CONCURRENT EXERCISE AND THE POTENTIAL ROLE OF AQUATIC TREADMILL RUNNING FOR PROMOTING RATHER THAN IMPEDING SKELETAL MUSCLE GROWTH AND STRENGTH DEVELOPMENT

A Dissertation

by

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ABSTRACT

The preservation of skeletal muscle mass, strength, and aerobic capacity have been demonstrated to be essential for maintaining one's health, preventing a wide range of cardio-metabolic diseases, and improving quality of life. Therefore, the American College of Sports Medicine prescribes a combination of both aerobic and resistance exercise for promoting optimal health. However, previous investigators have reported that aerobic training may interfere with skeletal muscle hypertrophy and strength development when performed concurrently with resistance training as opposed to performing resistance training in isolation. Within skeletal muscle, this interference has been hypothesized to occur as a result of competing intracellular factors within skeletal muscle which are regulated by energy balance, insulin signaling, and contractile activity. However, due to inconsistencies in the literature with regards to exercise mode, frequency, intensity, training volume, and subject population, certainty about exercise interference remains unclear. Recent findings from our laboratory indicate that aquatic treadmill (ATM) running, unlike standard land treadmill (LTM) running, may enhance rather than impede skeletal muscle growth and strength while additionally providing aerobic benefits.

In the investigation presented herein, we examined the exercise-induced adaptations to 12 weeks of concurrent resistance and ATM training (RT-ATM), concurrent resistance and land LTM training (RT-LTM), and resistance training (RT) alone in previously untrained subjects. Additionally, we utilized isotope labeling to analyze the acute effects of each on myofibrillar fractional synthesis rates. From our available tissue samples, we also elected to measure chronic alterations in the content of signaling proteins hypothesized to play a role in

exercise interference: protein kinase B (Akt), mammailian target of rapamycin (mTOR), and tuberous sclerosis complex 2 (TSC2) content.

Compared to RT and RT-LTM, concurrent RT-ATM exercise was found to enhance myofibrillar fractional synthesis when performed immediately following resistance exercise in the untrained state. These findings were concomitant with greater increases in lean mass and muscular strength following 12 weeks of training. Interestingly, RT-LTM training was found to yield greater reductions in fat mass than RT or RT-ATM training. Neither RT-LTM nor RT-ATM training was found to experience interference with strength or hypertrophy compared to the RT group.

The results of this investigation challenge the view that training for both strength and endurance are universally incompatible. They also highlight the importance of exercise mode selection when prescribing exercise programs for specific health or performance outcomes. In combination with RT, the novel use of ATM running may benefit those who desire to preserve strength and muscle mass while also promoting aerobic fitness.

DEDICATION

I would like to dedicate this dissertation to my wife Patti, my son Miles, and my new daughter Isla. My love for you inspired me daily to pursue this doctorate. Patti, you have supported me with complete faith and love while enduring the challenges that my academic pursuits have given us. Throughout all of this, you kept me humble and yet, at times you made me feel like I was capable of anything. I will forever be grateful and can only hope to one day return the favor and help to give you and the kids everything they deserve. Miles and Isla, while I can't say that having children during graduate school is the easiest thing in the world, raising you two with your mother has already fully surpassed the joy I will get from any of my past, present, or future accomplishments. As much as children sometimes want their parents to be proud of them, I promise you that I will always do my best to make you proud of me.

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when it seems like all the odds are against you. There are few who really get to know what that means beyond listening to coaches giving cliché half time speeches at sporting events in films. To my sister, Dessa, one of my greatest regrets during graduate school was not having enough time or money to see you more often. Hopefully, that can change soon. Either way, thanks for sticking by your brother (even from far away). Many thanks to my brother and sister-in-law, Andrew and Kristi Jastram, for helping us countless times with our kiddos when scheduling turned into a nightmare.

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While it is commonplace to put some sort of poetic quote from a famous or historical figure at the end of these kinds of things, I suppose I'll be a little different. I see a great problem in the scientific community and the public revolving around a mindset that science is closing in on the ultimate answers to things. In some cases, this is combined with an unnecessary amount of narcissism and elitism. However, thanks to my mentors and colleagues, I have come to understand that instead of scientific findings collapsing towards some sort of ultimate truth, each discovery elegantly blooms into infinite questions and possibilities for humanity to pursue. As such, I cannot help but feel humbled and blessed to be able to keep exploring and asking questions in a field that is dedicated to helping others.

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CHAPTER I

INTRODUCTION AND REVIEW OF LITERATURE

This dissertation adheres to the journal article format method for dissertations. This document is organized into three chapters (Chapter II is intended to serve as standalone manuscripts to be submitted for publication in peer-reviewed journals). In accordance with these guidelines, this chapter provides a review of pertinent literature and presents the questions to be addressed in Chapter II. Chapter III presents general conclusions to the dissertation as a whole.

Inter-related cardiovascular, musculoskeletal, and metabolic challenges currently face the Unites States population which coincide with a high prevalence of obesity, inactivity, and sarcopenia (in aging adults). The preservation of skeletal muscle mass, strength, and aerobic capacity have been shown to be essential for maintaining one's health, preventing a wide range of cardio-metabolic diseases, and improving quality of life (101, 124, 202, 264, 265). To achieve this, the American College of Sports Medicine prescribes a combination of both aerobic and resistance exercise for promoting optimal health (243).

Skeletal muscle is an organ with a great deal of plasticity in that it can respond quickly to various stimuli and specifically, physical activity. Because of this, skeletal muscle plays an important role in metabolism, physical function, and health. Resistance training has been shown to elicit increases in skeletal muscle mass and strength (56, 113, 213). Skeletal muscle hypertrophy as a result of chronic training represents the summation of acute increases in skeletal muscle protein synthesis following individual bouts of resistance exercise (45, 75, 95, 121, 145, 181). Within skeletal muscle, this process is regulated by complex intracellular signal transduction pathways (12, 74, 184). These pathways are also

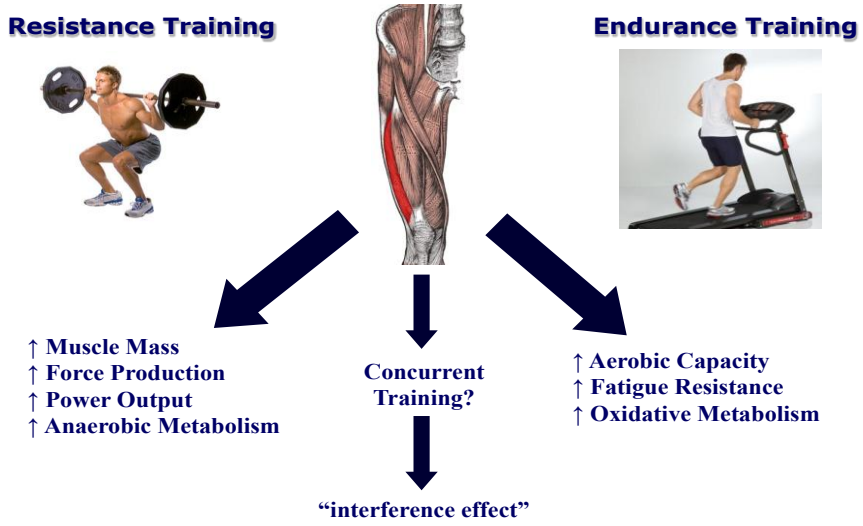
perturbed by endurance exercise, which has been observed to increase maximal oxygen uptake, skeletal muscle oxidative capacity, mitochondrial function, and elicit a shift in skeletal muscle to a more oxidative or, "Type I like" phenotype (10, 128, 194, 236). However, our laboratory (98) as well as others (8, 12, 24, 78, 108, 118, 143) have shown that when performed concurrently, endurance and resistance training may result in adaptation interference in which training adaptations are diminished compared to either mode performed in isolation. In other words, reduced gains in strength and muscle mass compared to resistance alone as well as reduced gains in aerobic capacity compared to endurance training alone. While not completely understood, there is evidence to suggest that within skeletal muscle, this interference may be a result of intracellular cross talk between diverging cell signaling transduction pathways that regulate skeletal muscle growth, metabolism, and function (10, 12, 55, 260). However, because of inconsistencies between previous concurrent training investigations with regards to exercise mode selection, training frequencies, exercise intensities, and subject populations used, a broad generalization of exercise interference (interference occurring under all concurrent training paradigms) is difficult at this time (152, 153, 261). The following section is a review of literature for acute and chronic physiological responses to concurrent exercise.

The Physiology of Concurrent Exercise

Introduction and Historical Perspectives

In 1980, Dr. Robert Hickson (118) published an investigation titled "Interference with Strength Development while Simultaneously Training for Strength and Endurance". His investigation was the first to experimentally observe concurrent training interference and thus demonstrate the important role of training specificity (118). In this investigation, 23 recreationally active participants (18-37yr, 17♂, 6♀) were divided into 3 separate training groups: Endurance training (cycling 3x·wk and running 3/wk, 30-40min at maximum achievable pace), Resistance training (high intensity lower body resistance exercise 3x·wk, repetition based exercise 2x·wk), Concurrent training (performed both training regimens with 2h of rest between resistance and endurance exercise sessions). Following 10 weeks of training, the concurrent training group experienced a lower degree of strength development compared to the resistance training group. In a final statement Hickson presented an important question regarding whether or not the outcomes of the study were directly related to an inability of skeletal muscle to simultaneously adapt to both endurance and resistance training. Given the results, it was suggested that for those desiring the development of strength and hypertrophy, simultaneously performing strenuous endurance exercise may be detrimental (118). Because both endurance and resistance exercise elicit unique adaptations, it has since been hypothesized that concurrent training prevents optimal conditions for adaption to either mode (Figure 1, following page).

Figure. 1 - Mode Specific Adaptations of Skeletal Muscle to Resistance and Endurance Training



General hypothesis for the interference effect.

Factors Affecting Concurrent Training Outcomes

Since Hickson's original investigation, others have attempted to further expand the current understanding of exercise training specificity and how it may shape human adaptation to exercise. Subsequent investigations have both supported (24, 54, 55, 98, 108, 133, 143, 152) and refuted (5, 67, 72, 161, 222) the presence of exercise interference. Furthermore the characterization of the conditional or molecular causes of interference has proven to be difficult (261).

Exercise Volume and Overtraining

Overtraining is a condition that occurs when the volume and intensity of an individual's exercise training exceeds their recovery capacity (38). Previous research

suggests that performing high volume training for both strength/power and aerobic fitness ultimately results in overtraining (24, 108, 143). Thus, while the typical adaptations to each style of training may be observed, the inability to achieve maximal training volume without overtraining may cause training improvements to be smaller. For example, in Hickson's original study, the concurrent training group performed nearly twice as many exercise sessions as either of the single mode groups (118). Therefore, it is reasonable to hypothesize that the exercise interference that was observed resulted from overtraining.

Successive bouts of high volume exercise (resistance or endurance) can produce chronically reduced muscle-glycogen levels over time (59, 184, 240). Creer et al. (61) reported that chronic reductions in muscle-glycogen with concurrent training that resulted in impaired intracellular anabolic signaling compared to resistance training in isolation. Additionally, Kraemer et al. (143) reported that concurrently performing resistance and endurance training at high training volumes resulted in significant elevations in serum cortisol, a stress hormone commonly associated with overtraining. Overtraining has also been observed to elicit increases in circulating catecholamines concomitant with increased catabolism (228). Together, these data indicate that training programs which involve high training frequencies or excessive training volumes may impair recovery, increase catabolism, reduce exercise performance in subsequent exercise sessions, and as a result, reduce the magnitude of training adaptations (184). At present, endurance training has been more frequently reported to interfere with resistance training adaptations compared to vice versa (261).

To determine if factors other than overtraining contribute to exercise interference, it is crucial to reduce total training volume to levels which will minimize the risk for overtraining

but still promote increases in muscle mass, strength, and aerobic capacity. Of note, exercise interference has been observed in training studies where lower total training volumes (<3/week per training mode) were used. Hakkinen et al. (108) reported that low volume concurrent training (2 sessions/wk) still resulted in interference with strength development. These data indicate that exercise interference may be caused by more than overtraining alone. Therefore designing training programs which minimize interference may be equally important for those trying to improve or maintain fitness as it is for those training for maximal physical performance.

Identifying factors other than overtraining which may contribute to interference from applied physiological data gathered during chronic training interventions is fundamentally difficult because of the challenge of equating total exercise volume between concurrent and single mode training programs (71). Consider a study involving the following training groups: resistance training, endurance training, and concurrent training. If the resistance and endurance training groups perform their respective modes of exercise 3 times per week and a concurrent training group performs a combination of both programs, they would be performing twice as many exercise sessions. Therefore, differences in physiological adaptations to training could reasonably be attributed to partially result from the increased total exercise volume. However, if the concurrent group only performed a fraction of the resistance or endurance training bouts so that total exercise sessions were matched, it could be hypothesized that reductions in resistance or endurance training volume relative to the groups performing each mode in isolation would result in under stimulation of adaptive mechanisms to either mode.

Exercise Intensity

Low intensity endurance training (<70% VO_{2max}) has been reported to elicit increases in pulmonary diffusion, cardiac output, and blood hemoglobin (38, 71, 214). As training intensity increases, there is an increase in the adaptive responses of peripheral musculature in the form of increased intramuscular angiogenesis, oxidative enzyme activity, mitochondrial density, and myoglobin (25, 38, 71, 120, 214). Acutely, increased endurance exercise intensity also yields a greater recruitment of Type II muscle fibers (15, 77, 116, 215). Accordingly, the long term training effects of endurance exercise result in Type II fibers with increased oxidative but reduced glycolytic capacity (12, 38, 116). Because of an increased recruitment of Type II fibers during high intensity endurance exercise and the subsequent oxidative adaptations of those fibers, it has been postulated that either high intensity or high volume endurance training can each negatively impact resistance training adaptations (71, 261). However, the degree to which either volume or intensity independently contribute to interference has not been established.

Exercise intensity also affects physiological adaptations to resistance training. Acutely, resistance exercise stimulates an increase in skeletal muscle protein synthesis that ultimately results in skeletal muscle hypertrophy (74). With regards to resistance training, intensity is commonly expressed as a percentage of an individual's one-repetition maximum (1RM: the maximum resistance that can be lifted) (15). The traditional intensity range for stimulating skeletal muscle hypertrophy has been reported to be between 60-85% of 1RM for a performance of 8-12 repetitions per set (15, 89). Resistance exercise performed within this range for multiple fatiguing sets have been reported to acutely promote increases in protein synthesis to a greater degree than high intensity low volume exercise (40). However,

exercise volume may also be thought of in terms of total time under tension which refers to the amount of time per set that a muscle is producing force. Accordingly, both the number of repetitions performed and time under tension per contraction have been reported to determine the anabolic effects of resistance exercise (40, 193).

Motor unit recruitment plays an equally important role in the development of muscular strength (108). Aagaard et. al (2) demonstrated an increase in rapid force development and motoneuron firing frequency following 14 weeks of high intensity resistance exercise. Resistance training has also been observed to increase motor unit recruitment and synchronization while decreasing inhibitory proprioceptive mechanisms which can limit maximal contractile force (38, 108, 134). High intensity exercise (>90%) is most closely associated with adaptations in neural components of strength development such as motor unit recruitment (2, 71, 109). At high intensity a greater number and synchronization of motor units is required to overcome the imposed mechanical demands of heavy resistance exercise (38). Therefore, differing training protocols (↑intensity/↓volume vs ↓intensity/↑volume) may increase strength through different mechanisms.

Depending on the concurrent exercise training protocol, interference may occur peripherally at the level of individual muscle fibers, centrally at the level of neural activation of motor units, or both depending on the volume and intensity of resistance or endurance exercise (71, 261). Based on previous evidence which indicated that high intensity endurance exercise and high volume resistance exercise both elicit peripheral adaptations at the level of skeletal muscle, Docherty et al. (71) proposed a concurrent training adaptation model with the hypothesis that high intensity endurance training paired with high volume / low intensity resistance training would yield the greatest level of peripheral interference.

However, this model for interference may be oversimplified as it does not consider the roles of contraction velocity or differences in neural adaptation between endurance and resistance exercise.

Contraction Velocity

In addition to volume and intensity, contraction velocity during exercise has been implicated in affecting concurrent training adaptations (51, 108, 109). The specificity of training principle suggests that training at high velocities would be the most appropriate way to foster increases in contractile velocity and thus power (50, 51). Compared to endurance exercise, resistance exercise involves rapid muscular force production over a relatively short duration (10, 38, 108, 207). In contrast, endurance exercise involves rhythmic movements that are less powerful in nature but repeated over a long duration (10, 38, 108, 207). As such, it has been proposed that adaptations to the specific muscle contractions required for each mode of exercise are inherently divergent (108, 143, 184, 207, 209).

Contraction velocity has also been shown to affect adaptation to specific types of resistance exercise as well. With regards to concurrent training, Hakkinen et al. (108) reported that rapid force production and muscular power may be more susceptible to interference than muscular hypertrophy or maximal strength development. Similarly, our laboratory (98) observed that concurrent resistance and treadmill training impaired muscular power development without interfering with improvements in strength development gains in muscle. While low velocity resistance training has been reported to stimulate hypertrophy because of increased time under tension, performing high velocity resistance exercise has been reported to yield greater increases in skeletal muscle power (34, 51, 84, 165).

At present, contraction velocity appears to have the greatest effect on central neural adaptations to exercise. In a study involving 63 subjects who were divided into groups by age (older vs. young) and resistance training group (high velocity vs. low velocity), Claflin et al. (51) observed similar increases in skeletal muscle hypertrophy following high velocity and low velocity resistance training and no differences at the single muscle fiber level with regards to contractile properties. Taken together, previous literature indicates that exercise interference has the potential to occur peripherally at the level of the muscle fiber as well as centrally with regards to neural adaptations to training. For those training for power development, training at high contraction velocities is most appropriate.

Muscle Fiber Adaptations

Because higher intensities of aerobic exercise require the recruitment of Type II muscle fibers, changes in muscle-fiber composition (particularly myosin heavy chain isoform shifts) have been considered to be partially responsible for endurance training-associated inhibition of strength development (143, 185). While strength training in isolation has been reported to elicit hypertrophy of Type II fibers (143, 227), intense endurance training has been observed to reduce fiber shortening speed of Type II fibers and alter myosin ATPase (38, 160, 227). Karavirta et al. (138) reported that only resistance training in isolation promoted increases in the cross-sectional area of Type II fibers compared to concurrent or endurance training. Additionally, Bell et al. (24) observed that along with diminished hypertrophy following concurrent compared to resistance training, there was a significant increase in capillary per fiber ratio following concurrent training. In summary, endurance exercise promotes a fast-to-slow shift in muscle fiber distribution, and when

performed concurrently with resistance training, results in a partial inhibition of hypertrophy in Type II fibers, reductions contractile shortening speed, and thus, strength and/or power development.

Exercise Mode Specificity

Given the variety of exercise activities that differ with regards to motor recruitment patterns, contraction frequencies, contraction velocities, and mechanical loads, the specific mode of exercise performed has been reported to play a critical role in adaptation to concurrent training (152, 261). In a recent meta-analysis, Wilson et al. (261) reported that endurance training mode appears to be a strong determinant for interference. It was also reported that exercise interference is body region specific because impaired adaptation was only found to occur in lower body in studies where the modes of endurance exercise used predominantly involved the legs.

Cycling and running are the most common modes of endurance exercise used in concurrent training investigations (261). When cycling is performed as opposed to running, incidents of exercise interference following concurrent training are rare (261). Wilson et al. (261) speculated this may be because cycling is more biomechanically similar to movements performed during resistance exercise and involves less impact than running. However, future investigations are needed to determine the degree to which specific modes of endurance exercise contribute to interference. These findings in conjunction with the integrated impact of volume, intensity, and contraction velocity on exercise adaptation further indicate that our present understanding of concurrent training adaptation is likely oversimplified.

Training History

For previously untrained or sedentary individuals, considerable increases in muscular strength have been observed shortly after beginning strength training (4-8wks) even in the absence of hypertrophy (38). These increases in strength have been previously attributed to neural adaptations to training (38, 108, 133). Furthermore, the degree of exercise intensity or mode specificity required to elicit significant improvements in strength or aerobic capacity in untrained populations is considerably less than for those who are already highly or moderately trained (261). Furthermore, prior training history has been shown to affect the adaptive responses to acute exercise (54). Coffey et al. (54) reported that prior training history in those who are primarily either endurance trained (distance runners) or resistance trained (power lifters) can effect transcriptional responses within skeletal muscle to either resistance or endurance exercise. The results from the study indicated that, independent of exercise mode, endurance trained athletes appear to be more sensitive to exercise stress than resistance trained athletes (54). It was also postulated that the chronic adaptive state of muscle following chronic resistance training may require a greater overload stimulus or repeated bouts of exercise to increase the transcriptional activity of myogenic genes in response to resistance exercise (54). At present, the degree to which training history may affect concurrent training outcomes is not clear. However, because training history has been shown to partially affect exercise adaptation, conclusions from concurrent training interventions are likely specific to the populations used.

Exercise Sequence

Intra-session exercise mode order (resistance followed by endurance vs. endurance followed by resistance) has been observed to affect both acute and chronic responses to

concurrent training (43, 44, 49, 55, 102). Chtara et al. (49) reported greater increases in aerobic performance when resistance exercise was performed immediately after endurance exercise within the same session. Following the study, it was suggested that when performed before endurance exercise, fatigue resulting from resistance exercise may have influenced aerobic performance and thus, the physiological adaptations to endurance training (49). While detriments to strength development were not reported in this study, it has also been previously proposed that endurance exercise prior to resistance exercise impairs resistance training intensity, resulting in less strength improvement (102). Cadore et al. 2012 and 2013 (43, 44) found no effect of exercise order on endurance performance but found that strength gains were greater in those who performed resistance exercise first. In an investigation of acute intracellular responses to concurrent exercise, Coffey et al. (55) reported that when endurance exercise was undertaken before resistance exercise, intracellular anabolic responses were diminished. In turn, it was cautioned that endurance after resistance exercise may exacerbate inflammation and protein degradation (55). These results provide support for the existence of exercise interference and indicate that performing divergent exercise modes in close proximity does not promote optimal activation of pathways to simultaneously promote both anabolic and aerobic responses.

Few have compared the effects of performing both endurance and resistance exercise concurrently on the same day versus on alternate days. In a study involving 15 young men, Sale et al. (216) observed that performing alternate day concurrent training resulted in greater strength gains compared to same day concurrent training with similar hypertrophic and aerobic adaptations observed with either (216). Regardless, these data add further support to

the hypothesis that exercise interference is more likely to occur when endurance and resistance exercise are performed within proximity to one another.

Summary

In summary, several factors may contribute to concurrent exercise interference. However, a great deal of research is still needed to characterize the specific conditions under which interference is most or least likely to occur. The present literature indicates the following:

- Overtraining can be a primary factor in concurrent exercise interference, partially due to depletion of muscle glycogen stores, reduced recovery time, and reduced performance in consecutive bouts of exercise.
- Endurance exercise is more likely to interfere with adaptations stimulated by resistance training (hypertrophy, strength) compared to vice versa (VO_{2max})
- Exercise intensity affects whether or not adaptation and/or exercise interference occurs peripherally or centrally.
- Velocity and frequency of muscle contractions result in fiber adaptations which suit the mechanical and metabolic demands of the exercise performed. Therefore interference may partially result from performing opposing types of contractile activity.
- Mode specificity is a factor in concurrent exercise interference with high intensity / high volume running being most associated with causing interference due to increased muscle damage and differences in motor-unit recruitment compared to cycling type exercise.

- Training history and physical condition of individuals influences responses to concurrent training. Because some degree of strength and cardiovascular fitness is needed to perform physical activity, several training modes (endurance or resistance) may simultaneously yield gains in muscle mass, strength, and aerobic capacity in previously sedentary individuals who are not accustomed to mechanical or metabolic stresses of physical work.
- Exercise sequencing plays a role in the adaptive responses to concurrent training. Preferential adaptation appears to occur for the mode performed first. Strength development appears to be most impaired when endurance exercise is performed first. The primary causes have been suggested to be pre-fatiguing of muscle which limits resistance training performance. Performing resistance and endurance exercise sessions in close proximity on the same day versus alternate day appears to exacerbate exercise interference.

Each of the above mentioned factors which have been observed to contribute to exercise interference are interrelated. Therefore, the development of exercise protocols to limit exercise interference must be highly specific to the training population with careful consideration for exercise mode, intensity, volume, and exercise session scheduling. At present, a great deal of further investigation is needed to better characterize and link acute concurrent responses and chronic physiological adaptations. The following section will address the proposed intracellular mechanisms which regulate skeletal muscle adaptations to exercise and how those mechanisms have been postulated to be partially responsible for concurrent training interference.

Intracellular Regulation of Skeletal Muscle Growth and Adaptation

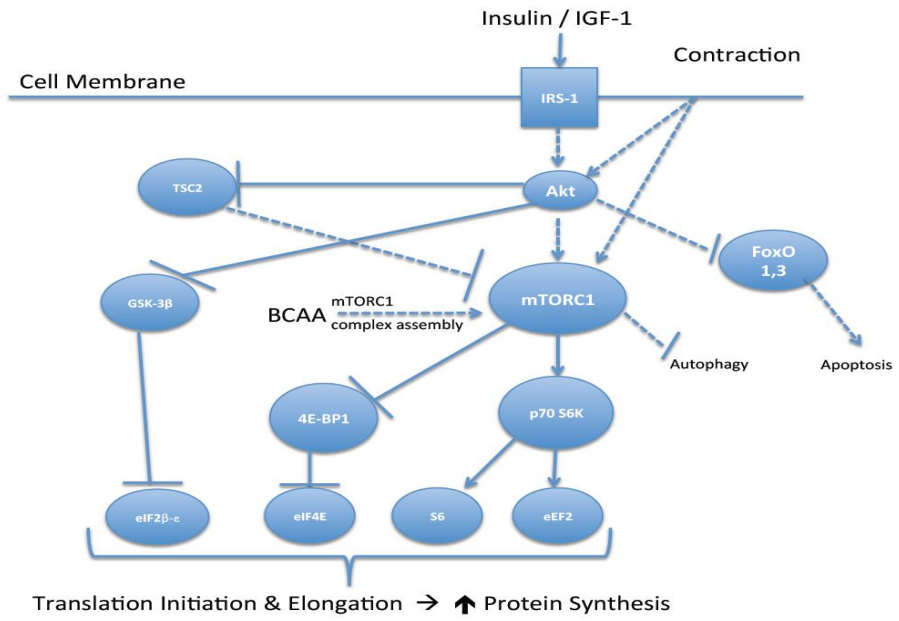
In recent years, much effort has been expended to characterize the intracellular responses to acute exercise and how those responses may govern adaptation. Regarding exercise interference, previous investigations have revealed what has been referred to as divergent cell signaling events following bouts of acute endurance and resistance exercise that play a role in directing chronic adaptive responses to exercise training (10, 55). The most popular hypothesis for exercise interference from a standpoint of cell signaling states that when intracellular energy is low, which comparatively occurs to a greater degree during endurance exercise than traditional resistance exercise, mitochondrial biogenesis and oxidative energy production become greater intracellular priorities than synthesis of contractile proteins (myofibrillar protein synthesis) and hypertrophy. Therefore, an adaptive shift towards less powerful but more fatigue resistant muscle fibers that better utilize oxidative metabolism is an appropriate response to endurance exercise. While the specific exercise stimulus to create conditions for interference to occur remain unclear, key regulatory mechanisms have been identified as probable role players in exercise interference (12).

The Akt-mTOR Pathway

Factors that influence metabolism, growth, degradation, and functional capacities of skeletal muscle are not entirely understood. However, in the past two decades, several investigations have provided a great deal of insight into the regulation of skeletal muscle growth and adaptation in response to exercise (31, 75, 150, 207). Protein synthesis is regulated primarily at translation by a number of proteins that are controlled by posttranslational modification (74, 75, 207). Eukaryotic initiation factor 2 (eIF2), eukaryotic

translation initiation factor 4E-binding protein 1 (4E-BP1), and the p70-S6 protein kinase (S6K1) are all highly involved in translation initiation and ribosomal assembly (74). As described below, the activity of all three proteins requires an important complex of proteins known as the mammalian target of rapamycin complex 1 (mTORC1) (31, 75, 150, 207). While the signaling is not entirely understood, insulin, insulin like growth factor-1 (IGF-1), amino acids, energy balance and contraction have been reported to regulate protein synthesis through mTORC1 (31, 74, 141, 150, 207). While other signaling mechanisms within skeletal muscle may also contribute, stimulation of protein translation through mTORC1 represents the primary mechanism by which muscle contraction and nutrition stimulate skeletal muscle growth (Figure 2).

Figure. 2 - Regulation of Protein Synthesis Through the Akt-mTOR Signaling Pathway (Abbreviated)



Dotted lines = indirect signaling **Solid lines = direct signaling.**

Definitions: 4E-BP1, eukaryotic initiation factor 4E-binding protein 1; Akt, protein kinase B; BCAA, Branched Chain Amino Acids; eIF2β-ε eukaryotic translation initiation factor 2β-ε; eIF-4E, eukaryotic translation initiation factor 4E, FoxO 1,3, forkhead box O 1,3; GSK-3β, glycogen synthase kinase 3; IRS-1, insulin receptor substrate-1; mTORC1, mammalian target of rapamycin complex 1; S6K1, p70 ribosomal S6 kinase 1; TSC2, tuberous sclerosis complex 2.

The mTOR protein exists *in vivo* as part of two distinct complexes within the cytosol (mTORC1 and mTORC2) and while many of the cofactors within each complex are similar, differing cofactors (ex. Raptor-mTORC1, Rictor-mTORC2) between the two dictate differing functional roles for each (123, 150). The specific role of mTORC2 remains elusive at this time. Recent studies have indicated that it may have potential roles in regulating cell survival, metabolism, cytoskeletal organization, and cross communication with mTORC1 and its downstream targets (123, 129, 150, 218). However, the role of mTORC2 in the downstream regulation of protein synthesis as well as its upstream signaling remains largely unknown and requires further investigation (129, 218).

By and large, the role of mTORC1 in skeletal muscle protein synthesis has been characterized to a greater extent than mTORC2. This is partially because of the practical use of rapamycin for selective inhibition of mTORC1 compared to the rapamycin-insensitive mTORC2 (75, 129). Therefore the ability to characterize mTORC1 function through its inhibition provide a clear model for investigating the degree to which it stimulates anabolism in response to various stimuli (75). Drummond et al. (75) demonstrated the importance of mTORC1 in regulation of exercise induced skeletal muscle protein synthesis in study involving 15 healthy men who were either assigned to a rapamycin group or a control group. After an overnight fast, the rapamycin treatment group ingested 12mg of rapamycin and both groups performed resistance exercise using a leg extension (75). Following the intervention, a significant increase in mixed muscle protein synthesis was observed in the control group but not the rapamycin group (75). A dissociation of the mTORC1 complex in the rapamycin group was observed as well (75). The results of this study demonstrate the importance of mTORC1 in resistance exercise-stimulated increases in skeletal muscle protein synthesis and

hypertrophy (31, 75, 141, 150, 207). This study also demonstrated the importance of the mTORC1 assembly as being necessary for mTOR function (75). Because mTORC2 has been found to be rapamycin insensitive and genetic knock out of mTORC2 has been shown to be fatal in mice, characterizing its specific role in skeletal muscle metabolism and function is difficult at this time (129, 218).

With regards to skeletal muscle protein synthesis, activated mTORC1 operates with a great deal of multifunctionality as it activates its downstream targets and consequently, the synthesis of myofibrillar proteins, mRNA biogenesis, ribosomal biogenesis, and mRNA transcription (64, 74, 121, 141, 150, 207). mTORC1 is primarily regulated by an upstream signaling cascade which begins at insulin receptors at the cell membrane (121, 150). Upon stimulation by either insulin or IGF-1, insulin-receptor-substrate-1 (IRS-1) is activated and facilitates the activation and translocation of phosphoinositide 3-kinase (PI3K) to the cell membrane (114, 154). Following its activation, PI3K begins production of phosphoinositol 3,4,5 tris phosphate (PIP3) at the cell membrane which then stimulates the co-localization of both, 3-phosphoinositide dependent protein kinase-1 (PDK1) and Protein Kinase B (Akt) leading to the subsequent phosphorylation and activation of Akt (12, 173). Of note, mTORC2 has also been reported to activate Akt (218). However, the mechanisms are less understood. Following activation, Akt serves pro-growth, pro-survival, and anti-apoptotic roles (29, 230). Akt has been reported to promote the activation of mTORC1 by phosphorylating proline-rich Akt substrate 40 (PRAS40), a competitive inhibitor of mTOR (254). Akt has also been shown to increase mTORC1 activity by phosphorylation and inactivation of tuberin (TSC2), another known inhibiter of mTORC1 that is activated by AMP activated protein kinase (AMPK) (12, 123, 150). Among other regulatory roles, Akt

has been linked to decreased Forkhead box protein (FOXO) activity (preventing apoptosis) and inhibition of Glycogen synthase kinase 3 beta (GSK-3β) (preventing inhibition of translation initiation) (12, 31).

Upon activation, mTORC1 elicits an increase in protein translation through phosphorylation of 4E-BP1 which removes its inhibition of eukaryotic translation initiation factor 4E (4E) (141). This results in increased capping of 5' mRNA and mRNA translocation to the ribosome (required for translation initiation) (141). mTORC1 also phosphorylates p70 S6K which has been shown to phosphorylate and activate ribosomal protein S6 (causes increased ribosomal biogenesis) and inhibit eukaryotic elongation factor 2 kinase (eEF2K) (an inhibitor or eEF2 and elongation) (132, 163, 208). S6 has also been reported to enhance ribosomal biogenesis by upregulating transcription of ribosomal mRNA (164, 208). In summary mTORC1 is a major regulator of anabolism that when activated, enhances translation initiation, elongation, as well as the transcription of ribosomal proteins. Stimulation through mTORC1 also partially inhibits autophagy.

Regulation of the Akt-mTOR Pathway

Energy balance is a key regulator of skeletal muscle growth and mitochondrial proliferation (12, 150). AMP-activated protein kinase (AMPK) has been shown to have a direct regulatory role in skeletal muscle energy homeostasis and skeletal muscle phenotype expression (3, 10, 128, 194, 200). Activation of AMPK, caused by an increased AMP:ATP ratio (↓energy) and an increase in intracellular calcium during exercise, has been shown to result in a partial fast to slow phenotype shift via activation of peroxisome proliferator

activated receptor-γ coactivator-1α (PGC-1α), a known regulator of mitochondrial biogenesis (12, 209). Furthermore, AMPK has been shown to be a key activator of angiogenesis (194).

AMPK has also been shown to regulate the mTOR pathway and myofibrillar protein synthesis through activation of tuberous scleroses complex 2 (10, 127). Understandably, the tuberous sclerosis tumor suppressing genes hamartin (TSC1) and tuberin (TSC2) have been a key interest in many fields involving the study of cell metabolism, growth, and cancer. Specifically, the unique ability for TSC2 to act as a "metabolic switchboard" for cell signaling has been reported to integrate cellular signaling responses to stress, energy availability, anabolic signaling, and the signaling involved in apoptosis (62, 123). In other words, pathways involved in both cell growth and degradation appear to converge at TSC2 with its activation or inhibition resulting in cellular responses that dictate the metabolic fate of a cell. The TSC2 gene was identified in 1993 and referred to as the tuberous sclerosis gene as a deletion of the TSC2 coding sequence was found to be present in patients with tuberous sclerosis complex who were found to have a reduced expression of TSC2 compared to normal controls (241). Briefly, tuberous sclerosis complex refers to a disorder involving excessive tumor growth in both children and adults that often results in neurologic disorders, facial angiofibromas, renal angiomyolipomas, and pulmonary lymphangiomyomatosis (62). In contrast, over expression of TSC2 has been shown to result in a marked reduction in cell size (91). Following the identification of the TSC2 protein, research studies over the last decade and a half have characterized TSC2 as a key regulator of cellular growth.

TSC2 has been observed to function as a GTPase activating protein (92, 269). While the functional components of the TSC1-TSC2 complex appear to be limited to TSC2 only, TSC1 is required to stabilize the complex and prevent ubiquitin-mediated degradation (46).

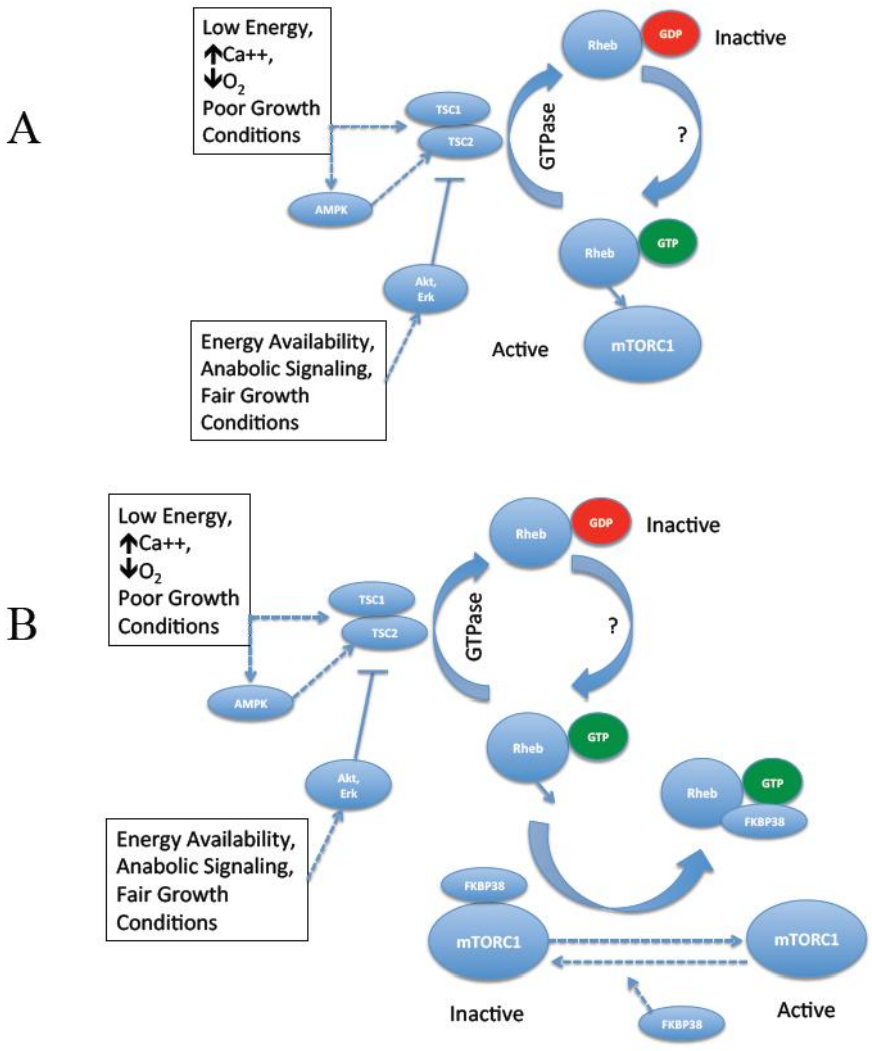
TSC2 largely acts on mTOR through interaction with ras-like proteins (Rheb) (123). The GTPase activity (normally low in comparison to other G-proteins) of Rheb is stimulated by TSC2 to enhance the conversion of Rheb-GTP to Rheb-GDP (126, 275). The affinity of TSC2 for Rheb implies a strong role for it in cellular signaling.

GTP bound Rheb has been observed to stimulate mTOR resulting in the phosphorylation of S6K and 4E-BP1 (126, 219, 231). This was reported by by Inoki et al. (126) in cell culture experiments where Rheb was either preferentially expressed or not expressed in vitro. It was found that when Rheb was not expressed, there was no phosphorylation of S6K or 4E-BP1. Furthermore, it was also demonstrated that in the presence of Rheb as well as rapamycin (inhibitor of mTOR), there was no effect of Rheb on the phosphorylation of S6K or 4E-BP1 suggesting that Rheb lies upstream of mTOR and plays a role in its activation (123, 126). Therefore, Rheb represents a link by which TSC2 regulates mTOR. The mechanism of TSC2 inactivation of mTOR through Rheb is not entirely understood, however there have been 2 hypotheses (123). The first suggests that under poor growth conditions (low energy state, hypoxia, ↓amino acids, cell damage, ↑Ca^{++}), the TSC1-TSC2 complex stimulates the conversion of Rheb-GTP to Rheb-GDP thus dissociating it from mTOR resulting in reduced mTOR activity (Figure 3a, next page) (238). The second suggests that Rheb activates mTOR by binding to FK506-binding protein 38 (FKBP38) and removing its inhibition on mTOR (Figure 3b, next page) (123). Support for this was provided by Bai et al. (17) who reported that FKBP38 is an endogenous inhibitor of mTOR, whose inhibitory activity is antagonized by Rheb in response to growth factor stimulation and nutrient availability. While further research is necessary to determine the specific mechanisms for TSC2-Rheb-mTOR signaling, a significant evidence exists which

suggests that TSC2 is a major regulator of mTOR.

Akt has been observed to deactivate TSC2 as well as cause destabilization of its heterodimer complex with TSC1 ultimately resulting in its degradation (201, 203). It has also been reported that the anabolic response in skeletal muscle following resistance exercise,

Figure 3 - Proposed Models of mTORC1 Regulation by TSC2



Dotted lines = indirect signaling **Solid lines = direct signaling.**

Adapted from Huang and Manning, 2008 (123). **A**. Hypothesis of direct stimulation of mTORC1 by Rheb. **B**. Hypothesis of Rheb removal of FKB38 inhibition for increased mTORC1 activation. Definitions: Akt, protein kinase B; AMPK, AMP-activated protein kinase; Erk, Extracellular-signaling-regulated kinase; FKBP38, FK506-binding protein 38; mTORC1, mammalian target of rapamycin complex 1; Rheb, ras-like protein expressed in brain; TSC1-TSC2, hammartin-tuberin components of tuberous sclerosis.

may be partially caused by an "override signal" from Akt to TSC2 which may inactivate TSC2 and its inhibition of mTOR regardless of AMPK→TSC2 signaling (31, 55). Thus along with activation of mTOR, Akt also increases cell anabolism via its inhibition of TSC2.

Deptor and has recently been characterized as an inhibitor of mTORC1(199, 221). Recently, Deptor has been associated with reduced mTOR activity (150). Additionally, upon activation of mTOR, Deptor has been reported to dissociate from the mTORC1 (150). While the exact mechanisms of Deptor action are not well understood, Liu et al. 2010 (158) reported that increased Deptor-mTOR association reduced activity of mTORC1. However, whether or not Deptor-mTOR interaction is affected by activity, stress, and energy balance is not known.

Mitogen Activated Protein Kinase (MAPK) Signaling

MAPK signaling refers to a family of proteins which regulate cellular response to stress (144). These include Extracellular-signaling-regulated kinase (ERK) proteins, p38 mitogen activated protein kinase, c-Jun NH_2-terminal kinase (JNK), and nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) (144). Each is stimulated by cytokines (particularly tumor necrosis factor alpha (TNF-α)), growth factors, metabolic stress, and mechanical stress (including exercise) (87, 147). Depending on the stimulus, MAPK pathways may stimulate cell growth, glucose uptake, fat metabolism, structural remodeling, and apoptosis (144). Following activation, MAPK signaling regulates metabolism and cell growth through both transcription and translation (85, 87, 147). ERK proteins have been reported to indirectly act on the mTOR pathway through inhibition of TSC2 (162). Insulin mediated stimulation of protein synthesis through ERK and its

subsequent phosphorylation of S6K has also been observed to occur independent of mTOR (85, 144). Therefore the regulation of cell growth is dependent on and sustained by multiple signaling mechanisms. MAPK signaling has also been shown to regulate growth and metabolism from at the level of transcription through interrelated but separate signaling cascades involving ERK, p38, and JNK (144). NF-κB has been reported to be a first responder to harmful cellular stimuli. Known inducers of NF-κB activity are highly variable and include reactive oxygen species, tumor TNF-α, and alterations in pH initiated by cell membrane damage (16). Upon activation, NF-κB is primarily involved in inflammation and transcriptional regulation of cellular remodeling and autophagy (16). The nature of how MAPK pathways interact is dependent on the degree and duration of cell stress (hypoxia, infection, mechanical damage) as well as anabolic, catabolic, or inflammatory signaling (144). The integration of MAPK signaling mechanisms may allow for the cell to determine the need for adaptation and repair versus apoptosis.

Direct and Indirect Stimulation of Protein Synthesis by Amino Acids

Previous research (31, 141, 145, 146, 181) has demonstrated the effectiveness of resistance exercise on increasing skeletal muscle protein synthesis rates. Amino acids (particularly leucine) ingestion has also been shown to enhance the effects of resistance exercise on protein synthesis rates (76, 204). Drummond et al. (74) compiled data from numerous studies and compared 4 groups of human subjects who either performed resistance exercise, consumed a carbohydrate/leucine enriched supplement, consumed the same supplement before resistance exercise, or consumed the supplement following resistance exercise. The compiled findings indicate an additive effect of combining resistance exercise

with branched-chain amino acid (BCAA) supplementation. Moore et al. (181) also demonstrated that increases in myofibrilar protein synthesis following resistance exercise were enhanced with amino acid supplementation. These data indicate that both amino acid ingestion (particularly BCAA) and resistance exercise may be required to maximally stimulate protein synthesis.

The recommended dietary intake of protein is currently 0.8-1.2g/kg body weight for mature adults in the general population (274). Furthermore, the American Dietetic Association recommends a daily protein intake of 1.2-1.7g/kg for optimal performance, recovery, and health (1). Current evidence indicates that the feeding of certain amino acids as well as complete protein elicits an increase in skeletal muscle protein synthesis through both increased intracellular amino acid availability, insulin secretion, and a direct stimulation of the mTOR pathway (31, 70, 90, 142, 188, 266). However, it should be cautioned that the supply of any amino acids in the fasted state or deficiency of any essential amino acid may greatly affect protein synthesis (↑AA in fasted state → ↑AA Pool → ↑protein synthesis , ↓AA → ↓Translation → ↓protein synthesis) based on substrate availability. Nonetheless, current findings indicate that amino acid supplementation can stimulate protein synthesis, and that sufficient dietary protein is required to maximize the anabolic response to exercise.

In particular, leucine has been reported to be a potent stimulator of the mTORC1 (74). Interestingly, stimulation of this pathway appears to occur at mTORC1 and at its downstream targets rather than upstream of mTORC1. Croizer et al. 2005 (63) demonstrated the impact of leucine on protein synthesis using a rat model. In this investigation, it was shown that a dose of 0.14 g leucine/kg produced a "near maximal" increase in protein synthesis (63). The results of this study also reviled that even at lower physiologically relevant doses of leucine,

increases in the phosphorylation of both 4E-BP1 and P70 S6K were observed (63). However, it should be cautioned that the experiment was carried out while the rats were in a food deprived state (18h fast) (63). Regardless, oral ingestion of leucine by humans has since been reported in many instances to be associated with increases in skeletal muscle protein synthesis (70, 74, 76, 191).

The mechanisms related to the stimulation of the mTOR pathway by L-leucine are not entirely understood at this time. However, there is evidence to suggest that activation of mTOR requires both leucine and glutamine (187). Furthermore, leucine may be crucial for mTORC1 assembly and activation (particularly Raptor-mTOR association) as amino acid deprivation has been shown to cause inactivation and dissociation of mTORC1 (217). Human studies involved in oral leucine supplementation have commonly used values of ~0.12g/kg (76).

In conjunction with leucine, glutamine may be an indirect regulator of the mTOR pathway as it is required for leucine transport (187). Because of this, the intracellular/ extracellular concentrations of both leucine and glutamine play a key role in the ability leucine to effect the mTOR pathway (30). The effect of leucine on the phosphorylation of p70 S6K has also been reported to be increased when combined with glutamine (68). Although the signaling mechanisms are not fully understood, glutamine appears to play a supportive role in promoting protein anabolism via possible regulation of mTOR and amino acid transport (266).

While not currently recommended by the FDA as an essential amino acid, some investigators have shown that arginine may play a critical role in the protein metabolism of neonates (267). With regards to the mTOR pathway and skeletal muscle protein synthesis,

the effects of arginine have only recently been investigated in vivo. Yao et al. 2008 demonstrated that in the case of neonatal pigs, supplementing milk with L-arg resulting in an increased phosphorylation of mTOR in skeletal muscle as well as an increase in the phosphorylation of 4E-BP1 as illustrated in Figure 6 (273). However, further research is required to determine if this phenomenon occurs in adult humans. It is conceivable that the stimulated increase in mTOR phosphorylation observed in neonatal pigs could be because both neonatal pigs and humans have been shown to be arginine deficient resulting of an inability to produce arginine from glutamine in the small intestine (268). Therefore, the role of arginine-mTOR signaling in humans requires further investigation. Regarding the mTOR pathway, arginine also indirectly stimulates its activation via its stimulation of insulin and IGF-1 release (266).

Intracellular Regulation of Exercise Training Adaptation and Interference

Exercise has been shown to perturb mechanisms which regulate both skeletal muscle transcription and translation (12, 53, 184, 207). Because of this, specific modes of exercise play a key role in adaptations and thus reinforce the principle of training specificity (12, 53, 144, 184, 207). Exercise also acts as a stress stimulus which activates similar intracellular mechanisms that are commonly associated with chronic inflammation, and programmed cell death (137, 144). Together these acute responses mediate the appropriate adaptive that are specific to the imposed exercise stimulus.

Exercise and Intracellular Conflict

Exercise causes alterations in intracellular energy availability (12). Therefore, depending on the degree of energy depletion, AMPK may be differentially activated with resistance compared to endurance exercise (10, 53, 54, 237). AMPK also plays a key role in transcription by phosphorylating PCG1-α (10, 55, 117, 200). Activation of PCG-1α is associated with the transcription of mRNA for genes involved in oxidative metabolism, and mitochondrial proliferation, as a partial fast-to-slow phenotypic shift in skeletal muscle (215). Because of this, endurance exercise has been reported to activate AMPK and PGC1-α to a greater extent than traditional resistance exercise (53). Given that AMPK has a regulatory effect on mTOR through activation of TSC2, endurance exercise inhibition of mTOR signaling has been postulated to be partially responsible for exercise interference (53). Partial support for this was given by Atherton et al. (10) in an experiment involving subjecting rat muscle to long duration low frequency stimulation (simulating endurance exercise) and short duration bursts of high frequency stimulation (simulating resistance exercise). Following the study, AMPK was reported to be activated to a greater degree following the simulated endurance exercise (10) in accordance with the hypothesis that endurance exercise yields elevated intracellular AMP concentrations compared to resistance exercise. Additionally, only the short bursts of high frequency stimulation (simulated resistance exercise) elicited increases in both myofibrillar and sarcoplasmic protein synthesis (10). Notably, signaling through mTOR and its downstream targets were also preferentially activated by short burst / high frequency stimulation (10). Wilkinson et al. (260) used a novel acute bilateral exercise model to compare the effects of resistance exercise and endurance exercise in humans. Following exercise, greater myfribrillar protein synthesis

rates were recorded following resistance compared to endurance exercise with upstream signaling similar to that shown by Atherton et al. 2005 (10). While these results provide support for the acute intracellular cross signaling that may determine chronic adaptations to concurrent exercise training, it should be cautioned that in the aforementioned investigations, acute signaling measures were made in the fasted state and chronic training outcomes were not observed. Furthermore, Vissing et al. 2013 (251) recently reported that activation of AMPK was not dissimilar following either resistance or endurance exercise but that anabolic signaling through mTOR was more robust following resistance exercise. Because additional mechanisms have been shown to influence skeletal muscle anabolism, AMPK-TSC2 inhibition of mTOR following endurance exercise should only be considered as a portion of the potential mechanisms which contribute to exercise interference.

Current hypotheses about the intracellular mechanisms responsible for exercise interference are largely based upon cell signaling responses to either resistance or endurance exercise in isolation. Few have actually characterized intracellular signaling events in humans during and following a session of concurrent exercise. Coffey et al. (55) observed greater Akt activation but no differences in mTOR activity, subsequent phosphorylation of p70S6k, or expression of PGC-1α mRNA immediately following resistance exercise compared to endurance when both were performed in close proximity. However, it was reported that in comparison to previous investigations of single mode exercise, a session of concurrent exercise reduced the molecular responses to either mode (anecdotal comparison) (55). These data provide further rationale for the hypothesis that additional intracellular signaling mechanisms may contribute to exercise interference. Given that feeding has been shown to stimulate mTOR signaling (70) and that training history has been shown to affect

acute responses to exercise (54, 96), more research is needed to determine how these acute responses are affected by feeding and how or if they differ in the trained versus the untrained state. Nonetheless, current literature does support the hypothesis that endurance exercise promotes a greater intracellular priority for increasing oxidative energy production by increasing mitochondrial biogenesis at the expense of reducing the synthesis of contractile protein (53). This falls in line with previous chronic training investigations where researchers hypothesized that concurrent training would result in a reduced hypertrophic response following concurrent training as opposed to resistance training in isolation.

Exercise Intensity and MAPK Signaling

Exercise intensity (metabolic stress and mechanical loading) may also be a factor in exercise mode specific responses to training (144). Specifically, MAPK pathway proteins are activated by both mechanical and chemical stimuli (144). Although not completely understood, both exercise mode and intensity determine which MAPK pathways are activated, how they interact, and the extent of their effects on the cell (85, 144, 147). For example when comparing passive, concentric, isometric, and eccentric contractions rat muscle, Martineu et al. 2001 (166) reported that there was a preferential activation of ERK (anabolic) during concentric contractions and JNK (degradation/remodeling) proteins during heavy eccentric contractions. This suggests a preferential signaling for growth from the concentric contractions but a greater inflammatory / remodeling signaling from high intensity from eccentric contractions. Therefore load specificity differences between and within various modes of endurance and resistance exercise may contribute to differential adaptations to chronic training.

Endurance exercise induces a shift to a more oxidative phenotype through mitochondrial biogenesis, increased oxidative metabolism, and intramuscular capillarizaiton for increased oxygen supply (194, 272). Compared to resistance exercise, endurance exercise produces a high flux of electrons through the electron transport chain that consequently results in a greater absolute amount of electron leakage and subsequent reactive oxygen species (144, 271, 272). Hypoxia and oxidative stress have been previously reported to stimulate p38 signaling within skeletal muscle resulting in a subsequent increase in PGC-1α expression and mitochondrial biogenesis (144, 271, 272). In response to endurance exercise, p38, AMPK, and PGC-1α activation stimulate the transcription of angiogenic growth factors, mitochondrial genes, PGC-1α mRNA, and Type I contractile proteins (272). Importantly, this provides a secondary mechanism independent of mTOR inhibition, whereby endurance exercise may interfere with resistance exercise-stimulated hypertrophy.

High intensity eccentric resistance exercise has been shown to cause calcium channel deregulation in the sarcoplasmic reticulum, as well as the activation of proteins involved in autophagy and remodeling (JNK proteins and NF-κB) (144, 166). Because JNK and NF-κB signaling have been observed to be activated in response to high force production and mechanical loading, it has been suggested that these pathways may be involved in skeletal muscle restructuring at the onset of heavy resistance training to prevent later damage (144, 166).

Intracellular Calcium

Endurance exercise produces greater increases in intracellular calcium over time compared to traditional resistance exercise (212). This type of contractile activity has been

shown by some to result in an increased activation of calcineurin (responds to changes in intracellular calcium monitor) which results in transcription of mRNA coding for Type I myosin heavy chain isoform (271). Increased intracellular calcium also stimulates calmodulin-dependent kinase (CaMK), an inhibitor of eEF2 and translation elongation (212). Rose et al. 2005 (212) reported that 90 minutes of submaximal cycling resulted in a calcium-CaMK dependent inhibition of eEF2. These results were similar to those reported by Atherton et al. 2005 (10) who reported inhibition of eEF2 immediately and 3 hours following endurance exercise. These responses differ from resistance exercise, which has been demonstrated to increase eEF2 activity through activity through mTORC1 signaling. Therefore, acute increases in intracellular calcium following exercise also represent an avenue of mTOR independent exercise interference.

Conclusions – Exercise Interference

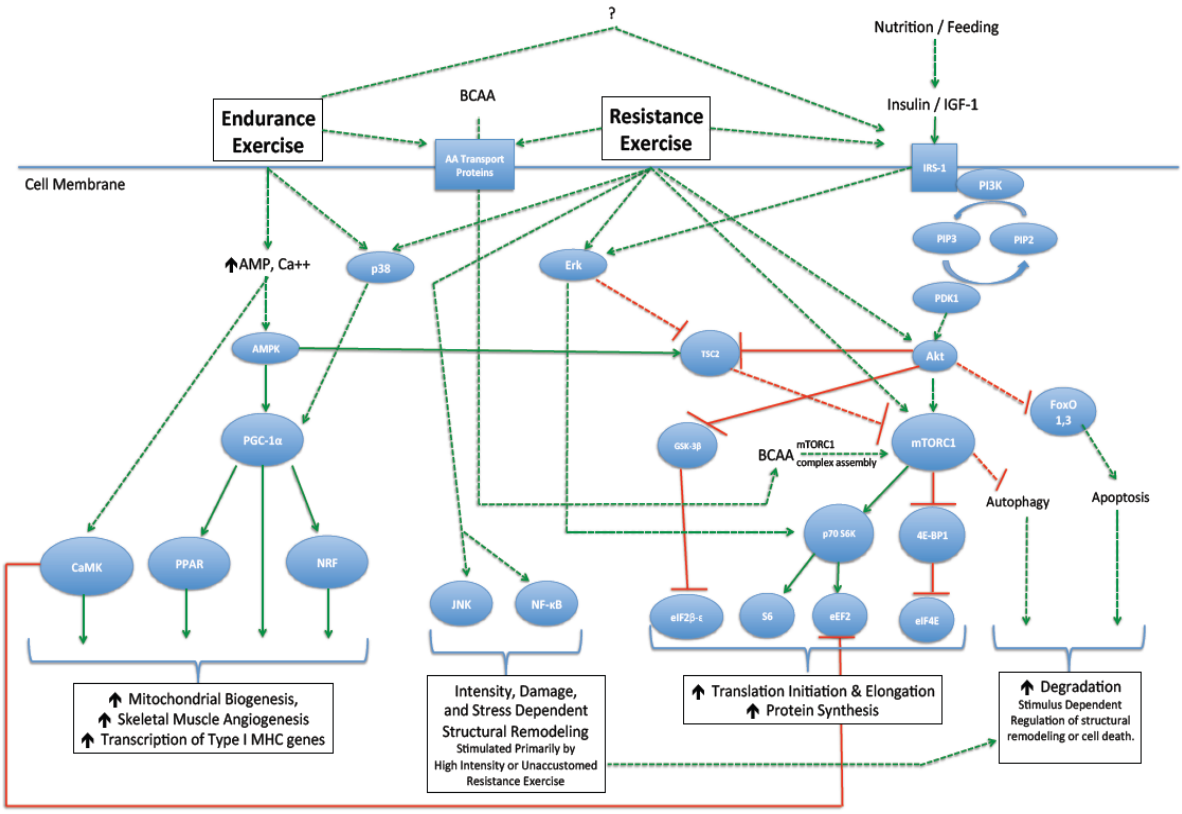
The intracellular signaling mechanisms that regulate skeletal muscle adaptation to exercise, while complex, are governed by intracellular energy availability, intensity of contractile activity, and duration of activity. Additionally, recent research provides further molecular support for the results reported in applied concurrent training investigations. Endurance training promotes enhanced oxidative capacity and reduced fatigueability in skeletal muscle by increasing mitochondrial biogenesis, angiogenesis, and stimulating a partial fast-to-slow fiber type shift. Resistance exercise results promote an increase muscular strength and size by increasing protein synthesis, anaerobic metabolism, and structural remodeling. However, the mechanisms responsible for resistance and endurance exercise adaptation are highly integrated. Given that several variables may affect concurrent training

outcomes, the simplistic approach of comparing steady state endurance training and traditional resistance training does not address the complexity of concurrent training. Both resistance and endurance training are commonly practiced in many forms. Therefore it may be more applicable to consider adaptive responses to exercise to occur on a continuum. Importantly, the aforementioned literature is a report on physiological tendencies for adaptation in response to resistance and endurance exercise. In other words, it would be inaccurate to claim that resistance exercise does not have the potential to partially stimulate mitochondrial biogenesis (18), nor would it be correct to state that endurance exercise is incapable of stimulating skeletal muscle hypertrophy (70) under certain conditions. As previously stated, exercise intensity, mode selection, training, frequency, and subject population all contribute to the adaptive outcomes of a given training stimulus. At present, the degree to which endocrine and immune function also contributes to concurrent training interference is not well known. Given the present limitations in the literature and concurrent training program design, a challenge still remains for identifying and implementing concurrent training programs, which minimize exercise interference and maximize adaptations.

General Molecular Hypothesis for Exercise Interference

Figure 4 (following page) represents a summary for the aforementioned intracellular signaling mechanisms that have been proposed to play a role in concurrent exercise interference. However, the time course for these signaling events following exercise and the degree to which each individual signaling cascade contributes to exercise interference is unknown.

Figure 4 - Intracellular Role Players in Exercise Interference.



Dotted lines = indirect signaling **Solid lines = direct signaling.**

Figure adapted from Laplante et al., 2010 (150), Kramer and Goodyear, 2007 (144), and Baar, 2006 (12). Abbreviations: 4E-BP1, eukaryotic initiation factor 4E-binding protein 1; Akt, protein kinase B; AMPK, AMP-activated protein kinase; CaMK, calmodulin-dependent kinase; eIF2β-ε, eukaryotic translation initiation factor 2β-ε; eIF-4E, eukaryotic translation initiation factor 4E, Erk, Extracellular-signaling-regulated kinase; FoxO 1,3, forkhead box O 1,3; GSK-3β, glycogen synthase kinase 3; IRS-1, insulin receptor substrate-1; JNK, c-Jun NH_2-terminal kinase; mTORC1, mammalian target of rapamycin complex 1; NRF, nuclear respiratory factor; NF-κB, Nuclear factor kappa-light-chain-enhancer of activated B cells; p38, p38 Mitogen activated protein kinase; PDK1, phosphoinositide-dependent kinase-1; PI3-K, phosphoinositide 3 kinase; PIP_2, phosphotydilinositol (4,5) bisphosphate; PIP_3, phosphotydilinositol (3,4,5) trisphosphate; PGC-1α, PPAR-γ coactivator 1-α; S6K1, p70 ribosomal S6 kinase 1; TSC2, tuberous sclerosis complex 2.

Aquatic Treadmill Exercise – Implications for Concurrent Exercise Research

Introduction

Aquatic exercise is becoming increasingly prevalent in clinical populations as a form of active rehabilitation for lower body injuries (259). Aquatic exercise has also been observed to be an effective therapy for those suffering from such conditions as arthritis, low back pain, fibromyalgia and others who may benefit from low impact exercise (9, 42, 155, 253). Consequently, aquatic exercise is becoming a valuable tool for increasing the activity levels of those with physical limitations that inhibit or deter them from performing traditional land based exercises. Presently, several modes of aquatic exercise have been under investigation. These modes include swimming, water aerobics, deep-water running (DWR), aquatic treadmill (ATM) running, and aquatic cycling. However, while aquatic exercise is growing in popularity, much is still uncertain with regards to acute and chronic physiologic responses to aquatic based training. Recently, our laboratory conducted a study comparing the efficacy of chronic ATM training with traditional land treadmill (LTM) training using a protocol similar to that recommended by the ACSM (106). Following training, increases in VO_{2max} and decreases in fat mass were similar regardless of exercise mode. Notably, leg lean mass (measured with DEXA) was significantly increased following ATM training (17.30±.80kg→18.10±.80kg, $p<0.05$), twice that of the LTM group. These data combined with other recent reports from our laboratory (105) indicate that ATM exercise may elicit different skeletal muscle adaptations compared to traditional LTM exercise.

The following section is review physiologic responses to water immersion, acute physiologic responses to common modes of aquatic exercise, the effects of chronic aquatic exercise training, therapeutic uses for a aquatic exercise, and the potential for aquatic

exercise in a concurrent training model. For the purposes of the investigation presented within this dissertation, the following review will primarily focus on head-out aquatic exercise with a heightened focus on aquatic running and cycling.

Physiological Adjustments to Water Immersion

Hydrostatic Pressure

When immersed in water, the hydrostatic forces acting upon the body are equal to: $P = Patm + g \bullet \rho \bullet h$ (257). P = water pressure; $Patm$ = atmospheric pres- sure (standard sea level 1013 hPa); g = gravity (9.81 m/sec^2); ρ = water density (1000 kg/m^3) and h = height of the water (m)

Therefore, on a body immersed in water, the pressure varies relative to depth such that for each cm of depth, there is an increase in external pressure of 0.74mmHg (257). In other words, the pressure gradient increases as depth increases which causes upward fluid and gas displacement within the body (257).

Cardiovascular Adjustments

Upon immersion in water up to the level of the neck, hydrostatic forces acting upon the body elicit an increased central blood volume (206). Due to the pressure gradient that arises, a redistribution of blood volume (~700ml) to the central cavity occurs (7). As a result, the heart receives approximately 200ml of this shifted blood volume (7, 206). Notably, increased cardiac preloads have been reported at water depths ranging from the waist to the neck (206). Because of increased preload, increases in cardiac stroke volume (~35%) and cardiac output have also been observed (206).

Increases in cardiac preload commonly increase stroke volume (232), contractility, and cardiac output as a result of the Frank Starling mechanism whereby the elastic properties of the heart enhance the force of cardiac contraction in response to stretch by optimizing the length tension relationship (214). During water immersion, the resulting increased cardiac stretch consequently stimulates baroreceptors that assist in regulating sympathetic and parasympathetic output. O'Hare et al. (110) and Norsk et al. (189) each observed depressed sympathetic activity during water immersion to the level of the neck. Norsk et al. (189) also reported that neck level immersion resulted in reductions in plasma norepinephrine levels that were mirrored by increases in stroke volume, systolic atrial pressure, and pulse pressure. Following this study, it was determined that reductions in catecholamine output resulted in a decreased resting heart rate.

Respiratory Adjustments

Increased hydrostatic pressure observed during water immersion at chest depth has been reported to decrease vital capacity as a result of an upward shift of the diaphragm (206). Accordingly, an increase in breathing frequency has been reported at maximal exercise efforts during aquatic running (206). Similarly, depth dependent reductions in functional residual capacity have also been reported during water immersion (206).

Renal Adjustments

Additional responses to water immersion (prolonged water immersion in particular) include alterations in renal function. Norsk et al. (189) observed an increase in natriuresis that was determined to be related to increases in thoracic blood volume and subsequent

altered baroreceptor stimulation. The mechanisms responsible have been hypothesized to be reductions in aldosterone section and increases in renal prostaglandin release (206). In a study involving 15 young men, Schou et al. (220) observed a suppression of angiotensin II and aldosterone production during a 3 hour water immersion protocol at neck depth with thermoneutral water temperatures (33°C). Therefore, these data suggest that an increase in central blood volume mediates compensatory responses through the angiotensin-renin system to re-equilibrate during water immersion.

Effects of Water Temperature

Water temperature, like air temperature, can influence cardiovascular responses to immersion with regards to thermoregulation. At cooler temperatures (<25°C), increased vaso-constriction causes an additional increase in central blood volume in addition to that elicited by hydrostatic pressures (206, 257). Similar to mechanisms elicited by hydrostatic pressure, increases in central blood during cold water immersion propagate an increase in cardiac preload (214). The resulting stimulation of stretch and baroreceptor in the heart cause increased parasympathetic tone and reductions in heart rate at rest and exercise (214). Due to increases in vasoconstriction to maintain core temperature, cold water immersion causes an increase in peripheral vascular resistance (214). Resultantly, decreases in cardiac output have also been observed during rest at neck depth during cold water immersion (32, 226). Although, to assist in the maintenance of core temperature, oxygen consumption and metabolism are typically increased with decreasing water temperatures while at rest (223, 226).

At warmer water temperatures (>35°C), an increase in skin temperature causes an

increase in peripheral vasodilation (32, 257). Heart rate also increases in response to hot water immersion (32, 257). The reductions in peripheral resistance combined with increases in heart rate yield increases in cardiac output. Because of an increase in subcutaneous blood flow, it has been hypothesized that hot water immersion could potentially reduce skeletal muscle blood flow (257). However, future investigations are needed to determine the interaction between vascular responses to heat which shunt blood flow to the skin in relation to competitive external hydrostatic pressures that exist during water immersion.

Previous investigations have yielded an established thermoneutral water temperature between 27-35°C at rest (32, 186, 189, 206, 257). Within this temperature range, heat dissipation and cardiovascular responses to exercise have been reported to be similar to land (257). During exercise the optimal temperature of water for thermoneutrality decreases slightly. Craig and Dvorak (60) found exercisers with a light work load to be able to maintain a thermoneutral condition at 34°C and with a heavy workload at 29°C. However, thermoneutral temperature ranges specific to various depths (hip, chest, neck) have not been fully established. Body composition has also been reported to play a role in thermoregulation during water immersion due to variance in insulation properties and abundance of subcutaneous lean versus fat tissue (172). Regardless, due to exaggerated cardiovascular and metabolic responses to water immersion outside of thermoneutral temperature ranges, researchers attempting to compare land and aquatic exercises at similar workloads should set water temperature within a thermoneutral range so as to not create exaggerated responses of physiological measures to extreme temperatures. This thermoneutral temperature may also be adjusted depending on the intensity of the activity.

Upright Aquatic Exercise

Cardiovascular Responses

At present, several investigations have compared the physiological responses of acute aquatic and land exercise (135, 139, 140, 167, 169, 175, 177, 178, 232, 252). At sub-maximal workloads, the relationship between heart rate and oxygen consumption (VO_2) has been found to be similar when comparing the same exercises in water and on land (103). Recently, our laboratory characterized the cardiovascular responses to ATM exercise (103). In this investigation, the model of ATM used (HydroWorx 1000 and 2000 series, HydroWorx International, Inc., Middletown, PA) incorporates a motor driven treadmill placed in the floor of a pool with pump-driven water jets, similar to those in commercial whirlpool baths, oriented to push against an exercising participant, thus providing resistance to forward ambulation. Following this investigation, similar cardiovascular responses were found between ATM and LTM exercise. While reductions in VO_{2max} have been consistently found when comparing DWR to LTM exercise (205, 206), comparisons of ATM or cycle erogmeter exercise to their land based counterparts have revealed no such differences (48, 57, 106, 224, 225). Because of the incorporation of jet based water resistance and involvement in the upper body, ATM exercise likely engages a greater muscle mass than DWR (106, 232). Also, a common limitation of maximal exercise testing during DWR in previous investigations was that stride lengths were self-selected and as a result, reduced when approaching VO_{2max} in order to maintain a specified stride cadence (232, 258). This may have been partially responsible for the previously observed reductions in VO_{2max} with DWR. In our investigation of ATM exercise, self-selection of work rate was removed as it was required that participants maintain velocity on a motorized treadmill belt against a jet

resistance (106). These results indicate that the testing parameters used in previous investigations may have been responsible for reported reductions in VO_{2max} during DWR and that it is possible to achieve comparable maximal aerobic workloads during aquatic exercise.

While similar cardiovascular responses have been reported between aquatic and land based exercise, there have been some exceptions. Similar to water immersion at rest, reduced catecholamine concentrations have been observed during aquatic versus land exercise (48, 57). In a study comparing aquatic versus land based cycle ergometer exercise, Connelly et al. (57) reported reductions in epinephrine, nor-epinephrine, and heart rate during head-out aquatic cycle ergometer exercise at intensities approaching VO_{2max} in water compared to land. Both Connelly et al. (57) and Christie et al. (48) also reported greater increases in pulmonary arterial pressure, end-diastolic volume, stroke volume, and ejection fraction associated with lower heart rates during aquatic cycle ergometer exercise. These findings are consistent with those made by Greene et al. (103) who observed reductions in maximal heart rate at VO_{2max}. Therefore, while measurements of hemodynamics are difficult during aquatic exercise, present data indicates that physiologic responses to aquatic exercise are similar to those observed with water immersion at rest.

Fuel Substrate Utilization

Svedenhag reported elevated respiratory exchange ratio (RER) and blood lactate concentrations during DWR at similar VO_2 (232). Michaud et al. (177) and Broman et al. (37) reported similar findings. Together, these data indicate the possibility of elevated carbohydrate oxidation and decreased lipid oxidation during deep water running compared to running on land. However, these findings are contrary to those by our laboratory (103, 106)

and others (57, 224, 259) who reported no difference in RER or blood lactate concentration between sub-maximal running exercise performed on land versus in water. Both Greene et al. (103) and Connelly et al. (57) also observed reductions in RER at VO_{2max} during aquatic versus land based exercise. Connelly et al. (57) also observed reductions in blood lactate concentrations during higher intensities of exercise (>90% VO_{2max}). Therefore, further comparative research is needed between DWR, ATM, and land based running under similar exercise testing conditions to determine if any differences in fuel substrate utilization exist between land and aquatic based exercises at similar intensities.

Biomechanics and Motor Recruitment Patterns

At present, there is limited information regarding biomechanical comparisons of aquatic versus land exercise. However, fundamental differences related to buoyancy, decreases in vertical load, increases in horizontal resistance, and increased density of water versus air provide rational for the potential presence of differing mechanical and metabolic demands on skeletal muscle. Expectedly, when examining ATM running, lower ground reaction forces, reduced joint compression, reduced stride frequency, and differences in skeletal muscle activation patterns have also been reported compared to LTM exercise (21, 22, 69, 210, 259). Moening et al. (180) performed video analysis of LTM and aquatic running and found differences in hip, knee, and ankle range of motion. Similar findings in a kinematic analysis of ATM running were reported as the transition of locomotion from walking to running was observed to occur at a lower absolute speed than LTM running (168). Silvers, Dickin, and Dolney used EMG analysis to evaluate lower limb skeletal muscle recruitment patterns during ATM and LTM exercise (259). Relative to LTM exercise, ATM

exercise resulted in greater activation of the biceps femoris, vastus medialis, tibialis anterior, and rectus femoris with reduced activation of the gastrocnemius (259). The investigators hypothesized that differences in skeletal muscle recruitment patterns between LTM and ATM were likely a result of reduced ground reaction forces and horizontal drag from the water. In the case of DWR, the lack of a ground support phase produces differing recruitment patterns than those reported with ATM exercise (195). Kaneda et al. (136) observed similarities between aquatic based walking and DWR but found further reductions in gastrocnemius and soleus activity with the removal of a ground support phase (136). In summary, differences in muscle recruitment exist between land and aquatic based running exercises. In general hip and knee joint extension and flexion appear to elicit greater activation in water compared to land with a greater range of motion achieved during aquatic exercise. However, reductions in gastrocnemius and soleus activation appear to occur during aquatic exercises that are dependent on reduced or absent ground reaction forces.

Physiological Adaptations to Chronic Aquatic Exercise Training

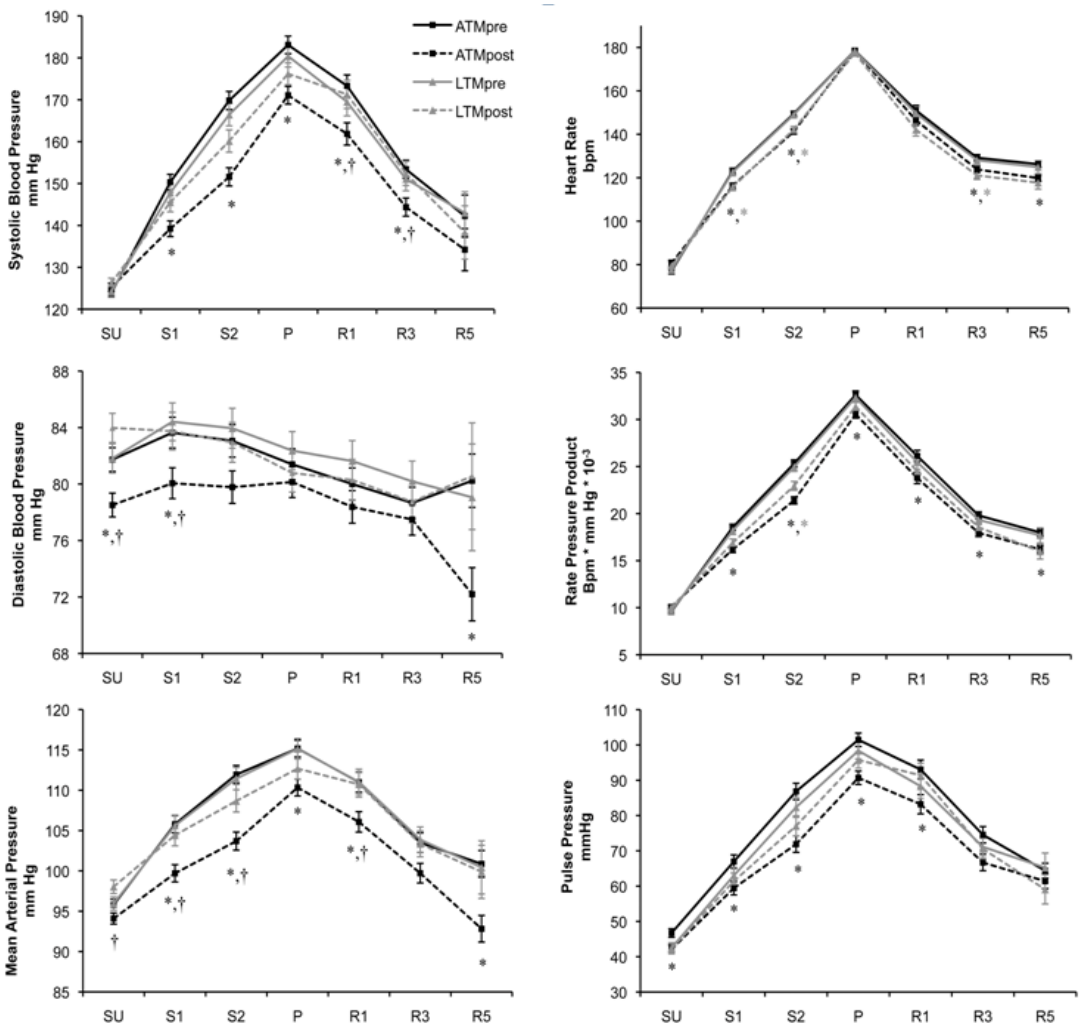
Cardiovascular Adaptation

Several studies (19, 20) have observed beneficial adaptations to chronic aquatic exercise. Increases in VO_{2max} have often been consistently observed in sedentary or recreationally active subjects (19, 36, 37, 105, 106, 233, 234). In our investigation of ATM training, 57 physically inactive, overweight, and obese men and women (Age: 44±2yr, Body Mass: 90.5±2.4 kg, BMI: 30.5±0.7 kg/m^2, VO_{2max}: 27.1±0.7 $ml \cdot kg \cdot min^{-1}$) were assigned to perform either LTM or ATM training 3 times per week for 12 weeks. Exercise programs were matched for training intensity and exercise volume. Similar increases in VO_{2max} were

observed in both training groups (+3.6± 0.4 ml·kg·min^{-1}) (106). In a follow-up investigation, we observed decreases in heart rate at submaximal workloads following either LTM or ATM training (105). These findings were similar those of Broman et al. (37) who found increases in VO_{2max} following DWR in elderly women.

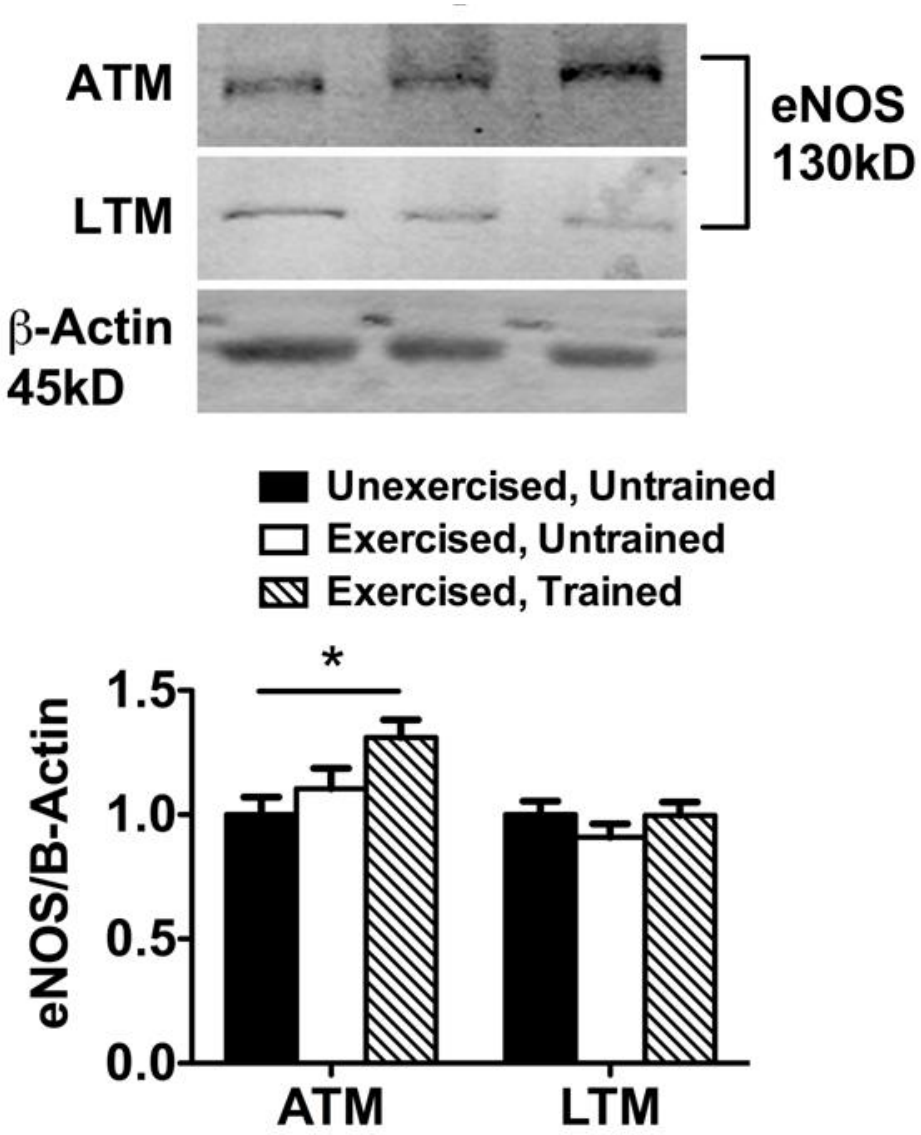
Along with improvements in aerobic capacity, additional cardiovascular adaptations to aquatic exercise training are beginning to surface. In our follow-up investigation comparing 12 weeks of ATM to LTM training, we observed that chronic ATM training elicited significant decreases in blood pressure during rest, submaximal, and maximal exercise in previously untrained men and women (Figure 5) (105). Importantly, these reductions were not observed following traditional LTM training. In an attempt to identify a possible mechanism, we analyzed muscle biopsy samples taken from 12 of our subjects who volunteered for biopsy sampling. It was determined that 12 weeks of ATM but not LTM exercise stimulated increases in endothelial nitric oxide synthase (eNOS) within skeletal muscle (Figure 6). Because eNOS is the primary means by which nitric oxide (NO) is produced to elicit vasodilation in smooth muscle (249), we suggest that ATM exercise (and potentially aquatic running in general) may increase the capacity for peripheral vasodilatation. This in turn, would aid in explaining the altered hemodynamic responses to exercise following training. At this time, we cannot discern if the increase was a result of an increased eNOS concentration in the endothelium or an indirect result of greater

Figure 5 - Blood Pressure Responses Before and During the Bruce Protocol Exercise Stress Test Before and After Twelve Weeks of Exercise Training Using Either Aquatic (ATM) or Land-based (LTM) Treadmills



This figure represents previous work recently published from our laboratory (105). Systolic blood pressure, diastolic blood pressure, mean arterial pressure, pulse pressure, and rate pressure product. *P<0.05 compared to pretraining value in same group. † P<0.05 between groups at same measurement time point. Data are adjusted means ± SEM. Pre: pre-training, Post: post-training. Testing stages: Supine (SU), Stage 1 (S1), Stage 2 (S2), Peak Exercise (P). One, three, and five minutes of recovery denoted by R1, R3, and R5.

Figure 6 - Influence of Exercise and Exercise Training on eNOS Content in ATM Compared to LTM Trained Individuals From Vastus Lateralis Biopsies



This figure represents previous work recently published from our laboratory (105). Upper panel: sample immunoblots of eNOS for both training groups and β-Actin loading control, samples organized from left to right are unexercised/untrained (UU), exercised/untrained (EU), and exercised/trained (ET). Lower panel: quantitation of the relative abundance of eNOS normalized to β-Actin control, densitometry for each subject is normalized to their own unexercised/untrained sample. *P<0.05 Compared to resting, untrained. Data are mean ± SEM.

angiogenesis following ATM training. Therefore, more investigation is needed to better characterize the mechanisms behind our observations. The findings of our investigation were similar to those found with swim training with regards to reductions in resting blood pressures (58, 192). Nualnim et al. (192) also observed improvements in baroreflex sensitivity and flow-mediated dilation following training. Given the previously found hemodynamic and cardiovascular adjustments to water immersion and acute aquatic exercise, the finding that hemodynamic adaptations to chronic aquatic exercise training differ from land based training is not unexpected. The implications of our findings and others with regards to possible therapeutic applications for heart cardiovascular disease will be discussed further in sections to come.

Body Composition

When performed at commonly prescribed thresholds for volume, intensity, and frequency, aquatic exercise has been shown to produce favorable changes in body composition (105, 106). In our previous study comparing ATM and LTM training (106), both groups were observed to have similar decreases in %body fat (-1.3 %BF). These findings are similar to those reported by others others (56, 155) with observed significant decreases in %BF following aquatic exercise training. While differences in training program design exist within the current literature, thresholds with regards to weekly exercise volume and caloric expenditure appear to be similar between aquatic and land based exercise training thus far. In addition to reductions in %BF, we have also previously observed significant increases in leg lean mass following 12 weeks of ATM training (106). While no statistically

significant differences were found between chronic LTM and ATM training, gains in leg lean mass were twice that of the LTM group on average.

Muscular Strength

While no measures of strength were taken during our original investigation, we suspected that the increases in leg lean mass we observed following ATM training may have also resulted in increased muscular strength. However present data reported in the literature regarding changes in muscular strength following aquatic training are difficult to interpret. Inconsistencies in program design and the incorporation of other equipment such as resistance bands or aquatic dumbbells make it difficult to determine the specific contributions of aquatic exercise to improvements in strength (19, 20). However, because of increased ambulatory resistance, decreases in vertical load, and differences in muscle recruitment patterns (259), we find it reasonable to suspect that mode specific differences in skeletal muscle adaptation may differ between aquatic and land based exercises. Further research is needed where land and aquatic exercise analogs are controlled for volume, intensity, and frequency to determine the specific effects of aquatic exercise on strength.

Considerations for Athletics

Much of the current literature on aquatic running is limited to sedentary, injured, or aging populations. As a result, further research is needed to determine the efficacy of aquatic based running for athletic populations who are already physically conditioned. Given the current findings with regards to increases in aerobic capacity, decreases in body fat, and potential increases in lean mass, exercises such as ATM running may have the potential to

increase athletic performance (259). While definitive data are lacking, it is notable that several collegiate and professional athletics organizations currently incorporate aquatic based exercises such as ATM running into their training programs (259). Therefore, future cooperation should be encouraged between research investigators, athletic training staff, and strength and conditioning professionals to characterize the physiological response to chronic aquatic running when incorporated into various sport specific athletic training programs.

Aquatic Exercise in Rehabilitation and Therapy

Aquatic based therapies are commonly practiced for those with lower limb injuries, spinal injuries, osteoarthritis, chronic inflammation, cardiopulmonary conditions, and fibromyalgia (259). The physical properties of water and acute physiological adjustments to water immersion discussed earlier provide specific benefits which have been reported to either enhance recovery, or provide an avenue for physical activity for those with limited mobility and functional capacity (9, 52, 111, 119, 131, 174, 242). The following section will briefly review current therapeutic applications of aquatic exercise with a focus on aquatic based running.

Osteoarthritis and Lower Back Pain

Because of reductions in impact, aquatic exercise has been demonstrated to be effective in reducing the symptoms of osteoarthritis while also improving joint mobility (66, 80). Anecdotally, aquatic therapy is also reported to have high rates of compliance in comparison to land based therapies (259). Denning et al. (69) reported reduced joint pain during ATM versus LTM walking in patients with osteoarthritis. Reductions in joint pain

from these studies have been determined to result from reductions in ground reaction forces generated during exercise (259). A further example of the effects of reduced vertical loading can be found in an investigation by Dowzer et al. (73) observed reduced spinal shrinkage during DWR compared to LTM exercise. A key finding in aquatic exercise research is that aquatic based aerobic and resistance exercises have been observed to be effective in eliciting increases in cardiovascular fitness and strength in patients with osteoarthritis (111, 112). Similar to those with osteoarthritis, aquatic based therapy has been found to be beneficial for those with various spinal conditions (253). Progressive aquatic therapies may also take advantage of manipulating water depth and thus, the degree to which the patient is unloaded (259). However, comparative studies are limited and it is unknown as to whether or not aquatic exercise provides greater benefits than comparable therapeutic land based exercises (253). Nonetheless, aquatic exercise appears to be an effective tool for promoting increases in fitness, reductions in pain, and improved joint mobility with a high rate of patient compliance.

Musculoskeletal Injury and Inflammation

Because of reductions in vertical load, aquatic exercise is commonly utilized in rehabilitation to maintain range of motion and function in individuals with lower limb injuries (259). Rational for this is that patients are able to continue to exercise at intensities which prevent deconditioning or atrophy as a result of injury induced inactivity (4). Because of the maintenance of physical function, aquatic therapies such as ATM running may potentially reduce injury recovery time.

Aquatic exercise therapy has also been proposed to reduce skeletal muscle edema and inflammation (257). In response to traumatic injury or a damaging bout of eccentric exercise edema has been reported to result in compression of localized capillaries and increase the transit time for delivery of oxygen and nutrients as well as the removal of metabolic waist (88, 190, 244). During immersion at rest, there is an increase in skeletal muscle blood flow elicited by the gradient which exists between internal tissue hydrostatic pressure and capillary filtration pressure (6). This gradient has been proposed to improve the reabsorption of interstitial fluids thereby reducing edema (257). Because an increased hydrostatic pressure gradient can also reduce cellular infiltration by inflammatory cytokines and white blood cell fractions (151, 179, 250), Wilcock et al. (257) hypothesized that water immersion and aquatic exercise may decrease secondary damage to tissue commonly caused by inflammation, and therefore improve recovery. While this hypothesis has not been systematically tested, it is reasonably supported by previous observations by our laboratory where ATM exercise was found to reduce delayed onset muscle soreness following intense sprinting in trained men compared to passive recovery (149). Therefore aquatic exercise appears to be an effective tool for pain management and functional recovery from either injury or strenuous physical activity. However, the extent to which aquatic exercise may improve recovery and reduce inflammation compared to other common therapies is not well understood at this time.

Osteoporosis

Because of reduced joint loading and impact, aquatic exercise is commonly prescribed to reduce risk of injury (Crouse book). However, because bone mineralization is

stimulated in part by weight bearing activity (65), further investigation is needed to evaluate the benefits of aquatic exercise versus land based weight bearing exercise. Bravo et al. 1997 (35) reported that one year of waist depth aquatic exercise involving aerobic and plyometric exercises (jumping, bounding) was effective at improving aerobic capacity, flexibility, and strength but did not increase either spine or femoral neck bone mineral density in postmenopausal women. On the other hand, Ay et al. 2003 (11) reported increases in calcaneal bone density following 6 months of aquatic exercise in a similar population. Therefore, because of limited and conflicting data, the degree to which aquatic exercises may be utilized to combat osteoporosis is unclear. Regardless, beneficial roles for aquatic exercise in patients suffering from osteoporosis have been identified in that various aquatic exercise programs have been observed to elicit improvements in cardiovascular fitness, strength, and motor function (97, 107, 156). Therefore adaptations to chronic aquatic exercise and the reduced risk of injury provide an important avenue of activity for those with osteoarthritis as long as weekly exercise regimens also incorporate land based exercises to achieve adequate loading to stimulate osteogenesis (259).

Cardiovascular and Cardiopulmonary Rehabilitation

While data are limited, there have been reports which indicate that water immersion and aquatic exercise therapy may benefit patients with congestive heart failure (239). Tei et al. (239) reported that immersion in warm water (41˚C) resulted in an increase in vasodilatation and subsequent decrease in peripheral resistance, and in response to being immersed in water, an increase in cardiac preload and stroke volume. Chronic responses to this treatment included increases in ejection fraction and reductions in left ventricular end-

diastolic volume. However, because of the effects of water immersion on blood volume distribution, catecholamine output, and cardiac stretch the severity of a patient's condition must be a determining factor when considering hot water therapy (176). Unfortunately, a threshold for whether or not such therapies are appropriate for a given cardiovascular condition has not been established and is therefore subjective to physicians on a case by case basis. Still, reports on the use of aquatic therapy for such data are promising (183).

While little is known about the potential for prolonged aquatic training in patients suffering from cardiovascular or cardiopulmonary diseases, findings by our laboratory (105) as well as Tei et al. (239) indicate a potential role of aquatic exercise in the prevention and treatment of hypertension. As previously stated, 12 weeks of chronic ATM training elicited chronic reductions in blood pressure at rest and during exercise (105). Although the investigation involved normotensive subjects, these findings suggest a therapeutic utility for this mode of exercise in the treatment and prevention of hypertension (81, 170), stroke (82), and atherosclerosis (171). Exaggerated SBP and MAP during exercise may be indicative of failure to reduce total peripheral resistance and of early structural changes in the vasculature which can lead to hypertension (196, 229, 262). Our observations of reduced SBP, DBP and MAP reactivity to exercise stress with ATM, but not LTM strongly suggest improved vessel compliance and a resultant reduced risk of future hypertension and related diseases in ATM trained subjects.

In our previous investigation we also observed a reduced reactivity to exercise stress in measures of both PP and RPP. Pulse pressure is proportional to stroke volume and widening of PP may serve as a marker of lost compliance of the vessel wall (171). The observed blunted increases in PP during exercise stress following ATM training may indicate

improved vessel compliance. RPP serves as an indicator of myocardial work/oxygen consumption (99), therefore reduced RPP during similar exercise stress is indicative of a reduced workload on the heart to perform equivalent total body work . Taken together these findings in previously inactive, normotensive adults demonstrate reduced blood pressure reactivity to physical stress following ATM training, which may have application in the treatment and prevention of hypertension. At present, we can only speculate as to how ATM training may affect these measures in a hypertensive population. However, previous data in more traditional exercise training modalities suggests that exercise is more likely to improve such measures in the hypertensive population (197). It would therefore be of great clinical interest to determine if ATM training may enhance such benefits in this population. Although we cannot be certain as to the similarity of the dynamics of immersion between swimming and ATM exercise, previous evidence suggests the efficacy of swim training to reduce resting blood pressures in both pre-hypertensive and hypertensive subjects (192, 235). Therefore, current literature does add support for the use of aquatic exercise in combating hypertension.

Analysis of muscle biopsy samples from our previous investigation revealed that eNOS content was enhanced only after exercise training in the ATM group with no change observed in the LTM group. Why such an adaptation would occur following ATM training but not LTM we can only speculate at this time. We suspect that the observed effects on ATM training on whole muscle eNOS expression may relate to similar improvements in flow-mediated dilation as seen with swim training (192).

Obesity

Aquatic exercise has been found to provide a safe environment for those with obesity to exercise at adequate intensities and volumes to elicit reductions in body fat with a reduced risk of injury due to reduced vertical loading (106). Aquatic exercises such as ATM running can also assist those with obesity in transitioning to land based exercises over time (259). As mentioned earlier, we have previously observed that chronic ATM training provides similar increases in aerobic capacity and improvements in body composition (106). The increases in lean mass observed in our previous investigation also suggest that ATM training may promote increases in strength and therefore functional capacity in obese and overweight individuals as well (106). Importantly, aquatic exercise regimens have also been reported to have a high rate of compliance among clinical populations (259). Therefore, if performed at appropriate exercise intensities and training volumes, aquatic exercise can be utilized as an effective exercise modality for improving body composition and health in obese populations.

Summary and Implications for Aquatic Exercise in Concurrent Training

In summary, exercise interference results from diverging adaptive processes within skeletal muscle that govern skeletal muscle growth, degradation, phenotype expression, and metabolic characteristics. While the specific mechanisms responsible are not entirely understood, adaptations appear to be largely governed by training volume, intensity, training history, and training mode. Because aquatic exercise elicits unique acute and chronic physiologic adjustments compared to land based exercise, it stands to reason that it may yield differential physiological responses when performed concurrently with resistance exercise.

Acutely, aquatic exercise increases central blood volume, cardiac preload, stroke volume, cardiac output, and barrow receptor firing with reduced catecholamine output, and angiotensin II production compared to land based endurance exercise performed at the same intensity. During DWR and ATM running, motor recruitment patterns differ from land-based exercise because of reduced vertical loading and increased horizontal resistance. Both aquatic and land base training has been previously observed to elicit similar increases in aerobic capacity and improvements in body composition. However, our previous work demonstrates that ATM training results in unique cardiovascular and skeletal muscle adaptations compared to standard LTM exercise. These adaptations include reductions in blood pressure at rest and during exercise stress, increases in skeletal muscle eNOS content, and increases in leg lean mass. In light of previous observations, we hypothesized that ATM running would not interfere with, but enhance skeletal muscle growth and strength development when performed concurrently with resistance training (RT-ATM) compared to concurrent RT-LTM training and RT alone. We also hypothesized that both concurrent RT-ATM and RT-LTM training would yield similar aerobic adaptations that would not be observed following resistance training alone (RT).

Aims of the Experiment

To test our hypotheses, we designed a 12 week training intervention. The ***purpose*** of the following investigation was to compare RT-ATM, RT-LTM, and RT with regards to chronic physiological adaptations to training, the acute anabolic response of skeletal muscle to a single session of exercise, and chronic alterations in intracellular regulators of skeletal muscle growth, degradation, and metabolism. Therefore, this dissertation addresses the following aims:

Specific Aim 1: Compare the physiological responses with regards to body composition lean mass, skeletal muscle strength, and aerobic capacity (VO_{2max}) to 12 weeks of chronic, RT, RT-LTM, and RT-ATM training.

Specific Aim 2: Compare myofibrillar fractional synthesis rates (FSR) measured 24h following acute RT, RT-ATM, and RT-LTM exercise in the untrained/sedentary state and following 12 weeks of chronic training (trained state).

Specific Aim 3: Compare the chronic effects of RT, RT-ATM, and RT-LTM exercise training on the content of signaling proteins that participate in the regulation of skeletal muscle metabolism (TSC2, mTOR, Akt).

Notably, we are among the first to examine chronic and acute responses to concurrent exercise within the same investigation. The data presented herein challenge the notion that endurance and resistance exercise are universally incompatible and further highlight the importance of exercise mode selection when designing exercise interventions for specific desired outcomes.

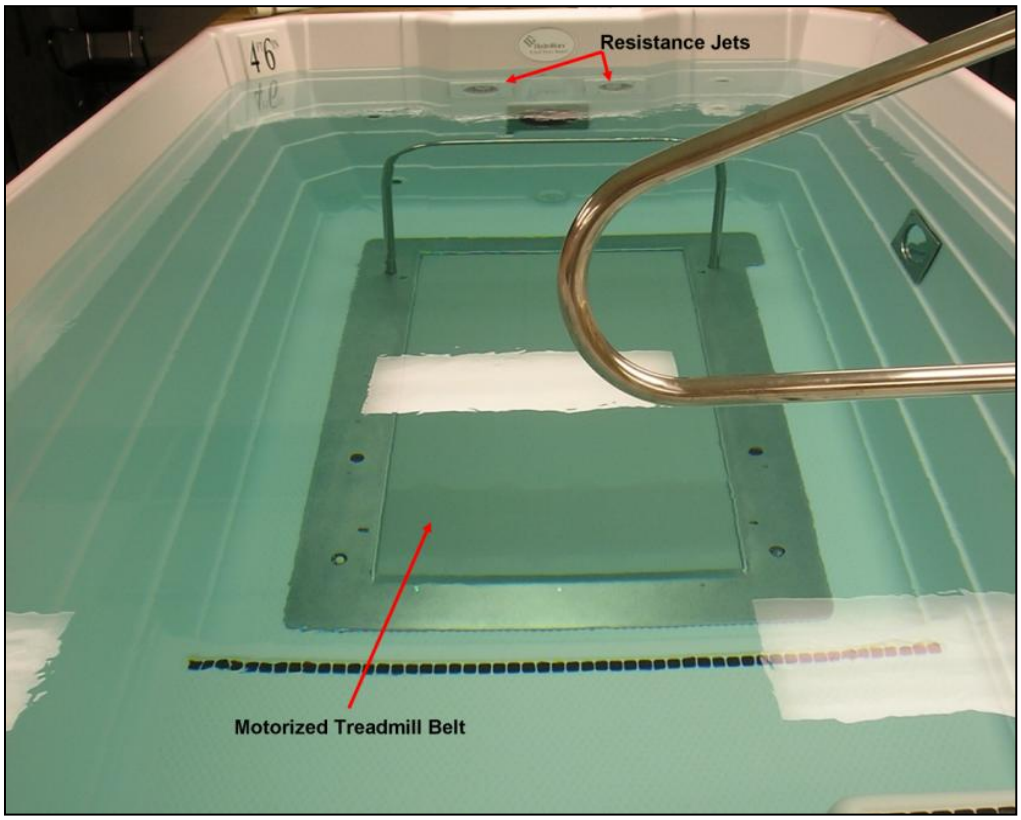
CHAPTER II

ANABOLIC RESPONSES TO ACUTE AND CHRONIC RESISTANCE EXERCISE ARE ENHANCED WHEN COMBINED WITH AQUATIC TREADMILL EXERCISE

Introduction

In recent years, aquatic exercise has grown in popularity in the general, overweight, elderly, and athletic populations as a mode of therapeutic or rehabilitative exercise (27, 73, 130, 248, 256). Aquatic based running exercises such as deep water running and aquatic treadmill (ATM) running (Figure 7) have also been shown to be an effective alternative to land based aerobic exercises for promoting increases in aerobic fitness (28, 37, 41, 83, 106, 174, 256). Recently, we compared the efficacy of ATM training with traditional land treadmill (LTM) training using a protocol similar to that recommended by the ACSM (106). Following training, increases in aerobic capacity and decreases in fat mass were similar regardless of training mode. However, leg lean mass (measured with DEXA) was significantly increased following ATM training, twice that of the LTM group. We suspected that because vertical load, lateral resistance, and skeletal muscle activation have been shown to differ between ATM exercise and traditional LTM exercise (259), chronic ATM training may also elicit unique mode-specific adaptive responses compared to LTM training.

Figure 7 - Aquatic Treadmill



HydroWorx 1000i series aquatic treadmill as used in the current study with markers denoting motorized belt and frontal resistance jets. The variable speed motorized treadmill from 0 to 200 mlminj1 (0–7.5 mph) allows for precise control of running velocity; in addition, variable-force resistance jets are configured to push against the subject, providing resistance to forward ambulation.

While no measures of strength were obtained during our original investigation (106), the gains in lean mass observed following training led us to consider a potential role for ATM exercise in a concurrent aerobic and resistance training model. Previous investigators (12, 13, 24, 118, 143) have reported that aerobic training may interfere with skeletal muscle hypertrophy and strength development when performed concurrently with resistance training, compared to performing resistance training in isolation. Primary adaptations to aerobic exercise include reductions in muscle fiber fatigue-ability and increases in aerobic capacity,

oxidative metabolism, and mitochondrial density (47, 117, 128, 185, 260, 271). On the other hand, primary adaptations to traditional resistance exercise typically include skeletal muscle hypertrophy, increases in strength, and an increase in glycolytic metabolism (31, 38, 85, 93, 207, 213). Because the principle of training specificity states that physiological adaptations to training are specific to the types of training performed (15, 38), some (12, 55, 108, 143, 152, 153) have presented hypotheses that link concurrent training interference to acute metabolic responses to exercise, exercise mode specific contractile characteristics, and overtraining. However, present findings are inconclusive since investigations exist which both support (54, 55, 98, 108, 118, 143, 152, 184) and refute (5, 67, 72, 161, 222) these hypotheses.

In recent years, intracellular signaling cascades which regulate skeletal muscle anabolism have been described following endurance and resistance-type exercise stimuli (10, 12, 55, 74, 85, 93, 95, 185, 260). Of note, interactions between protein kinase B (Akt), mammalian target of rapamycin (mTOR), and tuberous sclerosis complex 2 (TSC2) have been hypothesized to play a role in concurrent exercise interference (12, 184). Briefly, the Akt-mTOR pathway is regulated by energy balance, insulin signaling and skeletal muscle contraction, and when stimulated, has been shown to increase skeletal muscle myofibrillar fractional synthesis rates (myoFSR) (74). In times of reduced intracellular energy (↑AMP, ↓ATP), mTOR is negatively regulated by TSC2 and its anabolic signaling is reduced (127). TSC2 activation can be stimulated from multiple activation sites by proteins such as AMP activated protein kinase (AMPK), which also stimulates mitochondrial biogenesis (123, 127, 128, 200, 236). This information collectively precipitates the current interference hypothesis that when intracellular energy is low, which comparatively occurs to a greater degree during

endurance exercise than traditional resistance exercise, mitochondrial biogenesis and oxidative energy production become greater intracellular priorities than myoFSR and hypertrophy. However, because of inconsistencies between previous concurrent training investigations with regards to exercise mode selection, frequencies, intensities, and subject populations used, a broad generalization of exercise interference (interference occurring under all concurrent training paradigms) is difficult at this time (152, 153, 261).

In the present study we expanded on our previous findings (106) and examined the exercise induced adaptations to 12 wks of concurrent resistance and ATM exercise training (RT-ATM), concurrent RT-LTM training, and resistance training (RT) alone in previously untrained subjects (n=47). Additionally, we utilized isotope labeling to analyze the acute effects of RT-ATM, RT-LTM, and RT exercise on myoFSR measured for 24h following acute exercise before and after training in a subset of subjects who volunteered to undergo muscle biopsy sampling (n=25). From our available tissue samples, we also elected to measure chronic alterations in Akt, mTOR, and TSC2 content. We hypothesized that acute RT-ATM exercise would yield greater 24h myoFSRs than RT-LTM or RT and that 12wks of concurrent RT-ATM training would enhance rather than interfere with gains in lean mass and strength compared with 12wks of RT-LTM or RT alone. We also hypothesized that RT-ATM and RT-LTM training would elicit similar gains in aerobic capacity and reductions in fat mass, but that LTM exercise would interfere with strength and lean mass development when performed concurrently with RT. The findings presented herein demonstrate that concurrent RT-ATM exercise training may serve as a novel and effective tool for increasing or preserving muscular strength and skeletal muscle mass while also providing aerobic benefits.

Methods

All methods and procedures were approved by the Texas A&M University Institutional Review Board for Human Subjects in Research. Prior to participation, all subjects provided informed consent. Sixty-eight, untrained volunteers were recruited from Texas A&M University and the College Station, TX communities to participate in the study. Potential subjects were recruited through informational flyers, email, and by word of mouth. Volunteers were screened to ensure that they had not regularly performed planned exercise (>1/wk) for the previous 3 months. Prior to participation, all subjects were screened to ensure that they were healthy enough for exercise (<2 cardiovascular risk factors) (243). Screening was based on ACSM risk stratification criteria to exclude subjects with contraindications to exercise or those who were taking medications known to affect metabolism or blood clotting. For subjects with two or more risk factors for cardiovascular disease, examination and clearance from a cardiologist was required prior to participation. Of the 68 volunteers that were recruited, 47 (♂ n=23, 37±11yr, 182.7±6.7cm, 98.9±16.1kg | ♀ n=24, 38±12yr, 165.6±4.8cm, 82.1±19.1kg) completed all required aspects of the study which included all subject testing and completion of a at least 85% of all programmed training sessions. Additionally, rescheduled exercise sessions due to any unforeseen absences were required to be completed the week of the missed session. Baseline demographics for subjects who completed this investigation are shown in Table 1 (following page).

Prior to training, participants were asked if they would be willing to volunteer for an additional portion of the study which involved acute exercise and muscle sampling before and after training (methods to follow). Subjects were informed of all details related to

participation and compensation prior to consent. Of the original 47 subjects, 25 volunteers (♂ n=16, 40 ±4yr, 182.2 ±1.7cm, 93.8 ±5.5kg | ♀ n=9, 38 ±4yr, 166.3 ±2.0cm, 73.1 ±4.0kg) elected to participate in acute exercise testing and muscle sampling.

Table 1 - Pre-training Subject Demographics

	RT			RT-LTM			RT-ATM		
	Men	Women	Total	Men	Women	Total	Men	Women	Total
Number	7	8	15	8	8	16	8	8	16
Age (yr)	37 ± 5	37 ± 4	37 ± 3	37 ± 4	40 ± 4	38 ± 3	36 ± 3	40 ± 5	38 ± 3
Weight (kg)	96.1 ± 6.4	88.4 ± 7.4	92.0 ± 4.9	96.1 ± 6.7	79.0 ± 4.5	87.3 ± 4.5	104.2 ± 4.4	79.6 ± 8.1	91.9 ± 5.5
BMI ($kg \cdot m^{-2}$)	28.3 ± 1.5	31.9 ± 2.1	30.2 ± 1.4	28.4 ± 1.9	28.2 ± 2.0	28.3 ± 1.4	31.9 ± 1.3	28.5 ± 2.7	30.2 ± 1.5
%Body Fat	31.8 ± 2.7	49.3 ± 3.0	41.1 ± 3.1	31.7 ± 3.1	45.4 ± 2.2	38.5 ± 2.6	35.1 ± 2.4	43.0 ± 2.9	38.8 ± 2.1

Values are presented as means±SEM

General Study Protocol

Prior to participation, all subjects provided informed consent. Physiological and demographic assessments were completed on the second visit to the laboratory (methods to follow). After the completion of training, all physiological and demographic testing procedures were repeated within 4 days after the final exercise training session.

Diet and Activity Logs

Subjects were instructed to maintain their accustomed dietary and activity habits throughout the course of the study. No attempt was made to modify diet or activity outside of the study protocol. To verify compliance with these instructions, dietary and activity habits were assessed on two occasions coinciding with the beginning and end of exercise training using methods previously described (26). Briefly, subjects were instructed to complete dietary and physical activity records on days which would best represent their

normal daily habits. On both occasions dietary records were recorded for three consecutive days, including one weekend day. The 3-day dietary records were analyzed for total caloric intake and for carbohydrate, fat, and protein composition using commercially available computer software (Nutribase®, Cybersoft Inc., Phoenix AZ). Activity records were recorded for seven consecutive days and were analyzed for total energy expenditure. Because activity records were used to compare the energy expenditure of daily living before and after training, exercise participation in the study was excluded from the final activity logs.

Physiological Assessments

Body composition, including whole body percent fat, fat mass and lean body mass, were assessed using DEXA. An incremental maximal graded exercise test (GXT) was conducted on a motor-driven treadmill according to the Bruce protocol (39). Oxygen consumption during exercise was assessed using a calibrated metabolic gas-analysis system (Ultima®, Medical Graphics, Minneapolis, MN). VO_{2max} was taken as the highest 15 s average oxygen uptake achieved during the exercise test. Heart rate (HR) and rhythm were monitored continuously from a 12-lead electrocardiogram. Ratings of perceived exertion (263) using a Borg 15-point scale ranging from 6-20 (33) and manual blood pressures (BP) were obtained during the last 30 s of each treadmill stage and at maximal exercise. At least two of the following criteria were required for the maximal exercise test to be considered valid: 1) achievement of maximum heart rate within 10 bpm of the age-predicted maximum; 2) rating of perceived exertion ≥ 18; 3) respiratory exchange ratio >1.1 at maximal exertion;

or 4) O_2 uptake plateau despite further increases in workload. The same skilled laboratory personnel consistently performed all physiological measurements.

Strength Assessment

All subjects were tested and trained using Keiser® resistance training equipment (Keiser Corporation, Cherry Ave Fresno, CA). Prior to the strength assessment, subjects performed a standardized warm-up protocol involving three minutes of light cycling followed by a series of standardized stretching exercises. After completion of warm-up, subjects were tested on the following exercises in order: leg press, chest press, leg curl, lat pull, leg extension, triceps push down, and biceps curl. Following a series of warm-up sets involving increasing perceived intensities (50→90% of perceived maximum) and reduced repetitions (10→2) per set, subjects performed repetitions to failure at a resistance perceived to be near maximum. Following strength assessment, one-repetition-maximum (1RM) was calculated using an equation adapted from Baechle et al. 2010 (14). This process was again repeated during mid-point and final strength assessments where warm-up sets were set at percentages of each subject's previous 1RM values and progressed as follows: 50%(10reps), 65%(6reps), 75%(4reps), 80%(2reps), 85%(2reps).

Exercise Training

Subjects RT-LTM and RT-ATM groups performed resistance exercise immediately followed by LTM or ATM twice per week separated by one session of either LTM or ATM performed in isolation (Total of 3 sessions/wk). Subjects in the RT group performed resistance exercise in isolation twice per week. The same resistance exercise-training program was performed by all groups. Resistance exercise consisted of the same exercises

Table 2 - Training Progression

RESISTANCE TRAINING PROGRESSION Performed by All Groups				
Training Week	**Frequency (sessions / week)**	**Intensity (% of 1RM)**	**Sets · Repetitions**	**Progression**
Weeks 1-6	2	50% Warmup Set 60% Working Sets	1 x 12 3 x 12	↑ 5% of baseline 1RM if all working sets are completed with 12 repetitions
Week 7 - RESASSESSMENT OF STRENGTH				
Weeks 8-12	2	65% Warmup Set 80% Working Sets	1 x 8 3 x 8	↑ 5% of midpoint 1RM if all working sets are completed with 8 repetitions

AEROBIC TRAINING PROGRESSION: Concurrent Training Days Performed by the RT-LTM and RT-ATM Groups Only			
Training Week	**Frequency (sessions / week)**	**Intensity (% of VO_{2max})**	**Energy Expenditure (kcal)**
Week 1	2	60	250 - Resistance Exercise Expenditure
Week 2	2	65	300 - Resistance Exercise Expenditure
Week 3	2	70	350 - Resistance Exercise Expenditure
Week 4	2	75	400 - Resistance Exercise Expenditure
Week 5	2	80	450 - Resistance Exercise Expenditure
Week 6	2	85	500 - Resistance Exercise Expenditure
Week 7 - REASSESSMENT OF VO_2max			
Weeks 8-12	2	85	500 - Resistance Exercise Expenditure

AEROBIC TRAINING PROGRESSION: Non - Concurrent Training Days Performed by the RT-LTM and RT-ATM Groups Only			
Training Week	**Frequency (sessions / week)**	**Intensity (% of VO_{2max})**	**Energy Expenditure (kcal)**
Week 1	1	60	250
Week 2	1	65	300
Week 3	1	70	350
Week 4	1	75	400
Week 5	1	80	450
Week 6	1	85	500
Week 7 - REASSESSMENT OF VO_2max			
Weeks 8-12	1	85	500

Weekly Training Order			
Training Group	**DAY 1**	**DAY 2**	**DAY3**
RT	Resistance Exercise		Resistance Exercise
RT-LTM	Resistance Exercise followed by LTM	LTM only	Resistance Exercise followed by LTM
RT-ATM	Resistance Exercise followed by ATM	ATM only	Resistance Exercise followed by ATM

Resistance training progression performed equally by all groups. The aerobic training progression (shown above) was additionally performed by the RT-LTM and RT-ATM groups twice per week immediately following resistance training and once per week in isolation. For concurrent training groups, the volume of aerobic exercise on concurrent training days was determined by subtracting the kcal expenditure of resistance training from the total prescribed kcal expenditure for the day. Resistance exercise kcal expenditure was approximated by the following proprietary equation: kcal = [2.251 • Height cm] + [0.140 • Lean Mass kg] + [1.263 • VO_{2max} ml·kg·min^{-1}] + [0.002 • (total volume $^{sets \bullet reps \bullet resistance}$)].

and exercise sequence used during strength assessment. The RT-ATM and RT-LTM groups trained at equivalent caloric expenditures and relative intensities (Table 2). ATM training was conducted using a HydroWorx 1000 series treadmill (HydroWorx International® Inc., Middletown, PA). LTM training was conducted on a standard motor-driven treadmill (Quinton TM65, Quinton® Inc., Bothell, WA). Treadmill velocity and grade/jet resistance were adjusted as necessary during the training session to attain the HR and RPE which matched the prescribed intensity. Each individual's exercise prescription was adjusted for increases in VO_2max during week 6 such that the prescribed intensity and duration were maintained throughout the study. During aerobic exercise (LTM or ATM), individual energy costs ($kcal \cdot min^{-1}$) were estimated as the product of VO_2 ($LO_2 \cdot min^{-1}$) and the respiratory exchange ratio energy-oxygen equivalent ($kcal \cdot LO_2^{-1}$) measured during the GXT at each respective intensity of interest. Using this relationship, the exercise duration required to expend the required kcal of energy per exercise session was calculated for each subject (23). Heart rate and rate of perceived exertion were recorded during each exercise session as a means of tracking intensity. As an additional precaution, a metabolic cart was used to sample VO_2 from each subject during a training session to ensure correct exercise intensities and volumes were being achieved (wks 2, 4, 8,10). Caloric expenditure of resistance exercise was approximated using the

following proprietary equation: Resistance Exercise Kcal Expenditure = [2.251 • Height cm] + [0.140 • Lean Mass kg] + [1.263 • VO_{2max} ml·kg·min] + [0.002 • (total volume $^{sets \bullet reps \bullet resistance}$)].

The prescribed exercise progression was such that by week 6 subjects expended approximately 1500 $kcal \cdot wk^{-1}$ in exercise training. On concurrent training days, the

prescribed caloric expenditure was met by following resistance training with the appropriate volume of aerobic exercise to achieve the prescribed total for a given week. On days where aerobic exercise was performed in isolation, the total prescribed caloric expenditure was performed aerobically (Table 2). While time of day was not controlled for subject training, sessions were evenly separated throughout each training week to avoid back-to-back sessions. Each session was also monitored one-on-one for each subject by a trained member of the laboratory staff.

Acute Exercise Blood and Muscle Sampling

Methods for tissue collection have been previously published (93, 104). Blood samples were obtained on 6 occasions and muscle samples were obtained on 4 occasions. Muscle sample #1 and blood sample #1 were obtained ~3 days prior to acute exercise (resting/untrained state). Resting samples were taken following at least 72hr without strenuous activity. For blood and muscle sampling, each subject reported to the laboratory, (time of day controlled [between 5am-11am]), after a 12hr fast (water allowed *ad libitum*). Prior to sample collection, subjects completed a form reporting their physical activity and dietary adherence over the previous 24hr and the time of their last meal. Blood samples were drawn without stasis from an antecubital vein with the subject seated at quiet rest into Vacutainer tubes containing 10.5 mg Na-EDTA for plasma collection. Plasma samples were immediately isolated by centrifugation at 1500 x g for 30 minutes at 4°C. Aliquots of plasma were stored at −80°C for later analysis. Biopsies were taken from the vastus lateralis under local anesthesia (1% Xylocaine HCl) using a 5-mm needle. All muscle samples were

cleaned of visible fat, connective tissue, and blood. Muscle samples were immediately frozen in liquid nitrogen (−190ºC), and then stored at −80ºC until analyzed.

On the morning of acute exercise, subjects arrived to the laboratory and performed a standardized warm-up (previously described) followed by a single bout of resistance exercise. The intensity and caloric volume of the prescribed acute exercise bouts were matched to Week 1 (1st acute session/Untrained) and Week 12 of training (2nd acute session/Trained) (training description to follow). The rationale for this was to analyze the response of each group to exercise in the context of the volumes and intensities that might be achieved when untrained or trained. Resistance exercises occurred in the same order as listed for strength assessment. Heart rate and oxygen consumption were continuously measured using a metabolic cart (CPX Express, Medical Graphics, Minneapolis, MN) and caloric expenditure was determined using indirect calorimetry. Additionally, subjects in the RT-LTM and RT-ATM groups performed either LTM or ATM exercise immediately following resistance exercise. The prescribed caloric expenditure was met by following resistance training with the appropriate volume of aerobic exercise to achieve the prescribed total for training Week 1 (1st acute session / untrained / 250kcals) and Week 12 (2nd acute session / trained / 500kcals). Acute LTM exercise protocols began with a 3 min warm-up period at 53.6 $m \cdot min^{-1}$ at a 0% grade (RT-LTM group). Acute ATM exercise protocols began with a 3 min warm-up period at 53.6 $m \cdot min^{-1}$ at a 0% jet resistance (RT-ATM group). The duration of each acute exercise session was defined as the time required to expend the remaining volume of kcals need to reach a total of 250 kcals (250 - resistance exercise expenditure) at 60% of VO_2max (1st acute session / untrained) or 500 kcals at 85% of VO_2max, based on the most recently acquired VO_2max. HR, RPE and VO_2 were measured every 5 min at the

beginning of exercise to adjust treadmill velocity and grade until the required VO_2 was achieved; thereafter VO_2 measurements were taken every 5 min until the cessation of exercise, and minor adjustments were made as necessary to the treadmill velocity and grade to maintain the required VO_2, as well as, exercise time to ensure the correct kcal expenditure. Subjects were asked to avoid any physical exertion until after all blood collection procedures were completed.

Deuterium Administration and Isotope Tracing

The following methods have been previously published (93). Immediately following acute exercise, subjects received their 2nd blood draw and their first of 4 boluses of 70% ^2H_2O (men, 4 ml/kg; women, 3 ml/kg) (Cambridge Isotopes, Andover, MA) to achieve approximately 0.4% to 0.8% 2H-labeling of body water. The remaining boluses were given 2, 7.5, and 9.5 hours following acute exercise. Thirty minutes following exercise, participants received their first of 5 meals (Boost Nutritional Energy Shake; Novartis Medical Nutrition, Fremont, IN), which supplied the subjects with 8037 kJ, 52% carbohydrate, 20% protein, and 28% fat. The remaining 4 meals (Boost) were provided at 3, 5.5, 8.5, and 11 hours following acute exercise. Total supplemented energy intake was matched to each subject's baseline dietary analysis. Subjects returned to the laboratory 24h following cessation of exercise for the 3rd blood draw and 2nd vastus lateralis muscle biopsy. This process was again repeated following training 5 days of the end-of-study physiological assessments (exercised/trained state) for the remainder of muscle and blood sample collection.

Analysis of Myofibrillar FSR

Analysis of ^{2}H-labeling of body water and protein-bound alanine was determined as previously described (93-95). Briefly, 20 μL of plasma was reacted with 2.0 μL of 10NNaOH and 4.0 μL of a 5%(vol/vol) solution of acetone in acetonitrile for 24 hours. Acetone was removed by the addition of 0.6 mL of chloroform and 0.5 g Na2SO4. To determine myofibrillar FSR, approximately 40mg of wet muscle was homogenized on ice in 0.4 mL of 1× Norris Buffer (25 mmol/L Tris-HCl, 5 mmol/L β-glycerophosphate, 2 mmol/L dithiothreitol, 0.1 mmol/L Na3VO4, 10mmol/L$MgCl_2$; Cell Signaling Technologies, Danvers, MA) and 0.01% Triton. Homogenates were centrifuged at 14,000 rpm @ 4°C for 30 minutes, the supernatant containing the cytosolic and membrane portion was then saved and stored at −80ºC for Western Blot Analysis (methods to follow). An aliquot (100μL) of the hydrolysate was dried, and a 3:2:1 ratio (0.1 mL) of N,N-dimethylformamide dimethyl acetal (Methyl-8 reagent; Pierce, Rockford, IL), methanol, and acetonitrile was added to the residue to determine the 2H-labeling of alanine on its methyl-8 derivative. All samples were analyzed using an Agilent 5973N-MSD (Agilent Technologies, Santa Clara, CA) equipped with an Agilent 6890 GC system and a DB17-MS capillary column (30m × 0.25 mm × 0.25 μm).

Western Blot Analysis

Western blot analysis of proteins was performed as previously described (79) with minor modifications (104). Samples for Western blot analysis were collected in the rested state before and after exercise. Briefly, an aliquot of the cytosol-rich immunoblotting fraction was diluted in an equal volume of Laemmli buffer (125 mM Tris, pH 6.8, 4% SDS,

20% glycerol, 200 mM DTT, and 0.002% bromophenol blue) and subjected to separation based on protein size via sodium dodecyl sulfate -polyacrylamide gel electrophoresis (SDS-PAGE) using precast 4-20% gradient gels (Lonza info). Following separation, proteins were transferred to a nitrocellulose membrane (Amersham Biosciences, Piscataway, NJ) using a semidry transfer technique. Membranes were then incubated in a blocking solution (containing 5% nonfat dried milk in Tris-buffered saline); 5% milk/TBS at room temperature for 1hr. Following blocking, membranes were incubated overnight at 4°C in a solution of 5% milk/ TBS with specific antibodies added at 1:1000 to detect proteins of interest. Anti-mTOR, anti-Akt, and anti-TSC2 were all obtained from Cell Signaling Technology (Danvers, MA) for analysis of total protein expression.

The membranes were then briefly washed 3 times in TBS and incubated again in 5% milk/TBS with 1:2000 of an anti-rabbit IgG secondary antibody coupled to horseradish peroxidase (Cell Signaling) for 1hr at room temperature, before a final series of brief rinses and visualized using chemiluminescence (Alpha Innotech, FluorChem SP, San Leandro, CA). Luminescence was normalized to a protein standard (obtained from human vastus lateralis) loaded on each gel and expressed as normalized absorbance units (AU).

Statistical Analysis

A 3(group) x 2(time) x 2(gender) mixed-model ANCOVA (covariate = baseline measures) repeated across training was used to detect group x time interactions for maximal strength, VO_{2max}, body composition, dietary recall, and daily energy expenditure before and after training. A 1x3 Mixed Model ANOVA was used to analyze changes in the above variables following training: Change = (Post-training value) – (Pre-training value). A

3(group) x 1(time) x 1(gender). A mixed-model ANOVA was used to compared 24h myoFSR between groups following acute exercise before (untrained state) and after (trained state) training. 3(group) x 2(time) x2(gender) Mixed -model ANOVA repeated across training was used to detect changes in mTOR, Akt, and TSC2 skeletal muscle protein content before and after training. The comparison-wise error rate, α, was set at 0.05 for all statistical tests. Where significant F ratios are found a Tukey's post hoc analysis was performed to determine difference among groups. All data were analyzed using SAS Enterprise Guide (version 4.3, SAS,Cary, NC).

Results

Pre-training physiologic characteristics of subjects in each group by gender are shown in Table 1. No significant differences in any of these characteristics were found between training groups at the beginning of exercise training. Our statistical analyses showed that there were no differential effects of gender on exercise training outcomes (i.e., no interaction due to gender); therefore, all exercise training data were collapsed across gender for subsequent analysis and for the presentation of results that follow. Pre and post training values for all independent variables are listed in Table 3. No significant within or between group interactions were found for dietary intake and daily energy expenditure. Statistical analysis of pre and post training values revealed significant group x time interactions for body composition, strength, and aerobic capacity ($p<0.05$) as well as skeletal muscle mTOR and Akt content ($p<0.05$). Significant group interactions were observed for change in body composition, strength, and aerobic capacity ($p<0.05$). Lastly, a significant group interaction was observed for 24h post exercise myoFSR measured before training (untrained state).

Table 3 - Pre and Post-Training Data

	RT			RT-LTM			RT-ATM		
Variable	**Pre Training**	**Post Training**	**Sig.** Within Group	**Pre Training**	**Post Training**	**Sig.** Within Group	**Pre Training**	**Post Training**	**Sig.** Within Group
Diet and Physical Activity									
Caloric Expenditure ($kJ \cdot d^{-1}$)	11,740.00 ±441.53	11,807.53 ±424.90	NS	11,368.75 ±552.72	11,297.25 ±532.68	NS	11,802.75 ±553.96	11,755.25 ±577.08	NS
Total Dietary Intake ($kJ \cdot d^{-1}$)	9,231.01 ±704.87	9,458.56 ±988.28	NS	9,264.58 ±833.68	9,231.10 ±1000.80	NS	11,101.73 ±1,207.01	9,398.55 ±916.69	NS
Relative Protein Intake (g/kg)	1.24 ±0.20	1.10 ±0.17	NS	1.07 ±0.09	1.02 ±0.10	NS	1.14 ±0.12	1.03 ±0.07	NS
Relative Carbohydrate Intake (g/kg)	3.43 ±0.41	3.42 ±0.44	NS	3.04 ±0.27	3.31 ±0.38	NS	3.37 ±0.37	3.18 ±0.27	NS
Relative Fat Intake (g/kg)	0.98 ±0.10	0.95 ±0.08	NS	1.01 ±0.11	0.98 ±0.11	NS	1.18 ±0.12	0.95 ±0.08	NS
Maximal Aerobic Capacity									
VO_{2max} ($ml \cdot kg^{-1} \cdot min^{-1}$)	29.48 ±1.80	31.27 ±1.97	<0.01	31.48 ±1.88	37.33 ±1.95	<0.0001	30.53 ±1.67	33.89 ±1.87	<0.0001
GXT Time To Exhaustion (min)	8.44 ±0.48	8.88 ±0.55	<0.05	8.84 ±0.51	10.30 ±0.54	<0.0001	8.68 ±0.41	9.49 ±0.50	<0.0001
Total Body Composition									
Body Mass (kg)	91.99 ±4.91	92.53 ±4.57	NS	87.27 ±4.50	86.63 ±4.25	NS	91.93 ±5.47	93.04 ±5.58	NS
BMI ($kg \cdot m^{-2}$)	30.20 ±1.36	30.33 ±1.29	NS	28.28 ±1.35	28.51 ±1.14	NS	30.20 ±1.50	30.59 ±1.50	NS
%Body Fat	41.11% ±3.05	40.51% ±2.95	NS	38.54% ±2.55	35.75% ±2.44	<0.0001	38.84% ±2.07	37.26% ±2.04	<0.01
Fat Mass									
Fat Mass (kg)	36.57 ±3.74	36.16 ±3.48	NS	32.12 ±3.02	30.42 ±3.01	<0.001	34.10 ±2.90	33.17 ±2.82	<0.05
Trunk Fat Mass (kg)	20.45 ±1.91	20.11 ±1.80	NS	17.68 ±1.68	15.79 ±1.95	<0.01	19.27 ±1.80	18.83 ±1.83	NS
Total and Regional Lean Mass									
Lean Mass (kg)	50.86 ±4.50	51.91 ±4.50	<0.05	50.87 ±3.08	52.32 ±3.12	<0.01	53.23 ±3.40	55.71 ±3.60	<0.0001
Trunk Lean Mass (kg)	23.98 ±1.53	24.44 ±1.47	NS	23.58 ±1.39	24.29 ±1.37	NS	24.86 ±1.53	26.10 ±1.76	<0.01
Legs Lean Mass (kg)	17.82 ±1.12	18.24 ±1.13	<0.05	17.71 ±1.19	18.28 ±1.27	<0.01	18.14 ±1.80	18.96 ±1.83	<0.0001
Arms Lean mass (kg)	6.42 ±0.51	6.67 ±0.54	<0.01	6.13 ±0.46	6.26 ±0.44	NS	6.55 ±0.59	6.81 ±0.61	<0.01
Strength									
Total Strength (sum of maxes, lbs)	1,428.63 ±77.14	1,861.40 ±113.42	<0.0001	1,500.25 ±110.02	1,864.63 ±137.79	<0.0001	1,523.94 ±122.77	2,110.31 ±191.70	<0.0001
Leg Press (lbs)	668.03 ±38.04	848.47 ±48.48	<0.0001	689.31 ±48.43	841.19 ±66.08	<0.0001	715.00 ±59.13	1,014.25 ±96.24	<0.0001
Chest Press (lbs)	94.00 ± 9.45	116.00 ±11.47	<0.0001	98.25 ±10.56	117.31 ±10.59	<0.0001	103.25 ±12.40	136.25 ±15.73	<0.0001
Leg Curl (lbs)	144.40 ±8.42	188.33 ±11.94	<0.05	157.00 ±11.04	196.25 ±14.98	<0.05	157.94 ±11.39	208.31 ±16.66	<0.01
Lat Pull (lbs)	135.47 ±10.49	170.60 ±13.39	<0.0001	140.69 ±11.51	167.81 ±13.35	<0.0001	143.25 ±11.89	173.56 ±14.66	<0.0001
Leg Extension (lbs)	120.80 ±8.39	163.80 ±11.45	<0.0001	138.69 ±11.65	181.06 ±16.29	<0.0001	123.25 ±10.87	172.19 ±15.96	<0.0001
Triceps Pushdown (lbs)	222.07 ±12.11	314.27 ±22.22	<0.0001	233.88 ±20.10	304.38 ±22.51	<0.0001	235.06 ±21.24	346.44 ±37.03	<0.0001
Biceps Curl (lbs)	43.87 ±5.25	59.93 ±6.70	<0.0001	42.44 ±4.84	56.63 ±5.71	<0.0001	46.19 ±5.31	59.31 ±6.49	<0.0001

Values are represented as means±SEM for daily caloric expenditure on non-exercising days, daily dietary intake, maximal aerobic capacity, body composition, and strength assessed before (pre-training) and after (Post-training) 12 weeks of resistance training (RT), concurrent resistance and land treadmill training (RT-LTM), or concurrent resistance and aquatic treadmill training (RT-ATM).

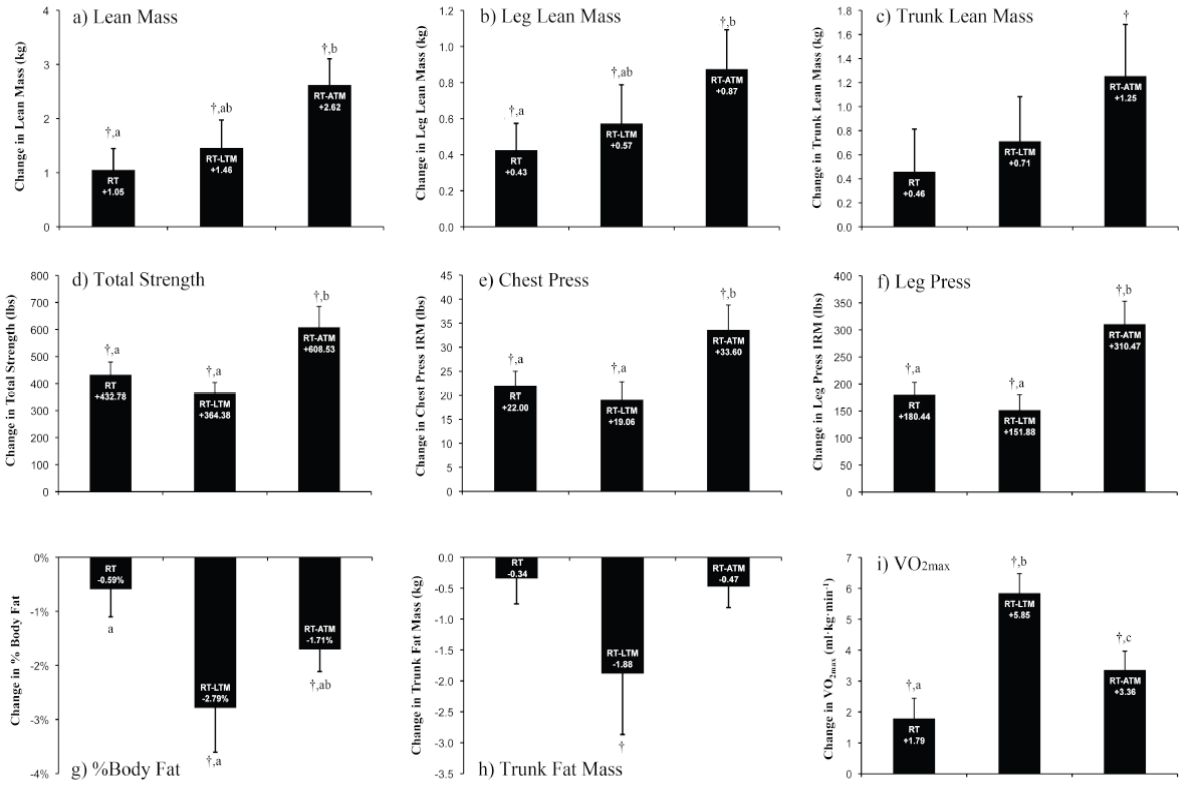
Body Composition, Strength, and Aerobic Capacity

Statistical analysis of pre and post training values revealed significant group x time interactions for body composition, strength, and aerobic capacity ($p<0.05$). Total lean mass (LM: 1.05-2.62kg) and leg lean mass (LLM: 0.43-0.87kg) were significantly increased following training in all groups. The highest gains were observed in the RT-ATM group, which were found to be significantly greater than the RT group (Figure 8). Significant increases in arm lean mass (~0.25kg) were observed following training in the RT-ATM and RT groups, but were not observed in the RT-LTM group. A significant increase in trunk lean mass was observed in the RT-ATM group only. Percent body fat (%BF: -1.71-2.79%) and fat mass (FM: -1.10-1.70kg) was reduced after exercise training in the RT-LTM and RT-ATM groups with the greatest decrease found in the RT-LTM group for %BF. Additionally, a significant decrease in trunk fat mass (-1.88kg) was observed in the RT-LTM group only.

Significant increases in strength were observed in all groups for all exercises, however, significantly greater increases in total strength (SUM of predicted 1RM values for all lifts), leg press, and chest press strength were observed in the RT-ATM group compared to RT and RT-LTM groups (Figure 8, to follow). The RT-ATM group also exhibited significantly greater gains in triceps push down than the RT-LTM group. No differences were observed between groups for gains in leg curl, lat pull, leg extension, or biceps curl.

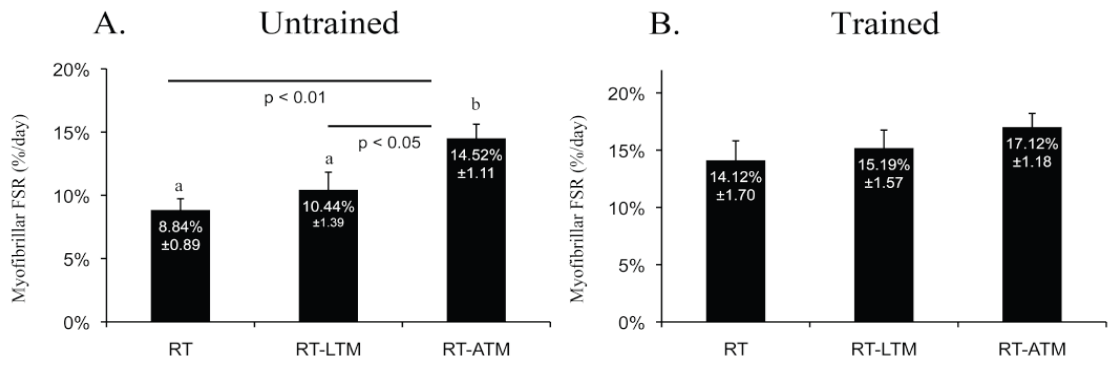
VO_{2max} (+1.79-5.85 ml·kg·min) and time to exhaustion measured during maximal exercise treadmill testing (GXT) were increased in all groups following exercise training (Figure 8). The RT-LTM group was found to have significantly greater increases in both variables compared to the RT or RT-ATM groups, although the RT-ATM group did demonstrate a greater increase in VO_{2max} (ml·kg·min) than the RT group.

Figure 8 - Physiological Adaptations to Chronic Training



Values are shown as mean±SEM for change from baseline for body composition, strength and VO_{2max} following 12 weeks of resistance training (RT), concurrent resistance and land treadmill training (RT-LTM), or concurrent resistance and aquatic treadmill training (RT-ATM). †= significantly different from baseline. Letters indicate between group interaction with like letters indicating no significant differences between groups. Type I Error set at α=0.05.

Figure 9 - Effects of acute RT, RT-LTM, and RT-ATM exercise on 24h myoFSR



Values are presented as mean±SEM for myofibrillar fractional synthesis rates (myoFSR) measured fed state for 24h following acute RT, RT-LTM, or RT-ATM exercise in the untrained state (Figure 3a) before training and in the trained state (Figure 3b). Letters indicate a significant between group interaction with like letters indicated no significant differences between groups ($p<0.05$).

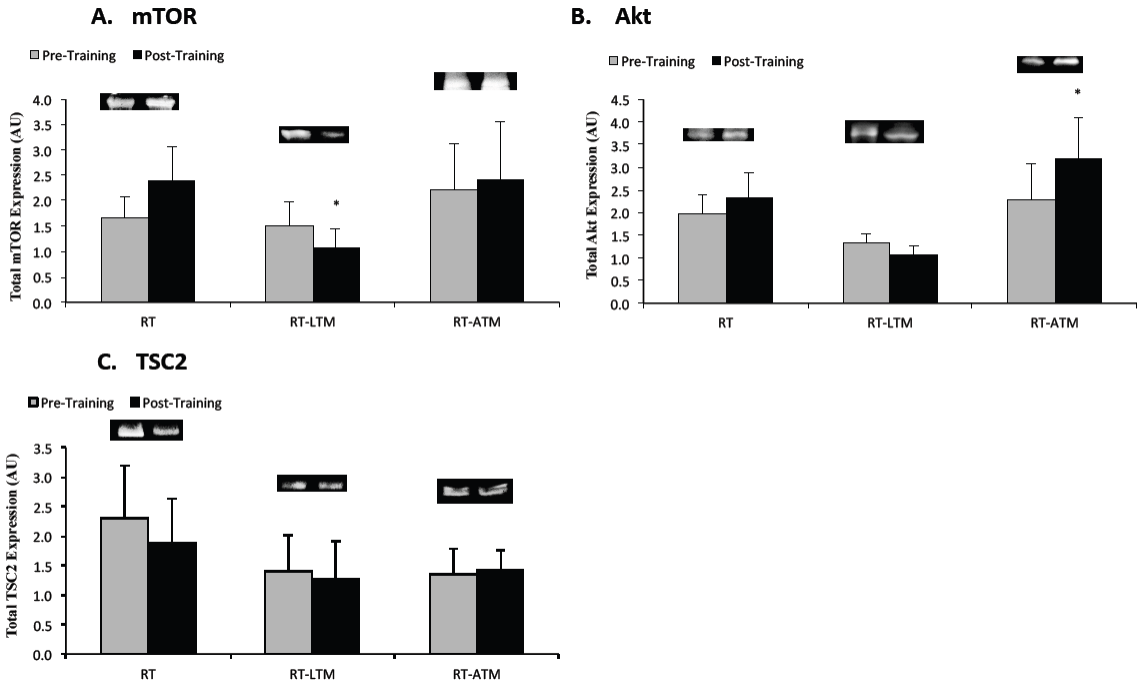
Acute Exercise: 24-hour Myofibrillar Fractional Synthesis Rates

In the untrained state (prior to training), acute RT-ATM exercise was found to elicit higher 24h myoFSRs compared to RT (5.68 %/d, $p<0.01$) and RT-LTM (4.08 %/d, $p<0.05$) (Figure 9a). Following training, acute RT-ATM resulted in the highest myoFSR values on average but no differences between groups were observed (Figure 9b). No differences in myoFSR were observed between acute RT and RT-LTM exercise.

Chronic Alterations in mTOR, Akt, and TSC2 Content

Following training, total mTOR content was decreased in the RT-LTM group (-34.57% ± 14.56, Figure 10a). Total Akt content was significantly increased (53.93% ± 23.37) following RT-ATM training only (Figure 10b). No chronic alterations in total TSC2 content were observed in any of the training groups (Figure 10c).

Figure 10 - Pre and Post training mTOR, Akt, and TSC2 Skeletal Muscle Protein Content



Values are presented as mean±SEM for total mTOR(A), Akt(B) and TSC2(C) content measured in the rested state before (pre-training) and after (post-training) twelve weeks of either RT, RT-LTM, or RT-ATM training. * = significant difference from pre-training value within group ($p<0.05$).

Discussion

Consistent with our hypothesis, RT-ATM exercise elicited a greater anabolic response myoFSRs compared to acute RT-LTM exercise and RT alone, which coincided with enhanced skeletal muscle growth and strength following chronic training (Figures 8, 9). Regional body composition measures made from DEXA analysis also revealed that RT-ATM training produced a significant increase in trunk lean mass (+1.25 kg) that was not observed in the other groups. Expectedly, gains in lean mass in this study were also accompanied by greater improvements in total strength (+608.53 lbs), chest press strength (+33.60 lbs), and leg press strength (+310.47 lbs) in the RT-ATM group in comparison to the RT and RT-LTM groups (Figure 8). Therefore, augmentation of muscle growth and strength was not limited to

the legs alone. These findings suggest that the novel addition of low impact ATM exercise following resistance exercise in a concurrent training program may particularly benefit elderly populations, those who have been previously bedridden, those recovering from injury, and athletic populations (9, 52, 115, 119, 206, 242).

We are the first to examine the acute effects of concurrent RT-ATM exercise on myoFSR and to compare 24h myoFSR following acute resistance exercise and concurrent exercise before and after chronic training. Consistent with the findings of Donges et. al. 2012 (72), the addition of aerobic exercise following a bout of resistance exercise did not result in suppression of myoFSR compared to resistance exercise alone in previously untrained subjects (Figure 9). Consequently, these data are at odds with hypothesis that reductions in anabolism occur following concurrent exercise compared to resistance exercise in isolation (12, 184). However, we acknowledge that the specific population used, exercise modes selected, exercise intensities, frequencies, and volumes may have been a factor in the lack of interference observed in this investigation (261) compared to previous investigations using trained or athletic populations (54, 143).

At present, the specific causes of the elevated protein synthesis response to RT-ATM exercise are unclear. However, findings from this study and others (29, 105, 245) may provide some direction for further investigation. A summary of proposed intracellular signaling mechanisms responsible for concurrent exercise interference is presented in Figure 11. In this investigation, we measured total protein content of mTOR, Akt, and TSC2 in the rested state before and after training. While we did not collect data related to the time-course of cell signaling responses to acute exercise, we did observe chronic increases in Akt expression following RT-ATM training (Figure 10B) and lower expression of mTOR with

RT-LTM. Akt is a Ser/Thr kinase that plays an important role in upregulating glucose uptake, glycogen synthesis, and protein synthesis (29, 207). Upon, activation through either nutritional stimulus or certain types of contractile activity, Akt activation leads to the stimulation of mTORC1 and the deactivation of glycogen synthase kinase 3–β (GSK3-β), which when active, is a potent inhibitor of eIF2β-ε, often considered a rate-limiting factor of peptide-chain initiation (29, 74). While we did not determine if Akt activity was chronically enhanced following acute exercise, increased Akt expression following training may suggest an increased anabolic signaling potential following RT-ATM training. This is supported by observations by Bodine et. al, 2001 (29) who observed increases in Akt expression during hypertrophy and decreases during skeletal muscle atrophy.

Figure 11 - Previously Proposed Intracellular Signaling Mechanisms for Concurrent Exercise Interference (10, 12, 150, 184)

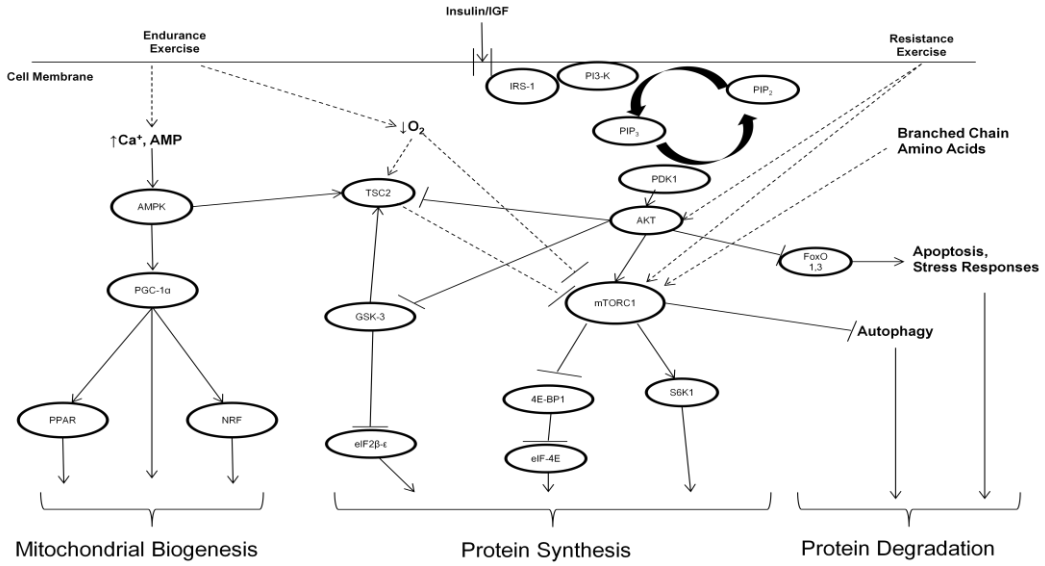


Figure adapted from Laplante et al., 2010 (150) and Baar et al., 2006 (12). Abbreviations: 4E-BP1, eukaryotic initiation factor 4E-binding protein 1; Akt, protein kinase B; AMPK, AMP-activated protein kinase; eIF2β-ε, eukaryotic translation initiation factor 2β-ε; eIF-4E, eukaryotic translation initiation factor 4E, FoxO 1,3, forkhead box O 1,3; GSK-3, glycogen synthase kinase 3; IRS-1, insulin receptor substrate-1; mTORC1, mammalian target of rapamycin complex 1; NRF, nuclear respiratory factor; PDK1, phosphoinositide-dependent kinase-1; PI3-K, phosphoinositide 3 kinase; PIP_2, phosphotydilinositol (4,5) bisphosphate; PIP_3, phosphotydilinositol (3,4,5) trisphosphate; PGC-1α, PPAR-γ coactivator 1-α; S6K1, p70 ribosomal S6 kinase 1; TSC2, tuberous sclerosis complex 2.

Following training, mTOR content was found to be decreased in the RT-LTM group only. Briefly, the mTOR protein functions as part of the mTORC1 and mTORC2 complexes. Upon removal of inhibition by Akt, amino acids, and other mechanisms, active mTORC1 phosphorylates its downstream targets which include eukaryotic translation initiation factor 4E-binding protein 1 (4E-BP1), ribosomal protein s6 kinase (S6K), and eukaryotic elongation factor 2 kinase (eEF2K) which ultimately results in an increase in protein synthesis (Figure 11) (74). However, because additional intracellular pathways contribute to protein anabolism in skeletal muscle (85), it is difficult at this time to determine if a decrease in mTOR content across training affected the outcomes observed here. Furthermore, while LTM exercise was not additive, acute and chronic anabolic responses to RT-LTM exercise were not found to be reduced compared to the RT group. While further investigation is needed, the observation that no reductions in mTOR content occurred following RT-ATM training compared to RT-LTM training may further indicate the presence of mode specific training adaptations. Speculation regarding the impact of these signaling intermediates on the basis of protein content should be guarded with caution, primarily because the changes in protein content were not always concomitant with changes in myoFSR among the groups.

A recent study from our laboratory (105) may also provide additional rationale for the observed outcomes in this study. We compared acute hemodynamic responses to acute exercise stress following 12wks of either ATM or LTM training. The aerobic training prescription was identical to the present investigation with regard to intensity and frequency. In conjunction with significant reductions in blood pressure, skeletal muscle endothelial nitric oxide synthase (eNOS) expression was increased following ATM training compared to LTM training. Because of the role of eNOS in the regulation of endothelial mediated

vasodilation, (249) those results suggested that ATM exercise may potentially enhance skeletal muscle blood flow. Recent findings by Timmerman et al. 2012 (245) have shown that any compromises in blood flow will have deleterious effects on skeletal muscle anabolism, perhaps as a result of diminished nutrient delivery. Therefore, future investigations will be needed to determine if skeletal muscle blood flow is enhanced following ATM or RT-ATM training. The possibility that our ATM protocol enhances blood flow, even in the rested state, may optimize FSR over the course of the 24-h period by facilitating nutrient delivery. Those results are consistent with the heightened and similar myoFSR responses in the RT-ATM group when compared to other groups.

During this investigation, both the RT-LTM and RT-ATM groups performed at equivalent training volumes, intensities, and frequencies. Because the RT group performed only resistance exercise twice per week, overall training volume was lower compared to the concurrent training groups (Weeks 6-12: RT, <1000kcal·wk; RT-LTM & RT-ATM, 1500kcal·wk). While it was expected that both the RT-ATM and RT-LTM would demonstrate greater decreases in %BF and fat mass than the RT group, the RT-LTM group experienced significantly greater reductions in %BF than the RT-ATM group (Figure 8). DEXA analysis further revealed that this decrease in %BF was primarily driven by decreases in fat mass and more specifically, trunk fat mass which was found to be only significantly decreased in the RT-LTM group. Given that the RT-LTM and RT-ATM groups expended the same weekly caloric volumes, these findings further highlight the importance of exercise mode selection for individual exercise training goals.

The results of this study are at odds with those of Gappmaier et al. 2006 (92) who reported no differences in %BF loss between 10wks of either walking on land, walking in

water, or swimming where all subjects exercised at the same intensity and duration. Additionally, in the previous study performed in our laboratory by Greene et al. 2009 (106) which compared 12wks of ATM and LTM exercise, decreases in both %BF and fat mass were nearly identical between groups. In the present investigation, all training groups were regularly given nutrition and activity instructions to maintain their normal diets and activities which they reported at the beginning of the screening process. Analysis of pre and post training dietary and daily activity records revealed no statistical interactions regarding daily activity or nutritional intake. Because subjects were also selectively randomized into groups and matched for age, gender, and body composition, we find the possibility of group specific non-compliance in the form of a nutritional or activity shift to be unlikely. Of note, Svedenhag et al. 1992 (232) reported elevated respiratory exchange ratio (RER) and blood lactate concentrations during DWR at similar VO_2. Michaud et al. 1995 (177) and Broman et al. 2006 (37) reported similar findings. Together, these data indicate the possibility of elevated carbohydrate oxidation and decreased lipid oxidation during deep water running compared to running on land. However, these findings are contrary to those by our laboratory (103) and others (57, 224, 259) who reported no difference in RER or blood lactate concentration between sub-maximal running exercise performed on land versus in water. Both Greene et al. 2011 and Connelly et al 1990 (57) observed reductions in RER at VO_{2max} during aquatic versus land based exercise. Therefore, further comparative research is needed between ATM and LTM running to determine if any mode-specific differences in fuel substrate utilization exist during exercise and recovery.

In addition to greater decreases in fat mass, the RT-LTM group demonstrated greater improvements in aerobic capacity and time to exhaustion than the other groups (Figure 8).

However, we suspect that the RT-LTM group may have had an advantage over the other groups in that they were trained on standard land-based treadmills which were identical to the treadmills that they were tested on. Therefore, while our results indicate that concurrent RT-LTM exercise may be more effective in increasing aerobic capacity, we caution that factors related to training specificity may have affected these outcomes. This was an unforeseen limitation as our previous investigation resulted in no statistical difference between ATM or LTM exercise training performed in isolation (106). Future investigations comparing ATM and LTM exercise may avoid this limitation by also testing subjects using a cycle ergometer to overcome training specificity factors.

ATM exercise provides a unique exercise stimulus in that is performed with reduced vertical load, increased lateral resistance, and an increase in lower body positive pressure as opposed to running on land. As a result, lower ground reaction forces, reduced joint compression, reduced stride frequency, and differences in skeletal muscle activation patterns have also been reported compared to LTM exercise (21, 22, 69, 210, 259). Because, skeletal muscle adaptation has been shown to be highly dependent on both contraction frequency and intensity (10, 207), we find it probable that ambulation through water at chest depth as opposed to air may have been a factor in producing the observed outcomes. The low impact nature of ATM exercise along with our past and present results also serve as an impetus for further investigation into inflammatory and endocrine responses to ATM exercise which have been shown to effect skeletal muscle adaptation (122, 143).

In summary, we observed that ATM exercise does not interfere with, but augments skeletal muscle growth and muscular strength when performed concurrently with resistance exercise. In addition, 12wks of concurrent RT-ATM training resulted in significant increases

in skeletal muscle Akt content compared RT-LTM or RT training. In combination with RT, the novel use of ATM running may benefit those who desire to preserve strength and muscle mass while also promoting aerobic fitness. RT-LTM training was found to result in greater decreases in fat mass compared to RT or RT-ATM training. Notably, neither concurrent training group (RT-LTM or RT-ATM) experienced acute or chronic anabolic interference although total mTOR content was decreased following RT-LTM training. Because a land treadmill was utilized for measuring aerobic capacity, further investigation is required to discern if training mode specificity was a factor in the aerobic adaptations observed in this investigation. Regardless, the results of this investigation challenge the view that training for both strength and endurance are universally incompatible and highlight the importance of exercise mode selection when prescribing exercise programs for specific health or performance outcomes. However, we acknowledge the need for further investigation into the effectiveness of concurrent RT-ATM exercise for promoting skeletal muscle growth in specialized populations such as athletes, the elderly, or those suffering from various chronic diseases. Additional exploration is also needed to further characterize the intracellular mechanisms responsible for the outcomes observed in this study. Nonetheless, in light of our results, concurrent RT-ATM training may serve as a novel, low impact training modality for simultaneously promoting increases in skeletal muscle mass, strength, and aerobic fitness.

CHAPTER III

CONCLUSIONS AND DIRECTIONS FOR FUTURE RESEARCH

This study was a continuing extension of our previous investigations which indicated that ATM training may induce a greater hypertrophic response than standard LTM training in previously untrained men and women (106). Because endurance training is not typically considered to be a strong stimulator of muscle growth, we elected to explore the potential use of ATM in a concurrent training model where endurance exercise has been purported to interfere with resistance exercise-stimulated hypertrophy and strength development. Within this study we characterized the chronic physiological adaptations to RT-ATM, RT-LTM, and RT as well as the acute stimulatory effects of each on 24h post exercise myoFSR following a single session of exercise before and after training. To date, this was among the largest human training investigations to examine acute molecular responses to exercise in conjunction with applied adaptations to training. Findings from this investigation provide new perspective on training specificity and highlight the importance of exercise mode selection for desired adaptive outcomes. Because of the nature of human training studies and the regular acquisition of supportive data and human tissue samples, it is likely that serendipitous discoveries still await us upon further analysis guided by the results in the current study. While much is still unknown about the factors which govern physiological responses to either concurrent training or aquatic exercise, the present study provides support for the supportive use of low impact ATM training for populations in need of preserving/increasing skeletal muscle mass and improving strength while simultaneously improving aerobic fitness.

Conclusion #1

Aquatic treadmill training enhances lean mass and strength gains when performed concurrently with resistance exercise. In the present investigation we hypothesized that twelve weeks of concurrent RT-ATM training would result in greater gains in lean mass and strength compared to twelve weeks of concurrent RT-LTM training with similar gains in aerobic capacity and reductions in fat mass. RT-ATM training was found to elicit greater increases in total lean mass (+2.62 kg) compared to the RT group (+1.05 kg). Regional body composition measures made from DEXA analysis also revealed that only the RT-ATM group was found to have a significant increase in trunk lean mass from baseline (+1.25 kg). This suggests that augmentation of muscle growth was not limited to the legs. Expectedly, gains in lean mass in this study were also accompanied by greater increases in total strength (+608.53 lbs), chest press strength (+33.60 lbs), and leg press strength (+310.47 lbs) in the RT-ATM group in comparison to the RT and RT-LTM groups (Figure 4). Similar to the lean mass gains revealed by our body composition analysis, augmented gains in strength were not limited to the lower body. At present, we can only speculate that ambulation through water at chest depth as opposed to air may have been a factor in producing the observed outcomes. These findings confirm a portion of our initial hypothesis and suggest that combined RT-ATM training may serve as a novel training modality which may benefit not only those in the general population, but clinical populations in need of improving daily functional capacity, reducing risk for injury, preserving lean mass, or reversing sarcopenia (101, 125, 264).

Conclusion #2

When low-moderate training volumes are used, neither land nor aquatic treadmill running interfere with gains in skeletal muscle mass or strength when performed concurrently with resistance training. Notably, we did not observe an interference effect with the development of strength or lean mass during this study. This was shown as the RT-LTM group demonstrated similar strength and lean mass gains compared to the RT group. These specific findings are similar to those found by Lundberg et al. 2012 and Shaw et al 2009 who did not observe any interference of endurance exercise with strength development (161, 222). Factors such as the population used as well as training intensities, volumes, mode selection, and frequency should be considered here and have shown to play a factor in concurrent training outcomes (261). It has been previously speculated that muscular power may be more affected by concurrent endurance and resistance exercise (108). Therefore, further investigations will be required to examine how either mode of training may have influenced rapid force development and motor unit recruitment. This may be of importance for athletic populations where power development is often a focus of training.

Conclusion #3

Aquatic treadmill exercise enhances 24h -post exercise myofibrillar protein synthesis and chronically increases Akt when performed immediately following resistance exercise. In the present study, we hypothesized that acute RT-ATM exercise would result in elevated myoFSRs compared to acute RT-LTM exercise and RT alone. In both the untrained and trained states, RT-ATM exercise yielded the highest myoFSRs and was found to be significantly elevated compared to the RT-LTM and RT groups in the untrained state (Figure 1). Neither the RT-LTM nor the RT-ATM groups were found to have diminished anabolic responses to acute exercise compared to the RT group which performed resistance exercise in isolation. Similar to our chronic training results, these findings and others (5, 67, 72, 159, 222) challenge the view that endurance and resistance exercise are universally incapable with regards to both chronic training adaptations and the acute response of skeletal muscle to exercise.

While we did not collect data related to the time-course of cell signaling responses to acute exercise in this investigation, we did observe chronic increases in Akt expression following RT-ATM training. Therefore, increased Akt expression following training may suggest an increased anabolic signaling potential following RT-ATM training. This is supported by observations by Bodine et. al 2001 (29) who observed increases in Akt expression during hypertrophy and decreases during skeletal muscle atrophy.

Conclusion #4

Land treadmill exercise chronically decreases skeletal muscle mTOR content but does not suppress 24h-post exercise myofibrillar protein synthesis when performed immediately following resistance exercise compared to resistance exercise alone. Neither the RT-LTM nor the RT-ATM groups were found to have diminished anabolic responses to acute exercise compared to the RT. Consistent with the findings of Donges et. al 2012 (72), performing endurance exercise immediately after resistance exercise did not result in suppression of myoFSR compared to resistance exercise alone. These data are at odds with hypothesis that reductions in anabolism occur following concurrent exercise (12, 184). However, the specific population used, exercise modes selected, exercise intensities, frequencies, and volumes may have been a factor in the lack of interference observed in this investigation (261) compared to previous investigations using trained or athletic populations (54, 143).

Following training, mTOR content was found to be decreased in the RT-LTM group only. However, because additional intracellular pathways contribute to protein anabolism in skeletal muscle (85), it is difficult at this time to determine if a decrease in mTOR content across training affected the outcomes observed here. Furthermore, while LTM exercise was not additive, acute and chronic anabolic responses to RT-LTM exercise were not found to be reduced compared to the RT group. While further investigation is needed, the observation that no reductions in mTOR content occurred following RT-ATM training compared to RT-LTM training may further indicate the presence of mode specific training adaptations. Speculation regarding the impact of these signaling intermediates on the basis of protein content should be guarded with caution, primarily because the changes in protein content were not always concomitant with changes in FSR among the groups.

Conclusion #5

Concurrent RT-LTM training causes greater reductions in body fat than concurrent RT-ATM training or RT alone. During this investigation, both the RT-LTM and RT-ATM groups performed at equivalent training volumes, intensities, and frequencies. While it was expected that both the RT-ATM and RT-LTM would demonstrate greater decreases in %BF and fat mass than the RT group, the RT-LTM group experienced significantly greater reductions in %BF and fat mass (particularly trunk fat mass) than the RT-ATM group. DEXA analysis further revealed that this decrease in %BF was primarily driven by decreases in fat mass and more specifically, trunk fat mass that was found to be significantly decreased in only the RT-LTM group. The results of this study are at odds with those of Gappmaier et al. 2006 (92) who reported no differences in %BF loss between 10wks of either walking on land, walking in water, or swimming where all subjects exercised at the same intensity and duration. Additionally, in the previous study performed in our laboratory by Greene et al. 2009 (106) which compared 12wks of ATM and LTM exercise, decreases in both %BF and fat mass were nearly identical between groups. Therefore, it may stand to reason that there is a metabolic interaction between RT and LTM exercise when performed concurrently that differs when RT and ATM are performed concurrently. These findings further highlight the importance of exercise mode selection for individual exercise training goals.

Conclusion #6

Concurrent RT-LTM training causes greater increases in aerobic capacity than RT-ATM and RT. In addition to greater decreases in fat mass, RT-LTM training elicited greater increases in aerobic capacity than RT or RT-ATM training. These results differ from our previous investigations of ATM and LTM where both training modes were found to produces similar increases in VO_{2max} (105, 106). Similar to our previous investigation, a Bruce protocol maximal GXT was used to assess VO_{2max}. Regardless, we suspect that the RT-LTM group may have had an advantage over the other groups in that they were trained on standard land-based treadmills, which were identical to the treadmills that they were tested on. Given, the nature of specificity of training, making a conclusion based on the present results is somewhat difficult at this time. Therefore, while our results indicate that concurrent RT-LTM exercise may be more effective in increasing aerobic capacity, we caution that specificity factors within our training groups may have affected these outcomes. While not entirely similar, these results mimic those found in comparisons of DWR and LTM exercise (232). In future investigations, it may be more appropriate to measure maximal aerobic capacity on a cycle ergometer so that both ATM and LTM groups are equally novice to the testing conditions.

Directions for Future Research

Further Characterization of Acute Exercise Responses

Our present results indicate that ATM training has the capacity to increase lean mass and strength, particularly when combined with RT. ATM exercise was also found to enhance the anabolic response to acute exercise when performed immediately following resistance exercise. At this time, the mechanisms responsible for our observed outcomes are not entirely understood. Because both mTOR and MAPK signaling have been observed to contribute to exercise stimulated increases in skeletal muscle protein synthesis (85), an investigation of the time course of acute intracellular signaling events will be required to determine which pathways are differentially affected by ATM versus LTM exercise.

Skeletal Muscle Fiber Adaptations

Both endurance and resistance training elicit unique muscle fiber adaptations. While strength training in isolation has been reported to elicit hypertrophy of Type II fibers (143, 227), intense endurance training has been observed to reduce fiber shortening speed of Type II fibers and alter myosin ATPase (38, 160, 227). In our initial investigation, ATM training was observed to elicit a greater hypertrophic response compared to LTM training, which is not commonly associated with muscle growth (106). Enhanced skeletal muscle anabolism and strength gains following concurrent RT-ATM training warrants further investigation into fiber specific adaptations to ATM and concurrent RT-ATM training compared to standard land based training. Based on our current data, it is reasonable to hypothesize that increases in the cross-sectional area of Type I and II muscle fibers would not be impaired by concurrent RT-ATM training. The effects of RT-ATM or ATM exercise on myosin heavy

chain phenotype expression are also unknown. Therefore, the characterization of fiber specific adjustments to ATM and RT-ATM training may provide insight into the physiological adaptations observed in this investigation.

Sarcopenia

Aging is commonly associated with reductions in skeletal muscle protein synthetic responses to exercise and nutrition (70, 165, 211, 245). In addition to reduced anabolic endocrine signaling with aging, reduced skeletal muscle blood flow has also been implicated as a potential cause for blunted protein synthesis observed in older subjects (245). Given the findings of our present study and those of our previous work which indicated that ATM training increases skeletal muscle eNOS (a strong stimulator of vasodilation) (105), elderly populations at risk for sarcopenia may receive great benefit from ATM or concurrent RT-ATM training. Concurrent training may also be of benefit for others who are at risk for sarcopenia as well such as those suffering from obesity, cancer, previously injury, or those who have been recently bed-ridden. The low impact nature of ATM running and previously reported high rates of compliance with aquatic exercise (259) also add further support for exploring ATM exercise as a potential treatment intervention for these populations.

Hypertension and Chronic Heart Failure

Concomitant with the results of this study, our recent findings of reduced blood pressure and increased skeletal muscle eNOS following chronic ATM training in normotensive subjects (105) strongly indicate that both concurrent RT-ATM and ATM may also provide benefits for those with, or at risk for hypertension. In accordance with previous

findings, reductions in blood pressure indicate a potential reduction in peripheral vascular resistance. The observed blunted increases in PP during exercise stress following ATM training may indicate improved vessel compliance. Additionally, reductions in RPP following training indicates a reduced workload on the heart during exercise stress. Therefore, like other forms of aquatic exercise (259), ATM exercise may be an appropriate therapy for those suffering from chronic heart failure. Further investigation is warranted to target these populations and examine both acute vascular responses to exercise as well as chronic training outcomes.

Inflammation

Because of the vertical unloading and reduced ground reaction forces during exercise, ATM exercise can be performed with a reduced risk of injury (9, 42, 253, 255). Also, aquatic exercise therapy has also been reported to reduce pain and tissue inflammation (257) which may improve performance in subsequent exercise bouts. Acute inflammatory signaling mechanisms have recently been reported to influence skeletal muscle and metabolic responses to exercise (100, 122, 198, 228). Recent pilot data from our laboratory indicate that ATM training may reduce post exercise muscle soreness and enhance recovery from intense sprint exercise in 20 trained men (149). In our pilot study, subjects performed a warm-up followed by 16 maximal 100 yard sprints. Work to rest ratio was set at 1:3. Following exercise, the half of the men performed ATM running at 5mph, 50% maximal jet resistance, and water (33°C) level at chest depth for 10 minutes (ATMRec). The other half performed a cool down involving light stretching exercises (PRec). Both groups then evaluated their level of body region specific soreness/pain using a numerical rating scale

(NRS: 0-10, 0=no pain, 10=worst pain) immediately following all exercise (IPE), 24h, and 48h post exercise. Following exercise, ratings of soreness/pain were markedly lower for the majority of the evaluated body regions across the measurement time points (Table 4).

Table 4 - ATM Running Reduces Muscle Soreness Following Intense Sprint Exercise in Trained Men

Independent Var.	Group	IPE	24h	48h
LEGS	ATMRec	3.3 ± 0.3 †	3.7 ± 0.4 †	3.2 ± 0.7
	PRec	4.5 ± 0.7 [a]	5.2 ± 0.5 [a]	3.3 ± 0.4 [b]
BACK	ATMRec	1.3 ± 0.4 [a]	0.9 ± 0.3 [a] †	0.5 ± 0.3 [b] †
	PRec	2.5 ± 0.9	2.7 ± 0.7	1.8 ± 0.6
HIPS	ATMRec	1.2 ± 0.4 [a] †	2.1 ± 0.5 [b]	1.3 ± 0.4 [a]
	PRec	2.5 ± 0.7 [a]	2.6 ± 0.5 [a]	1.2 ± 0.3 [b]
ABDOMEN	ATMRec	0.8 ± 0.4 †	1.1 ± 0.3 †	0.8 ± 0.2
	PRec	2.3 ± 0.5 [a]	2.6 ± 0.6 [a]	1.4 ± 0.4 [b]
OVERALL	ATMRec	2.0 ± 0.3 [a] †	3.0 ± 0.4 [b]	1.9 ± 0.5 [a]
	PRec	3.2 ± 0.5 [a]	3.5 ± 0.4 [a]	2.1 ± 0.3 [b]

Modified from Lambert et al. 2011 (149). Values are means ± SE for NRS scores (0-10, 0=no pain, 10=worst pain). Letter superscript = sig. diff. w/in groups across time, † = sig. diff. between groups at same measurement time point (comparisonwise $\alpha = 0.05$).

These data and others suggest that ATM running may minimize post exercise muscle soreness, reduce inflammation and enhance recovery following intense exercise.

Finally, exercise training has been observed to reduce chronic cardiovascular inflammation commonly observed in those with obesity, Type II diabetes, insulin resistance, and atherosclerosis (198, 228). Chronic inflammation is associated with increased concentrations of inflammatory cytokines and white blood cell fractions (198). In a recent pilot investigation (148), we observed reductions in serum TNF-α concentrations (-13.5%) following RT-ATM but not RT-LTM training. TNF-α is largely associated with local inflammation and insulin resistance (137, 198). Upon signaling through its receptor at the

cell membrane, TNF-α also activates signaling cascades which promote autophagy and apoptosis. Because insulin signaling through the Atk-mTOR pathway is a major contributor to nutrition and exercise stimulated protein synthesis, the results of the present investigation may have been partially caused by chronic reductions in TNF-α. However, future research is needed to better characterize the potential acute and chronic anti-inflammatory effects of ATM running.

Water Temperature

Water temperature has been observed to effect acute cardiovascular responses to aquatic exercise (32, 110, 206). Thermoneutral water temperature (~29-35° C) allows for similar cardiovascular adjustments compared land exercise (206). Because the majority of recent research comparing land and aquatic training involves aquatic exercise at thermoneutral water temperatures, it is unknown how hot or cold-water immersion or activity may have affected our acute or chronic outcomes.

Heatshock proteins (HSPs) are highly conserved temperature and stress sensitive regulatory proteins that have been observed to play an important role in fundamental cell processes (86). HSPs are upregulated when core body temperatures approach ~37°C and in conditions of general thermoregulatory stress (246). In particular, the Hsp70 family of HSPs respond to hyperthermia, energy depletion, hypoxia, acidosis, reactive oxygen species, and infection (182). Hsp70 has been reported to be associated with the adaptive tolerance to each of the aforementioned stressors as well as reduced sensitivity to the inflammatory cytokine TNF-α (182). In terms of its functionality, Hsp70 has been reported to assist in the maintenance of cell structure, refolding of unfolded or misfolded proteins, protein

translocation across cell compartments, prevention of protein aggregation, and degradation of damaged proteins (182). Additionally, various HSPs have been shown to have either anti-apoptotic or pro-apoptotic functions. Both resistance and endurance exercise have been observed to increase the expression of Hsp70 in a manner that is somewhat proportional to the duration of exercise and degree of eccentric loading (86). Touchberry et al. 2012 (247), reported that pre-treatment with heat exposure enhanced the anabolic response to downhill running in Wistar rats in a manner that was independent of Akt or MAPK signaling. Additionally, Liu et al. 2012 (157) reported that overexpression of Hsp72 may reduce skeletal muscle damage induced by eccentric exercise. Conversely, Yamane et al. 2005 (270) observed that post exercise cold water immersion reduced the exercise induced upregulation of Hsp70. Following this study, it was also concluded that cold water immersion attenuated temperature/stress dependent processes which are essential for training adaptation (270).

There is little evidence on the chronic training effects of aquatic exercise on HSPs. During this study, water temperature was set at 33°C. Given that our subjects were progressed to high exercise intensities and that true thermoneutral temperatures have been reported shift down (~29°C) depending on exercise intensity (206), subjects exercising in the RT-ATM group may have been exposed to greater levels of heat stress compared to the RT or RT-LTM groups. Conversely, the RT-LTM group was ultimately exposed to the greatest amount of cumulative eccentric load. Therefore, future studies are needed to address the following with regards to HSP expression and function: (1) the effects of ATM versus LTM exercise, (2) the effects of water temperature during ATM exercise, and (3) the effects of RT, concurrent RT-LTM, and concurrent RT-ATM.

Fat Metabolism

During our investigation, the RT-LTM group was found to elicit greater reductions in body fat than the RT or RT-ATM group. As previously stated, this was a partially unexpected finding considering that the RT-ATM and RT-LTM groups expended equal weekly caloric volumes. Therefore future investigations are needed to address possible mode specific differences in metabolic fuel usage during exercise or alterations in post exercise metabolic rates. In two of our previous investigations (105, 106), no differences were observed between ATM or LTM training in isolation with regards to fat reduction. Furthermore, previous data published from our laboratory (104) found that chronic ATM and LTM exercise resulted in similarly beneficial changes in blood lipid profiles. Providing some support for our findings, Svedenhag et al. 1992 (232) reported elevated respiratory exchange ratio (RER) and blood lactate concentrations during DWR at similar VO_2. Michaud et al. 1995 (177) and Broman et al. 2006 (37) also reported similar findings. Therefore, further exploration is needed to determine if ATM and LTM exercise differentially affect fuel substrate utilization when performed in isolation or combined with resistance exercise.

Athletic Performance

Several sports require varying degrees of strength, power, anaerobic conditioning, and aerobic fitness (15). However, training for each may lead to overtraining and thus, interference (143, 261). While ATM exercise is commonly used in athletic rehabilitation, little is known about its use as a supportive exercise mode in athletic training. The sum of research data, including data from the present study, indicate that performing ATM training

may improve recovery, reduce muscle soreness from training, enhance lean mass, strength, and aerobic fitness. Distance runners, which often perform high volume training may also benefit from the incorporation of ATM running into their regimens because of its low impact and potentially anti-inflammatory properties (259). However, little is known about the effects of aquatic exercise on athletic performance. Given that training history has been reported to effect concurrent exercise outcomes (54), the incorporation of ATM exercise into athletic training programs where athletes are already accustomed to training may yield different results than those found in the present investigation. Therefore future investigation is required to determine the efficacy of incorporating ATM running in various athletic training programs.

Limitations and Delimitations

Limitations

Compliance

Dietary and activity analysis was based on self-reported information. During acute exercise / sample collection periods self-reported exercise abstinence was used. Because our subjects were randomly selected and assigned, we find it unlikely that group specific non-compliance occurred. Subjects were also reminded weekly to of the compliance requirements. All subjects with self-reported non-compliance were removed from our data sets.

Subject Population

Because the present investigation relied on volunteer participants, we were unable to control for race demographics. Within this study, all subjects resided in the same geographical area. Consequently, our subject population was made up of primarily Caucasian subjects. While not likely, it is unknown as to whether or not populations of different ethnicities would respond differently to those in the current investigation.

Tissue Sample Analysis

Because this study was conducted over a period of five years, certain tissue samples were stored at -80˚C for considerably longer than others (ex. A participant from 2008 vs. 2012). However, for consistency, we elected to analyze all of our tissue samples together.

Delimitations

Subject Specificity

In this study, we recruited subjects from the general population who were previously untrained. Accordingly, the results of this study are limited to the parameters of our subject population. Further investigation will be required to determine whether or not conclusions from this investigation translate into other specialized subject populations such as those who are already trained, athletic populations, and clinical populations.

Nutritional Control

Due to the fact that we chose a free living diet to mimic a "real world" lifestyle, there was reduced control over nutritional intake compared to supplied or regulated nutritional

intake during training. However, subjects were instructed and reminded to not change their daily eating habits throughout the study. It is unknown at this time how the addition of post exercise nutrition and chronic regulation of nutrient intake may have affected the observed outcomes in this study.

Graded Exercise Testing

In this study, a Bruce protocol graded exercise test using a standard land treadmill was used to assess VO_{2max}. This is a repeated procedure from our laboratory's original investigation (Greene citation). While our aerobically trained groups (RT-ATM and RT-LTM) were exercising at the same intensities, it is possible that training mode specificity (LTM vs ATM) may have played a role during the performance of this test. To simplify, the RT-LTM group performed their exercise training on a mode of exercise (LTM) that they were tested on versus the RT-ATM group which was less accustomed to LTM exercise. However, the testing methods used in this case were chosen because of their use in common clinical settings and applicability to physical exertion which may take place in day to day life. Future studies comparing ATM and LTM training may benefit from using training specific modes of graded exercise testing and/or a cycle ergometer for which neither group is accustomed.

Mode Selection, Exercise Order, Training Volume

In this particular study, we chose to mimic the training volume and intensity of our initial investigation (36). Additionally, the results of this study are limited to the training modes, the resistance exercises selected, and the order of resistance and aerobic training

during concurrent training sessions. However, the selection of exercises and orders are consistent with what is commonly prescribed by the American College of Sports Medicine for general health and fitness (10). With regards to exercise mode, we elected to use a three-group model (RT, RT-LTM, RT-ATM). Therefore, our present data do not allow for a comparison of the effects of LTM vs ATM exercise on the independent variables measured in this study.

Stable Isotope Labeling

In this study, the protocol for ingestion of deuterium oxide and nutritional manipulation 24h following acute exercise testing was matched to the protocol of Gasier et al. (93). However, compared to this protocol, plasma sampling only occurred before and 24h post acute exercise. Because of this, plasma enrichment of deuterated alanine was unknown except for at the 24h post exercise time point. However, previous unpublished observations in our laboratory taken during the experiments of Gasier et al. (94) have verified that plasma enrichment determined at the 24h post exercise time point is not significantly different than the average enrichment calculated across 24h. Because of this, we are confident in using plasma enrichment at 24h post acute exercise for calculations of myoFSRs. The limited number of blood draws was chosen as a result of high subject volume, limited personnel, and the locations of our acute exercise testing sights.

In this investigation, we elected to utilize a 24 deuterium oxide method as opposed to other stable isotopic methods for measuring myoFSR. Therefore, we do not know the immediate effects of exercise on myoFSR nor do we know if there was an interaction between the acute responses of exercise and post exercise nutrition.

Control Group

In this investigation, we elected not to utilize a non-exercise control group. Instead, the RT group serves as an active control group whereby the effects of adding either ATM or LTM exercise and training were compared to it. However, it may be advisable for future investigations to utilize a control group for comparisons of the physiologic responses to acute exercise and exercise training.

Data Interpretation – Intracellular Signaling and Skeletal Muscle Fractional Synthesis Rates

As previously mentioned, interpretation of the findings from this investigation is limited to the specific modes, intensities and duration of exercise utilized in the study (ATM, LTM, and machine based RT). The intensity and duration of exercise were chosen to mimic exercise recommendations prescribed by the American College of Sports Medicine. Because of limited sample, changes in mTOR, Akt, and TSC2 expression were only measured in the rested state before and after training. Consequently, the specific time course of activation for each is unknown. However, these data in conjunction with elevated myoFSR following RT-ATM compared to the other training modes add support to the overall conclusions of this study and further demonstrate the presence of mode specific differences between ATM and LTM exercise and training.

Acute Exercise Session Testing

In this study, we selected to match our acute exercise testing sessions to the intensity and volume prescribed during the first (untrained) and final (trained) weeks of training.

Therefore, the acute sessions themselves were not matched to each other with regards to intensity and duration. Therefore, it is inappropriate to compare acute 24h post exercise myoFSR responses before and after training. Although, similar between group differences were observed before and after training. Our current protocol was selected to observe the acute responses to exercise that would be prescribed to individuals just entering an exercise program following prolonged inactivity (untrained) and to those who have vigorously trained for a period of 3 months (trained).

Significance of Findings and General Summary

With the availability of aquatic treadmill running to the general public increasing, these results suggest that ATM running may serve as an effective tool in conjunction with resistance exercise for the preservation of muscle mass and strength with added aerobic benefits as well. The results of this investigation confirm a portion of our initial hypothesis and suggest that combined RT-ATM training may serve as a novel training modality which may benefit not only those in the general population, but clinical populations in need of improving daily functional capacity, reducing risk for injury, preserving lean mass, or reversing sarcopenia. Also, the results of this investigation challenge the view that training for both strength and endurance are "universally incompatible" and highlight the importance of exercise mode selection when prescribing exercise programs for specific health or performance outcomes.

Questions still remain as to whether or not ATM or RT-ATM training might be effective for previously trained populations such as athletes or if either are beneficial for clinical populations such as those suffering from hypertension, heart disease, or other chronic conditions. Additionally, the specific mechanisms responsible for the acute and chronic

outcomes measured in this study are still unknown. Further groundwork is also needed to characterize differences between ATM and LTM exercise and exercise training.

The work presented within this dissertation represents one of the largest single-institution training studies to date. We are also among the first to characterize both acute and chronic responses to concurrent exercise and training within the same study. While we acknowledge the need for further investigation, the current investigation indicates that concurrent RT-ATM training may serve as a novel, low impact training modality for simultaneously promoting increases in skeletal muscle mass, strength, and aerobic fitness.

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APPENDIX A
Informed Consent

***The study presented within this dissertation was conducted in conjunction with other investigations. Therefore, there are additional procedures mentioned within the informed consent document that were not included in the experiment described within this dissertation.**

Chronic effects of concurrent aerobic underwater treadmill training and progressive resistance training on various components of physical fitness characteristics

Introduction

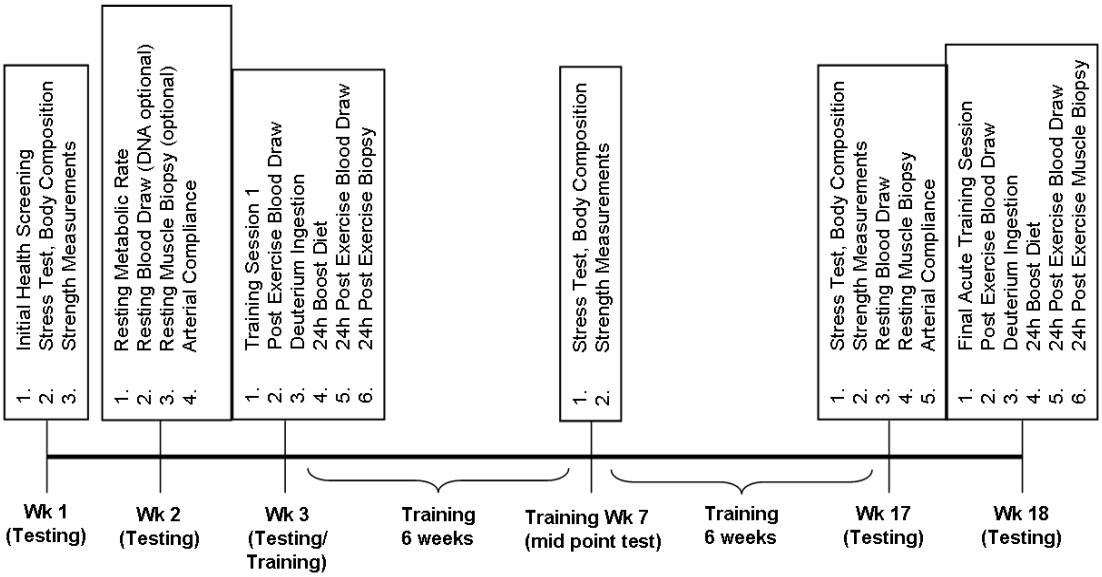
The purpose of this form is to provide you information that may affect your decision as to whether or not to participate in this research study. If you decide to participate in this study, this form will also be used to record your consent.

You have been asked to participate in a research project studying the physiological effects of aerobic water exercise and resistance exercise. The purpose of this study is to compare the effects of chronic aerobic water exercise to the effects of resistance training as well as concurrent water or land treadmill exercise and resistance training in regards to various components of physical fitness such as cardiovascular fitness, muscular strength, blood pressure, cholesterol, and overall functional capacity. You were selected to be a possible participant because you currently meet the recruitment criteria for this project. This study is being sponsored/funded by HydroWorx International Inc.

What will I be asked to do?

Your participation is completely voluntary.

Project Testing/Training Timeline



- *Fitness Assessment and Health Screening*

If you agree to be in this study, you will be asked to perform several procedures requiring a total of about 4 hours in the laboratory to test your physical fitness and health. These tests may require that you visit the laboratory on two separate days. You will perform a graded exercise test (GXT) by walking or running on a land-based, motorized treadmill until you are exhausted. While you are doing this test, you will have electrodes attached to your chest to measure the activity of your heart through an electrocardiogram (ECG), you will breathe through a mouthpiece connected to a machine to measure the amount of oxygen your body is using, and your blood pressure will be measured. During the test, a licensed physician will be on site to review your ECG report to determine if there are any cardiovascular contraindications to exercise present. If there are any abnormalities shown to be present from your report, you will be given instructions on how to schedule further health screening tests elsewhere. Please note, that if you are not cleared by the physician during this testing day, you must be cleared by further cardiovascular testing elsewhere and provide clearance documentation from you doctor in order to be eligible to participate. After the GXT, you will have an earlobe stick with a small lancet like the ones used for finger sticks so that about two drops of blood can be collected to measure a substance in your blood (lactic acid) produced by exercise. You will also be asked to perform tests to measure your muscle endurance, and flexibility. Your body bone density and body fat will be measured by lying at rest wearing exercise clothing in a DEXA (Dual Energy X-ray Absorptiometry) scanning machine. This machine will scan your body with a small amount of X-ray radiation. The radiation exposure is comparatively less than the amount of natural radiation you would be subjected to flying in an airplane from Houston to Dallas. Anytime you feel uncomfortable in the machine you can remove yourself from it. You will also have seven-site skin fold circumference measures taken on parts of your body, including your hip and abdomen. You will be asked to breathe

through a mouthpiece attached to a machine to measure your breathing capacity and the health of your lungs. Please note that at no time will any of the project research team or Texas A&M University be responsible for any medical costs outside of normal testing procedures during participation in the testing or training during this study.

-**FEMALE PARTICIPANTS**: If you are pregnant or if there is a possibility that you might be pregnant, you will not be permitted to participate in this study due to the small amount of radiation exposure from DEXA scanning.

- *Strength Assessment*
Following the initial assessment of physical fitness you will be asked to attend a strength training session to learn and practice the exercises that will be used to assess your strength levels. This session will be scheduled at least 24 hours following the initial fitness assessment and will last for duration of 1-2 hours.
At least 24 hours following this practice session, you will be tested for maximal strength on the exercises that were reviewed. These exercises will involve all major muscle groups and all testing will be supervised by trained members of the research group at all times. For strength assessment, you will be asked to complete 3-5 repetitions with maximal effort at the highest level of resistance that can be safely achieve. Each strength measurement will be preceded by 2-3 warm up sets of each exercise. Again this testing session will last for a duration of 1-2 hours.

Again your participation is completely voluntary and if at any time you feel uncomfortable, you may remove yourself from testing.

- *Resting Metabolic Rate Measurements, Blood Draws, and Muscle Biopsy (optional)*
Following the first week of testing you will be asked to sign up for a time the following week for the measurement of your Resting Metabolic Rate which gives us a measure of your energy expenditure when you are at rest. This process will involve 1.5-2 hours of your time and will simply involve breathing into a mouthpiece which is connected to a machine used to measure the amount of oxygen that your body is using at rest.

Also, during the second and third weeks of testing, with your consent, you will be asked to give a small piece of muscle from your thigh as well as a small amount of blood. The first sample will be collected before you have done any exercise training at all and the second sample will be collected 24hours following an exercise bout during the third week of testing. Also, an additional blood sample will be collected immediately following the same exercise bout. NOTE: Research has demonstrated that a key time point to measure markers of inflammation occurs immediately following exercise as well as 24 hours following exercise. The amount of muscle that will be taken is about the size of a pea and the amount of blood drawn will be 4 tubes containing about 2-3 table spoons of blood. We will also collect DNA (the genetic code) from blood samples so that we may study how differences in the genetic code between individuals might change responses to exercise. Please note that all needles used for the initial anesthetic injection for each biopsy procedure and blood draws will be only used once. Also, medical instruments such as scalpels and biopsy needles will be thoroughly cleaned and sterilized in an autoclave immediately following the biopsy procedure. Finally, the biopsy site it self will be sterilized

and bandaged. Muscle samples will be stored for measurement of factors related to exercise adaptation of muscle and leftover samples will be stored by the Applied Exercise Science Laboratory (AESL) for potential future use as it relates to the context of this study. These samples will be used to measure cellular mechanisms and factors related to resistance and aerobic capacity before and after exercise. Blood and muscle samples will be stored by the AESL for potential future measurements related to the context of this experiment. These samples will be collected before and after **training.**

> *-Heavy Water Administration:* You will be asked to consume 4 ml per kilogram body weight of a stable water molecule isotope (not radioactive) over 4 different time points during the day on two different occasions (before the muscle biopsy procedure before and after training). The isotope will help us measure your ability to build muscle from the biopsy sample that collected. Protein Supplement and Meals: On the day of the study, you will only be allowed to consume only boost nutrition shakes which will be provided for you. The purpose for this will be to ensure that diet will not affect the results of either the blood draws or muscle biopsies.

NOTE: The Muscle Biopsy portion of this project is entirely optional and lack of participation from this portion of the project will not exclude you from participation in any other aspect of training or testing. If you do choose to participate in the muscle biopsy procedures, you will be compensated with a payment of $25 for each biopsy. The total amount of compensation will be $100 for both pre and post training measurements **(Total of 4 biopsies).**
NOTE: Testing will occur both before and after training

-Arterial Compliance Testing
Because arterial stiffness has been shown to be associated with high blood pressure and heart disease, you will be asked to be tested for arterial compliance (blood vessel elasticity) before and after training. This will be non-invasive and will involve a technician simply holding a sensor over a few artery locations.

- Exercise Training
Once you complete the initial testing, you will be assigned at random to complete an exercise training program performing either underwater treadmill exercise, resistance exercise, or a combination of resistance exercise and land treadmill exercise, or a combination of resistance exercise and underwater treadmill exercise. The training program will last 12 weeks, and require that you train 2 - 4 times per week for about 20 minutes to 1.5 hours each day. You will have a personal trainer from the Applied Exercise Physiology Laboratory staff assigned to supervise each training session, and each session will be personalized for you. For those involved in underwater treadmill exercise, you will be asked to walk or run on your assigned treadmill for each training session until you expend about 500 kilocalories of energy 3 times per week. The physical effort required to complete each exercise session will be easy to moderate at the beginning, but will steadily increase from moderate to hard as you get in better physical condition. For those involved in resistance exercise, you will be asked to complete 2-3 sets of 8-15 repetitions per exercise 2 times per week. These exercises will involve every major muscle group and each exercise session will last approximately 1 hour. Again, the each session will be easy to moderate at the beginning but will progress as the number of repetitions and level of resistance for each exercise will be personalized for you. For those involved in concurrent training (resistance + water or land treadmill exercise), you will perform resistance exercise 2 times per week

with either water or land treadmill exercise following resistance exercise. On a third day during the week, you will perform water or land treadmill exercise only. However, each session will still total progress to a total expenditure of 500 kilocalories for each session (for all exercise). This means that on days that you perform resistance exercise; you will spend less time doing aerobic exercise (water or land treadmill). Total exercise frequency for concurrent exercise groups will be 3 days per week. After 12 weeks of training, you will be asked to repeat all the measures taken at the beginning of the study, including blood sampling, maximal effort GXT, body composition, lung tests, and assessment of your muscle strength, endurance, and flexibility. Values obtained from these measurements will be used to compare to your pre-training values to see how well the training program worked.

- *Diet Records*

For the purpose of research precision, you will be asked to not change your daily eating habits during training however, you will be asked to periodically provide 3-day dietary intake records so that it can be determined whether or not diet played a role in your adaptation to the training program.

What are the risks involved in this study?

The physical exertion required of you in this study will range from easy to maximal effort. During exercise there are physical risks to you including: muscle and bone strains and sprains, abnormal blood pressure, fainting, abnormal heart beats, shortness of breath, and in rare instances, heart attack.

Blood Sampling:

Risks associated with blood sampling: Obtaining the blood samples by using a small needle or catheter inserted into the antecubital vein (for cholesterol and triglyceride analysis) is a routine procedure in the AESL and in many clinical settings with rare adverse effects, although the puncture of the skin is accompanied by minor discomfort and may result in the development of a minor bruise next to the puncture site. However, as with any similar procedure disrupting the skin barrier, there is a risk of contracting an infection. This risk to you (and to the technician) will be minimized through the use of accepted sterile procedures which include: (1) use of surgical rubber gloves by the technician; (2) antiseptic cleansing (70% alcohol) of the involved site prior to puncture; (3) use of sterile equipment and instruments for each sample; and (4) proper dressing of the wound with antiseptic and band-aid following sample collection.

Muscle Biopsy:

Dr. J.P. Bramhall has oversight of all skeletal muscle biopsies, which will be performed in the Read Building, room 149 (Dr. Steven E. Riechman's Laboratory). The procedure room is a separate room within Room 149 that is sterile, isolated, and secured. This procedure room will house all biopsy materials, including anesthesia, biopsy needles, and sterile wound closures (butterfly strips and gauze pads). All sensitive materials (e.g. anethesia) will be stored in a locked cabinet within the procedure room. Dr. Bramhall's role/oversight on this project will include preparation and sterilization of biopsy needles, preparation of the biopsy procedure room to ensure a sterile/aseptic environment, administration of local anesthetic, incision of the skin for biopsy procedure, obtaining the biopsied sample, application of pressure to the biopsy site and incision closures, along with providing instructions to the subject related to post biopsy healing. Potential complications with biopsy include soreness (100%), infection (<1%), and permanent numbness (<<1%). *However, all previous studies have resulted in no complications with this procedure.

What are the possible benefits of this study?
Your benefits for participation in this study include the benefit of physical training, weight loss, a free visit with a physician who will review your risk for cardiovascular disease, ECG to directly see the health of your heart, and a free cholesterol profile. Also, this research will provide much insight to the scientific community in regards to physical fitness and the body's ability to adapt to various forms of exercise. Also, You will be offered any and all of your results at the end of your participation in the study.

Do I have to participate?
No. Your participation is voluntary. You may decide not to participate or to withdraw at any time without your current or future relations with Texas A&M University or the Applied Exercise Science Laboratory being affected.

Will I be compensated?

For those participating in the muscle biopsy procedure, $25 will be provided as compensation for muscle biopsies before and after training for a total of $100. Again, the decision to not participate in the muscle biopsy procedure will not exclude you from participation in all other training or testing. Also, as a reward for participation, you may choose not to receive $100 compensation but to enter in to the Applied Exercise Science Lab based FITLIFE program free for one semester. FITLIFE is made up of a series of exercise classes run through the lab designed to promote health and overall physical fitness. The benefit of this program is that it will promote the continuing maintenance and improvement in physical fitness following participation on this study.

Confidentiality

Who will know about my participation in this research study?
The data collected during this study is confidential and the names of all the subjects will be entered as a code in data analysis to ensure the confidentiality. The records of this study will be kept private. No identifiers linking you to the study will be included in any sort of report that might be published. Research records will be stored securely and only Stephen F. Crouse and his research collaborators will have access to the records.

Your decision whether or not to participate will not affect your current relations with Texas A&M University. If you decide to participate, you are free to refuse any situations that may be objectionable. You can withdraw at any time without your relations with the university, job, benefits, etc., being affected.

Contact Information

Whom do I contact with questions about the research?
If you have questions regarding this study, you may contact

Brad Lambert
Cell: (832) 687-2483
Office: (979) 458-0805
Email: bradlambert@hlkn.tamu.edu

And/Or

The Applied Exercise Science Laboratory
Phone: (979) 845-9418
Fax: (979) 862-2207

Whom do I contact about my rights as a research participant?
This research study has been reviewed by the Human Subjects' Protection Program and/or the Institutional Review Board at Texas A&M University. For research-related problems or questions regarding your rights as a research participant, you can contact these offices at (979)458-4067 or irb@tamu.edu.

Signature
Please be sure you have read the above information, asked questions and received answers to your satisfaction. You will be given a copy of the consent form for your records. By signing this document, you consent to participate in this study.

Muscle Biopsy Procedure:
_____ **YES**, I agree to participate in the muscle biopsy procedure before and after training.
(Answering yes does not obligate you to participate; you may change your decision at any time if you wish)
_____ **NO**, I do not want to participate in the muscle biopsy procedure at any time.

DNA Collection:
_____ **YES**, I agree to have my DNA collected from my blood sample.
(Answering yes does not obligate you to participate; you may change your decision at any time if you wish)
_____ **NO**, I do not wish for my DNA to be collected during this study.

***Female Participants:**
-------- **Yes,** I am pregnant or may be pregnant at this time
_____ **No,** I am not pregnant at this time

Signature of Participant: _____ **Date:** _____

Printed Name: _____

Signature of Person Obtaining Consent: _____ **Date:** _____

Printed Name: _____

APPENDIX B

APPLIED EXERCISE SCIENCE LABORATORY
SEVEN DAY PHYSICAL ACTIVITY RECORD*

Name:_____ Age:_____ Ht:_____ Wt:_____

Address: _____ Phone:_____(W) _____
_____(H)
_____ Occupation:_____
_____

DIRECTIONS: This Seven Day Physical Activity Record is designed to measure your habitual physical activities over the course of one week. You are asked to record your sleep habits as well as the physical activities you participated in over the course of the past seven days; include both occupational and leisure-time physical activities.

1. **BEFORE READING ANY FURTHER, PLEASE REVIEW ATTACHMENT 1 FOR EXAMPLES OF LIGHT, MODERATE, HARD, AND VERY HARD PHYSICAL ACTIVITIES!**

2. **DO NOT RECORD LIGHT ACTIVITIES.** See Attachment 1 for examples of LIGHT ACTIVITIES. Most of you will spend the majority of your waking hours in light activity. For example, a laboratory worker may be on their feet all day and may feel "fatigued", but the energy cost is in the "light" category. However, we need you to record the number of hours you spend sleeping.

3. For all other physical activities, which may be classified as moderate, hard, or very hard, **DOCUMENT ONLY THE TIME ACTUALLY SPENT PERFORMING THE ACTIVITY**: Include both occupational and leisure-time activities. For example, the laboratory worker in the illustration given above may spend a number of hours stocking shelves with supplies, which would likely be moderate exercise. It is unlikely, however, that they would spend an 8 hour day performing this task, and time should be subtracted for lunch, breaks, etc. Similarly, being at the pool for 2 hours but swimming for 15 minutes should be recorded as 15 minutes, not 2 hours.

4. For this record to be representative of your normal physical activity habits, it is critical that the week's activities be "normal" for you. For example, a week in which you take a holiday or a few days vacation would clearly NOT be a "normal" week for you. **IF THE UPCOMING WEEK'S ACTIVITIES WILL NOT REPRESENT YOUR NORMAL ACTIVITY PATTERNS, THEN PLEASE DO NOT COMPLETE THIS FORM - WAIT FOR A WEEK THAT WILL REFLECT YOUR NORMAL PHYSICAL ACTIVITY PATTERNS.** Note that a week is not necessarily Sunday through Saturday, but may be any consecutive 7 day period.

5. Use the record forms beginning on the next page to record; (1) the physical activity, (2) the total hours/minutes spent performing the activity, (3) and rate how hard you worked at the particular physical activity. Use the following scale to rate how hard you worked.

6. Return this completed record to the laboratory staff at your next laboratory visit.

SCALE TO RATE HOW HARD YOU WORK

1 - Barely breaking a sweat; breathing just slightly elevated.
2 - Moderate sweating; breathing significantly above normal, but could talk normally.
3 - Heavy sweating; breathing very heavy to nearly winded, could NOT talk normally.

PLEASE GO TO THE NEXT PAGE TO BEGIN YOUR SEVEN DAY ACTIVITY RECORD

*From: Blair et al., Assessment of habitual physical activity by a seven day recall in a community survey and controlled experiments. Am. J. Epidem. 122:794-804, 1985.

DAY ONE

Date:_____ **Day of Week:**_____

Activity	TOTAL TIME (Hours:Minutes)	HOW HARD (1,2,3)
Sleeping, including naps		

DAY TWO

Date:_____ **Day of Week:**_____

Activity	TOTAL TIME (Hours:Minutes)	HOW HARD (1,2,3)
Sleeping, including naps		

DAY THREE

Date:_____ **Day of Week:**_____

Activity	TOTAL TIME (Hours:Minutes)	HOW HARD (1,2,3)
Sleeping, including naps		

DAY FOUR

Date:_____ **Day of Week:**_____

Activity	TOTAL TIME (Hours:Minutes)	HOW HARD (1,2,3)
Sleeping, including naps		

DAY FIVE

Date:_____ **Day of Week:**_____

Activity	TOTAL TIME (Hours:Minutes)	HOW HARD (1,2,3)
Sleeping, including naps		

DAY SIX

Date:_____ **Day of Week:**_____

Activity	TOTAL TIME (Hours:Minutes)	HOW HARD (1,2,3)
Sleeping, including naps		

DAY SEVEN

Date:_____ **Day of Week:**_____

Activity	TOTAL TIME (Hours:Minutes)	HOW HARD (1,2,3)
Sleeping, including naps		

CONCLUDING QUESTIONS

1. Would you say that during the past week you were (check one):

_____less active than usual
_____about as active as usual
_____more active than usual

2. Which statement most nearly describes your attitude toward leisure-time physical activity?

_____I absolutely detest physical activity and exertion of any type.
_____I do not enjoy physical activity or exertion of any type.
_____I do not like activities which make me sweat, but I do like some types of light activities.
_____I enjoy light physical activity of many types, and occasionally like hard physical activity.
_____I thoroughly enjoy all types of physical activities, even those which are hard and very hard.

3. When you have time off from work (weekends/vacations) or during work breaks (lunch, etc), how often do you participate in physical activities, including recreational sports, which would be considered moderate to very hard?

_____Never
_____Seldom
_____Sometimes/Irregularly
_____Frequently/Regularly
_____Almost Always

THANK YOU VERY MUCH FOR YOUR TIME AND ACCURACY IN COMPLETING THIS QUESTIONNAIRE. THIS INFORMATION IS INDISPENSABLE FOR OUR STUDY, AND WE THANK YOU FOR YOUR WILLINGNESS TO COOPERATE IN COMPLETING THIS FORM.

ATTACHMENT 1

CLASSIFICATION OF PHYSICAL ACTIVITY

LIGHT ACTIVITIES

Household/Occupational

- *Bakery, general*
- *Bookbinding*
- *Carpet sweeping*
- *Cooking*
- *Eating (sitting)*
- *Farming*
  - *driving harvester*
  - *driving tractor*
  - *milking by machine*
- *Ironing*
- *Knitting, sewing*
- *Lying at ease*
- *Machine-tooling*
  - *machining*
  - *working sheet metal*
- *Painting, inside*
- *Printing*
- *Shoe repair, general*
- *Sitting quietly*
- *Standing quietly*
- *Tailoring*
  - *cutting*
  - *hand-sewing*
  - *machine-sewing*
- *Typing (electric and manual)*
- *Wallpapering*
- *Watch repairing*
- *Writing (sitting)*

Sports/Recreational

- *Billiards*
- *Canoeing (leisure)*
- *Card playing*
- *Drawing (standing)*
- *Horse racing (walking)*
- *Music Playing*
  - *accordion (sitting)*
  - *cello (sitting)*
  - *conducting*
  - *flute (sitting)*
  - *horn (sitting)*
  - *piano (sitting)*
  - *trumpet (standing)*
  - *violin (sitting)*
  - *woodwind (sitting)*

MODERATE ACTIVITIES

Household/Occupational

- *Carpentry (general)*
- *Cleaning*
- *Electrical work*
- *Farming*
  - *feeding animals*
  - *milking by hand*
- *Food shopping*
- *Gardening*
  - *weeding*
  - *hedging*
  - *raking*
- *Sawing*
- *Woodworking*
- *Shopping/Walking*
- *Locksmith*
- *Machine-tooling*
  - *operating lathe*
  - *tapping and drilling*
  - *welding*
- *Mopping floor*
- *Painting (outside)*
- *Planting seedlings*
- *Plastering*
- *Scraping paint*
- *Stock clerking*
- *Pressing (tailoring)*
- *Window cleaning*

Sports/Recreational

- *Archery*
- *Croquet*
- *Cycling, leisure 5.5 mph*
- *Dancing (ballroom)*
- *Gymnastics*
- *Music playing*
  - *drums (sitting)*
  - *organ (sitting)*
- *Table tennis*
- *Treading water, normal*
- *Volleyball*
- *Walking, normal pace*

HARD ACTIVITIES

Household/Occupational

- *Coal Mining*
  - *drilling coal, rock*
  - *erecting supports*
  - *shoveling coal*
- *Farming*
  - *feeding cattle*
  - *shoveling grain*
- *Forestry*
  - *ax chopping, slow*
  - *hoeing*
  - *planting by hand*
  - *stacking firewood*
- *Furriery*
- *Scrubbing floors*
- *Steel mill, working in*
  - *fettling*
  - *forging*
  - *tipping molds*
- *Pushmowing yard*

Sports/Recreational

- *Badminton*
- *Canoeing (racing)*
- *Circuit training*
  - *Universal*
- *Nautilus*
- *free weights*
- *Cricket*
- *Cycling, leisure 9.4 mph*
- *Dancing (medium aerobic)*
- *Golf (without cart)*
- *Horse racing (trotting)*
- *Skiing, soft snow (leisure)*
- *Tennis*

VERY HARD ACTIVITIES

Household/Occupational

- *Farming (galloping)*
- *barn cleaning*
- *forking straw bales (70-145 per min)*
- *Forestry*
  - *ax chopping, fast 11 min. mile)*
- *Digging*
- *Horse grooming*
- *Marching, rapid*
- *Steel mill, working in*
  - *hand rolling*

Sports/Recreational

- *Basketball*
- *Boxing*
- *Circuit training*
- *Hydra-Fitness*
- *Climbing hills*
- *Horse racing*
- *Judo*
- *Jumping rope*
- *Racquetball*
- *Running (5 min.-*

barking trees
carrying logs
felling trees
sawing by hand
trimming trees

merchant mill rolling

removing slag
tending furnace

no load

5 kg load
10 kg load

20 kg load
Cycling (racing)

Dancing
aerobic (intense)
twist" and "wiggle"

Skiing, hard snow
Skindiving
Snowshoeing,

Squash
Swimming (all strokes)

Field hockey
Football

Activity Compliance Form

ACTIVITY COMPLIANCE

NAME:_____ DATE:_____

1. My activity level (**has / has not**) changed from the last activity record submitted.

2. My activities have changed as follows:

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

Printed Name _____

Signature _____

APPENDIX C

APPLIED EXERCISE SCIENCE LABORATORY
HYDROWORX PROJECTS
THREE DAY DIET RECORD

Name:_____ Age:_____ Ht:_____ Wt:_____

DIRECTIONS: This Three Day Diet Record is designed to measure your food intake over the course of three consecutive days. Please make sure that ONE recorded day is a weekend. Because of this requirement, this record should be filled out **Thursday, Friday, Saturday OR Sunday, Monday, Tuesday**.

1. Records should be kept over a time period that best represents your "normal" eating patterns for 2 weekdays and one weekend day. For example, if Monday is a work holiday, it is unlikely that you will eat as you normally would.

2. Record **ALL** food and drink (**including water**) that you consume on each day. Record both the type of food or drink and the amounts consumed.

3. Please be as specific on foods and amounts as possible. For example, if you eat a turkey sandwich, please record the type of bread (white, whole wheat, rye, etc), number of slices of meat, and any additional items (cheese, tomato, mayonnaise, etc). Also include brand names of items when possible. For help in determining what is considered a serving, see the serving size chart on page 2 for some common food items.

4. Page 3 shows a sample day of the diet record. Please read this to help you become familiar with the recording format.

5. If you have any questions about filling out the record, please contact laboratory staff for assistance.

6. Return this record to the laboratory staff once it is complete.

Please do not change your diet in any way during the course of the study. Maintain normal eating habits, please do not begin a "diet". If you travel, don't worry, these changes from normal are only temporary.

Serving Size Chart

1 Cup cereal flakes or 1 baked potato = size of a fist

½ cup cooked rice, pasta or potato = size of an ice cream scoop

1 pancake = size of a CD

1 cup of salad greens or 1 medium fruit = size of a baseball

½ cup fresh fruit or vegetables = size of a standard light bulb

¼ cup dried fruit = 1 large egg

3 oz. meat, fish, poultry = size of a deck of cards

2 Tbsp peanut butter = size of a golf ball

1 ½ oz. cheese = 4 stacked dice or 2 cheese slices; 1 tsp margarine, butter and spreads = 1 dice

DAY 1 **Date: _____** **Day of Week:_____**

Food Eaten	# of servings or amount	Food Eaten	# of servings or amount

DAY 2 **Date: _____** **Day of Week:_____**

Food Eaten	# of servings or amount	Food Eaten	# of servings or amount

DAY 3 **Date: _____** **Day of Week:_____**

Food Eaten	# of servings or amount	Food Eaten	# of servings or amount

DAY 1 **Date: SAMPLE** **Day of Week: _SAMPLE DAY__**

Food Eaten	# of servings or amount	Food Eaten	# of servings or amount
Breakfast			
coffee (caffinated)	1-8oz cup		
w/ half&half	2 Tbsp		
w/ Splenda	1 Tbsp		
Raisin Bran cereal	1 cup		
w/ 1% milk	1 cup		
Multivitamin	1 vitamin		
Lunch			
Turkey sandwich (homemade)			
w/ turkey deli meat	3 slices		
w/ Kraft American cheese	1 slice		
w/ Lite mayo	2 Tbsp		
w/ whole wheat bread	2 slices		
w/ mustard	1 tbsp		
apple	1 medium		
Lay's potato chips	1 snack bag		
Sprite	12oz can		
Snacks			
water	20oz bottle		
Nature's Own honey granola bar	2 bars		
Hershey's Kisses	3 kisses		
Lemon-lime Gatorade	32oz bottle		
Dinner			
McDonald's Big Mac			
w/ cheese and mayo			
french fries	medium		
Diet Coke	medium		
Bluebell Vanilla Ice Cream	2 scoops		

Diet Compliance Form

DIET COMPLIANCE

NAME:_____ DATE:_____

3. My diet (**has / has not**) changed from the last diet record submitted.

4. My diet changed as follows:

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

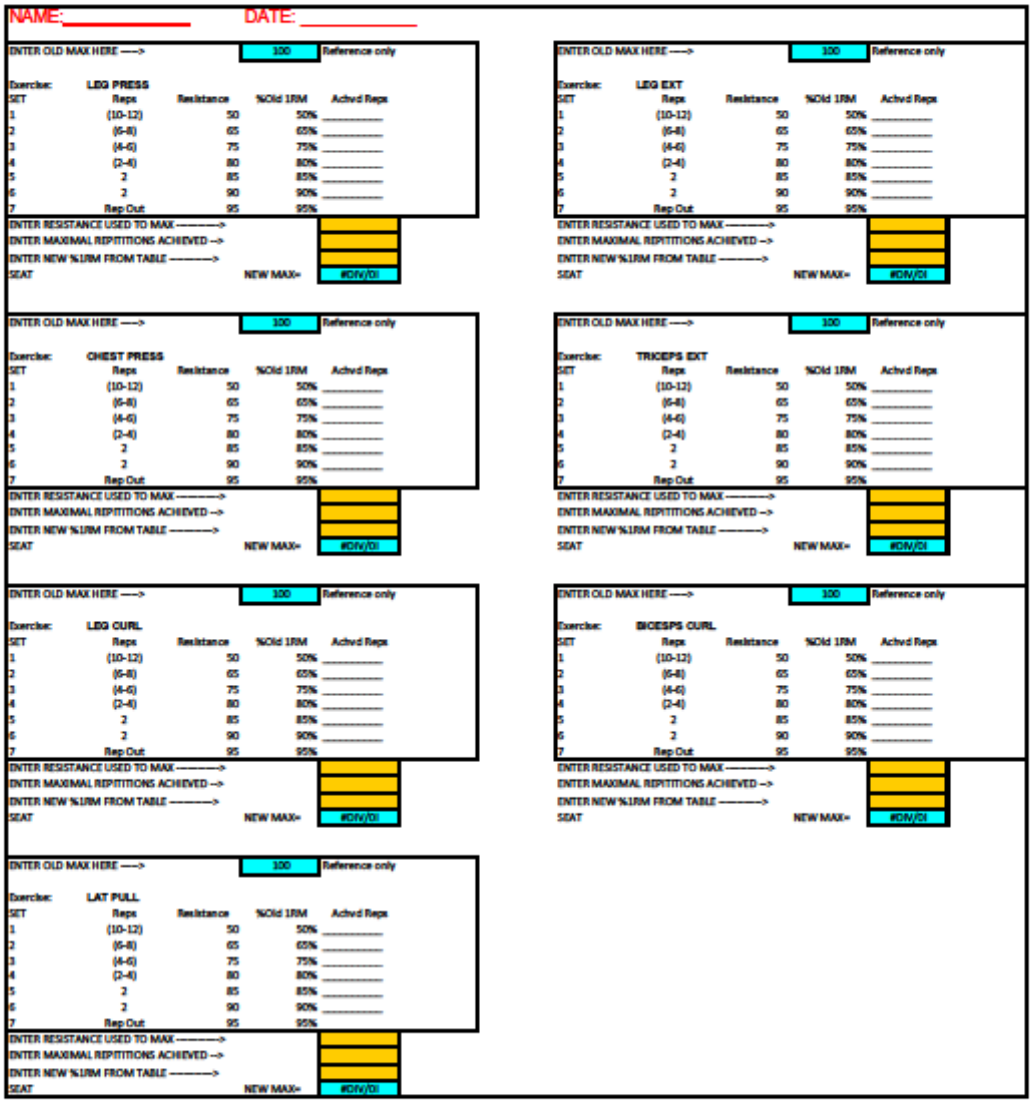
_____

Printed Name _____

Signature _____

APPENDIX D

SAMPLE STRENGTH TESTING FORM



NAME:_____ DATE: _____

ENTER OLD MAX HERE ---> 100 Reference only

Exercise: LEG PRESS

SET	Reps	Resistance	%Old 1RM	Actvd Reps
1	(10-12)	50	50%	_____
2	(6-8)	65	65%	_____
3	(4-6)	75	75%	_____
4	(2-4)	80	80%	_____
5	2	85	85%	_____
6	2	90	90%	_____
7	Rep Out	95	95%	

ENTER RESISTANCE USED TO MAX ---------->
ENTER MAXIMAL REPITITIONS ACHIEVED -->
ENTER NEW %1RM FROM TABLE ---------->
SEAT NEW MAX= #DIV/0!

ENTER OLD MAX HERE ---> 100 Reference only

Exercise: LEG EXT

SET	Reps	Resistance	%Old 1RM	Actvd Reps
1	(10-12)	50	50%	_____
2	(6-8)	65	65%	_____
3	(4-6)	75	75%	_____
4	(2-4)	80	80%	_____
5	2	85	85%	_____
6	2	90	90%	_____
7	Rep Out	95	95%	

ENTER RESISTANCE USED TO MAX ---------->
ENTER MAXIMAL REPITITIONS ACHIEVED -->
ENTER NEW %1RM FROM TABLE ---------->
SEAT NEW MAX= #DIV/0!

ENTER OLD MAX HERE ---> 100 Reference only

Exercise: CHEST PRESS

SET	Reps	Resistance	%Old 1RM	Actvd Reps
1	(10-12)	50	50%	_____
2	(6-8)	65	65%	_____
3	(4-6)	75	75%	_____
4	(2-4)	80	80%	_____
5	2	85	85%	_____
6	2	90	90%	_____
7	Rep Out	95	95%	

ENTER RESISTANCE USED TO MAX ---------->
ENTER MAXIMAL REPITITIONS ACHIEVED -->
ENTER NEW %1RM FROM TABLE ---------->
SEAT NEW MAX= #DIV/0!

ENTER OLD MAX HERE ---> 100 Reference only

Exercise: TRICEPS EXT

SET	Reps	Resistance	%Old 1RM	Actvd Reps
1	(10-12)	50	50%	_____
2	(6-8)	65	65%	_____
3	(4-6)	75	75%	_____
4	(2-4)	80	80%	_____
5	2	85	85%	_____
6	2	90	90%	_____
7	Rep Out	95	95%	

ENTER RESISTANCE USED TO MAX ---------->
ENTER MAXIMAL REPITITIONS ACHIEVED -->
ENTER NEW %1RM FROM TABLE ---------->
SEAT NEW MAX= #DIV/0!

ENTER OLD MAX HERE ---> 100 Reference only

Exercise: LEG CURL

SET	Reps	Resistance	%Old 1RM	Actvd Reps
1	(10-12)	50	50%	_____
2	(6-8)	65	65%	_____
3	(4-6)	75	75%	_____
4	(2-4)	80	80%	_____
5	2	85	85%	_____
6	2	90	90%	_____
7	Rep Out	95	95%	

ENTER RESISTANCE USED TO MAX ---------->
ENTER MAXIMAL REPITITIONS ACHIEVED -->
ENTER NEW %1RM FROM TABLE ---------->
SEAT NEW MAX= #DIV/0!

ENTER OLD MAX HERE ---> 100 Reference only

Exercise: BICEPS CURL

SET	Reps	Resistance	%Old 1RM	Actvd Reps
1	(10-12)	50	50%	_____
2	(6-8)	65	65%	_____
3	(4-6)	75	75%	_____
4	(2-4)	80	80%	_____
5	2	85	85%	_____
6	2	90	90%	_____
7	Rep Out	95	95%	

ENTER RESISTANCE USED TO MAX ---------->
ENTER MAXIMAL REPITITIONS ACHIEVED -->
ENTER NEW %1RM FROM TABLE ---------->
SEAT NEW MAX= #DIV/0!

ENTER OLD MAX HERE ---> 100 Reference only

Exercise: LAT PULL

SET	Reps	Resistance	%Old 1RM	Actvd Reps
1	(10-12)	50	50%	_____
2	(6-8)	65	65%	_____
3	(4-6)	75	75%	_____
4	(2-4)	80	80%	_____
5	2	85	85%	_____
6	2	90	90%	_____
7	Rep Out	95	95%	

ENTER RESISTANCE USED TO MAX ---------->
ENTER MAXIMAL REPITITIONS ACHIEVED -->
ENTER NEW %1RM FROM TABLE ---------->
SEAT NEW MAX= #DIV/0!

GRADED EXERCISE TESTING FORM

Applied Exercise Science Laboratory
Graded Exercise Testing Worksheet

Pre-exercise Data

Name: _____ Date of Test_____ Test Protocol: _____

Pertinent Medical History: _____

Pertinent Medications / Doses: _____

Supine HR _____ Supine BP _____

Pre-ex HR _____ Pre-ex BP _____ Predicted max HR _____ 85% Predicted max HR _____

Exercise Data

Time	Speed	Grade	HR	BP	RPE	Comments

Recovery Data

Time	HR	BP	Comments

Maximal Exercise Data

Max. Ex. Time _____ Peak HR _____ Peak BP _____

Reason for Stopping _____n

n

1 ST ↘or ↗ 2 mm
2 Chest Pain
3 Induced BB Block
4 Abnormal BP Response
5 V-Tach
6 Sust. A-Tach.
7 2nd or 3rd degree HB
8 Frequent PVC's
9 R on T PVC
10 Multifocal PVC's
11 Light Headedness
12 Dyspnea
13 Claudication
14 General Fatigue
15 Other _____

ECG Technician :_____ BP Technician : _____

APPENDIX E

EXERCISE SESSION DATA FORMS

HydroWorx Concurrent Training Study

LAND TREADMILL SESSION DATA

KCAL: ____ %VO2: ____ Heart Rate: ____
SPEED: ____ GRADE: ____ TIME: ____

Seesion 1		Session 2		Session 3	
DATE:	_____	DATE:	_____	DATE:	_____
Weight:	_____	Weight:	_____	Weight:	_____
RBP	_____	RBP	_____	RBP	_____
RHR	_____	RHR	_____	RHR	_____
Exercise HR	_____	Exercise HR	_____	Exercise HR	_____
RPE	_____	RPE	_____	RPE	_____
SPEED	_____	SPEED	_____	SPEED	_____
GRADE	_____	GRADE	_____	GRADE	_____
TIME	_____	TIME	_____	TIME	_____
POST BP	_____	POST BP	_____	POST BP	_____
POST HR	_____	POST HR	_____	POST HR	_____
PAIN	_____	PAIN	_____	PAIN	_____

COMMENTS: _____
_____

HydroWorx Concurrent Training Study

AQUATIC TREADMILL SESSION DATA

KCAL: ____ %VO2: ____ Heart Rate: ____
SPEED: ____ JET: ____ TIME: ____

Seesion 1		Session 2		Session 3	
DATE:	_____	DATE:	_____	DATE:	_____
Weight:	_____	Weight:	_____	Weight:	_____
RBP	_____	RBP	_____	RBP	_____
RHR	_____	RHR	_____	RHR	_____
Exercise HR	_____	Exercise HR	_____	Exercise HR	_____
RPE	_____	RPE	_____	RPE	_____
SPEED	_____	SPEED	_____	SPEED	_____
JET	_____	JET	_____	JET	_____
TIME	_____	TIME	_____	TIME	_____
POST BP	_____	POST BP	_____	POST BP	_____
POST HR	_____	POST HR	_____	POST HR	_____
PAIN	_____	PAIN	_____	PAIN	_____

COMMENTS: _____
_____

SUBJECT NAME: Session 1 5 Week of

Exercise Data Sheet - HydroWorx Study

Subject	Leg Press	Chest Press	Leg Curl	Lat Pull	Leg Ext	Triceps Ext	Biceps Curl			
	100	100	100	100	100	100	100			
BP Pre	_____						WT Start: _____			
BP Post	_____						Wt Fin: _____			_____

Exercise	Set #	Resistance	Goal Reps	Achvd Reps	Time Start	Time Fin	Time To Comp	HR Start	HR Fin	RPE
Leg Press	WU	60	8-12	_____	_____	_____	_____	_____	_____	_____
	1	75	4-8	_____	_____	_____	_____	_____	_____	_____
Pos: 5	2	75	4-8	_____	_____	_____	_____	_____	_____	_____
	3	75	4-8	_____	_____	_____	_____	_____	_____	_____
Chest Press	WU	60	8-12	_____	_____	_____	_____	_____	_____	_____
	1	75	4-8	_____	_____	_____	_____	_____	_____	_____
Pos: 3	2	75	4-8	_____	_____	_____	_____	_____	_____	_____
	3	75	4-8	_____	_____	_____	_____	_____	_____	_____
Leg Curl	WU	60	8-12	_____	_____	_____	_____	_____	_____	_____
	1	75	4-8	_____	_____	_____	_____	_____	_____	_____
Pos: 3	2	75	4-8	_____	_____	_____	_____	_____	_____	_____
	3	75	4-8	_____	_____	_____	_____	_____	_____	_____
Lat Pull Down	WU	60	8-12	_____	_____	_____	_____	_____	_____	_____
	1	75	4-8	_____	_____	_____	_____	_____	_____	_____
Pos: 2	2	75	4-8	_____	_____	_____	_____	_____	_____	_____
	3	75	4-8	_____	_____	_____	_____	_____	_____	_____
Leg Extension	WU	60	8-12	_____	_____	_____	_____	_____	_____	_____
	1	75	4-8	_____	_____	_____	_____	_____	_____	_____
	2	75	4-8	_____	_____	_____	_____	_____	_____	_____
	3	75	4-8	_____	_____	_____	_____	_____	_____	_____
Triceps Ext	WU	60	8-12	_____	_____	_____	_____	_____	_____	_____
	1	75	4-8	_____	_____	_____	_____	_____	_____	_____
Pos: 4	2	75	4-8	_____	_____	_____	_____	_____	_____	_____
	3	75	4-8	_____	_____	_____	_____	_____	_____	_____
Biceps Curl	WU	60	8-12	_____	_____	_____	_____	_____	_____	_____
	1	75	4-8	_____	_____	_____	_____	_____	_____	_____
Pos: 6	2	75	4-8	_____	_____	_____	_____	_____	_____	_____
	3	75	4-8	_____	_____	_____	_____	_____	_____	_____

APPENDIX F

ACUTE EXERCISE TESTING FORMS

ACUTE EXERCISE WORKSHEET (LAND TREADMILL)

PRE-EXERCISE DATA

Name: _____ Date: _____ Age: _____

Height: _____in Weight: _____lb Medical History: _____

Medications/Doses: _____

Target: Intensity _____% Duration _____min HR _____bpm VO_2 _____L RER _____

Target: Speed _____mph Grade _____% Energy expenditure _____kcal

EXERCISE DATA

Note: Collect and record data throughout warm-up, during the periods indicated below (15 min intervals) unless total prescribed duration is less than 65 min, and the last 2 minutes of the prescribed exercise session. Adjust the treadmill elevation as necessary to maintain the prescribed VO_2.

Time (min)	Speed (mph)	Grade (%)	HR (bpm)	BP (mmHg)	RPE	VO_2 (L/min)	RER	Comments
Warmup 1								
2								
3								
Exercise 3-5								
18-20								
33-35								
48-50								
63-65								

POSTEXERCISE DATA

Note: Immediately after exercise, escort subject to phlebotomy station for blood collection procedure. Do not cool down on treadmill.

Duration _____min Exercise Average: HR _____ VO_2 _____ RER _____

Total Kcal _____ Comments _____

ACUTE EXERCISE WORKSHEET (AQUATIC TREADMILL)

PRE-EXERCISE DATA

Name: _____ Date: _____ Age: _____

Height: _____in Weight: _____lb Medical History: _____

Medications/Doses: _____

Target: Intensity _____% Duration _____min HR _____bpm VO_2 _____L RER _____

Target: Speed _____mph Grade _____% Energy expenditure _____kcal

EXERCISE DATA

Note: Collect and record data throughout warm-up, during the periods indicated below (15 min intervals) unless total prescribed duration is less than 65 min, and the last 2 minutes of the prescribed exercise session. Adjust the treadmill elevation as necessary to maintain the prescribed VO_2.

Time (min)	Speed (mph)	JET (%)	HR (bpm)	BP (mmHg)	RPE	VO_2 (L/min)	RER	Comments
Warmup 1								
2								
3								
Exercise 3-5								
18-20								
33-35								
48-50								
63-65								

POSTEXERCISE DATA

Note: Immediately after exercise, escort subject to phlebotomy station for blood collection procedure. Do not cool down on treadmill.

Duration _____min Exercise Average: HR _____ VO_2 _____ RER _____

Total Kcal _____ Comments _____

APPENDIX G

SAMPLE STATISTICAL CODE AND RAW DATA FOR CHAPTER II

Independent Variables

DATA CODE	VARIABLE DEFINITION
SUBID	Unique Idendifier
GROUP	Exercise Training Group (RTATM - Combined Resistance and aquatic treadmill training, RTLTM - Combined Resistance and Land Treadmill Training, RT - Resistance training, ATM - aquatic treadmill training)
TIME	Time of measurement (Pre - pretraining, Post - Post training
GENDER	Gender M = male, F = Female
RACE	C = Caucasian, A = African American, H = Hispanic
HT	Height in Inches
HT cm	Height in Centimeters
WT	Weight in Pounds
WTKG	Mass in Kilograms
BMI	Percent body fat measured by DEXA
AGE	Age in Years

Dependent Variables

DATA CODE	VARIABLE DEFINITION
DXA%FT	%Body Fat Measured By DEXA
FM	Fat Mass in grams Measured by DEXA
LM	Lean Mass in grams Measured by DEXA
FM ARMS	Fat Mass of Arms Region in grams Measured by DEXA
LM ARMS	Lean Mass of Arms Region in grams Measured by DEXA
FM LEGS	Fat Mass of Legs Region in grams Measured by DEXA
LM LEGS	Lean Mass of Legs Region in grams Measured by DEXA
FM TRUNK	Fat Mass of Trunk Region in grams Measured by DEXA
LM TRUNK	Lean Mass of Trunk Region in grams Measured by DEXA
FM AND	Fat Mass of Android (mid torso) Region in grams Measured by DEXA
LM AND	Lean Mass of Android (mid torso) Region in grams Measured by DEXA
FM GYN	Fat Mass of Gynoid (glute) Region in grams Measured by DEXA
LM GYN	Lean Mass of Gynoid (glute) Region in grams Measured by DEXA
BMC	Bone Mineral Content in grams measured by DEXA
BMD	Bone Mineral Density (g/cm3) measured by DEXA
TOTAL TIME	Total time to exhaustion during bruce protocol GXT
VO2max ml/kg/min	Relative VO2max (ml/kg/min)
VO2max ml/kgLM	VO2max relative to lean mass (ml/kgLM/min)
VO2max L/min	Absolute VO2max (L/min)

MAX HR	Maximal heart rate recorded during Bruce protocol GXT
DAILY EXP	Daily caloric expenditure calculated from 7 day activity record analysis
TOT CAL	Average daily caloric consumption (kcals) calculated from 3 day diet record analysis
TOT Kj	Average daily consumption expressed in kilojoules from 3 day diet record analysis
CHO (g)	Average daily carbohydrate intake (grams) calculated from 3 day diet record analysis
REL CHO	Average daily carbohydrate intake relative to body mass (g/kg)
CHO%	Average %daily kcal intake from carbohydrate calculated from 3 day diet record analysis
PRO (g)	Average daily protein intake (grams) calculated from 3 day diet record analysis
REL PRO	Average daily protein intake relative to body mass (g/kg)
PRO%	Average %daily kcal intake from carbohydrate calculated from 3 day diet record analysis
TOT FAT (g)	Average daily fat intake (grams) calculated from 3 day diet record analysis
REL FAT	Average daily fat intake relative to body mass (g/kg)
TOTFAT%	Average %daily kcal intake from carbohydrate calculated from 3 day diet record analysis
MONO (g)	Average daily mono-unsaturated fat intake (grams) calculated from 3 day diet record analysis
POLY (g)	Average daily poly-unsaturated fat intake (grams) calculated from 3 day diet record analysis
SAT (g)	Average daily saturated fat intake (grams) calculated from 3 day diet record analysis
LEG PRESS	One repetition max for leg press (lbs)
CHEST PRESS	One repetition max for chest press (lbs)
LEG CURL	One repetition max for leg curl (lbs)
LAT PULL	One repetition max for lat pull down (lbs)
LEG EXT	One repetition max for leg extension (lbs)
TRI PUSH DOWN	One repetition max for triceps push down (lbs)
BICEPS CURL	One repetition max for bicep curl (lbs)
TOTALLFT	Sum of all one repetition max values for each exercise (lbs)
Plasma MPE (%)	Percent plasma enrichment of deuterium (plasma sample taken 24h following acute exercise)
Muscle MPE (%)	Percent myofibrillar protein enrichment of deuterium (muscle sample taken 24h following acute exercise)
FSR %/day	Myofibriallar fractional synthesis rate expressed in %/day (measured following acute exercise)
Akt	Total protein content of Protien Kinase B (Akt) expressed in arbirtrary units (measured in the rested state)
mTOR	Total protein content of mammalian target of rapamycin (mTOR) expressed in arbitrary units (measured in the rested state)
TSC2	Total protein content of tuberous sclerosis complex 2 (TSC2) expressed in arbitrary units (measured in the rested state)

STATISTICAL ANALYSIS

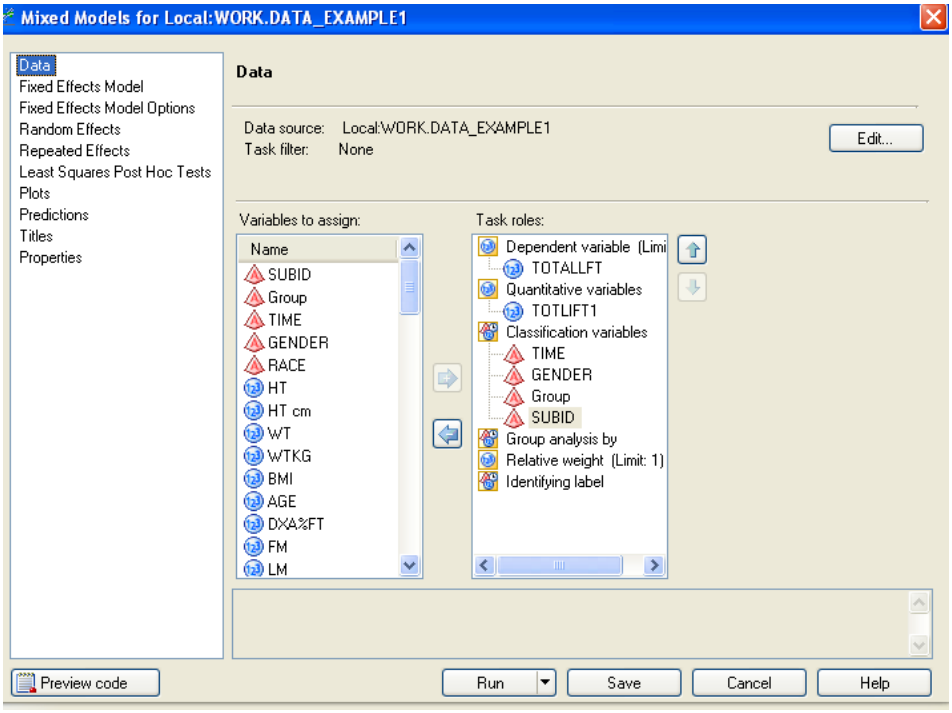
A 3(group) x 2(time) x 2(gender) mixed model ANCOVA (covariate = baseline measures) repeated across training was used to detect group x time interactions for maximal strength, VO_{2max}, body composition, dietary recall, and daily energy expenditure before and after training. A 1x3 Mixed Model ANOVA was used to analyze changes in the above variables following training: Change = (Post-training value) – (Pre-training value). A 3(group) x 1(time) x 1(gender). A Mixed Model ANOVA was used to compared 24h myoFSR between groups following acute exercise before (untrained state) and after (trained state) training. 3(group) x 2(time) x2(gender) Mixed model ANOVA repeated across training was used to detect changes in mTOR, Akt, and TSC2 skeletal muscle protein content before and after training. The comparison-wise error rate, α, was set at 0.05 for all statistical tests. Where significant F ratios are found a Tukey's post hoc analysis was performed to determine difference among groups. All data were analyzed using SAS Enterprise Guide (version 4.3) interfaced with Statistical Analysis System (version 9.3; SAS,Cary, NC).

Mixed Model ANCOVA with Repeated Measures

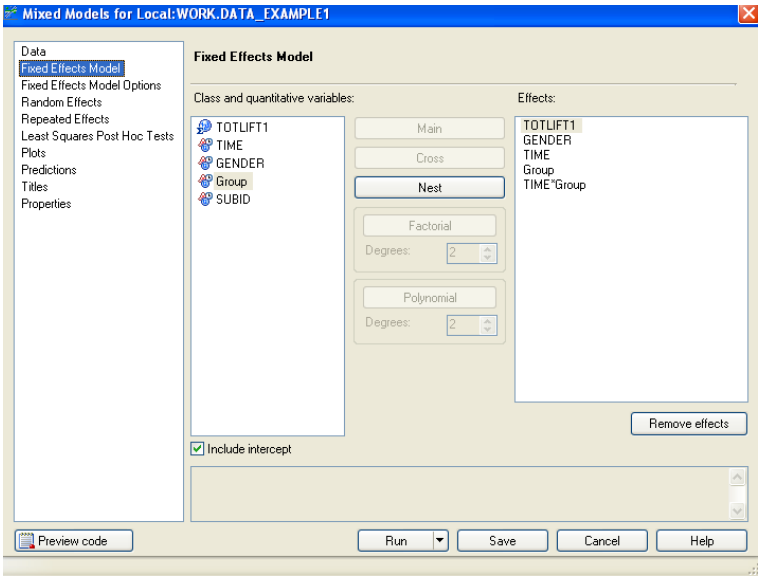
Within this model, baseline measures were selected as covariates. The procedure for running this model in SAS Enterprise Guide (version 4.3) involves the following.

1. For the variable of interest, first create a second column in the data sheet and that has the same variable name and then add a 1. For example, if the variable is Total Strength (TOTLIFT), a second covariate column will be created with the title TOTLIFT1.
2. Within this second column, paste pre time point values alongside both pre and post training values in the covariate column.
3. Save your data sheet with this new column.
4. Open SAS Enterprise Guide
5. Click file→open→data and select your data sheet and tab within the data sheet.
6. Click ANALYZE→ANOVA→MIXED MODELS

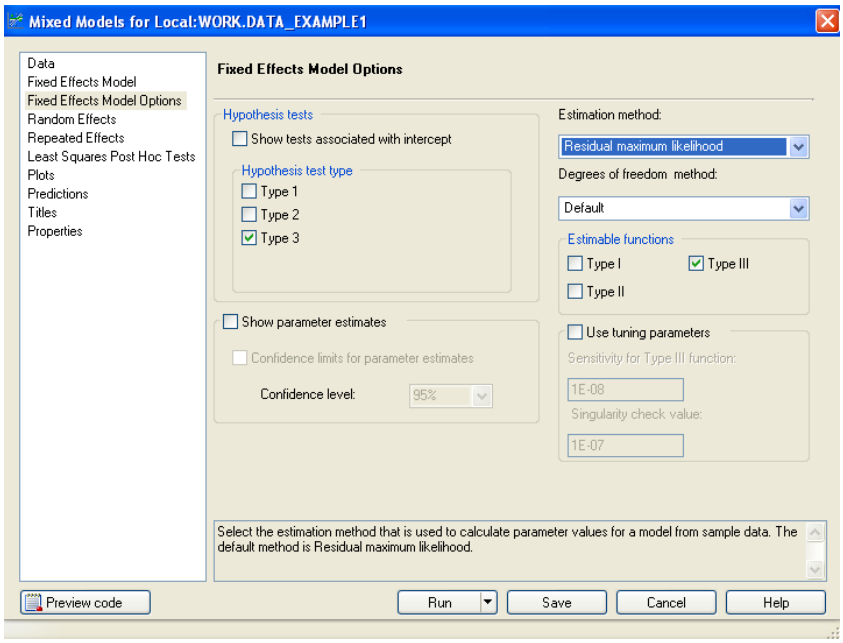
7. Under classification variables, select SUBID, GENDER, TIME, and GROUP
8. Under quantitative variables, select TOTLIFT1
9. Under dependent variables, select TOTLIFT



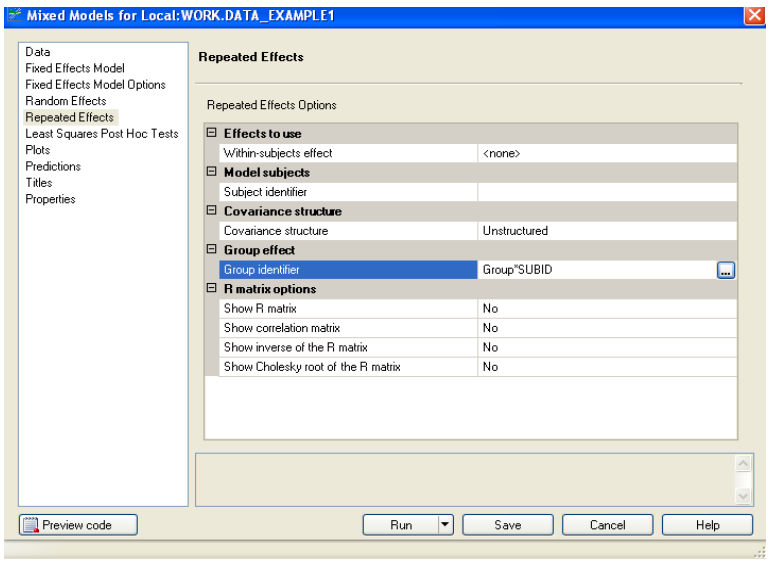
10. On the menu to the left, click FIXED EFFECTS MODEL
11. Select TOTLIFT1 and click MAIN to add it to the model
12. Do the same for GROUP, GENDER, and TIME
13. Hold control to select both GROUP and TIME and then click CROSS to add the interaction term to the model



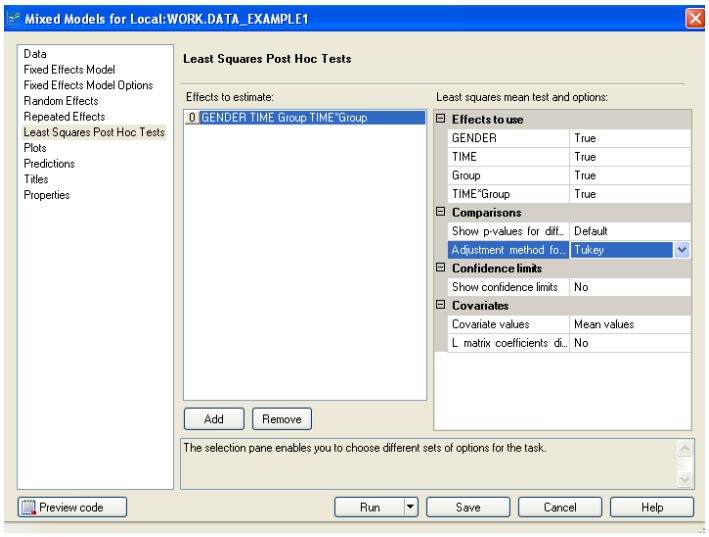
14. On the menu to the left, click FIXED EFFECTS MODEL OPTIONS
15. Under Hypothesis Test Type, select TYPE III
16. Under Estimable Functions, select TYPE III



17. On the menu to the left, click REPEATED EFFECTS
18. Under Within-subjects effects, select TIME
19. Under Subject Identifier, select SUBID
20. Under Co-variance structure, select Unstructured
21. Under Group Identifier, hold control to select both GROUP and SUBID and then click CROSS followed by OK



22. On the menu to the left, click LEAST SQUARES POST HOC TEST
23. Click ADD
24. Under Effects To Use, Change each term from False to TRUE
25. Under Comparisons/Show p-values, change None to DEFAULT
26. Under Comparisons/Show p-values, change Default to TUKEY



27. Click RUN

Following this, SAS Enterprise Guide will generate an Output and provide the input code for the analysis. The code that is generated can function in a standalone fashion using standard SAS software as well. The code below allows for the analysis of any main or interactive effects of gender, acute exercise, and exercise training with normalization to baseline for all subjects. The code for this analysis is as follows:

```
PROC MIXED DATA = WORK.SORTTempTableSorted
PLOTS(ONLY)=ALL
METHOD=REML
;
CLASS TIME GENDER Group SUBID
;
MODEL TOTALLFT=     TOTLIFT1 GENDER TIME Group TIME*Group
/
HTYPE=3
E3
;
;
LSMEANS GENDER TIME Group TIME*Group / PDIFF ADJUST=TUKEY ;
RUN;
QUIT;
```

Note: Within this study, Type 3 tests of fixed effects revealed that gender was not observed to significantly impact any of our statistical models, therefore all models were re-run without including gender under "classification data."

Mixed Model ANOVA with Repeated Measures

Because Akt, mTOR, and TSC2 content were normalized to internal standards, a Mixed Model ANOVA with Repeated Measures was used. The only difference in procedure is to not create or enter covariate values based on pre training measures (steps 1, 2, and 8).

Mixed Model ANOVA

Because acute exercise conditions were matched to either the 1st or 12th week of training, we chose not to analysis across training for 24h post exercise myoFSR's. Instead, a Mixed Model ANOVA was used to compared 24h myoFSR between groups following acute exercise before (untrained state) and after (trained state) training. Differences in procedure are as follows:

- Omit steps 1 & 2
- Step 7: Only enter SUBID, GENDER, and GROUP
- Omit step 8
- Omit step 11
- Step 12: Only enter GROUP and GENDER
- Omit step 13
- Omit steps 17-21

Note: These same procedures were used for analysis of change in maximal strength, VO_{2max}, and body composition between groups. All change variables were created using the following equation: Change = (Post-training value) – (Pre-training value).

RAW DATA / INDEPENDENT VARIABLES

SUBID	Group	TIME	GENDER	RACE	HT	HT cm	AGE
BE090	RTATM	PRE	F	w	65.5	166.37	42
CE033	RTATM	PRE	F	w	62.5	158.75	50
LA013	RTATM	PRE	F	w	65.5	166.37	34
LN005	RTATM	PRE	F	w	64	162.56	21
MA016	RTATM	PRE	F	w	68	172.72	32
MN052	RTATM	PRE	F	w	68.2	173.228	24
NY070	RTATM	PRE	F	w	63	160.02	58
RE081	RTATM	PRE	F	w	66	167.64	59
DG075	RTATM	PRE	M	w	70.5	179.07	42
DN050	RTATM	PRE	M	w	68	172.72	27
JF065	RTATM	PRE	M	W	69.5	176.53	28
JS063	RTATM	PRE	M	W	68	172.72	50
JY019	RTATM	PRE	M	w	73	185.42	45
MT008	RTATM	PRE	M	w	74	187.96	40
TT024	RTATM	PRE	M	w	71	180.34	33
TY010	RTATM	PRE	M	w	75	190.5	22
BE090	RTATM	POST	F	w	65.5	166.37	42
CE033	RTATM	POST	F	w	62.5	158.75	50
LA013	RTATM	POST	F	w	65.5	166.37	34
LN005	RTATM	POST	F	w	64	162.56	22
MA016	RTATM	POST	F	w	68	172.72	32
MN052	RTATM	POST	F	w	68.2	173.228	24
NY070	RTATM	POST	F	w	63	160.02	58
RE081	RTATM	POST	F	w	66	167.64	59
DG075	RTATM	POST	M	w	70.5	179.07	42
DN050	RTATM	POST	M	w	68	172.72	27
JF065	RTATM	POST	M	W	69.5	176.53	28
JS063	RTATM	POST	M	W	68	172.72	50
JY019	RTATM	POST	M	w	73	185.42	45
MT008	RTATM	POST	M	w	74	187.96	40
TT024	RTATM	POST	M	w	71	180.34	33
TY010	RTATM	POST	M	w	75	190.5	22
BA058	RTLTM	PRE	F	W	64	162.56	155.5
BH057	RTLTM	PRE	F	W	65	165.1	186
DE029	RTLTM	PRE	F	W	61	163	163
LE060	RTLTM	PRE	F	W	66.2	168.148	172.7
LN051	RTLTM	PRE	F	W	64.5	163.83	146.6
NY040	RTLTM	PRE	F	W	66.2	168.148	177

PI089	RTLTM	PRE	F	W	66	167.64	149.3
SE035	RTLTM	PRE	F	W	64.5	163.83	232.5
CS061	RTLTM	PRE	M	A	69	175.26	211.5
DD071	RTLTM	PRE	M	W	69	175.26	194.7
GT074	RTLTM	PRE	M	W	71	180.34	194
LN038	RTLTM	PRE	M	W	71	180.34	215
MW068	RTLTM	PRE	M	W	75	190.5	303
RR025	RTLTM	PRE	M	W	72.5	184.15	222.6
RY092	RTLTM	PRE	M	W	73	185.42	160
WL091	RTLTM	PRE	M	W	78.5	199.39	188.5
BA058	RTLTM	POST	F	W	64	162.56	154
BH057	RTLTM	POST	F	W	65	165.1	186.5
DE029	RTLTM	POST	F	W	61	163	161.5
LE060	RTLTM	POST	F	W	66.2	168.148	173
LN051	RTLTM	POST	F	W	64.5	163.83	152.5
NY040	RTLTM	POST	F	W	66.2	168.148	178.5
PI089	RTLTM	POST	F	W	66	167.64	147
SE035	RTLTM	POST	F	w	64.5	163.83	223
CS061	RTLTM	POST	M	A	66.2	168.148	208.7
DD071	RTLTM	POST	M	W	69	175.26	197
GT074	RTLTM	POST	M	W	71	180.34	193
LN038	RTLTM	POST	M	W	71	180.34	196
MW068	RTLTM	POST	M	W	75	190.5	297
RR025	RTLTM	POST	M	W	72.5	184.15	226.5
RY092	RTLTM	POST	M	W	78.5	199.39	161
WL091	RTLTM	POST	M	W	78.5	199.39	194
AN054	RT	PRE	F	W	65.5	166.37	197
BK088	RT	PRE	F	w	67.5	171.45	284.5
JL017	RT	PRE	F	w	70	177.8	219.4
KE067	RT	PRE	F	W	63	160.02	188
KY066	RT	PRE	F	w	66	167.64	202
MA037	RT	PRE	F	H	64	162.56	185.6
PI006	RT	PRE	F	w	62	157.48	131
SN009	RT	PRE	F	w	64	162.56	147.6
AW021	RT	PRE	M	w	74	187.96	179.8
BE085	RT	PRE	M	A	71	180.34	186.5
DD015	RT	PRE	M	w	71	180.34	182.8
JN001	RT	PRE	M	w	76	193.04	286.4
MK093	RT	PRE	M	W	70	177.8	206.7
SM072	RT	PRE	M	W	72	182.88	224
TS042	RT	PRE	M	w	72	182.88	214.2

RAW DATA / DEPENDENT VARIABLES / BODY COMPOSITION

SUBID	Group	TIME	DXA%FT	FM	LM	FM ARMS	LM ARMS
BE090	RTATM	PRE	43.70	30071.00	38806.00	27960.00	4611.00
CE033	RTATM	PRE	41.40	24969.00	35298.00	1866.00	3742.00
LA013	RTATM	PRE	39.90	24437.00	36788.00	2323.00	3902.00
LN005	RTATM	PRE	46.20	33232.00	38769.00	3013.00	4369.00
MA016	RTATM	PRE	49.10	48632.00	50389.00	5137.00	5574.00
MN052	RTATM	PRE	24.00	15299.00	48415.00	1363.00	5515.00
NY070	RTATM	PRE	47.70	29297.00	32097.00	2728.00	3143.00
RE081	RTATM	PRE	49.00	58134.00	60152.00	4545.00	4633.00
DG075	RTATM	PRE	44.30	45945.00	57815.00	3445.00	8075.00
DN050	RTATM	PRE	27.30	20927.00	55649.00	1381.00	7944.00
JF065	RTATM	PRE	39.90	38424.00	57928.00	3473.00	6587.00
JS063	RTATM	PRE	39.30	39415.00	60930.00	3763.00	9307.00
JY019	RTATM	PRE	40.10	47823.00	71309.00	4416.00	9268.00
MT008	RTATM	PRE	31.60	31221.00	67505.00	2498.00	8494.00
TT024	RTATM	PRE	32.00	33956.00	72062.00	2918.00	9999.00
TY010	RTATM	PRE	25.90	23855.00	68179.00	1517.00	9594.00
BE090	RTATM	POST	43.80	30696.00	39452.00	2867.00	4783.00
CE033	RTATM	POST	41.70	24955.00	34889.00	1856.00	4008.00
LA013	RTATM	POST	39.50	24739.00	37874.00	2339.00	3790.00
LN005	RTATM	POST	42.20	30145.00	41362.00	2633.00	4251.00
MA016	RTATM	POST	46.30	47668.00	55185.00	4704.00	5576.00
MN052	RTATM	POST	25.50	16691.00	48792.00	1359.00	5811.00
NY070	RTATM	POST	47.00	28514.00	32198.00	2550.00	3407.00
RE081	RTATM	POST	48.60	57809.00	61094.00	4418.00	5025.00
DG075	RTATM	POST	41.50	43927.00	61964.00	3497.00	9173.00
DN050	RTATM	POST	24.50	19474.00	60004.00	1368.00	8640.00
JF065	RTATM	POST	35.90	34089.00	60748.00	3017.00	7347.00
JS063	RTATM	POST	38.20	39286.00	63553.00	3584.00	9004.00
JY019	RTATM	POST	37.30	46573.00	78219.00	4699.00	9058.00
MT008	RTATM	POST	28.90	28670.00	70440.00	2305.00	9111.00
TT024	RTATM	POST	30.80	32876.00	74000.00	2769.00	10279.00
TY010	RTATM	POST	24.40	22974.00	71193.00	1542.00	9702.00
BA058	RTLTM	PRE	50.60	33557.00	32771.00	2689.00	3795.00
BH057	RTLTM	PRE	54.60	43116.00	35848.00	3751.00	4535.00
DE029	RTLTM	PRE	43.30	30434.00	39915.00	2696.00	4842.00
LE060	RTLTM	PRE	47.00	35006.00	39409.00	3059.00	4249.00
LN051	RTLTM	PRE	44.70	28154.00	34835.00	2484.00	3759.00
NY040	RTLTM	PRE	39.40	30245.00	46602.00	2544.00	4492.00

PI089	RTLTM	PRE	34.70	22325.00	42104.00	2199.00	4713.00
SE035	RTLTM	PRE	48.80	48807.00	51250.00	4304.00	5638.00
CS061	RTLTM	PRE	28.60	26237.00	65509.00	2097.00	9407.00
DD071	RTLTM	PRE	36.70	31005.00	53463.00	2458.00	6681.00
GT074	RTLTM	PRE	30.60	25390.00	57607.00	1940.00	7794.00
LN038	RTLTM	PRE	34.00	31884.00	61825.00	3108.00	7400.00
MW068	RTLTM	PRE	49.30	65393.00	67306.00	4680.00	7413.00
RR025	RTLTM	PRE	28.00	27050.00	69531.00	2026.00	8966.00
RY092	RTLTM	PRE	20.40	14188.00	55384.00	1183.00	6770.00
WL091	RTLTM	PRE	25.90	21192.00	60502.00	1488.00	7669.00
BA058	RTLTM	POST	46.20	30560.00	35555.00	2479.00	3918.00
BH057	RTLTM	POST	41.10	43363.00	36727.00	3702.00	4743.00
DE029	RTLTM	POST	42.60	29736.00	40033.00	2902.00	5146.00
LE060	RTLTM	POST	46.10	34743.00	40582.00	3282.00	4511.00
LN051	RTLTM	POST	41.20	26813.00	38287.00	2210.00	4026.00
NY040	RTLTM	POST	40.20	30949.00	46126.00	2743.00	4792.00
PI089	RTLTM	POST	30.70	19645.00	44363.00	1905.00	4738.00
SE035	RTLTM	POST	48.20	46779.00	50264.00	3700.00	5654.00
CS061	RTLTM	POST	26.30	23978.00	67347.00	1828.00	9454.00
DD071	RTLTM	POST	34.10	29487.00	56912.00	2162.00	6860.00
GT074	RTLTM	POST	30.90	25783.00	57601.00	1824.00	7687.00
LN038	RTLTM	POST	30.40	25917.00	59378.00	2458.00	7568.00
MW068	RTLTM	POST	48.30	62497.00	67030.00	4380.00	7387.00
RR025	RTLTM	POST	24.30	23994.00	74877.00	1736.00	8356.00
RY092	RTLTM	POST	17.30	12250.00	58365.00	1012.00	7181.00
WL091	RTLTM	POST	24.10	20257.00	63752.00	1400.00	8274.00
AN054	RT	PRE	54.70	45989.00	38110.00	4187.00	5102.00
BK088	RT	PRE	53.30	65924.00	57811.00	5817.00	5272.00
JL017	RT	PRE	55.90	52958.00	41730.00	4050.00	5052.00
KE067	RT	PRE	54.30	43737.00	36827.00	3455.00	4156.00
KY066	RT	PRE	55.10	47678.00	38924.00	3679.00	4499.00
MA037	RT	PRE	47.50	38119.00	42077.00	3332.00	4575.00
PI006	RT	PRE	31.70	17992.00	38678.00	.	.
SN009	RT	PRE	41.80	27142.00	37801.00	2046.00	4233.00
AW021	RT	PRE	25.10	19541.00	58432.00	1605.00	8042.00
BE085	RT	PRE	23.90	19382.00	61564.00	1795.00	9886.00
DD015	RT	PRE	26.30	21053.00	58949.00	1600.00	7880.00
JN001	RT	PRE	42.00	51039.00	70379.00	3515.00	7267.00
MK093	RT	PRE	31.50	28335.00	61701.00	2719.00	8220.00
SM072	RT	PRE	35.40	34178.00	62465.00	2706.00	8235.00
TS042	RT	PRE	38.10	35445.00	57481.00	2746.00	7488.00
AN054	RT	POST	55.70	46996.00	37408.00	4458.00	5282.00
BK088	RT	POST	50.80	60582.00	58560.00	5379.00	5142.00

JL017	RT	POST	54.80	53498.00	44211.00	4598.00	5325.00
KE067	RT	POST	55.00	44729.00	36622.00	3505.00	4669.00
KY066	RT	POST	50.10	44135.00	44014.00	3509.00	4627.00
MA037	RT	POST	48.20	39446.00	42374.00	3509.00	4479.00
PI006	RT	POST	32.60	18365.00	37888.00	.	.
SN009	RT	POST	41.90	27875.00	38633.00	2087.00	4319.00
AW021	RT	POST	24.10	19224.00	60623.00	1551.00	7973.00
BE085	RT	POST	24.60	20772.00	63553.00	1983.00	10272.00
DD015	RT	POST	26.20	21212.00	59634.00	1611.00	7995.00
JN001	RT	POST	41.00	49438.00	71013.00	3570.00	8330.00
MK093	RT	POST	32.20	29440.00	62094.00	2621.00	8563.00
SM072	RT	POST	36.80	36307.00	62417.00	3009.00	8643.00
TS042	RT	POST	33.70	30317.00	59667.00	2459.00	7732.00

SUBID	Group	TIME	FM LEGS	LM LEGS	FM TRUNK	LM TRUNK	FM AND
BE090	RTATM	PRE	11218.00	12801.00	15196.00	18312.00	2239.00
CE033	RTATM	PRE	10219.00	11750.00	12110.00	16892.00	2230.00
LA013	RTATM	PRE	9361.00	11819.00	11984.00	18232.00	1835.00
LN005	RTATM	PRE	13061.00	13242.00	16268.00	18194.00	2567.00
MA016	RTATM	PRE	19388.00	18566.00	23019.00	23118.00	3960.00
MN052	RTATM	PRE	6016.00	16641.00	7451.00	22980.00	1163.00
NY070	RTATM	PRE	8528.00	9732.00	17104.00	16331.00	3039.00
RE081	RTATM	PRE	19546.00	18955.00	32712.00	32879.00	6426.00
DG075	RTATM	PRE	12216.00	19590.00	29164.00	26156.00	5888.00
DN050	RTATM	PRE	6033.00	19297.00	12880.00	24536.00	2019.00
JF065	RTATM	PRE	9306.00	19738.00	24584.00	27393.00	4997.00
JS063	RTATM	PRE	11123.00	20348.00	23463.00	27044.00	4115.00
JY019	RTATM	PRE	13373.00	23878.00	29042.00	34255.00	5902.00
MT008	RTATM	PRE	8309.00	23510.00	19557.00	30974.00	3660.00
TT024	RTATM	PRE	10454.00	26076.00	19688.00	31198.00	3782.00
TY010	RTATM	PRE	7508.00	24224.00	14167.00	30229.00	2277.00
BE090	RTATM	POST	11605.00	13129.00	15282.00	18336.00	2375.00
CE033	RTATM	POST	10131.00	11768.00	12087.00	15997.00	2039.00
LA013	RTATM	POST	9575.00	12336.00	12091.00	18988.00	1909.00
LN005	RTATM	POST	12468.00	14744.00	14165.00	18990.00	2385.00
MA016	RTATM	POST	18406.00	21075.00	23247.00	24533.00	4003.00
MN052	RTATM	POST	5781.00	16352.00	9015.00	22982.00	1215.00
NY070	RTATM	POST	8733.00	10354.00	16240.00	15449.00	2810.00
RE081	RTATM	POST	18795.00	19479.00	33024.00	32021.00	6014.00
DG075	RTATM	POST	10087.00	19124.00	29152.00	29323.00	5511.00
DN050	RTATM	POST	6856.00	21471.00	10619.00	25592.00	1719.00
JF065	RTATM	POST	8611.00	20950.00	21414.00	27656.00	4166.00

JS063	RTATM	POST	10134.00	21026.00	24608.00	29458.00	4628.00
JY019	RTATM	POST	11723.00	25669.00	29298.00	39891.00	6182.00
MT008	RTATM	POST	7706.00	24620.00	17920.00	32354.00	3517.00
TT024	RTATM	POST	9876.00	26308.00	19378.00	32714.00	3696.00
TY010	RTATM	POST	7102.00	24899.00	13708.00	32361.00	2248.00
BA058	RTLTM	PRE	15172.00	11809.00	14756.00	14652.00	2242.00
BH057	RTLTM	PRE	15900.00	12350.00	22430.00	16273.00	3554.00
DE029	RTLTM	PRE	9492.00	12792.00	17437.00	19410.00	2964.00
LE060	RTLTM	PRE	13391.00	13075.00	17538.00	18983.00	3044.00
LN051	RTLTM	PRE	10231.00	12920.00	14570.00	15223.00	2882.00
NY040	RTLTM	PRE	7562.00	14916.00	19283.00	23837.00	3390.00
PI089	RTLTM	PRE	8412.00	14606.00	11108.00	19919.00	1487.00
SE035	RTLTM	PRE	14521.00	16662.00	28834.00	25370.00	5057.00
CS061	RTLTM	PRE	11565.00	25353.00	11862.00	26494.00	1875.00
DD071	RTLTM	PRE	9333.00	19026.00	18400.00	24185.00	3538.00
GT074	RTLTM	PRE	8556.00	20306.00	14236.00	25753.00	2675.00
LN038	RTLTM	PRE	10137.00	20794.00	17801.00	29746.00	3184.00
MW068	RTLTM	PRE	24285.00	24873.00	35364.00	31412.00	7411.00
RR025	RTLTM	PRE	7277.00	24936.00	17079.00	31569.00	3216.00
RY092	RTLTM	PRE	4486.00	17820.00	7918.00	26458.00	1391.00
WL091	RTLTM	PRE	4901.00	21073.00	14205.00	28025.00	2346.00
BA058	RTLTM	POST	15206.00	12329.00	11995.00	16603.00	1862.00
BH057	RTLTM	POST	16722.00	12490.00	21931.00	16994.00	3819.00
DE029	RTLTM	POST	9330.00	12880.00	16743.00	19189.00	3018.00
LE060	RTLTM	POST	13107.00	13562.00	17392.00	19408.00	3103.00
LN051	RTLTM	POST	10095.00	13670.00	13720.00	17478.00	2752.00
NY040	RTLTM	POST	7860.00	15218.00	19485.00	22759.00	3435.00
PI089	RTLTM	POST	7506.00	14887.00	9706.00	21898.00	1327.00
SE035	RTLTM	POST	13578.00	17473.00	28328.00	23503.00	4706.00
CS061	RTLTM	POST	11076.00	26341.00	10460.00	27401.00	1742.00
DD071	RTLTM	POST	9187.00	20153.00	17311.00	25938.00	3427.00
GT074	RTLTM	POST	8197.00	20245.00	15083.00	25800.00	2749.00
LN038	RTLTM	POST	8260.00	19026.00	1480.00	28883.00	2522.00
MW068	RTLTM	POST	23454.00	25695.00	33643.00	30420.00	6975.00
RR025	RTLTM	POST	6385.00	27307.00	15290.00	35240.00	2881.00
RY092	RTLTM	POST	3976.00	19060.00	6750.00	27763.00	1238.00
WL091	RTLTM	POST	4898.00	22145.00	13381.00	29437.00	2101.00
AN054	RT	PRE	19594.00	13454.00	20945.00	16394.00	3180.00
BK088	RT	PRE	25916.00	19690.00	33107.00	29982.00	6713.00
JL017	RT	PRE	22576.00	15434.00	25160.00	18212.00	4294.00
KE067	RT	PRE	17714.00	13181.00	21394.00	16441.00	3864.00
KY066	RT	PRE	18153.00	13963.00	24692.00	17650.00	4250.00
MA037	RT	PRE	10393.00	13546.00	23463.00	20892.00	4388.00

PI006	RT	PRE	.	.	.	.	.
SN009	RT	PRE	9158.00	11648.00	15124.00	19025.00	2629.00
AW021	RT	PRE	6370.00	19479.00	10903.00	26790.00	1784.00
BE085	RT	PRE	5467.00	20942.00	11481.00	26365.00	2066.00
DD015	RT	PRE	8038.00	20056.00	10830.00	27369.00	1612.00
JN001	RT	PRE	13998.00	25140.00	32506.00	34228.00	6381.00
MK093	RT	PRE	8155.00	21553.00	16729.00	27968.00	2864.00
SM072	RT	PRE	10254.00	22376.00	20316.00	27694.00	4023.00
TS042	RT	PRE	11988.00	18949.00	19713.00	26732.00	3578.00
AN054	RT	POST	20313.00	13513.00	20936.00	15414.00	3324.00
BK088	RT	POST	23352.00	20883.00	30898.00	29677.00	6380.00
JL017	RT	POST	23801.00	16124.00	23949.00	19688.00	4494.00
KE067	RT	POST	18253.00	12822.00	21839.00	16280.00	4128.00
KY066	RT	POST	17593.00	14612.00	22005.00	21682.00	4166.00
MA037	RT	POST	10095.00	13442.00	24896.00	21402.00	4706.00
PI006	RT	POST	.	.	.	.	.
SN009	RT	POST	9362.00	12272.00	15602.00	19079.00	2560.00
AW021	RT	POST	5759.00	20527.00	11289.00	28057.00	1822.00
BE085	RT	POST	5892.00	21030.00	12182.00	27742.00	2152.00
DD015	RT	POST	8721.00	21288.00	10319.00	26704.00	1641.00
JN001	RT	POST	12672.00	24685.00	32230.00	34242.00	6394.00
MK093	RT	POST	8510.00	21915.00	17568.00	27737.00	3019.00
SM072	RT	POST	10558.00	22448.00	21721.00	26740.00	3845.00
TS042	RT	POST	10839.00	19803.00	16130.00	27723.00	2923.00

SUBID	Group	TIME	LM AND	FM GYN	LM GYN	BMC	BMD
BE090	RTATM	PRE	2444.00	6662.00	6155.00	2893.00	1.23
CE033	RTATM	PRE	2516.00	5249.00	5342.00	2630.00	1.24
LA013	RTATM	PRE	2643.00	5451.00	5245.00	2596.00	1.14
LN005	RTATM	PRE	2397.00	6798.00	6227.00	2910.00	1.22
MA016	RTATM	PRE	3443.00	9263.00	8408.00	3356.00	1.29
MN052	RTATM	PRE	3273.00	3910.00	6861.00	3047.00	1.30
NY070	RTATM	PRE	2418.00	5201.00	4773.00	2568.00	1.17
RE081	RTATM	PRE	5422.00	9707.00	9314.00	2802.00	1.20
DG075	RTATM	PRE	4389.00	7019.00	8758.00	3920.00	1.36
DN050	RTATM	PRE	3439.00	3816.00	8116.00	3436.00	1.31
JF065	RTATM	PRE	4421.00	5360.00	9067.00	3890.00	1.41
JS063	RTATM	PRE	4303.00	6738.00	8095.00	3781.00	1.33
JY019	RTATM	PRE	5267.00	7096.00	10299.00	3590.00	1.30
MT008	RTATM	PRE	4648.00	5387.00	10469.00	4102.00	1.46
TT024	RTATM	PRE	4388.00	6247.00	11244.00	3988.00	1.40
TY010	RTATM	PRE	4579.00	4801.00	10433.00	3997.00	1.31

BE090	RTATM	POST	2466.00	6831.00	6083.00	2881.00	1.22
CE033	RTATM	POST	2275.00	5001.00	5026.00	2737.00	1.26
LA013	RTATM	POST	2759.00	5539.00	5795.00	2579.00	1.11
LN005	RTATM	POST	2470.00	5988.00	6427.00	2751.00	1.24
MA016	RTATM	POST	3679.00	8302.00	9476.00	3233.00	1.32
MN052	RTATM	POST	2998.00	3767.00	6586.00	3102.00	1.32
NY070	RTATM	POST	2251.00	4978.00	4526.00	2573.00	1.17
RE081	RTATM	POST	4833.00	9289.00	9186.00	2795.00	1.22
DG075	RTATM	POST	4441.00	6568.00	8884.00	4059.00	1.38
DN050	RTATM	POST	3644.00	3986.00	8733.00	3292.00	1.32
JF065	RTATM	POST	4141.00	4678.00	8820.00	3968.00	1.43
JS063	RTATM	POST	4663.00	6160.00	8983.00	3682.00	1.35
JY019	RTATM	POST	6365.00	7261.00	11875.00	3392.00	1.29
MT008	RTATM	POST	4746.00	5040.00	11401.00	4023.00	1.44
TT024	RTATM	POST	4939.00	5520.00	11785.00	3976.00	1.41
TY010	RTATM	POST	4607.00	4707.00	11100.00	3887.00	1.29
BA058	RTLTM	PRE	2293.00	7586.00	5213.00	3153.00	1.24
BH057	RTLTM	PRE	2673.00	8624.00	6052.00	3386.00	1.26
DE029	RTLTM	PRE	2889.00	5244.00	5705.00	2794.00	1.25
LE060	RTLTM	PRE	2915.00	7137.00	5957.00	2840.00	1.25
LN051	RTLTM	PRE	2407.00	5764.00	5983.00	2650.00	1.12
NY040	RTLTM	PRE	3712.00	4429.00	6981.00	3035.00	1.27
PI089	RTLTM	PRE	2635.00	5061.00	6060.00	2891.00	1.26
SE035	RTLTM	PRE	3689.00	7819.00	7354.00	3492.00	1.39
CS061	RTLTM	PRE	3628.00	5223.00	9258.00	3860.00	1.42
DD071	RTLTM	PRE	3760.00	5353.00	8103.00	3195.00	1.23
GT074	RTLTM	PRE	3723.00	5275.00	8689.00	3213.00	1.25
LN038	RTLTM	PRE	4486.00	5569.00	9509.00	3363.00	1.26
MW068	RTLTM	PRE	4859.00	12918.00	10665.00	3852.00	1.34
RR025	RTLTM	PRE	4722.00	4715.00	11184.00	4610.00	1.50
RY092	RTLTM	PRE	3857.00	3001.00	8014.00	2943.00	1.14
WL091	RTLTM	PRE	4014.00	3769.00	9674.00	3909.00	1.34
BA058	RTLTM	POST	2467.00	6977.00	5318.00	2978.00	1.28
BH057	RTLTM	POST	2921.00	9048.00	6004.00	3436.00	1.25
DE029	RTLTM	POST	2906.00	5132.00	5877.00	2735.00	1.25
LE060	RTLTM	POST	2936.00	6858.00	6168.00	2767.00	1.26
LN051	RTLTM	POST	2631.00	5650.00	6277.00	2449.00	1.15
NY040	RTLTM	POST	3556.00	4630.00	6869.00	3043.00	1.27
PI089	RTLTM	POST	2867.00	4690.00	6549.00	2756.00	1.24
SE035	RTLTM	POST	3497.00	7352.00	7398.00	3710.00	1.39
CS061	RTLTM	POST	3650.00	4983.00	9842.00	3731.00	1.42
DD071	RTLTM	POST	3962.00	5082.00	8758.00	3115.00	1.24
GT074	RTLTM	POST	3696.00	5152.00	8549.00	3243.00	1.22

LN038	RTLTM	POST	4174.00	4426.00	9038.00	3311.00	1.23
MW068	RTLTM	POST	4958.00	12183.00	12183.00	3907.00	1.33
RR025	RTLTM	POST	5489.00	3955.00	12884.00	4370.00	1.49
RY092	RTLTM	POST	4050.00	2541.00	8817.00	2836.00	1.15
WL091	RTLTM	POST	4078.00	3660.00	10257.00	3828.00	1.33
AN054	RT	PRE	2654.00	9371.00	6003.00	3920.00	1.33
BK088	RT	PRE	4657.00	11551.00	8652.00	3073.00	1.28
JL017	RT	PRE	2961.00	11373.00	7013.00	3845.00	1.28
KE067	RT	PRE	2740.00	8527.00	5675.00	3203.00	1.26
KY066	RT	PRE	2962.00	9073.00	6135.00	3254.00	1.20
MA037	RT	PRE	3053.00	5627.00	6062.00	2384.00	1.13
PI006	RT	PRE	.	.	.	2638.00	1.21
SN009	RT	PRE	2842.00	5722.00	5581.00	2336.00	1.12
AW021	RT	PRE	3618.00	4016.00	8725.00	3201.00	1.24
BE085	RT	PRE	3713.00	3121.00	9118.00	3841.00	1.45
DD015	RT	PRE	3873.00	4637.00	8675.00	3607.00	1.24
JN001	RT	PRE	5318.00	7927.00	11586.00	3891.00	1.34
MK093	RT	PRE	4256.00	4799.00	9416.00	3811.00	1.44
SM072	RT	PRE	4482.00	5089.00	9310.00	4010.00	1.42
TS042	RT	PRE	4161.00	6147.00	8432.00	3874.00	1.32
AN054	RT	POST	2478.00	9509.00	5604.00	3900.00	1.32
BK088	RT	POST	4581.00	10557.00	9345.00	3014.00	1.29
JL017	RT	POST	3009.00	11727.00	7506.00	3720.00	1.31
KE067	RT	POST	2776.00	9007.00	5834.00	3274.00	1.25
KY066	RT	POST	3204.00	9170.00	6731.00	2862.00	1.26
MA037	RT	POST	3134.00	5953.00	6117.00	2488.00	1.10
PI006	RT	POST	.	.	.	2660.00	1.22
SN009	RT	POST	2614.00	5966.00	5762.00	2324.00	1.10
AW021	RT	POST	3907.00	3873.00	9413.00	3192.00	1.25
BE085	RT	POST	3935.00	3261.00	9305.00	3946.00	1.39
DD015	RT	POST	3857.00	4810.00	8777.00	3585.00	1.29
JN001	RT	POST	5336.00	7316.00	12025.00	3968.00	1.31
MK093	RT	POST	4374.00	5010.00	9571.00	3797.00	1.41
SM072	RT	POST	4112.00	5702.00	8314.00	4184.00	1.41
TS042	RT	POST	4255.00	5628.00	8537.00	3730.00	1.33

RAW DATA / DEPENDENT VARIABLES / AEROBIC CAPACITY

SUBID	Group	TIME	TOTAL TIME	VO2max ml/kg	VO2max L/min	MAX HR
BE090	RTATM	PRE	7.42	24.50	1.76	175
CE033	RTATM	PRE	7.13	27.6	1.75	171

LA013	RTATM	PRE	7.95	27.9	1.797	183
LN005	RTATM	PRE	9.66	37.4	2.86	208
MA016	RTATM	PRE	6.83	26.2	2.717	191
MN052	RTATM	PRE	10.30	36.6	2.457	201
NY070	RTATM	PRE	7.93	29.10	1.85	179
RE081	RTATM	PRE	6.12	18.00	2.26	163
DG075	RTATM	PRE	8.38	26.10	2.84	182
DN050	RTATM	PRE	11.16	39.6	3.17	197
JF065	RTATM	PRE	8.98	34.30	3.50	170
JS063	RTATM	PRE	7.28	24.5	2.615	170
JY019	RTATM	PRE	8.27	28.9	3.606	165
MT008	RTATM	PRE	9.75	32.2	3.316	187
TT024	RTATM	PRE	9.66	31	3.39	195
TY010	RTATM	PRE	12.06	44.6	4.362	195
BE090	RTATM	POST	9.00	28.80	2.12	175
CE033	RTATM	POST	8.46	30.5	1.928	174
LA013	RTATM	POST	7.90	31.6	2.089	185
LN005	RTATM	POST	10.57	39	2.923	210
MA016	RTATM	POST	8.15	26.6	2.841	188
MN052	RTATM	POST	11.75	43.9	3.038	198
NY070	RTATM	POST	7.75	29.20	1.86	185
RE081	RTATM	POST	6.25	21.10	2.63	162
DG075	RTATM	POST	9.00	29.80	3.30	185
DN050	RTATM	POST	12.75	45.3	3.76	193
JF065	RTATM	POST	10.55	36.6	3.6	180
JS063	RTATM	POST	7.50	26.5	2.873	164
JY019	RTATM	POST	8.00	29.4	3.829	163
MT008	RTATM	POST	10.75	38.6	4.02	182
TT024	RTATM	POST	10.25	38.9	4.298	190
TY010	RTATM	POST	13.13	46.5	4.571	197
BA058	RTLTM	PRE	7.36	25.4	1.791	187
BH057	RTLTM	PRE	6.50	22	1.852	184
DE029	RTLTM	PRE	6.56	28.7	2.098	178
LE060	RTLTM	PRE	7.86	27.1	2.116	171
LN051	RTLTM	PRE	8.46	28.8	1.916	189
NY040	RTLTM	PRE	6.85	22.9	1.842	149
PI089	RTLTM	PRE	11.10	43.1	2.92	203
SE035	RTLTM	PRE	6.75	24.2	2.56	191
CS061	RTLTM	PRE	11.23	39.6	3.798	200
DD071	RTLTM	PRE	10.22	36.8	3.258	171
GT074	RTLTM	PRE	12.32	42.2	3.712	192
LN038	RTLTM	PRE	6.93	22.7	2.288	192
MW068	RTLTM	PRE	7.40	27.3	3.754	185

RR025	RTLTM	PRE	11.26	39.5	3.986	173
RY092	RTLTM	PRE	10.20	37.8	2.751	191
WL091	RTLTM	PRE	10.45	35.6	3.043	190
BA058	RTLTM	POST	9.53	31.70	2.212	192
BH057	RTLTM	POST	7.53	24.50	2.074	175
DE029	RTLTM	POST	7.45	29.40	2.153	173
LE060	RTLTM	POST	7.95	30.80	2.414	170
LN051	RTLTM	POST	10.25	37.80	2.612	190
NY040	RTLTM	POST	8.50	30.20	2.445	149
PI089	RTLTM	POST	13.25	48.70	3.250	203
SE035	RTLTM	POST	7.41	29.70	3.006	190
CS061	RTLTM	POST	12.68	45.90	4.350	202
DD071	RTLTM	POST	11.50	39.80	3.574	171
GT074	RTLTM	POST	12.62	47.90	4.214	192
LN038	RTLTM	POST	8.67	32.80	2.918	185
MW068	RTLTM	POST	10.50	35.60	4.791	189
RR025	RTLTM	POST	12.50	47.50	4.885	179
RY092	RTLTM	POST	11.75	42.60	3.118	185
WL091	RTLTM	POST	12.75	42.40	3.729	188
AN054	RT	PRE	7.08	25.6	2.287	180
BK088	RT	PRE	5.23	18	2.321	181
JL017	RT	PRE	6.60	24.5	2.436	160
KE067	RT	PRE	7.68	24.6	2.101	181
KY066	RT	PRE	6.92	24.6	2.251	177
MA037	RT	PRE	6.1	23.8	1.997	180
PI006	RT	PRE	11.03	38.8	2.303	181
SN009	RT	PRE	7.15	23	1.539	178
AW021	RT	PRE	10.75	39.9	3.289	202
BE085	RT	PRE	10.5	37.3	3.153	188
DD015	RT	PRE	10.43	39.4	3.272	200
JN001	RT	PRE	8.83	29.2	3.79	171
MK093	RT	PRE	9.82	34.6	3.323	171
SM072	RT	PRE	9.57	31	3.154	182
TS042	RT	PRE	8.88	27.9	2.708	192
AN054	RT	POST	7.30	26.2	2.375	170
BK088	RT	POST	5.75	20.60	2.56	177
JL017	RT	POST	7.00	24	2.471	177
KE067	RT	POST	7.00	25.00	2.14	182
KY066	RT	POST	7.25	24.00	2.22	176
MA037	RT	POST	6.13	24.7	2.113	175
PI006	RT	POST	11.10	38.1	2.251	194
SN009	RT	POST	7.12	26.8	1.859	180
AW021	RT	POST	11.30	42	3.5	201

BE085	RT	POST	10.00	39.30	3.45	181
DD015	RT	POST	12.00	43.4	3.67	190
JN001	RT	POST	9.50	27.7	3.454	170
MK093	RT	POST	10.70	38.70	3.68	176
SM072	RT	POST	10.80	32.20	3.33	183
TS042	RT	POST	10.25	36.3	3.426	188

RAW DATA / DEPENDENT VARIABLES / DIET AND ACTIVITY

SUBID	Group	TIME	DAILY EXP	TOT CAL	TOT Kj	CHO (g)	REL CHO	CHO%
BE090	RTATM	PRE	8467	2488	10414.77	352.00	4.90	0.57
CE033	RTATM	PRE	7912	897	3754.84	117.00	1.84	0.52
LA013	RTATM	PRE	7981	1442	6036.21	137.00	2.12	0.38
LN005	RTATM	PRE	9680	2037	8527.93	332.60	4.34	0.65
MA016	RTATM	PRE	11125	2843	11900.80	.	.	.
MN052	RTATM	PRE	8412	2223	9305.48	296.00	4.40	0.53
NY070	RTATM	PRE	8181	.	.	.	.	.
RE081	RTATM	PRE	12670	.	.	.	.	.
DG075	RTATM	PRE	12554	2447	10243.14	179.00	1.65	0.29
DN050	RTATM	PRE	10600	1943	8133.40	247.00	3.08	0.51
JF065	RTATM	PRE	12734	2126	8899.44	218.00	2.13	0.41
JS063	RTATM	PRE	12391	2416	10113.38	245.00	2.29	0.41
JY019	RTATM	PRE	13858	3405	14253.33	394.00	3.15	0.46
MT008	RTATM	PRE	12065	4192	17546.37	448.46	4.33	0.43
TT024	RTATM	PRE	13097	3845	16095.17	415.00	3.79	0.43
TY010	RTATM	PRE	12346	4826	20199.96	568.51	5.80	0.47
BE090	RTATM	POST	8606	2540	10632.44	365.00	4.96	0.57
CE033	RTATM	POST	7842	1353	5663.66	190.00	3.00	0.54
LA013	RTATM	POST	8050	1731	7245.97	196.00	2.96	0.45
LN005	RTATM	POST	9483	1756	7351.54	228.43	3.05	0.52
MA016	RTATM	POST	11345	960	4018.56	117.00	.	0.49
MN052	RTATM	POST	8695	1903	7965.96	218.00	3.13	0.45
NY070	RTATM	POST	8181	.	.	.	.	.
RE081	RTATM	POST	12670	.	.	.	.	.
DG075	RTATM	POST	12635	2509	10502.67	189.00	1.70	0.30
DN050	RTATM	POST	10891	2058	8614.79	275.00	3.31	0.48
JF065	RTATM	POST	12443	1937	8108.28	243.00	2.46	0.37
JS063	RTATM	POST	12554	.	.	.	.	.
JY019	RTATM	POST	14347	3373	14119.38	402.00	3.08	0.48
MT008	RTATM	POST	12146	2317	9698.25	239.42	2.30	0.41

TT024	RTATM	POST	13183	2992	12524.51	368.00	3.33	0.44
TY010	RTATM	POST	12443	3759	15735.17	476.00	4.83	0.42
BA058	RTLTM	PRE	8397	944	3951.58	113.00	1.60	0.48
BH057	RTLTM	PRE	9726	2517	10536.16	224.00	2.65	0.36
DE029	RTLTM	PRE	8917	1964	8221.30	238.00	3.21	0.48
LE060	RTLTM	PRE	9285	1686	7057.60	256.00	3.26	0.61
LN051	RTLTM	PRE	8412	2396	10029.66	276.00	4.14	0.46
NY040	RTLTM	PRE	9358	1483	6207.84	164.00	2.04	0.44
PI089	RTLTM	PRE	8506	1707	7145.50	174.00	2.56	0.41
SE035	RTLTM	PRE	11271	2103	8803.16	245.00	2.32	0.47
CS061	RTLTM	PRE	12555	.	.	.	.	.
DD071	RTLTM	PRE	10924	2260	9460.36	275.00	3.11	0.49
GT074	RTLTM	PRE	11376	.	.	.	.	.
LN038	RTLTM	PRE	12069	1357	5680.40	176.00	1.80	0.52
MW068	RTLTM	PRE	16806	3224	13495.66	446.00	3.24	0.55
RR025	RTLTM	PRE	11902	2690	11260.34	319.00	3.15	0.47
RY092	RTLTM	PRE	9620	2851	11934.29	372.00	5.12	0.52
WL091	RTLTM	PRE	11040	3297	13801.24	371.00	4.33	0.43
BA058	RTLTM	POST	8328	1280	5358.08	185.00	2.64	0.58
BH057	RTLTM	POST	9726	2089	8744.55	237.00	2.80	0.45
DE029	RTLTM	POST	8843	1501	6283.19	178.00	2.42	0.47
LE060	RTLTM	POST	9285	1284	5374.82	167.00	2.12	0.52
LN051	RTLTM	POST	8601	2570	10758.02	295.00	4.26	0.46
NY040	RTLTM	POST	9358	1690	7074.34	195.00	2.40	0.46
PI089	RTLTM	POST	8412	.	.	.	.	.
SE035	RTLTM	POST	10903	2621	10971.51	335.00	3.30	0.51
CS061	RTLTM	POST	12454	.	.	.	.	.
DD071	RTLTM	POST	11005	2231	9338.97	281.00	3.14	0.50
GT074	RTLTM	POST	11376	.	.	.	.	.
LN038	RTLTM	POST	11298	1236	5173.90	235.00	2.64	0.53
MW068	RTLTM	POST	16502	2266	9485.48	287.00	2.13	0.51
RR025	RTLTM	POST	12065	2558	10707.79	300.00	2.91	0.47
RY092	RTLTM	POST	9620	3052	12775.67	431.00	5.89	0.57
WL091	RTLTM	POST	11212	4290	17957.94	563.00	6.38	0.53
AN054	RT	PRE	10963	2894	12114.28	362.00	4.04	0.50
BK088	RT	PRE	12965	.	.	.	.	.
JL017	RT	PRE	10410	2457	10284.33	343.24	3.44	0.56
KE067	RT	PRE	9438	.	.	.	.	.
KY066	RT	PRE	11160	.	.	.	.	.
MA037	RT	PRE	9653	1150	4813.90	.	.	.
PI006	RT	PRE	8002	2590	10840.44	335.42	5.63	0.52
SN009	RT	PRE	8401	2344	9811.31	272.04	4.05	0.46
AW021	RT	PRE	11138	1911	8000.24	277.48	3.40	0.58

BE085	RT	PRE	10598	2626	10992.44	260.00	3.07	0.40
DD015	RT	PRE	10891	2777	11626.03	416.66	5.01	0.60
JN001	RT	PRE	14265	2233	9349.05	260.20	2.00	0.47
MK093	RT	PRE	11331	1817	7605.84	185.00	1.97	0.25
SM072	RT	PRE	11983	.	.	.	.	.
TS042	RT	PRE	11983	1458	6103.19	161.00	1.65	0.44
AN054	RT	POST	11062	.	.	.	.	.
BK088	RT	POST	12597	2693	11272.90	386.00	3.10	0.57
JL017	RT	POST	10618	2457	10284.33	343.24	3.32	0.56
KE067	RT	POST	9438	.	.	.	.	.
KY066	RT	POST	11260	.	.	.	.	.
MA037	RT	POST	9799	1123	4700.88	109.00	1.27	0.39
PI006	RT	POST	7904	2588	10833.37	309.00	5.23	0.48
SN009	RT	POST	8549	2405	10068.59	276.00	3.97	0.46
AW021	RT	POST	11341	2103	8803.16	267.00	3.20	0.47
BE085	RT	POST	10842	2258	9451.15	245.00	2.78	0.43
DD015	RT	POST	11085	2874	12030.56	398.00	4.70	0.46
JN001	RT	POST	14102	3712	15540.44	631.62	4.95	0.68
MK093	RT	POST	11413	1564	6546.90	97.00	1.02	0.25
SM072	RT	POST	11983	.	.	.	.	.
TS042	RT	POST	11812	1511	6326.26	163.00	1.72	0.43

SUBID	Group	TIME	PRO (g)	REL PRO	PRO%	TOT FAT (g)	REL FAT
BE090	RTATM	PRE	81.00	1.13	0.13	84.00	1.17
CE033	RTATM	PRE	33.00	0.52	0.15	33.00	0.52
LA013	RTATM	PRE	39.00	0.60	0.11	82.00	1.27
LN005	RTATM	PRE	35.30	0.46	0.07	62.85	0.82
MA016	RTATM	PRE	.	.	.	.	.
MN052	RTATM	PRE	73.00	1.09	0.13	83.00	1.23
NY070	RTATM	PRE	.	.	.	.	.
RE081	RTATM	PRE	.	.	.	.	.
DG075	RTATM	PRE	129.00	1.19	0.21	135.00	1.24
DN050	RTATM	PRE	88.00	1.10	0.18	67.00	0.84
JF065	RTATM	PRE	156.00	1.53	0.29	70.00	0.68
JS063	RTATM	PRE	107.00	1.00	0.18	112.00	1.05
JY019	RTATM	PRE	158.00	1.26	0.19	133.00	1.06
MT008	RTATM	PRE	164.85	1.59	0.16	193.16	1.87
TT024	RTATM	PRE	166.00	1.52	0.17	169.00	1.54
TY010	RTATM	PRE	177.90	1.82	0.15	204.44	2.09
BE090	RTATM	POST	90.00	1.22	0.13	80.00	1.09
CE033	RTATM	POST	56.00	0.88	0.17	41.00	0.65

LA013	RTATM	POST	77.00	1.16	0.18	71.00	1.07
LN005	RTATM	POST	68.92	0.92	0.16	62.98	0.84
MA016	RTATM	POST	33.00	0.31	0.14	40.00	0.37
MN052	RTATM	POST	89.00	1.28	0.18	75.00	1.08
NY070	RTATM	POST	.	.	.	.	.
RE081	RTATM	POST	.	.	.	.	.
DG075	RTATM	POST	148.00	1.33	0.24	129.00	1.16
DN050	RTATM	POST	91.00	1.09	0.16	66.00	0.79
JF065	RTATM	POST	86.00	0.87	0.13	69.00	0.70
JS063	RTATM	POST	.	.	.	.	.
JY019	RTATM	POST	151.00	1.16	0.18	129.00	0.99
MT008	RTATM	POST	89.70	0.86	0.15	111.15	1.07
TT024	RTATM	POST	128.00	1.16	0.15	112.00	1.01
TY010	RTATM	POST	115.00	1.17	0.10	155.00	1.57
BA058	RTLTM	PRE	51.00	0.72	0.22	32.00	0.45
BH057	RTLTM	PRE	133.00	1.57	0.21	121.00	1.43
DE029	RTLTM	PRE	64.00	0.86	0.13	84.00	1.13
LE060	RTLTM	PRE	71.00	0.90	0.17	42.00	0.54
LN051	RTLTM	PRE	98.00	1.47	0.16	100.00	1.50
NY040	RTLTM	PRE	56.00	0.70	0.15	67.00	0.83
PI089	RTLTM	PRE	75.00	1.11	0.18	79.00	1.16
SE035	RTLTM	PRE	76.00	0.72	0.14	91.00	0.86
CS061	RTLTM	PRE	.	.	.	.	.
DD071	RTLTM	PRE	119.00	1.34	0.21	76.00	0.86
GT074	RTLTM	PRE	.	.	.	.	.
LN038	RTLTM	PRE	71.00	0.73	0.21	41.00	0.42
MW068	RTLTM	PRE	135.00	0.98	0.17	100.00	0.73
RR025	RTLTM	PRE	106.00	1.05	0.16	110.00	1.09
RY092	RTLTM	PRE	91.00	1.25	0.13	111.00	1.53
WL091	RTLTM	PRE	136.00	1.59	0.16	141.00	1.65
BA058	RTLTM	POST	45.00	0.64	0.14	40.00	0.57
BH057	RTLTM	POST	76.00	0.90	0.15	93.00	1.10
DE029	RTLTM	POST	60.00	0.82	0.16	61.00	0.83
LE060	RTLTM	POST	64.00	0.81	0.20	40.00	0.51
LN051	RTLTM	POST	91.00	1.31	0.14	114.00	1.64
NY040	RTLTM	POST	61.00	0.75	0.15	74.00	0.91
PI089	RTLTM	POST	.	.	.	.	.
SE035	RTLTM	POST	75.00	0.74	0.11	109.00	1.08
CS061	RTLTM	POST	.	.	.	59.00	0.62
DD071	RTLTM	POST	117.00	1.31	0.21	71.00	0.79
GT074	RTLTM	POST	.	.	.	.	.
LN038	RTLTM	POST	74.00	0.83	0.17	.	.
MW068	RTLTM	POST	104.00	0.77	0.18	78.00	0.58

RR025	RTLTM	POST	101.00	0.98	0.16	106.00	1.03
RY092	RTLTM	POST	125.00	1.71	0.16	92.00	1.26
WL091	RTLTM	POST	145.00	1.64	0.14	162.00	1.84
AN054	RT	PRE	114.00	1.27	0.16	110.00	1.23
BK088	RT	PRE	.	.	.	.	.
JL017	RT	PRE	80.98	0.81	0.13	84.44	0.85
KE067	RT	PRE	.	.	.	.	.
KY066	RT	PRE	.	.	.	.	.
MA037	RT	PRE	.	.	.	.	.
PI006	RT	PRE	165.19	2.77	0.26	65.25	1.10
SN009	RT	PRE	113.85	1.70	0.19	88.92	1.33
AW021	RT	PRE	79.65	0.97	0.17	53.63	0.66
BE085	RT	PRE	104.00	1.23	0.16	130.00	1.53
DD015	RT	PRE	101.82	1.23	0.15	78.16	0.94
JN001	RT	PRE	94.46	0.73	0.17	90.53	0.70
MK093	RT	PRE	100.20	1.07	0.29	75.13	0.80
SM072	RT	PRE	.	.	.	.	.
TS042	RT	PRE	64.00	0.66	0.18	62.00	0.64
AN054	RT	POST	.	.	.	.	.
BK088	RT	POST	96.00	0.77	0.14	85.00	0.68
JL017	RT	POST	80.98	0.78	0.13	84.44	0.82
KE067	RT	POST	.	.	.	.	.
KY066	RT	POST	.	.	.	.	.
MA037	RT	POST	48.00	0.56	0.17	55.00	0.64
PI006	RT	POST	149.00	2.52	0.23	84.00	1.42
SN009	RT	POST	110.00	1.58	0.18	95.70	1.38
AW021	RT	POST	90.00	1.08	0.16	75.00	0.90
BE085	RT	POST	101.20	1.15	0.18	97.00	1.10
DD015	RT	POST	100.00	1.18	0.12	98.00	1.16
JN001	RT	POST	51.52	0.40	0.06	108.88	0.85
MK093	RT	POST	114.00	1.19	0.29	80.00	0.84
SM072	RT	POST	.	.	.	.	.
TS042	RT	POST	78.00	0.82	0.21	60.81	0.64

SUBID	Group	TIME	TOTFAT%	MONO (g)	POLY (g)	SAT (g)
BE090	RTATM	PRE	0.30	11.00	4.00	24.00
CE033	RTATM	PRE	0.33	2.66	2.44	11.31
LA013	RTATM	PRE	0.51	6.00	8.00	33.00
LN005	RTATM	PRE	0.28	27.97	8.03	20.65
MA016	RTATM	PRE	.	.	.	.

MN052	RTATM	PRE	0.34	10.00	5.00	32.00
NY070	RTATM	PRE	.	.	.	.
RE081	RTATM	PRE	.	.	.	.
DG075	RTATM	PRE	0.50	46.00	7.00	52.00
DN050	RTATM	PRE	0.31	9.00	5.00	18.00
JF065	RTATM	PRE	0.30	16.00	6.00	21.00
JS063	RTATM	PRE	0.42	18.00	5.00	38.00
JY019	RTATM	PRE	0.35	40.60	13.57	45.29
MT008	RTATM	PRE	0.41	53.15	20.15	73.24
TT024	RTATM	PRE	0.40	40.39	26.22	48.23
TY010	RTATM	PRE	0.38	54.06	9.75	83.12
BE090	RTATM	POST	0.30	10.00	4.00	22.00
CE033	RTATM	POST	0.29	6.00	4.00	14.00
LA013	RTATM	POST	0.37	6.00	4.00	25.00
LN005	RTATM	POST	0.32	8.60	6.70	22.37
MA016	RTATM	POST	0.38	2.66	2.44	11.31
MN052	RTATM	POST	0.35	5.00	1.00	23.00
NY070	RTATM	POST	.	.	.	.
RE081	RTATM	POST	.	.	.	.
DG075	RTATM	POST	0.46	38.00	9.00	49.00
DN050	RTATM	POST	0.26	5.00	5.00	19.00
JF065	RTATM	POST	0.24	1.00	0.01	19.00
JS063	RTATM	POST	.	.	.	.
JY019	RTATM	POST	0.34	39.00	12.20	43.00
MT008	RTATM	POST	0.43	22.55	0.81	38.13
TT024	RTATM	POST	0.30	15.00	7.00	32.00
TY010	RTATM	POST	0.31	13.00	5.00	47.00
BA058	RTLTM	PRE	0.31	3.00	1.00	9.00
BH057	RTLTM	PRE	0.43	19.00	8.00	33.00
DE029	RTLTM	PRE	0.38	14.71	6.44	28.00
LE060	RTLTM	PRE	0.22	0.00	0.00	14.00
LN051	RTLTM	PRE	0.38	9.00	3.00	31.00
NY040	RTLTM	PRE	0.41	7.00	5.00	26.00
PI089	RTLTM	PRE	0.42	32.00	14.00	24.00
SE035	RTLTM	PRE	0.39	14.00	5.00	33.00
CS061	RTLTM	PRE	.	.	.	.
DD071	RTLTM	PRE	0.30	12.00	15.00	13.00
GT074	RTLTM	PRE	.	.	.	.
LN038	RTLTM	PRE	0.27	9.00	5.00	14.00
MW068	RTLTM	PRE	0.28	4.00	7.00	39.00
RR025	RTLTM	PRE	0.37	32.01	16.18	36.83
RY092	RTLTM	PRE	0.35	22.00	10.00	36.00
WL091	RTLTM	PRE	0.37	26.00	12.00	47.00

BA058	RTLTM	POST	0.28	8.00	3.00	11.00
BH057	RTLTM	POST	0.40	12.00	3.00	31.00
DE029	RTLTM	POST	0.37	6.00	1.00	21.00
LE060	RTLTM	POST	0.28	4.00	2.00	14.00
LN051	RTLTM	POST	0.40	16.00	11.00	29.00
NY040	RTLTM	POST	0.39	9.00	11.00	26.00
PI089	RTLTM	POST	.	.	.	.
SE035	RTLTM	POST	0.37	24.00	9.00	40.00
CS061	RTLTM	POST	0.30	10.00	6.00	19.00
DD071	RTLTM	POST	0.29	11.00	15.00	11.00
GT074	RTLTM	POST	.	.	.	.
LN038	RTLTM	POST	.	.	.	.
MW068	RTLTM	POST	0.31	4.00	2.00	29.00
RR025	RTLTM	POST	0.37	30.01	15.00	35.00
RY092	RTLTM	POST	0.27	37.00	12.00	31.00
WL091	RTLTM	POST	0.34	27.00	20.00	52.00
AN054	RT	PRE	0.34	20.00	9.00	35.00
BK088	RT	PRE	.	.	.	.
JL017	RT	PRE	0.31	20.67	12.96	30.02
KE067	RT	PRE	.	.	.	.
KY066	RT	PRE	.	.	.	.
MA037	RT	PRE	.	.	.	.
PI006	RT	PRE	0.23	14.47	9.63	21.20
SN009	RT	PRE	0.34	7.36	5.64	19.36
AW021	RT	PRE	0.25	8.88	5.77	18.03
BE085	RT	PRE	0.45	48.00	21.00	34.00
DD015	RT	PRE	0.25	11.98	5.72	31.07
JN001	RT	PRE	0.36	22.89	9.28	28.42
MK093	RT	PRE	0.46	28.00	12.00	32.00
SM072	RT	PRE	.	.	.	.
TS042	RT	PRE	0.38	16.00	4.00	20.00
AN054	RT	POST	.	.	.	.
BK088	RT	POST	0.28	11.98	5.72	31.07
JL017	RT	POST	0.31	20.67	12.96	30.02
KE067	RT	POST	.	.	.	.
KY066	RT	POST	.	.	.	.
MA037	RT	POST	0.44	20.00	8.00	20.00
PI006	RT	POST	0.29	5.00	8.00	24.00
SN009	RT	POST	0.36	8.50	5.64	21.36
AW021	RT	POST	0.30	7.00	4.00	22.00
BE085	RT	POST	0.39	24.00	18.00	31.00
DD015	RT	POST	0.26	13.00	5.00	35.00
JN001	RT	POST	0.26	4.17	6.71	16.38

MK093	RT	POST	0.46	28.00	12.00	32.00
SM072	RT	POST	.	.	.	.
TS042	RT	POST	0.36	16.00	4.00	20.00

RAW DATA / DEPENDENT VARIABLES / STRENGTH

SUBID	Group	TIME	LEG PRESS	CHEST PRESS	LEG CURL	LAT PULL	LEG EXT
BE090	RTATM	PRE	449	57	100	102	82
CE033	RTATM	PRE	402	47	107	80	83
LA013	RTATM	PRE	300	50	108	78	59
LN005	RTATM	PRE	578	66	144	102	92
MA016	RTATM	PRE	824	72	165	147	120
MN052	RTATM	PRE	580	86	158	149	124
NY070	RTATM	PRE	395	40	102	75	69
RE081	RTATM	PRE	897	77	112	108	88
DG075	RTATM	PRE	789	115	169	159	133
DN050	RTATM	PRE	856	151	158	190	169
JF065	RTATM	PRE	771	97	188	139	151
JS063	RTATM	PRE	758	124	170	176	95
JY019	RTATM	PRE	869	176	200	188	170
MT008	RTATM	PRE	1092	144	163	172	194
TT024	RTATM	PRE	1030	200	253	220	163
TY010	RTATM	PRE	850	150	230	207	180
BE090	RTATM	POST	526	75	120	114	115
CE033	RTATM	POST	533	71	133	97	91
LA013	RTATM	POST	453	61	137	97	93
LN005	RTATM	POST	640	103	179	132	141
MA016	RTATM	POST	1054	112	207	155	180
MN052	RTATM	POST	704	102	215	156	178
NY070	RTATM	POST	647	60	108	100	93
RE081	RTATM	POST	1278	102	157	137	122
DG075	RTATM	POST	1102	145	212	194	150
DN050	RTATM	POST	1278	200	244	215	238
JF065	RTATM	POST	1059	113	219	167	219
JS063	RTATM	POST	1114	164	208	215	142
JY019	RTATM	POST	1229	260	291	252	241
MT008	RTATM	POST	1670	175	289	239	276
TT024	RTATM	POST	1554	222	297	260	199
TY010	RTATM	POST	1387	215	317	247	277
BA058	RTLTM	PRE	374	42	106	86	86

BH057	RTLTM	PRE	622	51	103	97	91
DE029	RTLTM	PRE	659	91	131	124	74
LE060	RTLTM	PRE	446	42	94	75	78
LN051	RTLTM	PRE	618	62	123	97	121
NY040	RTLTM	PRE	528	61	105	87	88
PI089	RTLTM	PRE	618	78	156	117	142
SE035	RTLTM	PRE	705	80	188	133	139
CS061	RTLTM	PRE	974	168	169	195	216
DD071	RTLTM	PRE	715	118	165	185	173
GT074	RTLTM	PRE	813	178	188	226	166
LN038	RTLTM	PRE	699	115	172	151	139
MW068	RTLTM	PRE	774	133	208	162	180
RR025	RTLTM	PRE	1176	134	251	200	218
RY092	RTLTM	PRE	557	104	158	160	140
WL091	RTLTM	PRE	751	115	195	156	168
BA058	RTLTM	POST	524	56	119	97	100
BH057	RTLTM	POST	789	75	148	107	129
DE029	RTLTM	POST	742	105	141	134	107
LE060	RTLTM	POST	489	58	109	98	113
LN051	RTLTM	POST	753	99	155	116	152
NY040	RTLTM	POST	642	73	129	116	123
PI089	RTLTM	POST	705	92	181	184	152
SE035	RTLTM	POST	1111	100	192	140	159
CS061	RTLTM	POST	1288	194	278	238	321
DD071	RTLTM	POST	825	144	239	229	214
GT074	RTLTM	POST	931	159	231	219	206
LN038	RTLTM	POST	818	135	206	167	188
MW068	RTLTM	POST	1018	145	274	199	244
RR025	RTLTM	POST	1459	174	263	257	276
RY092	RTLTM	POST	679	109	189	181	167
WL091	RTLTM	POST	686	159	286	203	246
AN054	RT	PRE	553	74	140	124	72
BK088	RT	PRE	867	66	149	124	103
JL017	RT	PRE	597	74	144	126	133
KE067	RT	PRE	641	69	100	86	84
KY066	RT	PRE	510	56	131	91	94
MA037	RT	PRE	599	64	124	97	97
PI006	RT	PRE	635	75	108	90	92
SN009	RT	PRE	373	48	88	82	82
AW021	RT	PRE	684	135	189	204	163
BE085	RT	PRE	819	164	168	159	156
DD015	RT	PRE	699	130	172	189	150
JN001	RT	PRE	947	140	129	172	133

MK093	RT	PRE	821	111	167	176	139
SM072	RT	PRE	630	110	205	156	157
TS042	RT	PRE	645	94	152	156	157
AN054	RT	POST	745	91	173	124	142
BK088	RT	POST	867	86	168	182	157
JL017	RT	POST	798	92	159	129	152
KE067	RT	POST	754	82	135	114	116
KY066	RT	POST	619	63	157	112	122
MA037	RT	POST	832	66	151	102	126
PI006	RT	POST	840	98	151	121	144
SN009	RT	POST	538	68	115	107	100
AW021	RT	POST	769	153	234	230	235
BE085	RT	POST	1064	210	212	222	182
DD015	RT	POST	886	151	222	226	202
JN001	RT	POST	1336	180	276	247	244
MK093	RT	POST	1016	135	222	237	210
SM072	RT	POST	856	134	249	204	135
TS042	RT	POST	807	131	201	202	190

SUBID	Group	TIME	TRI PUSH DOWN	BICEPS CURL	TOTALLFT
BE090	RTATM	PRE	191	31	1012
CE033	RTATM	PRE	142	20	881
LA013	RTATM	PRE	118	17	730
LN005	RTATM	PRE	198	30	1210
MA016	RTATM	PRE	213	44	1585
MN052	RTATM	PRE	222	56	1375
NY070	RTATM	PRE	121	17	819
RE081	RTATM	PRE	161	24	1467
DG075	RTATM	PRE	222	60	1647
DN050	RTATM	PRE	343	52	1919
JF065	RTATM	PRE	230	47	1623
JS063	RTATM	PRE	259	57	1639
JY019	RTATM	PRE	309	76	1988
MT008	RTATM	PRE	265	54	2084
TT024	RTATM	PRE	400	84	2350
TY010	RTATM	PRE	367	70	2054
BE090	RTATM	POST	212	39	1201
CE033	RTATM	POST	177	33	1135
LA013	RTATM	POST	167	28	1036
LN005	RTATM	POST	284	37	1516
MA016	RTATM	POST	237	53	1998

MN052	RTATM	POST	282	51	1688
NY070	RTATM	POST	195	25	1228
RE081	RTATM	POST	234	34	2064
DG075	RTATM	POST	312	60	2175
DN050	RTATM	POST	469	68	2712
JF065	RTATM	POST	395	62	2234
JS063	RTATM	POST	427	82	2352
JY019	RTATM	POST	468	97	2838
MT008	RTATM	POST	564	91	3304
TT024	RTATM	POST	650	101	3283
TY010	RTATM	POST	470	88	3001
BA058	RTLTM	PRE	121	13	828
BH057	RTLTM	PRE	152	32	1148
DE029	RTLTM	PRE	237	33	1349
LE060	RTLTM	PRE	132	20	887
LN051	RTLTM	PRE	180	19	1220
NY040	RTLTM	PRE	137	21	1027
PI089	RTLTM	PRE	223	35	1369
SE035	RTLTM	PRE	245	39	1529
CS061	RTLTM	PRE	360	74	2156
DD071	RTLTM	PRE	246	48	1650
GT074	RTLTM	PRE	405	74	2050
LN038	RTLTM	PRE	225	41	1542
MW068	RTLTM	PRE	286	60	1803
RR025	RTLTM	PRE	314	57	2350
RY092	RTLTM	PRE	244	53	1416
WL091	RTLTM	PRE	235	60	1680
BA058	RTLTM	POST	156	28	1080
BH057	RTLTM	POST	234	41	1523
DE029	RTLTM	POST	306	43	1578
LE060	RTLTM	POST	175	30	1072
LN051	RTLTM	POST	275	33	1583
NY040	RTLTM	POST	181	29	1293
PI089	RTLTM	POST	235	46	1595
SE035	RTLTM	POST	321	42	2065
CS061	RTLTM	POST	428	88	2835
DD071	RTLTM	POST	396	69	2116
GT074	RTLTM	POST	370	89	2205
LN038	RTLTM	POST	338	59	1911
MW068	RTLTM	POST	367	86	2333
RR025	RTLTM	POST	447	80	2956
RY092	RTLTM	POST	283	62	1670
WL091	RTLTM	POST	358	81	2019

AN054	RT	PRE	216	34	1213
BK088	RT	PRE	185	32	1526
JL017	RT	PRE	215	29	1318
KE067	RT	PRE	170	22	1172
KY066	RT	PRE	186	18	1086
MA037	RT	PRE	194	29	1204
PI006	RT	PRE	211	24	1235
SN009	RT	PRE	140	25	838
AW021	RT	PRE	328	80	1783
BE085	RT	PRE	217	58	1741
DD015	RT	PRE	287	65	1692
JN001	RT	PRE	242	59	1822
MK093	RT	PRE	247	64	1725
SM072	RT	PRE	246	68	1572
TS042	RT	PRE	247	51	1502
AN054	RT	POST	303	36	1614
BK088	RT	POST	261	49	1770
JL017	RT	POST	249	41	1620
KE067	RT	POST	231	39	1471
KY066	RT	POST	252	34	1359
MA037	RT	POST	253	33	1563
PI006	RT	POST	237	43	1634
SN009	RT	POST	200	32	1160
AW021	RT	POST	486	112	2219
BE085	RT	POST	357	81	2328
DD015	RT	POST	394	80	2161
JN001	RT	POST	412	95	2790
MK093	RT	POST	425	79	2324
SM072	RT	POST	366	72	2016
TS042	RT	POST	288	73	1892

RAW DATA / DEPENDENT VARIABLES / Myofibrillar FSR

SUBID	Group	TIME	Plama MPE(%)	Muscle MPE(%)	FSR %/day
BE090	RTATM	PRE	0.926524658	0.4193425	0.122323578
CE033	RTATM	PRE	0.962054497	0.530577461	0.149055292
LA013	RTATM	PRE	0.769633571	0.461722261	0.162141836
LN005	RTATM	PRE	.	.	.
MA016	RTATM	PRE	0.845165021	0.357156075	0.114212806
MN052	RTATM	PRE	0.924749494	0.658898702	0.19257186
NY070	RTATM	PRE	.	.	.

RE081	RTATM	PRE	.	.	.
DG075	RTATM	PRE	0.786530297	0.451729541	0.155224873
DN050	RTATM	PRE	0.643587967	0.350848564	0.147336403
JF065	RTATM	PRE	0.792773868	0.291042023	0.09922124
JS063	RTATM	PRE	0.579911642	0.432484989	0.201561456
JY019	RTATM	PRE	0.69851372	0.433974776	0.167914354
MT008	RTATM	PRE	0.961563326	0.302877611	0.085130965
TT024	RTATM	PRE	.	.	.
TY010	RTATM	PRE	.	.	.
BE090	RTATM	POST	0.655366995	0.491443308	0.202668912
CE033	RTATM	POST	.	.	.
LA013	RTATM	POST	0.908254863	0.621392225	0.18490828
LN005	RTATM	POST	.	.	.
MA016	RTATM	POST	1.809227697	1.080651576	0.161432413
MN052	RTATM	POST	0.570916804	0.292586884	0.138509737
NY070	RTATM	POST	.	.	.
RE081	RTATM	POST	.	.	.
DG075	RTATM	POST	0.842844728	0.494751752	0.158649257
DN050	RTATM	POST	0.689703823	0.501190932	0.196398808
JF065	RTATM	POST	0.999089836	0.568169699	0.15369927
JS063	RTATM	POST	0.521280559	0.471576034	0.24449978
JY019	RTATM	POST	0.822108095	0.290901001	0.095634495
MT008	RTATM	POST	0.808531733	0.566633111	0.189410109
TT024	RTATM	POST	.	.	.
TY010	RTATM	POST	1.109702065	0.602734788	0.146797324
BA058	RTLTM	PRE	1.07000089	0.713024642	0.180102058
BH057	RTLTM	PRE	.	.	.
DE029	RTLTM	PRE	.	.	.
LE060	RTLTM	PRE	.	.	.
LN051	RTLTM	PRE	2.313421867	0.977378987	0.114184311
NY040	RTLTM	PRE	.	.	.
PI089	RTLTM	PRE	0.605465639	0.226415409	0.101068252
SE035	RTLTM	PRE	.	.	.
CS061	RTLTM	PRE	.	.	.
DD071	RTLTM	PRE	.	.	.
GT074	RTLTM	PRE	1.001598602	0.34639416	0.093470621
LN038	RTLTM	PRE	.	.	.
MW068	RTLTM	PRE	.	.	.
RR025	RTLTM	PRE	1.013092559	0.307947607	0.082153484
RY092	RTLTM	PRE	0.952144962	0.334789806	0.095031466
WL091	RTLTM	PRE	1.748886632	0.419576364	0.064840691
BA058	RTLTM	POST	1.333012403	0.734340287	0.148888598
BH057	RTLTM	POST	.	.	.

DE029	RTLTM	POST	0.579323625	0.249578998	0.116435409
LE060	RTLTM	POST	.	.	.
LN051	RTLTM	POST	.	.	.
NY040	RTLTM	POST	.	.	.
PI089	RTLTM	POST	0.662871436	0.489605819	0.199625282
SE035	RTLTM	POST	.	.	.
CS061	RTLTM	POST	.	.	.
DD071	RTLTM	POST	.	.	.
GT074	RTLTM	POST	0.917583366	0.558679565	0.164556685
LN038	RTLTM	POST	.	.	.
MW068	RTLTM	POST	.	.	.
RR025	RTLTM	POST	0.550610436	0.371962473	0.182579899
RY092	RTLTM	POST	0.696618073	0.255736747	0.099219418
WL091	RTLTM	POST	.	.	.
AN054	RT	PRE	.	.	.
BK088	RT	PRE	.	.	.
JL017	RT	PRE	0.895142596	0.284245087	0.085822077
KE067	RT	PRE	2.152167487	0.781122987	0.098093816
KY066	RT	PRE	.	.	.
MA037	RT	PRE	.	.	.
PI006	RT	PRE	.	.	.
SN009	RT	PRE	.	.	.
AW021	RT	PRE	.	.	.
BE085	RT	PRE	1.159549097	0.237845226	0.055437492
DD015	RT	PRE	0.668443658	0.185225599	0.074891836
JN001	RT	PRE	0.980967851	0.387400957	0.106734345
MK093	RT	PRE	0.613376852	0.284914644	0.125541024
SM072	RT	PRE	0.959968573	0.256479433	0.072209411
TS042	RT	PRE	.	.	.
AN054	RT	POST	.	.	.
BK088	RT	POST	.	.	.
JL017	RT	POST	0.949489385	0.425922308	0.12123794
KE067	RT	POST	.	.	.
KY066	RT	POST	.	.	.
MA037	RT	POST	.	.	.
PI006	RT	POST	.	.	.
SN009	RT	POST	.	.	.
AW021	RT	POST	.	.	.
BE085	RT	POST	1.118944596	0.345645628	0.083487366
DD015	RT	POST	0.738035765	0.368798422	0.135054768
JN001	RT	POST	0.754197505	0.524042242	0.187793035
MK093	RT	POST	1.195422655	0.563456263	0.127390489
SM072	RT	POST	0.966476357	0.686643298	0.192016358

TS042	RT	POST	.	.	.

RAW DATA / DEPENDENT VARIABLES / WESTERN BLOT DATA

SUBID	Group	TIME	Akt	mTOR	TSC2
BE090	RTATM	PRE	0.519572954	0.244094488	.
CE033	RTATM	PRE	3.307692308	1.43902439	2.473684211
LA013	RTATM	PRE	.	.	
LN005	RTATM	PRE	5.857142857	.	0.1
MA016	RTATM	PRE	7.571428571	9.11	3.266666667
MN052	RTATM	PRE	.	.	.
NY070	RTATM	PRE	.	.	.
RE081	RTATM	PRE	.	.	.
DG075	RTATM	PRE	0.727272727	1.446808511	0.11444
DN050	RTATM	PRE	0.636085627	0.555944056	2.278688525
JF065	RTATM	PRE	0.4	0.681818182	0.807692308
JS063	RTATM	PRE	1.0559	.	.
JY019	RTATM	PRE	0.47826087	.	.
MT008	RTATM	PRE	.	2.672413793	0.768831169
TT024	RTATM	PRE	.	.	.
TY010	RTATM	PRE	.	2.034482759	1.083116883
BE090	RTATM	POST	0.398576512	0.488188976	0.166666667
CE033	RTATM	POST	6.615384615	1.731707317	2.842105263
LA013	RTATM	POST	.	.	.
LN005	RTATM	POST	7	.	.
MA016	RTATM	POST	7.714285714	11.44	2.566666667
MN052	RTATM	POST	.	.	.
NY070	RTATM	POST	.	.	.
RE081	RTATM	POST	.	.	.
DG075	RTATM	POST	1.25	1.484042553	0.95666
DN050	RTATM	POST	1.244648318	0.692307692	1.918032787
JF065	RTATM	POST	0.5	0.787878788	0.884615385
JS063	RTATM	POST	3.54037	.	.
JY019	RTATM	POST	0.925465839	.	.
MT008	RTATM	POST	.	2.017241379	0.846753247
TT024	RTATM	POST	.		
TY010	RTATM	POST	.	2.155172414	1.168831169
BA058	RTLTM	PRE	1.54696	3.428571429	0.454545455
BH057	RTLTM	PRE	0.869009585	0.7	.
DE029	RTLTM	PRE	1.693950178	0.826771654	.
LE060	RTLTM	PRE	.	.	.
LN051	RTLTM	PRE	1.871429	1.26	2.566666667
NY040	RTLTM	PRE	.	.	.

PI089	RTLTM	PRE	.	.	.
SE035	RTLTM	PRE	.	.	.
CS061	RTLTM	PRE	.	.	.
DD071	RTLTM	PRE	.	.	.
GT074	RTLTM	PRE	1.36453202	2.263157895	1.2
LN038	RTLTM	PRE	.	.	.
MW068	RTLTM	PRE	.	.	.
RR025	RTLTM	PRE	.	.	.
RY092	RTLTM	PRE	0.641943734	0.63	.
WL091	RTLTM	PRE	.	.	.
BA058	RTLTM	POST	1.54696	2.428571429	.
BH057	RTLTM	POST	1.460063898	0.765	0.818181818
DE029	RTLTM	POST	0.704626335	0.377952756	.
LE060	RTLTM	POST	.	.	.
LN051	RTLTM	POST	1.00006	0.90	2.533333333
NY040	RTLTM	POST	.	.	.
PI089	RTLTM	POST	.	.	.
SE035	RTLTM	POST	.	.	.
CS061	RTLTM	POST	.	.	.
DD071	RTLTM	POST	.	.	.
GT074	RTLTM	POST	1.461412151	2	0.475862069
LN038	RTLTM	POST	.	.	.
MW068	RTLTM	POST	.	.	.
RR025	RTLTM	POST	.	.	.
RY092	RTLTM	POST	0.199488491	0.04	.
WL091	RTLTM	POST	.	.	.
AN054	RT	PRE			
BK088	RT	PRE	0.306709265	1.8	3.090909091
JL017	RT	PRE	2.925266904	0.346456693	.
KE067	RT	PRE	.	.	.
KY066	RT	PRE	.	.	.
MA037	RT	PRE	.	.	.
PI006	RT	PRE	.	.	.
SN009	RT	PRE	2.26037196	2.50862069	2.553246753
AW021	RT	PRE	.	.	.
BE085	RT	PRE	1.692307692	0.682926829	0.210526316
DD015	RT	PRE	0.896797153	1.031496063	.
JN001	RT	PRE	3.425	2.045454545	1.076923077
MK093	RT	PRE	2.272727273	1.15	0.631147541
SM072	RT	PRE	.	3.7	0.618
TS042	RT	PRE	.	.	.
AN054	RT	POST	.	.	.
BK088	RT	POST	0.597444089	1.4	1.909090909

JL017	RT	POST	1.982206406	0.393700787	.
KE067	RT	POST	.	.	.
KY066	RT	POST	.	.	.
MA037	RT	POST	.	.	.
PI006	RT	POST	.	.	.
SN009	RT	POST	3.295622318	3.672413793	1.176623377
AW021	RT	POST	.	.	.
BE085	RT	POST	5.076923077	0.951219512	1.368421053
DD015	RT	POST	1.419928826	1.464566929	.
JN001	RT	POST	1.175	1.212121212	0.75
MK093	RT	POST	2.693181818	5.46	0.663934426
SM072	RT	POST	.	4.55	0.545
TS042	RT	POST	.	.	.

APPENDIX H

VITA

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EDUCATION

Bachelor of Science: Kinesiology, 2006
Department of Health and Kinesiology, Texas Lutheran University, Seguin, TX

Doctor of Philosophy: Kinesiology 2013
Department of Health and Kinesiology, Texas A&M University, College Station, TX

GRADUATE HONORS AND AWARDS

2013: American College of Sports Medicine (Texas Chapter)
Student Manuscript Award Winner, TACSM Annual Meeting

2012: Department of Education, Texas A&M University
Strategic Academic Fellowship: $20,000

2011: American College of Sports Medicine (Texas Chapter)
Student Research Presentation Award (2nd Place). TACSM Annual Meeting.

2010: Sydney & J.L. Huffines Institute for Sports Medicine and Human Performance, Texas A&M University
Graduate Research Grant: $1,000 Title: "Acute and chronic intracellular responses to concurrent aerobic and resistance exercise as well as the incorporation of underwater treadmill running."

2009: National Strength and Conditioning Association
Student Research Grant, Doctoral Category: $10,000
Title: "Acute and chronic intracellular responses to concurrent aerobic and resistance exercise as well as the incorporation of underwater treadmill running: A novel approach for minimizing the interference effect."

2009: Texas A&M University Student Research Week Award, April 2009.
Session winner award: $300.00

PROFESSIONAL MEMBERSHIPS

2008-present: American College of Sports Medicine
2009-present: Texas Chapter of the American College of Sports Medicine
2008-present: Collegiate Strength and Conditioning Coaches Association
2008-present: National Strength and Conditioning Association

PUBLICATIONS

Nicholas P. Greene and Brad S. Lambert (Co-First Authors), Alex T. Carradine, Dustin P. Joubert, James D. Fluckey, Steven E. Riechman, and Stephen F. Crouse. Aquatic Treadmill Training Reduces Blood Pressure Reactivity to Physical Stress. *Medicine & Science in Sports & Exercise* Publish Ahead of Print: 10.1249/MSS.0000000000000167, 2013.

Brad S. Lambert, Jonathan M. Oliver, John S. Green, Steven E. Martin, Stephen F. Crouse. DEXA or BMI: Clinical Considerations for Evaluating Obesity in Collegiate Division I-A American Football Athletes. *Clinical Journal of Sports Medicine* 22(5):436-438, 2012. PMID 22805182

Nicholas P. Greene, Steven E. Riechman, Brad S. Lambert, Elizabeth S. Greene, James D. Fluckey, and Stephen F. Crouse. Regulators of Blood Lipids and Lipoproteins? PPARδ and AMPK, Induced by Exercise, are Correlated with Lipids and Lipoproteins in Overweight/Obese Men and Women. *American Journal of Physiology-Endocrinology And Metabolism* 2012. 303(10):212-221, 2012. PMID 22990076

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