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Effects of Shroom Tech Sport Supplementation and Concurrent Training on Body Composition, Performance, and Health in Collegiate-Aged Men

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EFFECTS OF SHROOM TECH SPORT SUPPLEMENTATION AND CONCURRENT

TRAINING ON BODY COMPOSITION, PERFORMANCE, AND HEALTH IN

COLLEGIATE-AGED MEN

By

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This dissertation is dedicated to my family (Christine Kreipke, Tyler Kreipke, Donald Kreipke, and Shirley Kreipke) and friends. Your love and support has been my rock throughout this journey. Without you, none of this would be possible. Thank you. I love you all.

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ABSTRACT

Background: Skeletal muscle is highly responsive to exercise training stresses, resulting in specific performance improvements based on the type of training undertaken (65, 118). Among all the variations of exercise training there are two extremes: 1) resistance training (RT) and 2) aerobic training (AT). The combination AT and RT is termed concurrent training (CT). This combination has been shown to have positive effects on body composition through decreases in fat mass (92, 135, 180, 462) and aerobic performance (27, 55, 153, 193, 393, 420, 462). Despite these positive outcomes, there have been multiple studies suggesting that the combination of these two training modalities hinders increases in strength (27, 180, 222, 419), power (153, 419), and fat free mass (222, 237, 403, 419). Notably, CT composed of high intensity interval training (HIIT) and RT has been shown to positively affect aerobic performance without negatively affecting strength in recreationally active men (55, 432, 471) and women (432). In attempts to further augment performance, many individuals have looked to nutritional supplementation, consisting of both conventional and herbal ingredients. Interestingly, rhodiola rosea (RR) (33, 101, 370) and cordyceps sinensis (CS) (60) may have potential to enhance muscle endurance at high intensities. **Purpose:** To determine the effects of CT, composed of HIIT and RT, and Shroom Tech Sport[tm] (SUP), a multi-ingredient performance supplement (MIPS) containing RR and CS, on body composition, aerobic and strength performance, cardiometabolic profiles, and hormone concentrations in young recreationally active men. **Methods:** Recreationally active men were stratified and matched by age, total strength, relative VO_2max, percent body fat, and training years; then assigned to take SUP (n=10) or a placebo (PLA) (n=11). Participants completed a 12-week CT program (4 days per week; 2 days: total body RT; 2 days: HIIT). Supplements (1 capsule (792mg) per 23kg) were consumed 45 minutes before each training and testing sessions and at breakfast on non-training days. Body composition, blood draws, and strength, power and aerobic performance were tested at week 0, and after weeks six and 12 of training. Additionally, subjects completed three-day food logs for dietary intake. Data were reported as mean ± SD. Dependent variables were assessed by two-way (group x time) analysis of variance (ANOVA). Significance was accepted at $p<0.05$. **Results:** There were no differences between groups in any of the participant characteristics. There were no significant differences in body mass index, fat free mass or percent fat free mass. However, there was a significant time effect for percent body fat, with

both groups exhibiting decreases (SUP: pre $15.5 \pm 5.8\%$ v mid $14.8 \pm 7.2\%$ v post $14.2 \pm 6.6\%$; PLA: pre $16.2 \pm 6.7\%$ v mid $15.3 \pm 6.5\%$ v post $14.3 \pm 6.4\%$; p=0.0065), with no significant differences between groups. There were main group (p= 0.042) and time (p=0.016) effects for fat mass but no group x time interactions (SUP: pre 11.92 ± 5.28kg v mid 11.51 ± 6.22kg v post 11.10 ± 6.96 kg; PLA: pre 12.83 ± 6.55kg v mid 12.23 ± 6.61kg v post 11.32 ± 6.49kg). There were no significant differences in circumferences or lean mass index (LMI). There were no changes in VO$_2$max. Both groups improved bench (SUP: $2.6\pm3.0\%$; PLA: $5.4\pm5.2\%$) and squat (SUP: $7.2\pm6.6\%$; PLA: $8.8\pm5.4\%$) strength. There was a main effect for time in max (p=0.007) and average power (p=0.004) but no differences between groups. Notably, significant differences were observed between groups in average bench (SUP: 28 ± 1reps v PLA: 25 ± 3, p<0.05) and total (bench + squat) (SUP: 61 ± 4reps v PLA: 57 ± 4; p<0.05) training volumes at "moderate" (72.5-77.5%) intensities. Further, SUP also attenuated decreases in average running volume at 100% calculated max speed (CMS) when compared to those at 90% CMS versus PLA (SUP:-41±83secs v PLA:-135±118, p<0.05). There were no group x time interactions in any of the hormone concentrations. There were time effects for systolic blood pressure, total cholesterol, LDL, and HDL, with decreases in total cholesterol (SUP: Pre: 152 ± 22mg/dL to Mid: 142 ± 23mg/dl to Post: 147 ± 23mg/dl v PLA: Pre: 154 ± 29mg/dl to Mid: 142 ± 22mg/dl to Post: 143 ± 22mg/dl; p=0.009), LDL (SUP: Pre: 83 ± 26mg/dL to Mid: 74 ± 14mg/dl to Post: 80 ± 26mg/dl v PLA: Pre: 82 ± 24mg/dl to Mid: 70 ± 13mg/dl to Post: 76 ± 18mg/dl; p=0.047) and HDL (SUP: Pre: 48 ± 11mg/dL to Mid: 45 ± 10mg/dl to Post: 44 ± 7mg/dl v PLA: Pre: 60 ± 12mg/dl to Mid: 55 ± 12mg/dl to Post: 54 ± 10mg/dl; p=0.013). **Conclusion:** Supplementation with SUP, 45 minutes prior to exercise, enhanced moderate intensity resistance exercise performance and max intensity HIIT performance in recreationally trained men. Additionally, 12 weeks of CT protocol consisting of progressive RT and HIIT improved strength and power performance while decreasing fat mass; however, there were no differences between groups. Therefore, use of SUP (792mg per 23kg of body weight) for 12 weeks may be beneficial for resistance training at moderate intensities and aerobic training at maximal intensity may be beneficial for recreationally active men.

CHAPTER 1

INTRODUCTION

1.1 Background

Skeletal muscle is highly responsive to exercise training stresses. Depending on the training modality selected, skeletal muscle has been shown to exhibit an array of changes including: increases in size, contractile properties, size and number of mitochondrial content, and oxidative properties. These changes lead to specific performance improvements based on the type of training undertaken (65, 118). Among all the variations of exercise training there are two traditional modalities exist: 1) RT, often associated with high intensity (+60% of one rep max (1RM)) for short duration ($\leq$ 60 seconds per set of exercise), and 2) AT, consisting of lower intensity (< 60% VO_2max) repetitive movements for substantially greater durations, traditionally lasting longer than 20 minutes. Consequently, both modes of training elicit very different physiological adaptions. RT has been shown to stimulate myofibrillar protein synthesis resulting in muscular hypertrophy (124, 490) and enhanced muscle cell recruitment (120), leading to increases in maximal strength (120, 124, 490). Conversely, AT increases mitochondrial protein content (biogenesis) and respiratory enzyme activity, resulting in greater electron transport capacity and, thus, a rise in adenosine triphosphate (ATP) production (190). Interestingly, endurance trained muscle tissue exhibits altered substrate metabolism by lowering muscle glycogen and blood glucose dependency and promoting greater utilization of fat during exercise. As a result, aerobically trained muscle has lower lactate production during submaximal exercise (191). Together, these adaptations to AT result in increased aerobic capacity (173).

As the outcomes are vastly different from RT and AT, the molecular pathways that elicit skeletal muscle adaptations are also quite different. Interestingly, human skeletal muscle fibers exist in multiple phenotypes (Type I, IIa, and IIx), which display various capacities for different intensities and durations of physical activity. The expression of these differing phenotypes can be further enhanced with continuous bouts of the same modality of exercise, Indeed a single bout of either mode cannot elicit significant hypertrophic or mitochondrial biogenesis responses, but the accumulation of specific training overtime will alter muscle phenotypes (106, 118, 389), resulting in changes in specific protein expression and functional capacity (322).

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CT is the combination AT and RT. Though body composition can be altered through either increases in lean mass or decreases in fat mass, CT has been shown to have positive effects on body composition through decreases in fat mass (92, 135, 180, 462). Interestingly, CT has also demonstrated positive outcomes in aerobic performance such as increases in VO_2max (27, 55, 153, 193, 420, 462) and running economy (393). Despite these positive outcomes in body composition and AT, pioneering work by Robert Hickson (180) suggests that the CT hinders strength adaptations after 10 weeks of training compared to RT alone (CT: +25% :RT:+ 44%; p<0.05). These original data have been corroborated numerous times for muscle mass (222, 237, 403, 419) and strength (27, 222, 419) and power (153, 419) performance.

Conversely, not all research is in agreement that CT does hinder increases in lean body mass (27, 153, 222, 314, 315, 432) strength (55, 135, 153, 193, 222, 471) and muscular power (55, 135). These differences are often due to the differences in training methodology. For example, frequency (222, 315) chronological separation between exercise sessions (26, 153, 316), and AT modality (315, 316), duration of study (315, 316) and intensity (55, 432, 471) have been shown to influence CT outcomes (350).

Furthermore, dietary supplementation has become prevalent across multiple populations including military personnel (256) and all levels of athletics (123, 198, 535) contributing to $32 billion in annual sales for this market reported in 2012 (290). Performance enhancing supplements have become a popular subgroup of dietary supplements. Many of these ingredients have been shown in increase strength (15), endurance (189) and recovery (347), which can further influence body composition. These common ingredients found in performance enhancing supplements are often combined into blends for potential synergistic effects and are commonly referred to as multi-ingredient performance supplements (MIPS). Though these products are often comprised of a plethora of ingredients, creatine monohydrate, caffeine, beta-alanine, and branched-chain amino acids have come to the forefront and are the common ingredients for many of these MIPSs.

Additionally, herbs such as rhodiola rosea (RR) (33) and cordyceps sinensis (CS) (60) may also have potential to enhance performance. Indeed, RR has been shown to influence substrate use in favor of fat during submaximal exercise (382) and increase time to exhaustion (RR: 17.2 ± 0.8min v PLA: 16.8 ± 0.7min; p<0.05)) and VO_2 peak (RR: 52.9 ± 2.7ml/kg/min v PLA: 50.9 ±

1.8ml/kg/min) (33). Likewise, animals receiving CS supplementation also exhibited increases swim time to exhaustion by 1.79-fold when compared to PLA (287). Additionally, a combination of CS and rhodiola crenulata (RC), a herb in the same genus as RR which exhibits many of the same characteristics of RR, elicited significantly greater increases in time to exhaustion than the placebo intervention (59). The current literature suggests that both of these herbal supplements have potential to extend time to exhaustion, albeit in regards to aerobic training. These findings may greatly benefit RT and HIIT performance which has the potential to enhance body composition and aerobic and strength adaptions. To date, the potential benefits of supplementation with RR and CS in a MIPS has yet to be examined in combination with other exercise protocols.

1.2 Purpose

The purpose of the present study was to determine the effects of daily supplementation with Shroom Tech Sport (SUP) (792mg /23kg), a MIPS containing RR and CS, in combination with a 12-week CT protocol, consisting of total body RT and HIIT, on strength, power and aerobic performance, hormone concentrations, and cardiometabolic markers in recreationally trained collegiate aged men.

1.3 Specific Aims

The following specific aims were tested in the current project:

1. To what extent 12 weeks (792mg /23kg) of SUP in combination with 12 weeks of CT will improve body composition (fat mass and fat free mass) in recreationally trained collegiate-aged men?
2. To what extent 12 weeks (792mg /23kg) of SUP in combination with 12 weeks of CT will improve strength (squat and bench), power (Wingate), and aerobic (VO_2max and lactate threshold) performance in recreationally trained collegiate-aged men?
3. To what extent 12 weeks (792mg /23kg) of SUP in combination with 12 weeks of CT will alter resting hormonal (total and free testosterone, estrogen, cortisol, insulin, insulin-like growth factor-I) and damage marker (creatine kinase) concentrations in recreationally trained collegiate-aged men?

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4. To what extent 12 weeks (792mg /23kg) of SUP in combination with 12 weeks of CT will alter cardiometabolic (total cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein and glucose) profiles in recreationally trained collegiate-aged men?

1.4 Research Hypotheses

The working hypotheses are as follows:

1. Collegiate-aged recreationally trained men consuming SUP (792mg /23kg) will exhibit greater increases in fat free mass and greater decrements in fat mass compared to PLA (792mg /23kg).
2. Collegiate-aged recreationally trained men consuming SUP (792mg /23kg) will exhibit greater increases strength (bench and squat), power and aerobic (VO_2max and lactate threshold) and demonstrate attenuation of fatigue in anaerobic power (Wingate) performance compared to PLA (792mg /23kg).
3. Collegiate-aged recreationally trained men consuming SUP (792mg /23kg) will exhibit greater increases resting anabolic hormone and damage marker concentrations compared to PLA (792mg /23kg).
4. Collegiate-aged recreationally trained men consuming SUP (792mg /23kg) will exhibit similar cardiometabolic profiles compared to PLA (792mg /23kg).

1.5 Assumptions

Assumptions for the current study are as follows:

1. All participants gave full effort during training and performance testing sessions.
2. All tests were performed in a fasted state.
3. All participants followed non-training day prescribed supplementation protocol regarding SUP or PLA.
4. All participants accurately reported food consumption for the three day food log.
5. All participants accurately reported past emotions for the Profile of Mood States (POMS) questionnaire.

1.6 Delimitations

The delimitations of the current study are as follows:

1. Only collegiate aged men were allowed to participate in the current study.
2. All subjects are recreationally trained and meet the following criteria:
   a. All subjects had at least two years training experience
   b. All subjects were able to squat their body weight
   c. All participants had a VO_2max of at least 40ml/kg/min.
3. All training was supervised by either certified fitness professionals or individual who had received training in regards to exercise protocol and expectations
4. All training day supplementation was monitored by research personnel.
5. All subjects did not have any prior history of muscular or skeletal disorders.
6. All participants did not have any prior history of anabolic steroid use.
7. All participants were non-smokers.
8. All participants using supplements followed a four week wash-out period before participation.

1.7 Limitations

The limitations of the current study are as follows:

1. SUP is composed of a proprietary blend of ingredients. Thus, individual ingredients could not be adjusted for differing body masses among individuals.
2. Dosing of SUP was based upon body mass, as directed by the manufacturer, which may have resulted in individuals receiving various amounts of the ingredients.
3. Dietary intake was monitored through three-day food logs and not directly controlled. Thus, the present study relied on the honesty in recordings.

1.8 Definition of Terms

- Concurrent Training (CT): is the combination of resistance and aerobic training.

- Resistance Training (RT): Often is associated with high intensity (+60%) for short duration (≤ 60 seconds per bout of exercise) with the focus of muscle strength and/or hypertrophy. Further, this mode of exercise often uses free weights and machines for training specific body parts.

- Aerobic Training (AT): is training focused on increasing aerobic capacity. Traditionally, aerobic training consisting of lower intensity repetitive movements for substantially greater durations.

- High Intensity Interval Training (HIIT): Aerobic training that consists of repeated bouts of high intensity (+80% VO_2max) efforts.

- Multi-ingredient Performance Supplement (MIPS): is a nutritional supplement that consists of multiple ingredients in order to further augment either aerobic or resistance training.

- Lean Mass Index (LMI): represents the overall positive change in body composition, decreases in fat mass and increases in lean mass.

- One Rep Max (1RM): The maximal amount of weight that can be for one repetition.

CHAPTER 2

REVIEW OF LITERATURE

2.1 Skeletal Muscle Plasticity

2.1.1 Hypertrophy

2.1.1.1 Cellular pathway. Though the processes are still not fully understood, protein-kinase B (PKB; also known as AKT) is the main effector of mammalian target of rapamycin complex 1 (mTORC1), which is a pivotal mediator in increasing muscle protein synthesis. Consequently, muscle growth is dependent on the activation of this pathway in response to environmental stimuli (nutrient and hormonal growth factors, mitochondrial signals and RT) (35, 87, 95). Despite conflicting results (67, 86), there is overall supportive evidence for activation of PKB-mTORC1 signaling in anabolic processes from both acute (94) and chronic (297, 536) bouts of RT. Further, PKB has been shown to inhibit catabolic signaling (354, 493). Farther down the cascade, mTORC1 targets effectors 70kDa ribosomal protein S6 kinase (p70^{S6k}) and eIF4E-binging protein (4E-BP1) (36, 106). Additionally, it has been suggested that p70^{S6k} applies its effects through a multitude of substrate targets and has been implicated in the regulation of cell size and protein synthesis (65).

In addition to the PKB-mTORC1 pathway, RT has been shown to affect the mitogen-activated protein-kinase (MAPK) pathway, which is a regulator of gene expression, redox status and metabolism (279). With respect to RT, MAPK has been shown to link cellular stress in myocytes to modulating growth and differentiation responses (424). Continuing down this signaling cascade are three signaling proteins that are activated by MAPK, extracellular signal-related kinases (ERK 1/2), p38 MAPK, and c-Jun NH$_2$-terminal kinase (JNK). Of these three proteins, it has been suggested that JNK is the most responsive to mechanical tension and muscle damage. Activation of JNK through RT has been correlated to rapid rise in mRNA transcription factors that elicit cellular proliferation and DNA repair (11, 12).

Finally, calciuneurin (Cn) is the primary regulatory protein for a calcium dependent pathway for muscular hypertrophy. Cn is a downstream protein associated with PKB activation and is a pivotal component of hypertrophy via insulin-like growth factor-I (IGF-I) stimulation in type I

muscle fibers (431). Through Cn, myocyte enhancing factor 2, GATA transcription factors and nuclear factor of activated T (NFAT) cells, subsequently, promote cellular hypertrophy in type I muscle fibers (338). Additionally, Cn promotes the upregulation of myogenin (MEF) and the downregulation of myostatin; allowing for further promotion of muscle cell hypertrophy (431).

Though muscular hypertrophy is a primary contributor to muscular strength improvements, neural mechanisms also influence maximal strength. RT has been shown to elicit increases in muscle fiber recruitment (154), firing rate (84), and synchrony (340) resulting in more muscle fibers contracting in unison at faster rates and, ultimately, greater contraction strength. These neural adaptions have been shown to not only occur at the motor unit, but also in multiple locations throughout the entire nervous system including: cortical maps, motor command, descending drive, muscle activation, and sensory feedback mechanisms (98). This adaptation throughout this nervous system feedback loop allows for greater sensory of muscle contraction and limb speed, allowing for the nervous system to adjust efferent signals appropriately. Moreover, evidence demonstrates that neural adaptation is the primary mechanism for increases in muscle strength in the first five weeks of RT in untrained limbs, with hypertrophic responses becoming more dominant thereafter (344). Indeed, the combination of increased muscle cell cross sectional area and neural adaption both contribute to the increases in strength development (182).

2.1.1.2 Satellite cell activation. Skeletal muscle myogenesis is the result of the activation of skeletal muscle satellite cells. Initially, satellite cells lay dormant between the basal lamina and sarcolemma of their respective muscle fibers. These cells do not elicit any protein synthesis and have little gene expression. Additionally, skeletal muscle satellite cells must be activated through weight bearing activity, such as exercise, or trauma (143). Briefly, the activation of skeletal muscle satellite cells is reliant upon a multitude influences (immune responses, hormonal environment, autocrine factors and motor neuron input) (172).

Mechanical stretch in myofibers has also been shown to activate intercellular signals resulting in hepatocyte growth factor release and subsequent satellite cell activation (541). Further, this stretch also facilitates increases in nitric oxide concentrations; ultimately eliciting the release of follistatin (396) which has been shown to downregulate myostatin, commonly expressed in quiescent satellite cells. This expression may also aid in facilitating the activation of

satellite cells from quiescence. Further, fibroblast growth factors (FGF) have been shown to elicit MAPK signaling cascades (p38α/β-MAPK) which are necessary for the activation of satellite cells (221). Moreover, the bioactive lipid sphinogosine-1-phsophate (S1P) is required for the satellite cell to enter the cell cycle and facilitate muscle regeneration (309, 355). S1P facilitates the activation of adenylyl cyclase through binding to five G protein coupled receptors (321), eventually affecting cell survival, proliferation, migration and intercellular interaction (548). Likewise, p38α/β can alternatively be upregulated through the activation of the surface protein Cdo through interaction with scaffold protein JLP (484).

Once activated, satellite cells move outside the basal lamina, where they enter the cellular cycle (mitosis) and begin to coexpress pax7, MyoD (143), and CD56 (477). After multiple rounds of division, those cells committed to differentiation will down regulated pax7 and start to express myogenin and MyoD. These myocytes then align, fuse together, and form multinucleated myofibers (143). Alternatively, some cells will maintain Pax7 and downregulate MyoD expression. These cells ultimately leave the cell cycle (376, 552). These cells represent a self-renewing fraction of satellite cells. Interestingly, it has been shown that satellite cells can self-renew, replenish depleted pools, and the resultant cells of these processes are also capable of regeneration as well (70, 343).

Satellite cell myogenic capacity relies on the expression of pax7 and myogenic regulatory factors (MRFs; MyoD, Myf5, myogenin, MRF4). Further, the sequential activation and suppression of pax3/7 and MRFs mediates the progression of skeletal myoblasts through myogenesis (285, 452). While the role of pax7 is still not fully understood, a mouse model has shown that the regenerative abilities of satellite cells depends on the expression of pax7 (433). Additionally, the roles of MyoD and myf5 have been clearly defined. Foremost, MyoD aids in the facilitation of the differentiation potential of skeletal myoblasts (77, 429) while MyF5 moderates their proliferation rate and homeostasis (129, 500). Finally, Myogen and MRF4 are required for the formation of myotubes and fibers (257).

2.1.2 Skeletal Muscle Degradation

Skeletal muscle degradation (atrophy) is more than just the converse of muscle hypertrophy. It is characterized by active pathways stimulated by glucocorticoids and inflammatory cytokines resulting in reduced fiber cross sectional area, protein content which

leads to strength reduction, increased fatigability, and insulin resistance (214, 234). Further, multiple models including denervation, high-dose dexamethasone treatment, induction of inflammatory cytokines, and limb immobilization have been shown to induce muscle atrophy (107).

The muscle atrophy pathway is activated through three mediating proteins (Forkhead box O (FOXO), nuclear factor kappa light chain enhancer of B cells (NF$_K$B) and p38 MAPK) in response to a multitude of upstream stimuli. Notably, the binding of interleukin-1α (IL-1α) and tumor necrosis factor alpha (TNF-α) to their respective receptors initiates the upregulation of NF$_K$B-inducing kinase (NIK) and TGF-β activated kinase 1 (TAK1) converge in the upregulation of the I$_K$B kinase (IKK) complex which results in the expression of NF$_K$B (3, 176). It has been shown that TAK1 is the upstream regulatory protein of mitogen-activated protein kinase kinase 4 (MKK4) and subsequent p38 MAPK (497). The translocation of NF$_K$B and p38 MAPK across the myocyte membrane initiate the upregulation of two pivotal proteins: muscle RING finger-containing protein 1 (MuRF1) and muscle atrophy Fbox protein (MAFbx), which have both been shown to encode for E3 ubiquitin ligases (34, 138) (Figure 1).

Additionally, the binding myostatin, growth differentiation factor 11 (GDF11), activin-a and transforming growth factor beta (TGF-β) to their respective receptors initiates the upregulation of SMAD2,3 (107) resulting in the inhibition of PKB (498) (Figure 1). It has been shown the PKB expression downregulates the expression of FOXO transcription factor member, FKHRL1, which has been shown to induce apoptosis when translocated into the myocyte nucleus (48). Likewise, the expression of mammalian Ste20-like (MST1) kinase has been shown to induce skeletal muscle atrophy through the phosphorylation of FOXO (522). Further, translocation of FOXO across the myocyte nucleus has been shown to mediate the upregulation of MuRF1 (Figure. 1). Specifically, FOXO3 activation has been shown to be adequate to induce atrophy (323, 554). Additionally, the expression of FOXO1 resulted in an atrophic phenotype (336, 469).

MuRF1 elicits atrophy, at least in part, by directly affecting the muscle filament of the sarcomere and causes the proteolysis of myosin proteins (myosin light chain and myosin binding protein C) (69) and the inhibition of protein synthesis (64). Additionally, MuRF1 has been shown to facilitate ubiquitination of myosin heavy and light chains and myosin binding protein C

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(64, 69). Notably, ubiquitination is the joining of the protein ubiquitin to a given protein; resulting in the depletion of the affected proteins. MuRF1 induces the encoding of a protein that contains four domains. RING-finger requires MuRF1's ubiquitin ligase activity to bind to an E2 protein, which facilitates the transfer of ubiquitin to the substrate (219). The next domain in the cascade is a "B-box" which can mediate self-association. The B-box of MuRF1 self-associates in dimers with high affinity (348). The third domain is the "coiled-coil" domain, which may be necessary for the formation of heterodimers between MuRF1 and itself. Further, it may assist in the formation of heterodimers with MuRF2 (540). The final domain of MuRF1, the "MuRF" domain is shared among all three MuRF proteins (MuRF1, MurF2, and MuRF3) (145).

MAFbx contains an Fbox domain, commonly seen in the family of E3 ubiquitin ligases called SCFs (Skp1, Cullin, and Fbox). Fbox containing proteins mediate the binding of the Fbox to the Skp1-Cullin complex, ultimately joining substrates to the E2. Further, Rbx1, a RING-containing protein activates the E2 (232). Fbox containing proteins normally bind a substrate only after that substrate has been posttranslationally altered (539).

MAFbx has been shown to be an E3 ligase for a protein initiation factor, eIF3-f (300) and eIF3c (81, 288) suggesting that MAFbx activity causes muscle atrophy through the downregulation of muscle protein synthesis. Other substrates suggested for MAFbx (MyoD (Lagirand- Cantaloube) and calcineurin (299) though it has not been shown whether they are ubiquitnated by MAFbx in either skeletal muscle or under atrophic conditions.

2.1.3 Mitochondrial Biogenesis

The skeletal muscle adaptions associated with AT results from training stresses that produce significant metabolic challenges within the muscle milieu. In turn, cellular conditions are drastically altered with changes in intracellular concentrations of calcium (Ca^{2+}), oxygen, lactate, reactive oxygen species (ROS), and an increased adenosine monophosphate: adenosine triphosphate (AMP:ATP) and nicotinamide adenine dinucleotide to reduced NAD^+ reduced nicotinamide adenine dinucleotide ratio(NAD^+:NADH) (65). These stresses increase the activation of intercellular 5' adenosine-monophosphate-activated protein kinase (AMPK), Ca^{2+}/ calmodium-dependent protein kinase II (CaMK II), and p38 MAPK pathways. All of these signals converge to peroxisome proliferator-activated receptor-c coactivator-1 (PGC-1α),

ultimately promoting mitochondrial biogenesis (19, 394, 543) increased capillary density(130), and alter substrate utilization (190), resulting in greater aerobic capacity (173).

Prolonged moderate-intensity (60-70% of VO_2max) exercise increases sarcoplasmic reticulum Ca^{2+} uptake and number of active pumps removing Ca^{2+} from the cytoplasm (442). Accordingly, high intensity ($\geq100\%$ VO_2max) exercise has been shown to provoke 20-50% decreases in Ca^{2+} uptake from the cytoplasm and release back into the cytoplasm with a return to basal levels after 60 minutes of recovery (327). These acute changes in cytosolic Ca^{2+} may stimulate secondary events following increases basal concentrations. Likewise, repeated bouts of high intensity cycling produce less disturbance in Ca^{2+} uptake and release, subsequently improving resistance to fatigue in untrained men and women (192). Indeed, Cantrell et al. (55) demonstrate AT in the form of sprint training elicits increases in VO_2max and increases in time to exhaustion.

Further, the process of maintaining redox potential (NAD: NADH) is primarily a result of the catabolic actions occurring with glycolytic and lipolytic metabolism in the mitochondria (65). Maintenance of the redox potential generates ROS, which are then buffered by multiple antioxidant systems in skeletal muscle (9). Redox potential and ROS production during and after exercise may induce beneficial adaptive responses. First, redox state may have direct effects on transcriptional regulation and DNA binding specificity of transcription factors (56, 218). Additionally, ROS concentrations have effects on numerous components of cellular events, which may indirectly act on signaling via effects on mitochondrial metabolism and a decrease in myofilament Ca^{2+} sensitivity (466). In summary, increases in ROS concentrations may lead to adaptations that increase pivotal enzyme expression and muscle phenotype, ultimately resulting in greater aerobic capacity.

The resynthesis of ATP from ADP is produced by oxidative phosphorylation and/ or glycolysis. Consequently, concentrations of metabolites related to these processes of muscle phosphorylation (ATP, ADP and inorganic phosphate (P_i)) provide a feedback signal to balance ATP production with depletion (174). Any process that might cause an imbalance in concentrations between the three metabolites favoring ADP and Pi increases concentrations of intracellular AMP, which is a primary regulator of ATP degradation and synthesis pathways (430). This increase in AMP will then shift the AMP:ATP ratio, resulting in the activation of

AMPK in response to cellular energy depletions (13). Acute activation of AMPK is associated in enhancing ATP concentrations through increasing glucose transporter 4 (GLUT4) expression and insulin sensitivity, thus increasing insulin-dependent glucose uptake (175, 353, 357) and increasing fat oxidation (241, 295). Further, increases in contraction-mediated AMP have been implicated in activating transcription factors associated with mitochondrial fatty acid oxidation (37, 225, 295, 489), subsequently activating AMPK (333) leading to mitochondrial biogenesis.

The growth of the mitochondrial reticulum is highly regulated and complex process that requires the synchronization of multiple gene expression in both the nuclear and mitochondrial genomes (210, 211). While there is no single transcription factor found to be responsible for mitochondrial biogenesis, early growth response gene (Egr-1) and nuclear respiratory factor-1 and -2 (NRF1/2) appear to be the primary regulators (194). Egr-1 has been associated with promoting transcription of the electron transport chain protein cytochrome C oxidase (COX) (122), while NRF1 and NRF2 have been linked to the transcriptional control of multiple mitochondrial genes, including mitochondrial transcription factor A (Tfam) and identified mitochondrial transcription specificity factors including (134, 439). Interestingly, Egr-1 and NRF1/2 appear to respond to muscle contraction (72, 134, 211) and endurance training (19, 461). Additionally, PGC-1α has also been associated with biogenesis due to its apparent activation of multiple mitochondrial transcription factors (194). Thus, PGC-1 has been considered to be the "master" regulator protein of mitochondrial biogenesis (2, 440). Additionally, PGC-1 also mediates Tfam activation acting as a co-activator Tfam, a key component to mitochondrial DNA replication and transcription (235, 325).

PGC-1α also regulates the peroxisome proliferator activated receptor (PPAR) family (374, 503). The three PPAR subtypes regulate lipid homeostasis through the expression of genes involved in mitochondrial fatty acid oxidation (115, 293). Increased expression of PPAR subtypes has been associated with increased fat utilization during extended periods of exercise and may be linked to fast to slow fiber type conversion (317, 521).

Additionally, CaMKII and IV have been associated with the activation of gene expression of both contractile and mitochondrial proteins, respectively (119, 543). CaMKII expression has been shown to be the primary CaMK subtype responsive to endurance exercise, and is upregulated in an intensity-dependent manner (422). Although there is limited evidence,

CaMK activation has demonstrated downstream effects that may be partially mediated through NFAT signaling and histone deacetylase nuclear extrusion through Ca^{2+} signaling (18, 307).

2.1.4 Fiber Type Shifting

In conjunction with hypertrophy and mitochondrial biogenesis, skeletal muscle fibers also have the ability to change their type (i.e. from type I to IIa and IIx). Several factors (nerve patterns, mechanical loading, and hormonal environment) have been shown to influence muscle fiber type expression. Notably fiber-type change requires regulation and coordination of fast and slow gene programs. Present research suggests three mechanisms: 1) transcription factors acting as both activators and repressors 2) bidirectional promoters generating both sense and antisense transcripts and 3) miRNA hosted in Myosin Heavy Chain (MyHC) genes (443). Muscle fiber type switching is the consequence of the combination of these three mechanisms along with the activation of the associated pathways.

Cn is a Ca^{2+}/calmodulin-regulated protein that has been shown to be involved in fiber-type plasticity and fast-to-slow phenotype transformation (338, 360, 384, 486) through the transcription of NFAT (108) (Figure 2). Interestingly, mouse models over expressing Cn have been shown to have a higher increased amount of type I fibers (360). Granted, this increase may not be due to fiber type shifting but it may reflect inhibition of postnatal disappearance of type I fibers. Interestingly, there is also evidence suggesting that overexpression of Cn induces increases in myoglobin (360) and enzymes that facilitate mitochondrial oxidative phosphorylation and lipid metabolism (428, 549). Further, Cn expression upregulates the expression of PPAR β/δ and PGC-1α (549), two transcription factors that influence the upregulation of oxidative gene programing. Conversely, DSCR1 (aka MCIP1, calcipressin and RCAN1) has been shown to inhibit Cn signaling pathways (126, 423), through the binding of COOH-terminal domain to the enzyme active site (57). Further, Oh et al. (375) have shown that the overexpression of DSCR1 in mouse skeletal muscle exhibited normal muscle ratios in early development stages, but began to lose type I fibers in the soleus muscle at postnatal day seven. Further, mice lost all expression of type I by day 14 with all muscle fibers switching to type IIa. In summary, Cn is a pivotal protein in the maintenance and programming of type I muscle fibers.

Though NFAT transcription is mediated by Cn expression, it also acts as a nerve activity sensor in skeletal muscle that controls activity-dependent fiber type specification (443). Indeed,

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it has been shown that unstimulated mouse flexor digitorum brevis, composed primarily of fast-twitch muscle types, exhibited NFATc1-GFP localization in the cytoplasm. But when subjected to low-frequency stimulation, typical of type I fibers, NFATc1-GCP translocated to the nucleus (306). Interestingly, glycogen synthase kinase 3 beta (GSK3β) casein kinase 1 and 2, and dual-specificity tyrosin phosphorylation regulated kinase 1A (DYRK1A) appear to regulate NFACTc1 nuclear export after muscle activity in isolated human skeletal muscle (458) and thus inhibit myogenic differentiation (319).

Additionally, MEF2 transcription factors have been shown to be upregulated by the expression of Cn (542). Briefly, MEF2 has multiple splices (MEF2a, MEF2b, MEF2c and MEF2d) with further variants are generated by alternative splicing (30). Interestingly, these splices exist in equal concentrations in mouse slow and fast twitch muscle fibers (402). Over expression of MEF2 was reported to promote the formation of slow twitch muscle fibers in mouse muscle (402) and have been shown to be active in activity-dependent muscle fiber type remodeling (544).

Interestingly, overexpression of MEF2c (MEF2c-VIP) has been shown to upregulate PGC-1α, but not PGC-1β, in skeletal muscle. Further, it has been shown that Ca^{2+} and CaMK mediate MEF2 activity through class II histone deacetylases (HDACs). More specifically, Ca^{2+} and CaMK act as kinases for HDAC and cause phosphorylation and the removal of nuclear HDAC (335). Additionally, protein kinase D1 (PKD1) also assists in HDAC removal thus allowing for increases in MEF2 expression. Though PKD1 is not directly mediated by Ca^{2+}, it can be activated through protein kinase C (PKC) facilitated phosphorylation. PKD1 expression is greater in slow twitch muscles than fast twitch. And though over expression of PKD1 did lead to significantly reduced muscle size and increased type I and IIa fibers, there was not change in PGC-1α concentrations (250) suggesting the importance of PKD1 in fiber type shifting.

Interestingly, AMPK may also have mediating effects on MyHC gene expression. When compared to wild-type mice, transgenetic mice expressing the inactive subunit AMPKα2 show decreases in PGC-1α and citrate synthase activity. However, when these mice were subjected to running exercise, fiber type shifts from MyHC-IIb to –IIa and IIx were reduced compared to wild-type mice though other metabolic adaptations remained the same (416). Additionally,

sedentary transgentic mice expressing AMPK-active mutations exhibited 2.6 fold increases in type IIa and IIx fibers, though there were no further increases with the endurance training (416).

The presence of PPAR subfamilies have been shown to have influence on skeletal muscle fiber type (Figure. 2). Mouse models have shown that over expression of wild-type or mainly active PPARβ/δ leads to more oxidative fiber type characteristics with increases in mitochondrial DNA, upregulation in slow contractile protein genes, and increased resistance to fatigue (317, 521). Notably, Schuler et al.(448) have shown that the absence of PPARβ/δ causes a slow to fast fiber-type change, characterized by a down regulation of MyHC I and up regulation of MyHC IIb transcript concentrations in the gastrocnemius muscle. These changes were accompanied by changes in fiber type profiles with a downregulation of PGC-1α, mtTFA, and many other genes involved in oxidative phosphorylation, despite no change in mitochondrial DNA content. Likewise, the overexpression of PPAR-1α has also been shown to induce increases in oxidative fiber types (302, 528).

While the influence of the aforementioned proteins have been established to some degree, there is also evidence suggesting that the presence of ERK1/2, MyoD family proteins (MyoD and myogenin), Six1 and FOXO transcription factors may also contribute to changes in muscle fiber types. Despite these findings, there is evidence to the contrary for each of these proteins, suggesting a need for further research. Foremost, ERK1/2 activation by Ras mutation in rats can facilitate MyHC-slow expression in regenerating denervated soleus muscle (352). These findings have been further supported by Higginson et al. (183) who showed that pharmacological inhibition of ERK1/2 pathway decreases MyHC-β/slow and increases MyHC-IIx and –IIb. Conversely, Ras mutations that selectively activate the PI3K-Akt/PKB pathway, facilitates muscle cell hypertrophy but not fiber type specification in the same system (352). Likewise, pharmacological inhibition of ERK1/2 pathways in C2C12 muscle cells has shown increases in MyHC-β/slow promoter/reporter activity (459).

Similarly, data suggest MyoD and myogenin expression may contribute to muscle fiber type switching. Notably, MyoD has been shown to be prevalent in fast-twitch muscles while myogenin is more prevalent in slow twitch (201, 514), suggesting these two proteins may lead to muscle fiber type specification. Indeed, an E-box within MyHC-IIb gene promoter is bound by MyoD and is required for gene expression in fast muscle. Further, it has been shown that MyoD

activates the MyHC-IIb promoter in an E-box dependent manner, while myogenin activates this same promoter to a lesser degree and in an E-box-independent manner (532). Conversely, both proteins have been shown to be rapidly upregulated by denervation, which can be slowed by electrical stimulation (105). Additionally, changes in fast/slow fiber profiles elicited by hypothyroidism or low-frequency stimulation do not closely correlate with the relative expression of these proteins (281).

Transcription factor Six1 and its transcriptional coactivator, the protein phosphatase Eya 1, concentrations are greater in the nuclei of fast twitch muscles. Further, the forced expression of these proteins in mouse slow-twitch muscles leads to a fiber type switch from type I and IIa to IIx and IIb, and upregulation of proteins of the glycolytic pathway (147). Additionally, Richard et al. (413) have shown that the absence of Six1 and Six4 elicits the development of myofibers lacking the expression of fast-type muscle genes in embryonic mice. Despite these findings, it is still unclear if the Six1-Eya 1 system is controlled by activity patterns.

Finally, FOXO transcription factors have some supporting evidence that they might contribute to muscle fiber type shifting. Foremost, FOXO1 is more abundant in slow twitch muscles while FOXO4 is more abundant in fast twitch muscles (253). Indeed, mice overexpressing FOXO1 show more muscle atrophy and significant decreases in type I muscle fibers (231). Interestingly, muscle specific FOXO1 knockout C2C12 muscle exhibited a slow to fast fiber type switch (253). Despite this evidence, further research is needed to fully understand the relationship between FOXO transcription factors and muscle fiber type expression.

2.1.5 Evidence Supporting the Interference Theory

Original work completed by Robert Hickson (180).provided the first evidence of attenuated strength increases when RT is completed simultaneously with AT (which is known as CT) Evidence suggests a molecular mechanism associated with AMPK activation is responsible for the attenuation in strength performance with CT. Notably, rodent models indicate a negative correlation between AMPK activation and muscle hypertrophy (239, 492). AMPK activation has been shown to have significant negative effects on mTORC1 and its effectors (p70^{S6k} and 4E-BP1), resulting in attenuated protein synthesis and subsequent hypertrophy (16, 37, 151, 205–207). This molecular interference is caused by the direct phosphorylation of tuberous sclerosis complex 2 (TSC2) (207, 334) and the mTORC1 associated regulator, raptor (492) as a result of

AT. Activation of TSC2 by AMPK also has been shown to negatively affect mTORC1, and subsequent protein synthesis, through Ras-homologue enriched in brain (Rheb) (37, 94, 207). (Figure.2)

Moreover, AMPK regulation of mTORC1 may be isoform-specific. The AMPK-α1 catalytic isoform is acutely responsible for limiting skeletal muscle hypertrophy via mTORC1inhibition (334, 345, 346). Conversely, AMPK-α2 mediates metabolic adaptions within skeletal muscle (224, 334, 345). When compared to AMPK-α1 knock out mice, control mice subjected to chronic mechanical overload exhibited elevated levels of AMPK-α1 and blunted increases in hypertrophy to the plantaris muscle (346), supporting evidence of the selective role of AMPK-α1. Additionally, in vitro research suggests that AMPK activation may promote protein degradation through both the ubiquitin-proteasome and autophagy-lysosomal systems (435, 436). Specifically, AMPK activation elicits FOXO- dependent transcription of MaFbx and MuRF1 (435, 494).These factors disrupt the inhibitory effect of mTORC1 on Unc-51-like kinase 1 (ULK1),while also increasing ULK1 activity, leading to autophagy stimulation (227, 436). Taken together, AMPK activation from AT potentially mediates interference with muscle hypertrophy from RT through down-regulating the mTORC1 cascade, and subsequent protein synthesis while up-regulating protein degradation (65). (Figure.2)

Additionally, AT activates eurkaryotic elongation factor 2 Kinase (eEF2K) through the CaMK and AMPK pathways (421, 422) and has been shown to deactivate of eukaryotic elongation factor 2 (eEF2) through phosphorylation (45). The eEF2 factor is involved with the translocation of the ribosome along the mRNA (236). Conversely, *in vitro* studies suggest the activation of the mTORC1 and $p70^{S6K}$ pathways inhibit eEF2K activity, thus allowing for activation of eEF2 due to the elimination of its respective kinase. Ultimately, this would allow both increases in translation and protein synthesis (44, 46, 520). Activation of eEF2K by AT is another potential mechanism for the inhibition of muscle protein synthesis.

The upstream activation of regulated DNA damage and development 1 (REDD1) in response to AT has also been shown to inhibit mTORC1 and subsequent muscle protein synthesis (251, 468) in both rat (351) and human (96) models. Studies demonstrate that REDD1 prevents mTORC1 activity indirectly through releasing the inhibition of TSC2 caused by 14-3-3 protein binding (90, 112). REDD1 is activated by a number of stressors including ATP depletion (468)

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and hypoxia (47, 90, 112). In human models, it has also been shown that REDD1 mRNA is reduced three hours after low-intensity (20% one repetition maximum (1RM) performed for a total of four sets and 75 repetitions) exercise and blood flow restriction whilst mTORC1 mRNA expression increases in healthy males (96). This suggests that REDD1 activation through AT may be another furthering mechanism to inhibit muscle protein synthesis and subsequent hypertrophy associated with RT. (Figure 3)

Finally, the sirtuin (SIRT) deacetylase family of proteins are sensitive to metabolic stresses, such as increased NAD⁺ and lactate concentrations, and are active in skeletal muscle during AT (391). Of these proteins, SIRT1 is a regulator of mitochondrial biogenesis, partially because it has potential to regulate AMPK and PGC-1a activity (392). Further, SIRT1 also has been shown to negatively regulate mTORC1 activity through TSC2 activation (131), possibly through the inhibition of the upstream mTORC1-activator, Rheb (205). Consequently, the activation of SIRT1 is another potential mechanism for the inhibition of mTORC1 during the concomitant training of AT and RT. (Figure 3)
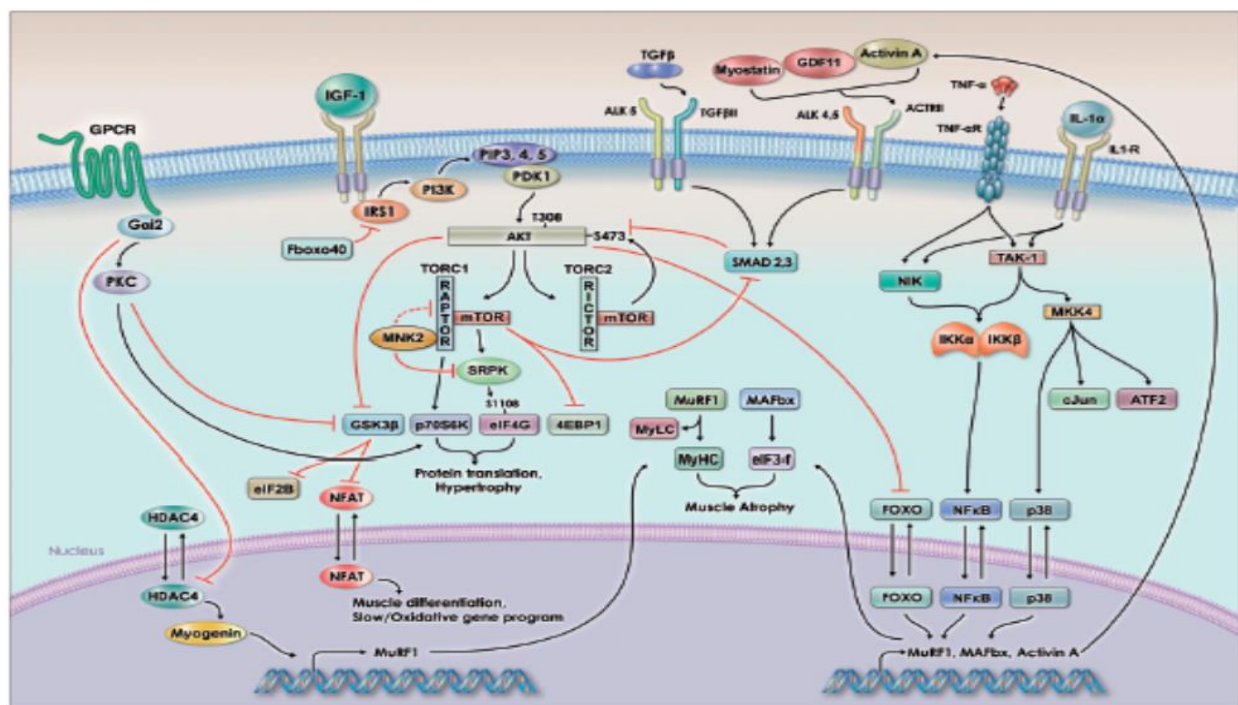
Figure. 1. Signaling Pathways Associated With Muscle Atrophy and Hypertrophy.

Modified from: Egerman, M and Glass D. *Crit. Rev. Biochem. Mol. Biol.* 49: 59–68, 2014.
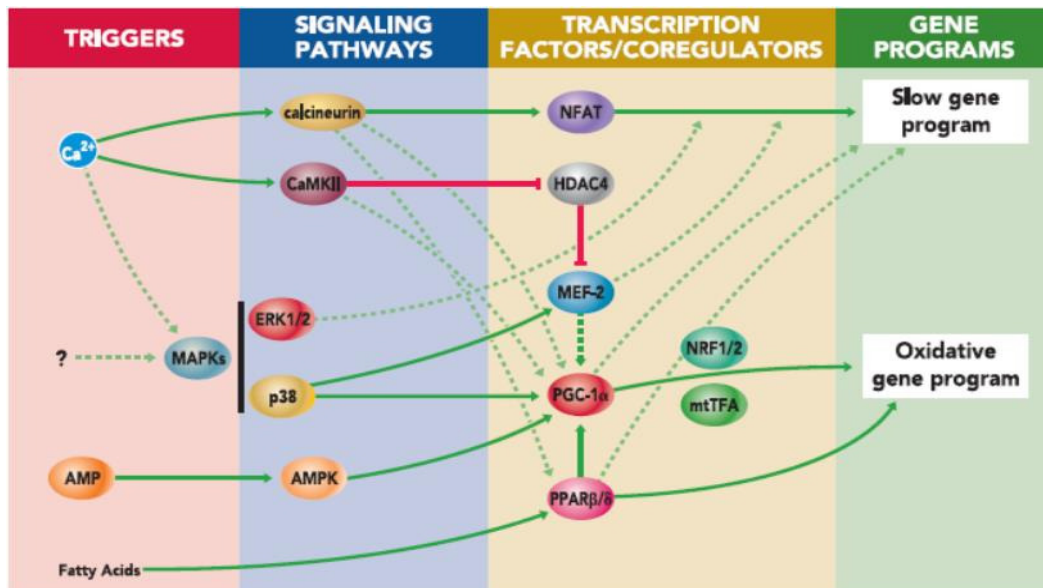
Figure 2. Scheme of Signaling. Solid lines represent established pathways. Dotted lines represent less established pathways. Red lines represent inhibition pathways. Modified from: Schiaffino, S et al. *Physiology.* 22:269-78, 2007
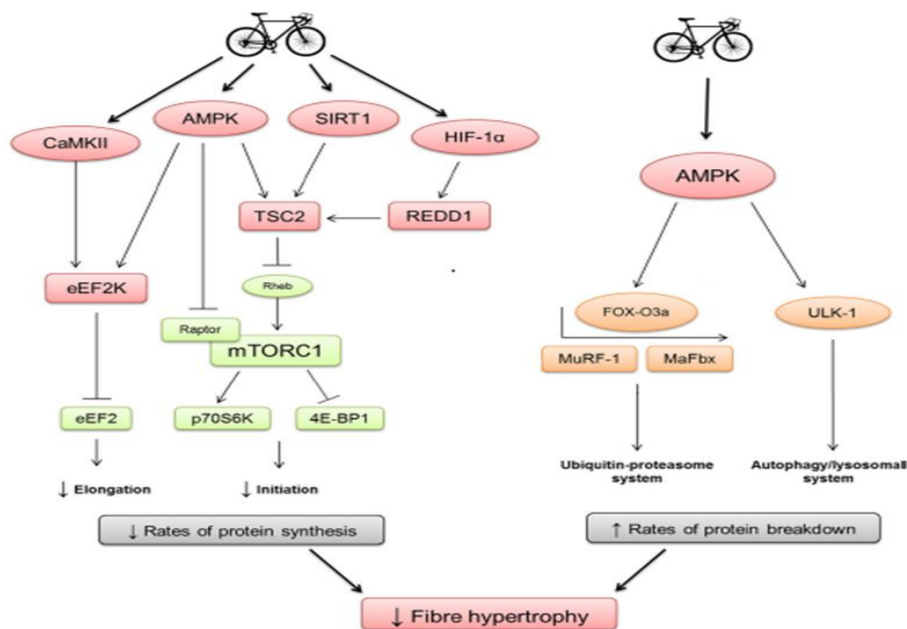
Figure 3. Cellular Pathways of Contributing to the Interference Theory.

Modified from: Fyfe et al. Sports Med (2014) 44:743–762

2.2 Influence of Concurrent Training on Body Composition, Performance and Hormones

2.2.1 Body Composition

Body composition can be positively influenced through either an increase of lean mass or a reduction of fat mass. This section will first focus on the effects of CT on lean mass followed by CT's effects on fat mass. Bone mineral density will not be discussed as it is beyond the scope of this review.

2.2.1.1 Effects of concurrent training on lean mass. The interference theory suggests that CT may not elicit the same changes in increases in lean mass as RT alone. Karavirta et al. (237) compared three, 21-week training protocols (CT, RT, and AT) in older men (56±7 years). Upon completion, the CT group (high intensity RT and AT, both twice a week) demonstrated increases (8±35%) in cross-sectional area of type II fibers, although the increase was not statistically significant. Moreover, high intensity RT elicited significant increases (26 ±22%) in type II muscle fiber types. Likewise, others compared 12 weeks of CT, RT, and AT protocols and demonstrated that CT increased only type IIa muscle fiber types (18%; $p<0.05$) while, RT increased both type I (17%) and type IIa (13%) fibers ($p<0.05$) in both men and women. The authors reported that RT resulted in a larger cross sectional area of both fiber types than the AT and CT groups (403). These findings suggest that despite the hypertrophic increases with CT, RT had the greatest effects on muscle fiber hypertrophy for both Type I and II fibers in young women and young and older men.

These increases in muscle fibers from RT lead to increases in total cross-sectional area of the muscle cell and muscle as a whole. Indeed, muscle cross-sectional area was shown to increase significantly in populations with no prior RT experience. After 12 weeks, both RT, (consisting of progressive heavy lower body RT (progressed: three sets of 10RM to three sets of 4RM) and CT (consisting of both heavy lower body RT and 9.9±1.1 hours of cycling per week)) provoked significant increases in knee flexors and extensors cross sectional area ($p<0.05$). Further, authors report significantly greater increases in total thigh muscle cross sectional area (sum of flexors and extensors) in the RT group (8.0± 0.8%) compared to the CT group (4.3±0.7%) (419). In addition, young men (23±0.6 years) and women (22±09 years) assigned to one of four 12-week training protocols (control or three days of AT (two days of cycling for 42

minutes and 1 day of high intensity intervals), progressive RT progressive (~70-85% 1RM) or CT (six nonconsecutive days consisting of both protocols)) demonstrated greater fast-to-slow fiber type transitions and blunted hypertrophy of type I fibers during the CT protocol. It was shown that the CT group increased vastus lateralis myosin heavy chain type IIa fibers after the 12 weeks of training. Moreover, when compared to the RT and AT groups, exhibited the greatest reduction in myosin heavy chain IIb at both six weeks and 12 weeks (p<0.05) (403). In summary, AT may attenuate or stop muscular growth in different age groups and physical activity levels.

Interestingly, despite much evidence supporting the blunting effects of CT on increases in lean mass associated with RT, not everyone agrees (27, 135, 153). Bell et al. (27) examined the effects of three, 12-week training protocols (AT, RT, and CT) in young men and women. For this study, RT consisted of a progressive total body RT protocol with lifts progressed 4% of 1RM every three weeks. AT consisted of cycling for 30 minutes at ventilatory threshold and was progressed to 42 minutes over the duration of the study. Additionally, the AT protocol had interval sessions (four sets of three minutes of work: three minutes active recovery) at power outputs equivalent to 90% of VO_2max and was progressed one set every four weeks. Finally, the CT group underwent both training protocols on alternating days. Interestingly, the RT group showed significant size increases in both type I (3250 ± 429 to $4137\pm386\mu m^2$) and II (3506 ± 480 to $4483\pm570\mu m^2$) muscle fibers, while the CT group exhibited significant increases in type II (3542 ± 292 to $4030\pm379\mu m^2$) muscle fibers after 12 weeks (p<.05), with no significant differences between the two groups. Further, McCarthy et al. (332) compared results of RT, AT and CT protocols lasting ten weeks in sedentary men. Total body, high intensity (6RM) RT took place three times a week. AT consisted of 50 minutes of cycling at 70% of heart rate reserve. Finally, the CT group completed both training protocols in a single training session. Upon completion, RT and CT elicited significant increases (p<.0001) in thigh extensor (12 and 14%, respectfully) and flexor/abductor (7% and 6%, respectfully) with no differences between groups. Additionally, both RT and CT groups had significant increases in type II fiber are a (24 and 28%, respectfully) and mean fiber area (21 and 23%, respectfully).

Taken together, the effects of CT on muscle fiber hypertrophy are inconclusive. Jones et al. (222) proposes that the a mount of exposure to low intensities may be a factor negatively

affecting RT outcomes in individuals with over two years experience with RT. Participants were assigned to one of three six week protocols. The RT group which completed five sets of six repetitions at 80±5% 1RM. Additionally, there were two CT groups. The first group trained aerobically (30 minutes at 30% 1RM knee extension) immediately after every RT sessions (1:1 training ratio). The second trained aerobically immediately after every third RT session (1:3 training ratio). Only those individuals who experienced the aerobic intervention every third day exhibited similar limb girth increases to the RT only group at both mid (1.7±0.9 and 1.7±0.4%, respectively) and post training (2.5±1.2 and 3.7±2.3%, respectively). Interestingly, the RT group also showed significant increases in circumference measurements when compared to the control and group that experienced AT every day of their RT. The 1:3 endurance to RT ratio group only showed significant increases in girth measurements against the control group ($p<.05$). These results suggest that hypertrophic adaptions elicited by 1:3 endurance to RT ratio group are is statistically different from those increases seen in the RT group and thus hypertrophy was not attenuated by the AT intervention as it was in the 1:1 endurance to RT protocol.

2.2.1.2 Effects of concurrent training on fat mass. Fat mass reduction is another important variable to consider when altering body composition. CT has been shown to significantly reduce fat mass in untrained (135) and active young men (92) and in middle-aged and elderly women (180). Healthy women (39 to 64years old) were assigned to one of three 21-week training groups (RT, AT, or CT). The RT protocol was divided into three seven-week training focuses, all consisting of periodized and progressed total body RT. The first section focused on muscular endurance with high repetition ranges (15-20 repetitions) and low loads (40-60% 1RM). The second focused hypertrophy with moderate repetition ranges (10-12 repetitions) and moderate loads (60-80%). The final section consisted of low repetition ranges (6-8 repetitions) and high loads (70-90%). The AT was also divided into three seven-week sections. Participants cycled twice a week for all sections of training. The first section consisted of 30-minute training sessions twice a week with varying intensities above and below aerobic threshold. The second section included 45-minute training sessions consisting of with varying intensities below aerobic threshold and above anaerobic threshold and 60-minute training sessions below aerobic threshold. Finally, the third section included varied durations of 60-to 90-minute sessions with constant intensity (under aerobic threshold) for 90-minute training sessions and 60-minute training sessions with varying intensities CT protocol included both of these training protocols

and were completed on different days. Upon completion of the training protocols, CT induced a significant reduction of fat mass (-4.8%) and trunk fat mass (-375±750g) as measured with body dual energy X-ray absorptiometry (DXA) scans and waist circumference measurements (-1.6±2,1cm) (462).

Moreover, Dolezal et al. (92) examined the effects of 10 weeks of AT, RT and CT protocols on metabolic rate. AT included a progressed AT program in both intensity (65 to 85% of age-derived maximum heart rate) and duration (25 minutes to 40 minutes). RT protocol included progressive and periodized total body RT. The CT protocol included both training protocols completed on the same day with the RT protocol always completed first. After the ten weeks, the CT provoked significant decreases in body fat (-3.5±1.8%), and fat mass (-2.6±1.8kg). Interestingly, these changes in fat mass and body fat were more significant than those in the AT and RT groups. Further, CT also significantly increased basal metabolic rate (7,455±964 to 7,802±981 kJ/day; 1,781.79±230.4 to 1,864.72±234.2kcal/day). While there is still conflict over CT's effects on lean mass, CT may aid in the increase of calories burning potential, aiding in fat mass reduction.

2.2.2 Performance

AT's blunting effects on skeletal muscle hypertrophy would also infer that AT may also hinder anaerobic muscle performance. This section will first focus on the effects of CT on strength followed by power performance.

2.2.2.1 Effects of concurrent training on muscular strength. Hickson et al. (180) were the first to compare strength changes among three training protocols (AT, RT, and CT). The aerobic protocol required participants to exercise six times per week, alternating progressive continuous running as fast as possible (30 minutes to 35 minutes to 40 minutes) and interval training session (six five-minute bouts separated by two minutes of rest) on an ergometer. The RT protocol consisted of lower body exercises performed three times a week. The CT protocol consisted of completion of both RT and AT protocols on the same day separated by two hours of rest. The authors reported CT induced significant improvement in leg strength in mix gender groups after week seven (+30kg, 34%) with a subsequent plateau then decrease at weeks nine and 10. It was further reported that the RT group continued to improve through week ten (+42kg, 44%). These findings for mix gender groups are further supported by Bell et al. (27) through

comparison of three training protocols (AT, RT and CT) in methods described above. Upon completion, RT and CT elicited significant increases in knee extension and leg press strength in both men and women (p<0.05), with RT eliciting significantly greater increases than CT. Both RT and CT increases were significantly greater than those in the AT group. Moreover, cyclist exposed to a previously described CT protocol exhibited strength increases in the CT group (109±5 to 147±6kg; p<0.05) but were significantly lower than that of the RT group (108±3 to 159±3kg) (p < 0.05). It was further reported that increases in average training load in leg exercises from week one to 12 was significantly greater in the RT group than the CT group in both absolute and relative measures (419). These findings support earlier work comparing circuit training protocols to two different circuit and AT combinations in male college physical education students. The circuit training protocol included a 12-week progressive program with a focus on total body strength endurance and power training. The CT groups completed the circuit training protocol but also completed AT which consisted of five high-intensity interval runs separated by active recovery at 60% VO_2max. Upon completion, circuit training produced greater strength increases (17%) than AT completed before (12.2%) and after (10.6%) circuit training (p<0.01) (62). Taken together, these studies suggest that though it is possible to increase maximal strength through CT, AT blunts the extent of these strength increases.

As with muscular hypertrophy, the amount of AT added to RT may also dictate if strength increases are hindered. As previously mentioned, Jones et al. (222) compared strength outcomes in three groups. The first underwent RT protocol. The other two included either AT after every completion of RT (1:1) or every third completion of RT (1:3). After three weeks, the RT only group displayed an increase (+12.4±3.9%; p=0.016) in maximal voluntary contractions of the knee extensor muscles while the two other groups did not. Moreover, the increase in the RT group was19.0±2.4% greater than the control group, while the groups with added AT were not different from the control group. Additionally, upon completion of the six- week training protocols, RT resulted in 22.7±5.9% (p=0.005) and 41±2.4% (p<0.001) increases in maximal voluntary contraction compared to both 1:1 endurance to RT and control groups, respectively Likewise, the 1:3 endurance to RT protocol group also had greater increases in maximal voluntary contractions compared to 1:1 endurance to RT and control groups (p=0.024 and p<0.001, respectively). Moreover, the authors report a 24.6±8.5 ("most likely") mean affect for the 1:3 endurance to RT group while 1:1 endurance to RT group exhibited a 7.2±6.1 ("likely")

effects on the increase in maximum voluntary contraction increases. Finally, upon completion of the six weeks of training, 1:3 endurance to RT group exhibited no difference from the RT group. These authors further report no increases from baseline in either the control or 1:1 endurance to RT ratio group in maximal voluntary contraction. These findings suggest the amount of exposure to low intensity AT may be a contributing factor to the blunting of strength increases.

Depending on intensity, aerobic based training may also elicit critical acute effects on strength when performed before strength testing sessions. For example, it has been shown that when exercise at low intensity (90% of anaerobic threshold for five kilometers) is undertaken 10 minutes before strength and strength-endurance testing, there is no significant effect on either 1RM in leg press or in repetitions to failure at 80% 1RM. But when strength and strength-endurance measures were assessed after intermittent exercise performed at VO_2max (1 minute:1 minute; running to rest ratio) for five kilometers, strength-endurance measures suffered as compared to strength and strength-endurance performance measures without running interventions beforehand (10.8±2.5 to 8.0±2.2 repetitions; p=0.03), though 1RM strength did not (470). These results suggest that lower (<90% anaerobic threshold) intensities of AT do not affect long term training outcomes 1RM for those exposed to CT. While training at higher intensities before RT may have further detrimental effects on strength performance due to decreased training volumes.

It has also been suggested that the blunting of strength increases from RT only happens in muscle experiencing both modes of exercise. Cadore et al. (52) studied elderly men, and reported that while lower-body strength increases were experienced in both CT and RT groups (+41.3±8.2 v +67.6±17.1%, respectively), the increases was significantly greater (p<0.001) in the RT group. The AT protocol consisted of cycling for a duration lasting 20 minutes at 80% of heart rate at ventilatory threshold and was progressed to 30 minutes at 90% of heart rate at ventilatory threshold (weeks 1-10). The last two weeks of AT (weeks 11-12) consisted of six sets of four minute intervals at 100% of heart rate at ventilatory threshold. Interestingly, participants in both groups exhibited significant increases in upper-body strength (RT: 32.6±10.8% v CT: 33.7±8.1%), with no significant difference between the two groups. These findings support earlier work conducted in men (18-40 years) exhibiting increases in upper-body strength in AT,

RT and CT groups. Despites these increases, RT and CT were both significantly higher than the endurance group (135).

In contrast, it has also been shown that after 10 weeks of CT or RT, RT still elicited greater improvements than CT in both bench press (24 v 19%; p<0.05) and back squat (23 v 12%; p<0.0.5) in active healthy young men. These findings suggest that CT may still inhibit increases in both upper and lower body strength though only the lower body experienced both endurance and RT interventions. Further research is needed to fully understand the outcomes of CT on all strength measures in all muscle groups.

Finally, though there is mounting evidence supporting the interference theory, data support that low intensity AT may not blunt strength increases elicited by RT. After 12 weeks, untrained men in the CT group exhibited no significant differences to the RT group in increases between in both leg press (40.8 v 39.4%) and bench press (21.2 v 30.5%) (135). These findings were later supported by Holviala et al. (193) suggesting that CT showed significant increases in single leg press measures compared to the control group, without significant difference from the RT only group in elderly men.

2.2.2.2 Effects of concurrent training on muscular power. Power output appears to also be hindered by CT, corresponding with attenuated strength increases as previously discussed. Skeletal muscle adaptations were compared in two 21-week training protocols. The first was protocol was comprised of progressive and periodized total body RT with a focus on leg extensors. The second was a CT protocol which included the aforementioned RT protocol and AT which progressed in both duration and intensity. The final weeks of the AT consisted of varying interval training, focusing on cycling speed and maximal endurance. Only RT resulted in significant increases in rate of force development and average force in first 500ms (p<0.01) in isometric knee extension, while CT groups had no changes (153). Likewise, the assessment of a progressive periodized RT protocol and the combination thereof with 9.9±1.1 hours of cycling per week in individuals with no prior RT six month prior to starting experimentation (12 well-trained cyclists and nine recreationally active individuals) revealed no increases in rate of force development in the CT group while the RT intervention elicited a 15±5% (p<0.05) improvement in peak rate of force development during isometric half squat measures. Moreover, these authors reported that the increases were reported to be significantly greater with RT than CT. Likewise, a

significantly higher percent increase in squat jump performance in the RT group (13±2.0%) was reported compared to the CT group (6.2±1.6%) (p<0.05) (419).

Conversely, power performance was assessed after three 12-week progressive training protocols (RT, AT, and CT). RT included, periodized total body RT protocol. The AT protocol progressed in both duration and intensity (percent of heart rate reserve). Finally, the CT consisted of the combination of both aforementioned protocols. Upon completion, only RT was shown to elicit significant increases in jump power (+5.7%) despite no differences in vertical jump height. However, the increase in the RT group was not significantly different from the CT group (+1.6%) but was significantly greater than the AT group (+0.4%). Though the RT group displayed significant changes in power in isokinetic knee flexion at 60°/sec (+10.1%), the CT did not. Despite the changes in RT group there were no significant difference between the two groups (135).

As with muscular hypertrophy and strength, there is also evidence suggesting that intensity of AT may be a factor in the development in power. As previously stated with muscular strength, many CT interventions using aerobic protocols consisting of either low intensity exercise for long durations (419) or a combination of low intensity exercise and high intensity interval training (62, 153) have reported attenuation of power outcomes compared to RT alone. Interestingly, after 12 weeks of CT, consisting of high intensity sprints and RT protocols, or RT, the authors reported a main effect for time with increases in average power in both groups (p=0.028) (55). These results suggest that the combination of high intensity sprints and RT may not blunt power increases.

2.2.2.3 Effects of concurrent training on aerobic performance. CT appears to have positive effects on aerobic performance by promoting improvements in VO_2peak (153), VO_2max (27, 55, 193, 462), mean power output (420) and running economy (393). Men and women were assigned to a progressive total body RT (three days/week), an AT (including both continuous and intermittent interval training (three days/week)) or CT (the combination of the two groups (six days/week)) for a total of 12 weeks. Upon completion, both CT and AT provoked significant improvements VO_2max in both men (4.27±0.18 to 4.54±0.22 l/min and 4.32±0.23 to 4.53±0.24 l/min, respectfully; p<0.05) and women (2.79±0.10 to3.00±0.09 l/min and 2.71±0.34 to 3.05±0.30 l/min, respectfully; p<0.05), without significant differences between the two groups.

Further, authors report that these improvements were significantly greater than the RT an control groups in both men and women (p<0.05) (27). Likewise, 12-week CT (combination of sprint interval training and RT) promoted significant increase in VO$_2$max (40.9±8.4 to 42.3±7.1 ml/kg/min; p < 0.05) while progressive RT had no effect. Further, it was reported that VO$_2$maxes were increased (42.3±7.1 v 36.0±3.0ml/kig/min; p<0.05) after the CT intervention (55). Recently, Rønnestad et al. (420) reported that 10 weeks of heavy RT in combination with continuous riding at various intensities provoked 6.5±5.7% (p<0.01) increase in mean power output in a 40-minute all out sprint, while continuous riding elicited no change in trained cyclists. This change was significantly larger than the continuous riding group (p<0.05). Though there is substantial evidence suggesting benefits of CT on aerobic performance, not everyone agrees (92, 135). Interestingly, despite CT's inability to elicit significant increases in VO$_2$peak (+2.8%), Glowacki et al. (135) reported that this response was not significantly different from the increases provided by the aerobic treatment (8%). Moreover, CT elicited significant increases strength measures. These findings are mimicked in Dolezal et al. (92) with no significant differences between AT and CT groups in VO$_2$max measures but significant increases in maximal strength measures for the CT group. Overall, findings suggest that CT protocols may be beneficial to aerobic performance with similar increases in aerobic performance with increases in maximal strength.

In summary, it would appear as if desired outcome is important when deciphering results in CT protocols. Indeed, CT has been shown to have multiple beneficial effects on aerobic performance and decreases in fat mass. In contrast, AT may elicit negative effects on increases in lean mass and strength and power performance, which may be due to many confounding variable. Of these factors, intensity of the AT during CT appears to be the primary determinant on strength and power outcomes. Exposure to low intensity AT negatively influences strength and power, while exposure to high intensity sprint protocols does not. Further, it can be suggested that the amount of exposure to low intensity training sessions affects strength and power performances, with one to one ratio of AT to RT exposure showing negative effects on strength performance while one to three did not. Despite these data, there is still evidence suggesting that exposure to low intensity AT does not affect strength or power performance at all. Interestingly, many of the studies reporting interference in strength and power performance had five or more total (combination of both RT and AT) training sessions per week (27, 62, 180)

while those that did not display attenuation of strength had less (222, 332). This suggests that outside factors such as depleted muscle glycogen or increased exposure to catabolic states from prolonged exercise causes the attenuation of strength and power typically observed with RT alone and lends support to the interference theory. These outside variables warrant further investigation into the interference theory of CT.

2.2.3 Hormonal Responses

This section will review the potential mechanisms that elicit acute and chronic responses in anabolic and catabolic hormone concentrations in regards to RT, AT and CT. Notably, this section will focus on responses in healthy individuals. Confounding factors such as overtraining or hormonal abnormalities will not be taken into consideration because they are beyond the scope of this review.

2.2.3.1 Testosterone. In men, testosterone is primarily produced in the leydig cells of the testes in response to luteinizing hormone from the pituitary (339). Notably, luteinizing hormone has been shown to fluctuate in pulse rate and amplitude in response to androgen concentrations in both animal (475) and men (505). In women, testosterone is produced in the ovaries and the adrenal glands. The primary precursor to testosterone production in the ovaries is androstrenedione. Then main precursors for the adrenal gland is dehydroepiandrosterone (DHEA) and dehydroepiandrosterone sulfate (DHEA-S) (148). Serum testosterone levels have been shown to be positively linked to performance outcomes (519) through both androgenic and anabolic effects on muscle cells (179). Additionally, testosterone interacts with the nervous system with receptors on neurons to increase neurotransmitter release, regenerate nerves, increase cell size and dendrite length and diameter (43, 356). Additionally, testosterone has been shown to enhance other hormonal interactions such as the secretion of growth hormone and the subsequent release of insulin-like growth factor (133). Finally, testosterone concentrations in the blood have been inversely linked to fat mass. Indeed, 18 months of testosterone replacement therapy (100mg/week) elicited a decrease in subcutaneous fat (-13±4%) in hypogonadal men (240) Interestingly, RT is identified as an effective means to elicit increases in total testosterone concentrations in men (58, 157, 181, 266, 278, 495, 525) and untrained women (326). The mechanism for RT to increase testosterone is multifaceted but may be due to adrenergic stimulation by the sympathetic nervous system and circulating catecholamine (217), lactate

stimulated secretion of testosterone, and adaptations in testosterone synthesis and production processes (125).

Despite these rises in total testosterone following RT, only a finite amount is readily available for androgen receptor interaction. Total testosterone is partially bound to sex-hormone binding globulin (SHBG). Only the unbound, or "free", testosterone is available to interact with androgen receptors. Concentrations of free testosterone are also dependent upon age. In healthy males between the ages of 20 and 50 years, the normal range of free testosterone is 5.5-20ng/100 ml and decreases with age (506). Testosterone (both free and total) has been shown to acutely rise for up to 15 minutes after RT sessions in both young and older men (270). The responses of free testosterone to RT have been shown to mimic those of total testosterone (6, 102, 270, 495), though there is evidence to the contrary (158, 160). These contradictions may lie in the length of study, level of training status of subject or the variance of training throughout the study (158, 160). Further, it has been shown that these responses may be augmented by chronic training. Kreamer et al. (270) suggests that after 10 weeks of periodized RT, free testosterone concentrations increased in both young and elderly men compared to pre-training levels. Likewise, resistance trained men exhibit a greater acute response to single sessions of RT than endurance trained men, further supporting this concept of augmented responses of testosterone to RT due to chronic training (495). RT has also been shown to elicit acute elevations of 25% in free testosterone levels in young women after six sets of 10RM squats with two minutes rest intervals (366), though this increase was not exhibited in middle-aged and elderly women (163).

Acute responses of testosterone to resistance training. Interestingly, evidence suggests that several factors impact acute elevation of total testosterone responses to RT. Foremost, exercise selection involving larger muscle groups such as those used in Olympic lifts (267), jump squats (512) and deadlifts (109) can potentially dictate testosterone responses. Perhaps obvious, these exercises have been shown to be metabolic stressors (409) which may be a stimulus for testosterone secretion (311). When comparing upper body training only and the combination of lower and upper body training, Hansen et al. (169) report acute increases of testosterone in response to a single bout of RT prior to chronic training (p< 0.05). Further, a trend towards significance was reported in acute testosterone response after nine weeks of RT (p=0.07) in the group that trained upper and lower body, where the group that only trained the upper body did

demonstrated no change in testosterone concentrations. This evidence suggests that the combination of lower- and upper-body exercises produce the greatest acute testosterone response and this has been confirmed in a later study comparing low and high endogenous hormone training environments produced by lower body exercises (529).

Additionally, volume, and rest duration between RT sets, have both been shown to acutely affect testosterone concentrations. Schwab et al. (449) reported that testosterone concentrations did not increase during the squat exercise until the completion of the fourth set, when intensity was held constant at 90-95% of their 6RM. These data are later supported in multiple studies that suggest that testosterone levels increase with greater total number of sets and thus an increase in training volume (40, 140, 409). Indeed, weightlifters performing larger training volume demonstrated significant increases in testosterone concentrations (2.56 ± 1.03 to 3.65 ± 0.66ng/ml; $p<0.01$) while weightlifters performing lower training volumes experienced no change (40).

Likewise, if volume is held constant, it has been shown that higher intensities provoke greater acute increases in testosterone concentrations. When working at 100% of their 3RM for back and front squats and their 6RM for knee extension, participants exhibited significant acute increases in testosterone levels (17%; $p<0.01$) as compared to 70% of their 6RM-where no change was demonstrated. Further, when analyzed for area under the curve, from baseline to three hours post training, the higher intensity exhibited a greater area under the curve ($p= 0.02$) (405). Similar results were found in a weightlifting population when subjected to high intensity protocols with testosterone concentrations increasing from 2.56 ± 1.03 to 3.65 ± 0.66ng/ml ($p<0.01$). Despite these findings, the same study also reported significantly decreased levels of testosterone immediately after the RT session in male sprinters (40).

Moreover, rest interval length between sets of RT has been show to effect levels of testosterone responses. Rahimi et al. (407) had resistance trained men undergo one of three RT protocols consisting of four sets of squat and bench press to failure with 85% 1RM. Each session was differentiated with a rest interval of 60, 90, or 120 seconds. Interestingly, serum testosterone concentrations were significantly greater immediately after the exercise bout with rest intervals of 120 seconds (+65%) and 90 seconds (+76%) when compared to 60 seconds ($p \leq 0.05$). Similarly, Kraemer et al. (271) reported significantly greater serum testosterone concentrations

after 5RM at when three minutes of rest between exercise was utilized compared to only one minute. Thus, rest intervals longer than 90 seconds may provoke greater increases in testosterone concentrations than short rest intervals (≤60 sec).

Additionally, acute responses of testosterone levels have been shown to be affected by age, training experience, starting baseline testosterone levels and gender. College-aged men (20±0.7 years) exhibit significant acute increases in testosterone levels (+1.1±.96ng/ml) while high-school (16±0.8 years) counterparts reported no significant changes in response to a single RT session (109). In addition, basal testosterone levels have been shown to be lower in mature men (62±3.2 years) when compared to younger counter parts (29.8±5.3 years). Moreover, mature men showed significantly lower responses to RT. Despite these blunted responses, the older population still attained significant increases in total testosterone concentrations in response to acute bouts of RT (~4.04 to ~4.61; p<0.05) (270).

RT experience also affects acute increases in testosterone concentrations in response to RT. Kraemer et al. (267) showed marked acute increases in testosterone (16.2±16.2 to 21.4±7.9nmol/l; p<0.05) in junior weightlifters (17.3±1.4 years) with two or more years lifting experience when exposed to a moderate to a high intensity lifting protocol as compared to lifters who had less than two years experience, who did not show any significant increases (15.7±5.1 to 16.7±6.0nmol/l). Likewise, testosterone concentrations only increased following acute RT after 10 weeks of training with weights in older men (269). Later findings suggest that 10 weeks of training in active older men result in greater acute responses to RT as compared to pre training values. Despite these data, there is evidence suggesting that chronic training does not promote acute responses in testosterone concentrations in young age groups, 29.8±5.3 years (270) and 34.4±4.4 years (5).

Finally, the gender of the individual could potentially influence acute testosterone responses to RT, though there appears to be some discrepancy with evidence suggesting limited (40, 157, 265, 478) and significant increases (82, 366) in women. Interestingly, despite hypertrophic and strength increases in response to RT protocols (162, 164), women do not demonstrate an acute increase in testosterone levels like their men counter parts upon completion of the same lifting (157, 303, 525), suggesting women may rely on a different hormonal mechanism for hypertrophy and strength development.

Testosterone responses to chronic resistance training. The impact of chronic RT on basal serum testosterone concentrations has been inconsistent or absent in both men and women (7, 162, 164, 401). Some studies suggest that RT will increase basal testosterone concentrations (5, 159, 270, 277, 326, 474) while others have shown no change (7, 160, 161, 163, 181, 329) or a reduction (5). It appears that training status does influence resting testosterone concentration (478). Conversely, volume may have significant effects on resting testosterone concentrations in untrained women who completed a 12-week high-volume protocols as compared to untrained women who completed single-set circuit training protocols (326). Similarly, Ahtianien et al. (5) reported resting total testosterone and free testosterone concentrations were significantly increased in male strength athletes when subjected to higher training volumes in the first 14 weeks of the training protocol. However, testosterone concentrations lowered with a decrease in training loads over the last seven weeks of the 21-week training protocol. Further, when young men were subjected to a two-week "heavy" phase after five weeks of normal training, they exhibited a 12±5% decrease in resting testosterone concentrations at day eight. Interestingly, these levels returned to baseline levels by the fourth day after completion of the heavy training protocol (406).

Acute responses of testosterone to aerobic training. While testosterone's anabolic properties often associate it with RT, there is potential that these properties may also prove beneficial to AT. Further, testosterone is acutely elevated following AT in both men (515) and women (73, 75). These responses have been made evident through multiple AT protocols (515). Further, these acute elevations in total testosterone to AT have been made evident in sedentary (496), recreationally active (216) and endurance trained individuals (515) across various modes of exercise (216, 515). Conversely, there is also evidence suggesting that AT causes acute decreases in both total and free testosterone concentrations in men (238) and no changes in women (73). These discrepancies may lie in differences in training volume.

Two training models are most common in AT protocols, high volume training, often associated with lower intensities and long durations, and interval training, which is the combination of low intensities and high intensities. High volume training is considered to be the more traditional protocol. When examining acute effects in women, 40 minutes of cycling at 75% of maximum heart rate elicited significant increases in testosterone concentrations

(+2nmol/l) (p<0.001) immediately post AT and returned to basal concentrations by 30 minutes post exercise (75). These findings were later supported by Wahl et al. (515), exhibiting evidence suggesting 120 minutes of cycling at 55% of peak power output elicits significant increases testosterone concentrations both immediately after and 30 minutes post (p<0.05) exercise compared to pre-exercise in triathletes and cyclist. Additionally, intermittent training (four sets of four minutes of cycling at 90-95% of peak power output) and sprint training also elicited significant increases in testosterone concentrations (p<0.01) as compared to baseline values. Moreover, intermittent training exhibited higher testosterone concentrations both immediately after and 180 minutes after exercise when compared to 120 minutes of continuous cycling (both p<0.01) and 60 minutes and 180 minutes after the all-out sprint training (both p<0.001). Though these two studies have used cycle ergometer protocols, results using treadmill running protocols have been shown to elicit similar acute responses in testosterone concentration (495).

Conversely, it would appear that duration may have significant negative effects on acute testosterone concentrations. When non-elite, middle aged, male marathon runners were tested immediately after running a marathon, it was found that both free (10.45 to 7.9ng/dl; p=0.05) and total testosterone levels (4.85 to 3.4ng/ml; p=0.013) were significantly reduced (238). These findings have been replicated in kayak races of 19km and 42km distances, though durations of this exercise intervention was roughly 4.4 hours, two-fold other high volume training studies (75, 515). This suggests that there may be a threshold of duration that may influence increases or decreases in testosterone concentrations. Earlier studies have suggested that this decrease in testosterone is in response in decreases in luteinizing hormone concentrations, amplitude and pulse rate (320, 454). Moreover, rodent model investigations in to this phenomenon suggest that testosterone levels decrease in order to limit amino acid use in muscle protein synthesis to spare serve as a gluconeogenic substrate (149). Interestingly, both total and free testosterone have been reported to return back to normal basal concentrations one week after completion of a marathon race, (238) possibly reflecting the return of glucose homeostasis.

Testosterone responses to chronic aerobic training. Chronic AT typically results in lower serum testosterone concentrations. Indeed, when compared against sedentary individuals, high mileage (108.0±4.5km/wk) endurance athletes have been shown to have a lower basal total (15.3±1.3nmol/l) and free testosterone (60.2±5.1pmol/l) concentration than sedentary individuals

(19.5±0.9nmol/l and 75.9±3.6pmol/l, respectively) (p<0.05) (472). Additionally, volume may provoke significant responses in testosterone concentrations as high volume runners exhibited lower total (15.3±1.3 nmol/l) and free (60.2±5.1pmol/l) testosterone levels than even the moderate volume (54.2±7.3km/wk) runners (21.4±1.6nmol/l and 86.0±6.1pmol/l, respectively) (p<0.05). No differences were exhibited between the moderate mileage and sedentary groups in total and free testosterone (472). When these findings are considered with data from MaConnie et al. (320) it is speculated that there is an upper threshold of endurance training duration decreases in both pulse and amplitude of luteinizing hormone as seen in runners who ran 125 to 200km/week. Indeed, Wheeler et al. (530) report no change in luteinizing hormone levels in individuals who ran an average of 56km/week. Together, these results support earlier data suggesting that men who ran an average of 64km/week exhibited significantly lower testosterone concentrations than sedentary men (531).

Conversely, evidence shows that after 12 weeks of one AT session per week of 60% VO$_2$max for 50 minutes, sedentary individuals did not exhibit a decrease in total testosterone concentrations as has been shown with high volume training protocols (184). More recently, Grandys et al. (144) reported that five weeks of the combination of interval (two times/week) and continuous (two times/week) aerobic protocols may be able to elevate resting total (18.84±5.73 to 22.03±6.61nmol/l, p = 0.0004) and free (374±116 to 470±153pmol/ l, p = 0.00005) testosterone concentrations in healthy young men. These effects may be gender specific as volume does not seem to affect basal testosterone levels in women, even in overtrained subgroups (501). Therefore, an upper- threshold of AT volume may elicit decreases in both luteinizing hormone and testosterone concentrations (320, 472, 530, 531), while training protocols with shorter mileages, have shown no change or increased testosterone concentrations in men (144, 184) .

Androgen receptors. Briefly, androgen receptors are nuclear receptors that bind to androgenic hormones such as testosterone in the cytoplasm of the cell and tanslocate into the nucleus (310). After translocation into the nucleus, androgen interaction with proteins within the nucleus promote either the upregulation or down regulation of gene transcription (177). Androgen receptor content is affected by muscle fiber type, contractile activity and testosterone concentration in animal models (42, 93). In rodent models, RT provokes significant increases in

androgen binding capacity in the extensor digitorum longus muscle but reduces androgen binding capacity in the soleus. Notably, the extensor digitorum longus is mostly comprised of type II fibers while the soleus is mostly made of type I fibers (104). Conversely, after AT, a significant increase in androgen binding capacity in soleus muscle but not the extensor digitorum longus muscle is reported (89). These findings suggest a fiber-type specific adaptation depending on training modality. Moreover, when subjected to electrical stimulation (to simulate RT), rat muscle exhibited a 25% increase in androgen receptor content at day three of the experiment that later plateaued at day five. This increase was associated with increases in muscle mass (208). Conversely, two weeks of both electrical stimulation and administration of androgen receptor antagonist treatment resulted in a significantly lower degree of rat muscle hypertrophy (102.30%) compared to the control group (107.41%) who did not receive the antagonist treatment (209). In summary, these findings demonstrate the importance of the interaction between testosterone and its respective receptor for optimal muscle hypertrophy.

In humans, RT also results in a muscle up-regulation of androgen receptor content. Both eccentric (110% 1RM) and concentric (85% 1RM) squats have been shown in elicit significant increases in androgen receptor mRNA in the vastus lateralis (63% and 102%, respectively) 48 hours after eight sets of eight repetitions (21). Further, Kadi et al. (228) suggests that androgen presence may significantly increase androgen receptor content, as power lifters who self-administered anabolic steroids exhibited higher percentage of androgen receptor positive myonuclei compared with untrained control subjects (p<0.05) and drug-free powerlifters (p<0.05). Additionally, Ratamess et al. (409) has shown significant correlations between androgen receptor content in the vastus lateralis and 1RM, further suggesting that androgen receptor content may assist in facilitating strength changes during RT. Interestingly, the same study suggests that training volume may also elicit changes in androgen receptor content as a single set of squats for 10 repetitions did not elicit any changes within the following hour. However, exercise consisting of six sets of 10 repetitions for squat exercises provoked significant decreased of 46% in androgen receptor content (28). This reduction in androgen receptor expression may be in response to catabolic environments within muscle protein milieu, which may occur once adequate training volume is reached. Muscle protein degradation has been shown up to three hours after high volume (five sets of 10 repetitions at 12RM and four sets of 10RM), total body RT (21) despite reported increases in testosterone concentrations (269),

suggesting there is a down-regulation in androgen receptors in response to exercise. These findings still warrant further investigation as the relationship between the initial down-regulation and subsequent up-regulation that occurs following exercise has not been fully explored (273).

Finally, age may hinder androgen receptor response to any type of exercise training. For example, after 21 weeks of RT, AT or CT protocols did not provoke any change in androgen receptor concentration in aged men (61±5 years) (4). Likewise, seven days of functional hind limb overload in aged rats (25 months) did not elicit significant hypertrophy nor increase soleus muscles androgen receptor expression (296). Thus, data suggest that age may have detrimental effects on androgen receptor response to exercise. Further research is warranted in this specific population as muscle wasting and strength loss are problems in older populations.

Sex hormone-binding globulin. Sex hormone-binding globulin (SHBG) predominantly acts as a transport protein for androgens circulating through the body. Concurrently, SHBG may also influence binding capacity of androgens to select binding sites and thus influence the magnitude of influence of the circulating androgens (229). In addition, SHBG controls the amount of free testosterone available to cross the cellular membrane and influence the intra-cellular mechanisms. Moreover, SHBG receptors have been identified on cellular membranes that possibly mediate the androgen actions through a cyclic adenosine monophosphate (cAMP) mechanism (229).

To date, SHBG responses to RT have been inconsistent. Acute elevations have been reported in men (409) and women (277) but not all studies agree (158). For example, chronic reductions and no change in SHGB following RT has been documented (160, 162–164, 329). Though inconsistent, these data suggest that increases in total testosterone and the stagnant levels of SHBG may further assist in the increased androgenic and anabolic effects of testosterone. It has been suggested that increases in maximal strength correlate to increased testosterone/SHBG ratios ($p<0.05$) (161).

The responses of SHBG to AT is much more consistent, as multiple studies have suggested no significant changes in SHBG concentrations in response to acute (110, 454) and chronic (152, 531) exercise, though not all agree (144). Indeed, there is data suggesting chronic AT (four times/week for five weeks), consisting of continuous cycling at 90% of lactate

threshold twice per week and intermittent training (consisting of four sets of six minutes of unloaded cycling and three minutes of loaded cycling which corresponded to a 50% change in power output) induced a significant decrease in resting SHBG concentrations (34.45 ± 11.26 to 31.95 ± 10.40nmol/l, $p = 0.01$) in healthy young men (144). Though not significantly, Remes et al. (411) reported that six months of activity required for military training elicited a 10% decrease in SHBG concentrations (29 ± 1.6 to 26 ± 1.5nmol/l). Additionally, when subjects were divided into two groups (poorly conditioned and well-conditioned), authors report a non-significant 16% decrease in the "poorly conditioned" subgroup (31 ± 2.1 to 26 ± 2.5nmol/l), but no change was reported in the well-conditioned group. These inconstancies in both AT and RT warrant further investigation.

2.2.3.2 Growth hormone. Growth hormone (GH) is produced by somatotroph cells in the anterior pituitary in response to growth hormone releasing hormone (GHRH) secretion from the hypothalamus and/or the reduction of somatostatin secretion. Upon entering the blood stream, GH interacts both directly and indirectly (via somatomedins produced by the liver) with body tissue resulting in altered body composition and energy metabolism through lipolytic, protein anabolic, and antinatriuretic mechanisms (186, 437).

Multiple peptides make up the super family of human growth hormone. The most commonly examined of these peptides is the 22kD molecule, consisting of 191 amino acids (125). There are also biologically active peptides such as a 20kD isoform, 5kD isoform and a 17 kD isoform. Further, the super family includes many other monomeric, dimeric, protein-bound and other combinations of GH. Though further research is needed, these variants seem to have similar physiological effects to those of the 22kD isoform (275).

Circulating GH is bound to proteins that extends the half-life and may have implications of both physiological impact and target destination. Two growth hormone-binding protein (GHBP) subtypes have been identified as high- and low-affinity GHBP with the high affinity binding protein considered to be the primary GHBP in circulation (400). Once bound to GH, GHBP complexes extend GH half-life, limit GH distribution through the body, and mediate GH's binding to tissue receptors (23). GHBP is produced through proteolytic cleavage of the extracellular domain of GH receptors (551). It is thought that the primary site for this process occurs in the hepatocytes, as it contains the most GH receptors, however, this process could

occur anywhere in the body that has growth hormone receptor sites. Further, recent studies suggest body mass index and adiposity (116, 417), leptin (29, 114, 280, 308) and intense RT (379, 426) and AT (418) can influence circulating of GHBP concentrations. Because of these confounding factors, GHBP concentrations are often difficult to interpret. Additionally, research concerning GHBP manipulation and exercise is scarce. As such, this section will focus on total GH concentrations.

Acute responses of growth hormone to resistance training. Muscle activation (330, 331, 518), particularly resistance exercise has been shown to elevate serum GH in both men and women (367). Using a large volume protocol, six set of 10RM, Hymer et al. (203) showed significant increases in three classifications of GH (> 60 kDa, 30-60 kDa, and < 30 kDa), in women. Interestingly, these GH responses may be dictated by muscular strength as Kraemer et al. (276) reported blunted responses in low molecular weight (<30kD) GH in stronger untrained women as compared to weaker participants, while both exhibited similar responses in the heavier molecular weight GH variants (>30kD). The 22kD GH will be the focus of the rest of the acute section.

As previously stated, RT has been shown to elevate GH levels up to 30 minutes following resistance exercise in men (1.47 to 25.0 ng/ml) and women (4.0 to 25.4 ng/ml) (367) with significantly higher basal concentrations found in women than men (187). Moreover, the extent of response seems to be mediated by exercise selection, and subsequently, amount of muscle mass recruited (169, 267), muscle action (102), intensity (6, 404, 502), volume (140, 188), rest interval length (268, 272, 407), and training status, as individuals with greater training status show a greater acute GH response to training (5, 426).

Similar to testosterone, the amount of muscle mass recruited during the exercise mediates the magnitude of elevation in plasma GH concentrations. When levels were measured after exercise, groups training both upper-and lower-body muscle groups exhibited higher plasma GH level than those training upper-body groups only (P<0.05) (169, 529). Indeed, an Olympic lifting protocol, which involves large muscle groups of the entire body, with high intensity and low volume provoked significant increases in GH (p<0.05) (267). Together, these findings suggest the recruitment of large muscle mass will elicit acute increases in GH.

Interestingly, the type of muscle contraction also has potential to elicit changes in acute GH response. When comparing concentric and eccentric movements, Durand et al. (102) reported that concentric only movements in a total body workout, elicit significant acute increases in GH (p<0.05) while the eccentric movement protocol did not. Authors further indicated that 37% of the variance in GH could be explained by the concentric intervention. Likewise, Kraemer et al (262), who found that after 19 weeks of RT, groups that trained only the concentric exhibited greater acute GH increases to the concentric exercise testing than the group that trained both eccentric and concentric muscle contractions, even when equated for volume (p<0.05). These findings imply a neuro-hormonal connection such that the anterior pituitary is stimulated by muscle contraction. It has been shown there are multiple nerve fibers in close proximity to endocrine gland cells, some even forming synapses with the glands and may regulate the secretions of the selected glandular secretions (226). Together, the concentric muscle contraction may act as a stressor and further stimulate the neuro-hormonal pathway, provoking acute increases in GH concentrations.

Exercise intensity also appears to regulate GH responses. Recreationally trained men underwent two different protocols: a maximal repetition protocol, where participants worked at their 12RM for four sets of multiple lower-body exercises and a forced repetition protocol, where participants worked at intensities 15% greater than their 12RM, requiring assistance to complete each of the four sets. Upon completion, both protocols stimulated significant increases in serum GH concentrations (maximal: 1.0 ± 1.9 up to $23.6\pm15.2\mu g/l$; p<0.001 and forced: $0.3\pm0.$ up to $28.6\pm16.2\mu g/l$; p<0.001). Relative changes in GH concentrations were greater after forced repetitions compared to maximal repetitions across all time points (6). Further, these responses are shown in both men and women as the heavy RT protocol (five sets of ten at 10RM) elicited significant increases in GH as compared to lower intensities (five sets of 10 repetitions at 70% and 40% 10RM) (303).

Once again, age may have a blunting effect on GH responses to RT. After undergoing training protocols at 60%, 70% and 85% of 1RM, young subjects (27 ± 1.6 years) exhibited non-significant increases in GH at 60% of their 1RM and progressively increased responses at 70% and 85% whereas, older subjects (72 ± 0.8 years) did not exhibit any responses (404). Interestingly, later findings suggest that moderate intensity, high repetition protocols may be

enough to elicit significant increases in GH in elderly men (69±5 years) (463). Therefore, greater intensities stimulate increases in GH concentrations, though confounding factors such as age may inhibit his response.

In conjunction with training intensity, volume also appears to significantly affect acute serum GH concentrations. When compared against each other, lighter intensity with higher volume (four sets of 15 repetitions at 60% 1RM) elicited greater increases in serum GH concentrations as compared to high intensity bouts with less volume (four sets of four repetitions at 90% 1RM (p<0.05) (188). These findings support earlier work exhibiting significant increases in GH (0.16±0.07 to 27.7±17.8μg/l; p<0.001) following a high volume fatiguing protocol (10 sets of ten at 70% 1RM) as compared to low volume protocols (20 sets of one at 100% 1RM) (from 0.31± 0.39 to 1.43± 0.89μg/l, p<0.01) (156). Moreover, when two, four, and six sets were compared against each other across three different protocols, maximum strength (five repetitions at 88% 1RM), muscular hypertrophy (ten repetitions at 75% 1RM), and muscular endurance (15 repetitions at 60% 1RM), four or more sets elicited significantly greater GH responses than two sets in all three training protocols (464).

Additionally, rest interval manipulation is another variable in RT sessions that influence GH responses. When compared with varying loads and rest interval times, a rest interval of 1 minute with a load of the participant's 10 repetition maximum was shown to elicit the greatest response at all time points and in area under the curve throughout the training session (271). Rahimi et al. (407) confirmed these findings by showing that a rest interval of 60 seconds elicited significantly greater GH responses than that of 90 or 120 seconds when completing four sets to failure at 85% 1RM.

Finally, training status appears to be another confounding factor in acute GH responses to RT. After 21 weeks of heavy RT, strength athletes exhibited significantly greater elevations in GH concentrations than untrained men 30 minutes after executing five sets of 10RM (p<0.05). Additionally, mean acute responses were also significantly greater in strength athletes 15 minutes after the training protocol (5). These findings were replicated in women by Taylor et al. (488) who found weight trained women had increased GH concentrations immediately, five and 60 minutes after a full body exercise protocol with each exercise consisting of three sets of 10RM than women who had no RT at least six months prior to testing.

It appears that lifting protocols that elicit high blood lactate responses also provoke greater GH responses (265). Indeed, multiple-set protocols produce greater lactate responses than single set protocols (79, 140, 265, 349). For example, 10 sets of 10 repetitions at 70% 1RM elicited significant increases in GH (0.16 ± 0.07 to $27.7 \pm 17.8 \mu g/l$; $p < 0.001$) in conjunction with significant increases in lactate (1.4 ± 0.3 to $15.0 \pm 0.4 mmol/l$; $p < 0.001$) (156). Gordon et al. (139) found that the GH response is attenuated during high-intensity cycling following induced alkalosis through ingestion of decaffeinated tea solution containing 0.3g Sodium bicarbonate/kg. Also, administration of sodium l-lactate while running at low intensities has resulted in elevated GH concentration (312). Moreover, hypoxia (485), acid-base shifts, and protein catabolism have been purported to stimulate GH release (265). Therefore, as long as proper workloads (as a product of rest interval, intensity, and volume) are met, RT could be considered a proper stimulus for acute GH increases (502).

Responses of growth hormone to chronic resistance training. RT does not appear to significantly affect resting GH levels as no changes have been shown in both men and women of differing ages (163, 270, 326, 329). Interestingly, it appears that women have a higher resting GH concentration than men (268). Likewise, training status does not significantly affect resting GH concentrations as strength athletes did not exhibit differences as compared to trained males men (5) or women (478). These findings suggest that GH concentrations only increase in acute instances, in response to exercise in order to aid in muscle tissue hypertrophy as significant correlations exist between muscle hypertrophy and mean GH concentration increases for both type I ($r = 0.70$, mid exercise and $r = 0.74$, post exercise) and type II ($r = 0.71$, post exercise) muscle fibers ($p < 0.05$) (329). Further, changes in GH receptor sensitivity, feedback loop mechanisms, insulin-like growth factor potentiation, and daily routines may also influence GH concentrations (275).

Acute responses of growth hormone to aerobic training. GH appear to have a much more immediate response to AT than RT as evidence suggests significant GH response 15 minutes into AT with concentrations peaking at or near the end of exercise (291, 410, 483). The intensity of exercise may also dictate the GH response (113). When duration was held constant (10 minutes of cycling) low intensity (below lactate threshold) elicited non-significant increases ($1.5 \pm 2.0 \mu grams/L$) in GH concentrations while high intensities (above lactate threshold)

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provoked a significant increases (+7.7±2.4μgrams/L) (p<0.05) (113). It would appear as if an intensity between 40% and 60% VO_2max is required to stimulate GH secretion (83, 111, 359). This shows that GH secretion is consistent with lactate threshold (136) and mimics responses in RT with significant elevations in GH concentrations reflect elevations of in lactate (79, 140, 349).

Moreover, when intensity is held constant, duration of exercise also seems to elicit significant responses in GH (113, 533). Wideman et al. (533) suggests that when intensity is held constant at 70% of peak oxygen consumption longer duration of exercise provoked increases in both men and women with 120 minutes provoking the greatest response, followed by 60 minutes then 30 minutes. Additionally, it has been shown that the minimum amount of time required for significant GH concentrations is 10 minutes when intensity is held about lactate threshold (113). Together, these studies suggest that duration and intensity significantly affect GH secretion, supporting early work suggesting that workload stands as a reliable predictor for GH response (50).

Moreover, age appears to blunt GH response to exercise compared to younger individuals (132, 526). Young men (27.2±1 years) have exhibited up to a 3.6-fold values were reported during exercise whereas older men (64.1±2.2 years) only exhibited a 1.89- fold increase in GH (526). Additionally, older men and women have shown a delay in GH response until exercise intensities reached 125%of lactate threshold compared to young men, who exhibited significant increases at 75% of lactate threshold and above. Further, young women demonstrated significant increases at 25% of lactate threshold and above (526). These studies suggest that aging blunts GH response in response to exercise at given intensities. Moreover, these studies suggest that greater intensity of exercise is required to elicit these responses.

Interestingly, the impact of AT status on the acute GH response to AT is not consistent. Data supports increases (32), decreases (50), and no impact (254) of training status on GH response to AT. When compared to controls who did not participate in regular physical activity, trained individuals demonstrated significantly higher GH concentrations after working for eight minutes at t 30%, 45%, 60% and 75% of maximal work rate (32). Likewise, Bunt et al. (50) report conflicting data suggesting that trained male runners had significantly higher GH responses to exercise after running 30 minutes (p < 0.01) as well as 3 and 15 minutes (p < 0.05)

post exercise than moderately active control participants. Interestingly, results suggest no significant differences between trained and untrained women (50). These discrepancies may be due to the both protocol designs, including mode of exercise and duration at higher intensities.

Growth hormone responses to chronic aerobic training. Chronic AT seems does not affect resting GH values in both men (32, 50) and women (50). Despite mounting data supporting chronic training's inability to impact on GH concentrations, Weltman et al. (527) report that three weeks of high intensity AT (20 minutes per session) blunts GH responses. It has further been suggested that chronic training may result in increased sensitivity to GH in a similar fashion as increased sensitivity to insulin, which has been shown to occur after several weeks of training (195, 196).

Despite these findings in both aerobically and resistance trained individuals, the pulsatility of GH concentrations makes the measurement of "resting" concentrations almost meaningless (479). Indeed, Kanaley et al. (233) examined the impact of AT on GH concentrations over 24 hours using frequent sampling (every 10 minutes). This study reported that AT had no impact on total GH secretion in the 24 hours compared to the controls. Likewise, heavy RT was reported to have no impact on12 hour total GH concentrations compared to controls who did not exercise prior to overnight (365).

2.2.3.2 Insulin-like growth factor-I. Insulin-like-growth factor-I (IGF-I) is a somatomedin produced in the hepatic cells in response to GH secretion. GH interacts with heptatic cells to produce IGF-I and IGF-II both of which have been shown to have systematic action in provoking whole body growth and anabolism (373). Due to very similar structure to proinsulin, IGF's has a very high affinity for insulin receptors (298, 373). After secretion, IGF-I influences multiple anabolic actions in bodily tissue such as: lipogenesis in adipocytes (441), protein synthesis in muscle cells (504) and bone growth (358). Though IGF-II still elicits some anabolic effects in adults, it has been shown to predominately affect fetal growth (168), Thus, the focus of this section will pertain to only IGF-I.

Once IGF-I binds to cellular receptors, it is spliced into three different isoforms, IGF-IEa, IGF-IEb, and IGF-IEc (mechano-growth factor; MGF). Interestingly IGF-IEa appears to be more GH responsive, while MGF is relatively GH insensitive (167) but shows significant response to

muscle stretch stimuli (545). These reactions may mirror their respective physiological roles as it has been suggested that the IGF-IEa splice is required for muscle maintenance and MGF is required for satellite cell activation (167). It has further been shown that MGF does not enter the blood stream and its E domain works independently of IGF-I receptors (546). Moreover, evidence suggests that these peptides respond primarily to muscle damage (21, 137). The rest of this section will solely focus on mature IGF-I hormone concentrations.

Circulating IGFs bind to insulin like growth factor binding proteins (IGFBP), which are abundant in most bodily tissue and act as mediators as IGF-I and IGF-II activity (220). When bound together, the complex not only serves as a reservoir for IGF-I release, but also increases the half-life to12-15 hours (150, 425). Additionally, the binding of IGF-I to IGFBP may assist in preventing cross-binding of IGF-I to insulin receptors (408). Moreover, it has been hypothesized that different forms of IGFBP are significant factors in carrying IGF-I to target tissues where IGF-I are released by proteolysis of IGFBP or the binding of the IGFBP to the extra cellular compartment (49, 383). These actions together likely regulate the actions of IGF-I through manipulation of IGFBP concentration levels in target tissues (97, 342).

There are an abundance of IGFBPs subtypes with an array of functions (128) which have been shown to have varying responses to different exercise interventions and training statuses. High intensity interval exercise has been shown to increase both IGF-I and IGFBP-3 concentrations. Despite this finding, only IGFBP-3 area under the curve was significantly greater than that of the resting control (76). An hour after heavy RT, participants exhibited significant differences in only IGFBP-3 after the first hour and increases in IGFBP-2 and decreases in acid-labile subunit concentrations in the overnight response compared to resting conditions (368). Together these studies suggest that IGFBP subtypes respond to high intensity, though the responses are not uniform. Finally, prolonged exercise elicited increases both during and after diet and 60-minute AT interventions (362). Despite these seemingly uniform findings, the mechanism is still unclear as there is not an evident trend among these responses to different types of exercise or within the same types of exercise.

Further, chronic training also seems to have mediating effects on binding protein levels as 16 weeks of AT elicited increases in IGFBP-3 in exercisers while controls over this time period showed decreases (39), while IGFBP-3 fragmentation and IGFBP-1 were both increased in

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response to ultra-endurance exercise over six days (369). Conversely, participants exhibited significant decreases in IGFBP-3 after eight weeks of exercise training and diet restrictions (364). Moreover, research comparing RT single set and three set interventions exhibited decreases in only the three set intervention at 13 and 25 weeks. It was also shown that there were not significant changes in IGFBP-1 in either training session (324). In summary, chronic exercise has been shown to manipulate the IGFBP family but without uniformity. This section will be further dedicated to total circulating IGF-I concentrations.

Acute responses of insulin-like growth factor-I to resistance training. IGF-I has exhibited conflicting data in immediate response to RT, as some studies have shown no response (58, 261, 278) while others have suggested acute elevations both during and after RT exercise (268, 271, 426). Rodent models using GH-deficient lit/lit dwarf mice showed that there was a distinct time delay in IGF-I splice mRNA expressions after GH administration. It was after four hours that both IGF-IEa and (MGF) expression had increased in the liver but only MGF was expressed in the muscle. But 12 hours after treatment, hepatic concentrations of both IGF splices had returned to baseline, while expression in the muscle had increased for both splices (204) further implying that once GH is secreted into the blood, there is still a time delay in IGF-I response. Kreamer et al. (268) has reported similar results in the both men and women in response to RT with initial increases in GH concentrations followed by increases in IGF-I.

Insulin-like growth factor-I responses to chronic resistance training. The effects of chronic RT have shown conflicting results in alteration of resting IGF-I, suggesting either no alteration in resting IGF-I concentrations during extended RT protocols (271, 329) or increases in both women (326) and men (259). Training status also alter resting IGF-I concentrations, as strength trained men have been shown to have higher resting concentrations (426). Moreover, training volume seems elicit significant effects in these responses as progressive swim training has shown to increase resting IGF-I concentration levels by 76% (p<0.05) as compared pre-training values (259). Furthermore, single sets of circuit training only increased IGF-I levels after 12 weeks while multiple sets increased resting levels at both 12- and 24-weeks (326). These results were later supported by Borst et al. (39), who reported resting IGF-I concentrations increased by nearly 20% (p=0.041) after 13-weeks of training for both single and multiple set

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programs. Despite conflicting data, volume of training and training status may also influence in chronic levels of circulating IGF-I concentrations.

Acute responses of insulin-like growth factor-I to aerobic training. While research examining the acute effects of AT on IGF-I concentrations in the blood is scarce, current literature has shown conflicting results as increases (379, 451) and no changes (75, 313) have both been reported in men and women. De Palo et al. (379) has shown evidence of increased IGF-I concentrations to both long duration (40 minutes exercise consisting of a ten minute warm-up, 15 minutes at 70-80% of VO_2max followed by 15 minutes of increasing workloads until exhaustion) and short duration (25 minute exercise consisting of the ten minute warm-up and 15 minutes of exercise at exhaustion) AT (66±10 to70±10nmol/l; p<0.05 and 55±14 to 61±15nmol/l; p<0.005, respectively). These results support earlier works suggesting that exercise performed at both high intensities and low intensities for 10 minutes can elicit increases in IGF-I concentrations (7.7±2.7%; p <0.05 and 13.3±3.2%; p < 0.002, respectively) (451) .

Conversely, evidence has suggested that 40 minutes of cycling at 75% of maximal heart rate did not provoke significant increases in IGF-I concentration levels in women regardless of age (75). Likewise, Wideman et al. (534) suggested that 30 minutes of constant load AT does not provoke significant increases in IGF-I concentration as compared resting concentrations. It would appear as if the differences in training protocols could be the possible reason for the differences in the aforementioned results. As such, the intensity of the AT is the potential key factor in provoking increases in IGF-I concentrations, though these responses may be unrelated to GH secretion (451).

Insulin-like growth factor-I responses to chronic aerobic training. While most of the literature suggests that chronic training has no effect on resting levels of IGF-I (10, 509, 550), conflicting data still exist suggesting both increases (259) and decreases (212, 361, 369). Most recent evidence of was reported in young sedentary women who underwent AT intervention for 16 weeks. Subjects were asked to exercise five times per week at a specific intensity based upon their age predicted heart rate maximum which was increased every four weeks. Despite showing slight decreases in IGF-I concentrations (-11.1±5.5ng/ml), no significant differences were observed compared to baseline or control measures (10). These data mimic earlier results in young and mature male cyclists, once again suggesting a slight, non-significant decrease in IGF-I

concentrations (274.4±78 to 227±23.2ng/mL and 149.5±14.1 to 123.4±16ng/mL, respectively; p>0.05) (550).

Other factors such as age (75, 550), health status (212, 361) and activity level (369) may contribute to the effects of chronic AT on IGF-I concentrations. As with many of the other hormone profiles, older individuals seem to exhibit lower IGF-I concentrations in both men (550) and women (75). Notwithstanding these decreased levels, most studies suggest that chronic AT does not elicit IGF-I changes in in aged populations (75, 509, 550), though there conflicting results exist (398).

Interestingly, evidence in obese population suggests that chronic AT for 60 minutes combined with a monitored diet elicited significant decreases (20%; p<0.01) in IGF-I after 11 days Further, serum IGF-I levels in a long-term (14.2±1.7 years) sub group were 55% lower than baseline (p<0.01) (361). Likewise, individuals who had not been active for at least two years demonstrated significant decreases in IGF-I concentrations (245±28 to 223±22ng/ml; p<0.05) after six weeks of low intensity AT (369). To any extent, it is not clear how the effects of chronic AT influence resting IGF-I concentrations and further investigation is required.

2.2.3.3 Cortisol. When subjected to stressful conditions, neuroendocrine response initiates the activation of the hypothalamus-pituitary-adrenal axis; allowing for adaptation to increased physiological demands and maintain homeostasis. Under these conditions, the hypothalamus secretes corticotropin-releasing hormone (CRH), which stimulates the secretion of adrenocorticoptropic hormone (ACTH) from the pituitary gland, ultimately, provoking the production of glucocorticoids from the adrenal cortex. The primary glucocorticoid in humans is cortisol, of which only 5-10% is unbound in the plasma and is biologically active (286). It has also been shown that cortisol has greater effects in type II muscle fibers than type I muscle fibers (274). Cortisol's catabolic effects on both skeletal muscle (328) and fat tissue (lipolysis) (387) make it of interest when considering both acute and chronic tissue remodeling after stressful environments such as exercise.

Acute responses of cortisol to resistance training. Much like GH, RT protocols that produce high amounts of lactate also have a strong correlation with creatine kinase (263) and cortisol production (264, 409). Indeed, when compared against each other, strength (four sets of

five at 88% 1RM with three minutes rest), hypertrophy (four sets of 10 repetitions at 75% 1RM) and strength endurance (four sets of 15 repetitions at 60% 1RM), hypertrophy and strength endurance protocols provoked significant increases in both lactate (1.17 ± 0.09 to 3.97 ± 0.41mmol/l and 1.25 ± 0.03 to 4.30 ± 0.31, respectively; $p<0.05$) and cortisol (325 ± 29 to 449 ± 78nmol/l and 335 ± 28 to 495 ± 54nmol/l, respectively; $p<0.05$) after 30 minutes of exercise in young men (551). Together, these correlations would suggest that cortisol responses to the high amounts of total volume common in hypertrophy protocols compared to strength or power training protocols, which have not shown significant changes in acute concentrations in cortisol 30 minutes after exercise (464, 551).

Additionally, manipulation of the factors making up training workload (sets, repetitions, and intensity) has been shown to increase cortisol concentration. When set number was held constant, higher rep schemes (hypertrophy: 10 repetitions and strength endurance: 15 repetitions) seemed to provoke greater acute cortisol responses than low reps schemes (strength: five repetitions) ($p<0.05$). Moreover, authors report that when repetitions were held constant were and sets were varied (two, four, and six sets), four and six sets of 10 repetitions elicited greater increases in cortisol levels ($p<0.05$), with now significant differences between the two (464). Likewise, manipulation in intensity has been shown to acutely increase cortisol levels. Indeed, during a forced repetition protocol with 15% greater training load demonstrated increases in cortisol concentrations (0.035 ± 1.1 to 0.65 ± 0.11μmo; $p<0.001$) (6). Finally, rest interval manipulation exhibits significant changes in acute concentrations as Kraemer et al. (265) reported rest intervals of one minute provoked greater elevations in cortisol concentrations than three minutes when loads were held constant ($p<0.05$). Despites the convincing evidence of relationship between high workloads and cortisol concentration elevation, there is still conflicting evidence, though concentration levels were trending post-exercise ($p=0.09$) (538). These acute responses may play a substantial role in the tissue reconstruction in response to resistance exercise.

Cortisol responses to chronic resistance training. Chronic RT has shown no change (5, 159, 160, 162–164, 401), to decreases (7, 161, 277, 326, 329), to increases (155) which appears to mirror long-term training stressors. Hence, it appears that acute responses in cortisol concentrations may insinuate previous metabolic stress while chronic elevated cortisol levels

may suggest adaptation in tissue homeostasis concerning protein metabolism (274). Further investigation is warranted to investigate factors influencing chronic concentrations and the implications thereof.

Acute responses of cortisol to aerobic training. Cortisol has been reported to consistently acutely increase in response to a single session of AT in men (238, 318, 454) and women (74). Marathon racing has been reported to significantly increase cortisol concentrations 30 minutes after race completion (338±147 to 1640±884mmol/l; $p<0.01$) in healthy males (454). Additionally, Karkoulias et al. (238) reports that cortisol concentrations remain elevated 60 minutes after race completion (13.4 to 24.4 µg/dl) in male non-athletes. Interestingly, authors reported cortisol levels were still slightly increased one week after the race (19.2µg/dl), though not significantly different from baseline values. Additionally, cortisol has been shown to increase with increases in volume. When cortisol levels were compared after 19km and 42km kayak races, it was shown that 42km post-race concentrations were significantly higher than 19km (0.447±0.110 to 1.005±.410µmol/l v 0.312±0.063 to 0.476±0.124µmol/l, respectfully; $p<0.05$) in elite male kayakers (318). Though the majority of literature suggests that AT elicits significant increases, there is evidence to the contrary. When 120 minutes of continuous cycling at 55% of peak power output was compared with two high intensity interval exercise protocols (four sets of four minute intervals at 90-95% peak power output and four sets of 30 second intervals at maximal effort sprints), continuous cycling provoked significantly lower cortisol concentrations ($p<0.001$) (515). Notably, authors suggest that these differences can be attributed to different training protocols than other studies. In summary, AT provokes increases in cortisol levels. It is possible that these increases are mediated by exercise volume as greater distances have been shown to elicit greater responses in cortisol.

Cortisol responses to chronic aerobic training. Chronic AT has shown to invoke no change (32, 152, 171, 184, 472, 496, 501) and increases (499) in basal cortisol concentrations which may reflect current long-term training stressors. While most of literature show no changes in basal cortisol levels, Tsai et al. (499) studied elite endurance athletes over the course of their competitive season and took blood samples at three time points (off season, mid-season, and late in the competitive season). Female athletes exhibited significant increases in basal cortisol levels from the off season to the third blood draw ($p<0.05$). Interestingly, authors reported that male

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athletes did not demonstrate the same trend. Despite this evidence, most of literature suggests that cortisol concentrations do not change with chronic AT.

2.2.3.4 Estrogen. In addition to its primary effects in the body, testosterone also acts as a precursor to estrogen production. Though the ovaries differentiate later than the testes, the mechanism is still the same, the aromatization of androgens via reactions with the enzyme 5-α-reductase. Although estrogen does not have the same androgenic and anabolic properties as testosterone, it has been shown to have specialized qualities such as reduction in bone reabsorption (372) and muscle damage (243), which may insinuate specific consequences in terms of adaptations to exercise. Estradiol is considered the most active from of estrogen in humans and is often the focus of study when estrogens are studied during exercise. Few studies have suggested acute elevations in estradiol concentrations following resistance exercise in women (74, 75, 260, 516) and men often experience no change in estradiol concentrations from training (161). When examined over time, evidence suggests that basal estradiol concentrations are not altered following 16 weeks of power training (164). In summary, the response and subsequent role of estradiol is still not fully understood in regards to muscle performance and adaptation.

2.2.3.5 Erythropoietin. Upon the decrease of oxygen concentrations (oxygen saturation) in the blood stream, the kidneys respond with the production and release of a protein hormone called erythroproietin (EPO). Further, it has been suggested that the liver may also produce small amounts of EPO, as it has been shown to be the main production site for fetal EPO (523). The primary role of EPO is to enhance the proliferation of erythrocyte precursor cells in the bone marrow into erythroblasts and, subsequently, differentiate erythroblasts into erythrocytes or red blood cells (RBC) (252). It has been purported that blood draws of 450ml elicit significant increases in EPO concentration within 24 hours of phlebotomy (100). Consequently, this elevation of RBC concentrations in the blood causes an increase in the content of the oxygen carrying protein, hemoglobin which leads to increases in oxygen carrying capacity to working muscle. Further, in order to elicit an increase in EPO, there must be a decline in arterial haemomoglobin saturation below 91% (415) compared to normal levels ($\geq$95%). Much data exists to support the EPO responses to hypoxic environments; however, there is scarce evidence

of its responses to both acute and chronic RT protocols. There is however, research regarding EPO and AT, which this section will focus of this section.

   Acute responses of erythropoietin to aerobic training. EPO has been studied across a multitude of endurance focused sports including cross-country skiing (255), cycling (255, 444), long distance running (450, 524) and biathlon (412). Among these varied studies, there is not a uniform response to AT as studies have shown both increases (100, 444) and no effects (100, 444). Interestingly, these responses appear to be influenced by outside factors, such as duration (450), intensity (415), and environment (100, 444). Though there is conflicting data (524), marathon running has been shown to significantly increase EPO concentrations in 15 well trained runners up to 30 hours after race completion (450). Conversely, shorter AT interventions of 60 minutes or less at moderate intensities have not been able to elicit these same responses (255). Together, these studies suggest there may be a duration of activity threshold for eliciting an increase in EPO concentration as marathon running takes over two hours to complete and in comparison to other interventions lasting only an hour or less.

   Additionally, intensity appears to influence EPO concentrations as three minutes of supramaximal (109±2.8% VO_2max) exercise provoked a significant 28% increase in EPO 24 hours post exercise in male athletes. Further, participants had ≤ 91% arterial oxyhaemoglobin saturation after supramaximal exercise (415). It is suggested that this drop in oxyhaemoglobin saturation is required to elicit increases in EPO concentrations (415, 444). Interestingly, maximal exercise to fatigue has not been shown to induce significant changes in EPO concentrations (444). Again, there appears to be a threshold that must be met in order to manipulate EPO levels as supramaximal intensities have been successful while maximal and submaximal intensities have not.

   Finally, the environment in which the exercise is being performed appears to be influential in eliciting significant increases in EPO concentrations. Increase in altitude (2005-2100 meters above sea level) has been shown to stimulate increases in EPO concentrations within hours of exposure to hypoxic environments (427). Likewise, blood removal via phlebotomy can be considered a hypoxic endogenous environment due to decreases in blood oxygen carrying capacity. Thus, phlebotomy of 450 ml has also been shown to elicit significant increases in EPO within 24 hours of intervention. Further, during incremental exercise following

phlebotomy there was a tendency for further increase in EPO concentration (p= 0.09) (100). These studies suggest as long as oxygen carrying capacity is hindered there will be an increase in EPO concentrations.

Erythropoietin responses to chronic aerobic training. Because tissue hypoxia is the primary stimulus for EPO production (415), effects of chronic training on EPO concentration levels is very scarce in the literature. Interestingly, male triathletes who swim, bike and run have been shown to have lower EPO concentrations (26.3U/ml) compared to distance runners (31.6U/ml) (p<0.05). Despite these differences, the mean concentration levels of both groups were not different from sedentary controls (26.5-35.3U/ml) (524). After a two-week detraining period, athletes who retrained for four weeks saw no increases in EPO concentrations (255). Again there is evidence that environmental factors may have substantial influence on EPO concentration levels. World class male biathlon athletes exposed to moderate altitude conditions (2050m above sea level), demonstrated increases in EPO concentrations after four days of exposure. Interestingly, there was no further increase in EPO concentrations over the course of training at altitude. Furthermore, 16 days after returning from altitude, EPO concentrations returned to those prior to the three-week training period (178). EPO concentrations are substantially influence by tissue environment as hypoxic environments have shown to elicit chronic increases in EPO concentrations, while current evidence infers that chronic training at normoxic conditions does not elicit the same response.

2.2.3.6 Hormonal Responses to Concurrent Training. Research on the effects of CT's influence on anabolic and catabolic hormonal profiles is very limited. Available research has examined an array of protocols including: chronic (27, 52), acute (66) and intra-exercise (51) in both men and women (27). However, despite this dearth of evidence, there is little effect of CT on anabolic and catabolic hormonal profiles. Bell et al. (27) reports that 12 weeks of CT (consisting of continuous exercise at ventilatory threshold and moderate to heavy intensity full body resistance) had no significant influence on testosterone, GH, or SHBG in both men and women. Ahtiainen et al. (4) further this notion by showing no significant change in serum testosterone concentrations after 21 weeks of CT.

Conversely, acute CT has been shown elicit increases in total testosterone in young (23.5 ±0.9 years) strength-trained men when strength training followed AT for two days. Additionally,

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cortisol was shown to increase after the initial exercise but returned to resting levels after the second modality of exercise, regardless of order (51). Finally, CT has been shown to decrease free testosterone in elderly men (52). These studies suggest that there is still not a definite finding on CT's influence on anabolic and catabolic hormones due to confounding factors such as training frequency, intensity, and duration; further suggesting a need for future research.

In conclusion, RT and AT modalities influence very different cellular pathways ultimately resulting in different outcomes in both cellular protein make-up and acute and chronic hormone levels. Though there is a sufficient amount of evidence to support the interference theory, the large number of variables that influence training adaptations (i.e. intensity, duration, and volume) still makes it difficult to clearly come to a conclusion. Further research is needed to fully explore these variables and the subsequent outcomes.

2.3 Influence of Nutritional Supplementation on Body Composition, Strength and Power

2.3.1 Primary Ingredients: Creatine Monohydrate, Caffeine, Beta-Alanine and Branch Chain Amino Acids

As previously mentioned, four ingredients have become very common in most MIPS products: creatine monohydrate (CM), caffeine, beta-alanine (BA) and branch chain amino acids (BCAAs). These main ingredients have been shown to have positive effects on body composition and/or most aspects of performance individually (31, 292, 513) and in combination (377). Briefly, supplementation with CM has been shown to significantly increase lean body mass without increases in fat mass (8, 25, 61, 213, 510, 511, 513). Similarly, BCAAs have also been shown to enhance increases in fat free mass in young (31, 54) and mature populations (249). Interestingly, the BCAA leucine seems to stimulate the activation of mTORC1 (146), one of the primary proteins in facilitating muscle protein synthesis. Conversely, caffeine has been shown to influence body composition through the loss of fat mass, rather than increasing lean mass (1, 142, 292). Finally, BA's effects on body composition are not very well understood as research shows conflicting results (244, 246, 284, 465). Overall, these four primary ingredients seem to elicit positive effects on body composition through manipulation in increases in lean mass or decreases in fat mass.

Additionally, these four primary ingredients also seem to also have positive influence on exercise performance. Indeed, a multitude of evidence suggests that CM increases strength performance (41, 61, 289, 510). Moreover, CM has also been shown to help improve aerobic performance though the attenuation of blood lactate accumulation (63, 141). Though BA (24) and Caffeine (230) do not have direct effects on maximal strength increases, both have been shown to have positive effects on strength and power endurance (88, 189, 230, 246, 480, 482). Further, these two ingredients have been shown to improve sprint performance (99, 446), suggesting they may elicit improvements in anaerobic power output. Likewise, caffeine and BA have also been shown to have positive influence on duration of AT at submaximal intensities (385, 395, 397, 556). This evidence suggests that chronic supplementation of BA and caffeine may lead to greater increases in exercise performance through the adaptations caused by increases in both AT and an RT volume. Similarly, BCAAs have not been shown to have a direct influence on strength performance. Regardless, BCAA's have been shown to have therapeutic effects on exercising muscle through reduction in delayed onset muscle soreness (DOMS) measures (197, 215, 371, 455, 460), which may contribute to the strength increases seen in BCAA supplementation studies (80, 249). Additionally, BCAA's have been shown to extend time to exhaustion in both mouse (53) and human models (341). In summary, supplementation with these primary ingredients has been shown to enhance exercise performance and the adaptations thereof.

Rhodiola rosea and Cordyseps sinensis are two other ingredients that may have potential in enhancing exercise performance. Despite the sparse research on these ingredients, there is evidence suggesting these ingredients may aid in improving endurance performance. The mechanisms of action and possible benefits for body composition and exercise performance will be focus of the rest of this section.

2.3.2 Rhodiola Rosea
     2.3.2.1 Mechanism of action. Rhodiola rosea (RR) has been reported to have direct effects on the central nervous system. Though the mechanism is still unclear, it has been suggested that RR works through a variety of mechanisms in rodent (388) and human (380, 473) models. RR is a root that primarily grows in Eastern Europe and Asia (242). Primarily, RR is part of the adaptogen family, which has been found to have chemical phenolic compounds

(phenylpropanoids and phenthylethane derivatives) structurally similar to catecholamines. RR, specifically, contains monoterpene glucoside rosiridin, which an *in vitro* study has suggested to inhibit monoamine oxidases A and B (91), which have been shown to deactivate neurotransmitters (438). Additionally, RR also contains the active compound tyrosol which has been shown to increase the phosphorylation of eNOS and FOXO3 and induces extended expression of SIRT1 (434), which has been shown to increase mitochondrial biogenesis through activation of AMPK and PGC-1α. Further, this activation hinders protein synthesis through negatively regulating mTORC1 through TSC activation (392). Moreover, evidence in an animal model suggests that tyrosine, a precursor to tyrosol synthesis, alleviates stress-associated depletion of brain catecholamines, norepinephrine and dopamine, resulting in improved task performance (completion of a task related skill) and reduced fatigue (378). Further, a few reviews reference Russian studies suggesting rhodiola rosea enhances the effects of these neurotransmitters by increasing the permeability of the blood brain barrier to precursors of dopamine and 5-HT (242, 248).

Likewise, extracts of RR have been shown decrease genes involved in adipocyte function, SLC2A4 and adipogenic factor FGF2, and significantly increase in the expression of genes involved in the inhibition of adipogenesis, GATA3, WNT3A, and WNT10B (399). Additionally, RR extracts have been shown to down-regulate PPAR-γ which is responsible for adipogenesis (399). These data suggest that RR may have both lipolytic and anti-adipogenetic properties.

2.3.2.2 Body composition. The effects of RR supplementation on body composition are quite scarce in the literature. Most recently, an *in vitro* study using two commercial extract from RR (salidroside and rosavines) in primary human visceral pre-adipocytes exhibited evidence suggesting rosavines extract was more effective in regulating the mechanisms of adipogenesis while salidroside induced lipolysis and the loss of differentiating cells by apoptosis (399). Further, when used in combination with citrus aurantium (bitter orange), RR provoked significant decreases in feeding (10.5%) in rats compared to RR or citrus aurantium alone. Additionally, animals ingesting this combination when on a high-fat diet for 13 weeks exhibited significantly lower visceral fat compared to paired fed animals and animals receiving RR or citrus aurantium alone (p<0.05). Further, differences between the RR and citrus aurantium group and the vehicle approached significance (p=0.09) (508). Moreover, it was shown that four weeks

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of 170mg RR supplementation in trained male athletes (25±5 years of age) resulted in significantly reduced serum free fatty acid concentrations levels at the immediate cessation of exercise (7.31±1.31mg/dl; p<0.05) and 30 minutes after maximal endurance exercise (7.01±1.16mg/dl; p<0.01) compared to a placebo group (12.86±1.62 mg/dl and 11.41±0.56 mg/dl, respectively) (382), suggesting the ability to alter substrate utilization during maximal AT. Conversely, when recreationally active young men supplemented with RR (3mg/kg body mass), no change in substrate utilization was shown during a 30-minute submaximal cycling trial (101). Due to this limited amount of evidence, the conclusion is still unclear as to RR effects on body composition and warrant further investigation.

2.3.2.3 Performance. Traditionally, RR is often used in combination for endurance related activity (33, 71, 103, 200, 370). De Bock et al. (33) reported that an acute dose of RR (200mg) significantly increased time to exhaustion (16.8±0.7 v 17.2± 0.8min) and VO_2peak (50.9±1.8 v 52.9±2.7ml/kg/min) on a cycle ergometer, compared to placebo. Interestingly, chronic (four weeks) supplementation without training did not provoke any differences in maximal aerobic capacity from PLA. These results have been mimicked in a rat model with rodents receiving chronic (two and four weeks) RR supplementation of varying doses (5mg, 25mg and 125mg). Indeed, after two weeks, 25mg and 125mg of RR supplementation elicited significantly increased swimming time to exhaustion 22.5% and 42.95, respectfully (p<0.05). Further, four weeks of 5mg, 25mg and 125mg RR supplementation increased swimming time by 20.9%, 49.9% and 65.0%, respectfully (p<0.05) (294). Additionally, chronic (four weeks) RR supplementation (170mg) has been shown to reduce lactate and creatine kinase concentrations in well-trained aerobic athletes (382). Conversely, there is evidence of RR supplementation having no significant effects on aerobic performances (71, 103, 382). Additionally, there is evidence suggesting that RR has no significant effect on isometric muscle contraction strength measures in either the acute (60 minutes prior) or chronic (four weeks) supplementation protocols (33).This limited, equivocal evidence merits further research into RR supplementation in combination with different training protocols.

2.3.3 Cordyceps Sinensis

2.3.3.1 Mechanism of action. Codryceps sinensis (CS) is a fungus that has long been used in traditional Chinese medicine for increased longevity, medical treatment, improvement of

quality of life and increases in athletic performance (386, 555). The fungus consists of many active components including adenosine, cordycepin, cordycepic acid, d-mannitol, polysacchardies, vitamins and other trace elements (287). Supplementation with CS have shown positive effect on endurance related exercise in both animal (287) and human models (60). Further investigation in animal models suggest that CS supplementation upregulates AMPK-1α, peroxisome proliferator-activated receptor- delta (PPAR-δ) and PGC-1α, key regulators in glycogen break down, glycolysis, glucose uptake and fatty acid oxidation metabolic processes (287). Both AMPK and PGC-1α proteins contribute significantly to the enhancement of endurance capacity. Further, PPAR-δ has been shown in muscle-specific transgenetic (PPAR-δ) rodent models to increase muscular fatty acid oxidation and glucose uptake and storage and mitochondrial pyruvate oxidation (127). Interesting, the same model suggests that increases in PPAR- δ result in lower lactate levels post high intensity exercise as compared to wild-type controls (127). Moreover, Wang et al. (521) suggest that increases in PPAR- δ muscle expression can lead to increases in oxidative enzyme concentration, mitochondrial biogenesis and production in type I fiber contractile proteins; the three trademarks of muscle fiber type switching.

Additionally, animal model evidence suggests CS supplementation enhances expression of monocarboxylate transporter 1, which is a sub group protein of monocarboxylate transporters responsible for the transportation of molecules consisting of one carboxylate group across cellular membranes, such as lactate (287). Indeed, reports of increased metabolic threshold, the moment when hydrogen ions stimulate ventilation, in human models further support this notion (60). Healthy mature (50-75 years of age) adults were divided into either a CS supplementation (999mg) or placebo group for 12 weeks. Upon completion of the study, CS supplementation resulted in improvements in metabolic threshold (+10.5%; 0.83$\pm$0.06 to 0.93$\pm$0.08 l/min (p =0.022)), while placebo exhibited no changes in maximal incremental exercise on a cycle ergometer (60).

Evidence also suggest that CS supplementation significantly increases glucose transporter 4 (GLUT4) expression in both sedentary and exercised CS animal groups compared to a control group, but were not different from animals in the exercise only group (287). These findings support earlier findings exhibiting lowered basal blood glucose and insulin levels with CS

supplementation suggesting enhanced glucose metabolism through improved insulin sensitivity (553).

Finally, CS supplementation in both sedentary and exercising animal models increased vascular endothelial growth factor (VEGF) (287) which is responsible for capillary angiogenesis (245). Consequently, increased expression of VEGF could lead to increases in capillary density, allowing for greater delivery of blood and subsequently oxygen to working muscles. Though many of these mechanisms have yet to be supported by human models, the evidence of purported responses to CS supplementation in animal models would accumulate into greater work capacity through both manipulation of metabolic mediating proteins and delivery systems.

2.3.3.2 Body Composition and performance. CS is another supplemental ingredient that has inadequate evidence supporting its efficacy in body composition measures as a primary supplement intervention or in combination with exercise interventions. Additionally, CS has primarily been studied in endurance exercise protocols (59, 71, 103, 287). Interestingly, Chen et al. (59) combined RC (1400 mg) and CS (600 mg) into a MIPS. Further, chronic supplementation was combined with high altitude training for two weeks. The authors reported that supplementation with the MIPS elicited increases in run time to exhaustion (5.7%) compared to the placebo (2.2%; $p<0.05$) in young male long distance track athletes (19.7±0.2 years). These findings support earlier results in an animal model suggesting CS supplementation extends time to exhaustion while swimming in rats (287). These scarce data warrant further investigation into the possible performance outcomes of supplementation with CS as a primary intervention and in combination with exercise protocols.

CHAPTER 3

RESEARCH DESIGN & METHODOLOGY

3.1 Experimental Approach to the Problem

The present study had a double-blind, randomized, placebo-controlled design. The supplement *Shroom Tech Sport* [TM] was chosen due to its main active ingredients, rhodiola rosea and cordyceps sinensis, which have been shown to individually attenuate fatigue in aerobic performance (33, 287). Despite these results, it is still unknown if these ingredients can improve anaerobic performance when combined with a high intensity CT protocol. For this reason, strength, and power performance will also be measured in conjunction with aerobic measures. Likewise, it is unknown whether this combination of ingredients improves overall health; therefore blood lipids and glucose markers will be tested.

3.2 Subjects

Thirty-four college-aged men were recruited to participate in this study. Participants were required to have at least two years of recreational exercise three times a week. Participants were not be admitted to the study if they had prior history of pre-existing skeletal muscular disorders or anabolic steroid use. Likewise, participants were non-smokers. Participants using supplements (with the exception of protein or multivitamins) were required to undergo a three-week wash out period prior to beginning this study. Participants were required to sign the written informed consent document and complete a medical history questionnaire prior to beginning the study. All procedures were approved by the Florida State University Human Subjects Institutional Review Board in accordance with the Helinski Declaration.

3.3 Procedures

3.3.1 Laboratory Testing

All testing procedures, except circumference measurements, took place at the Institute of Sports Science and Medicine (ISSM) at Florida State University in the morning (0500 to 1000 hours) under fasted conditions (≥8 hours after last meal). Circumferences were measured in the afternoon (1400 to 1700 hours) in William Johnson building at Florida State University. Each test was completed three times (baseline, mid-point, and post-training) (Figure. 1). Performance

testing began with strength and power testing no less than 72 hours after the final training session in order to avoid residual soreness from the final training session.
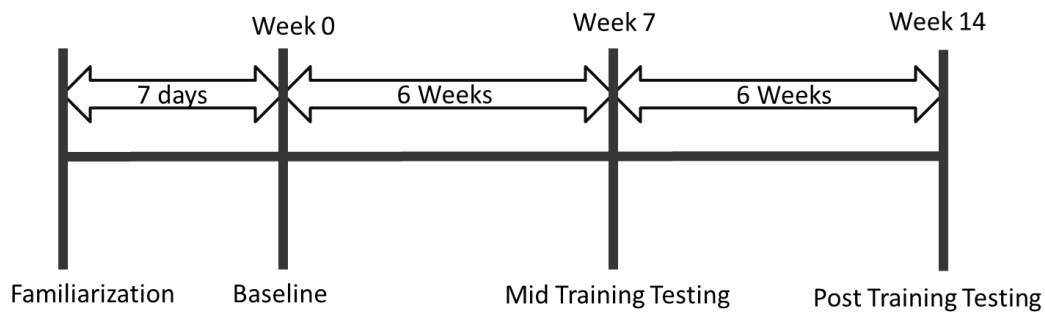
Figure 4. Timeline of Performance Test and Blood Draws

Table 1: Weekly Testing Schedule

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
Rest	Body Comp Blood Pressure Blood Draws	Maximum Strength Wingate	Rest	Body Scanner	VO$_2$Max Lactate Threshold	Rest

3.3.2 Questionnaires

Mood state was assessed via Profile of Mood State questionnaire, which is used to quantify tension, depression, anger vigor, fatigue and confusion based upon responses to 65 descriptors recalled over the past seven days (337). Participants completed this questionnaire in a fasted state, in a quiet room, during baseline and post-training testing periods. Subject did not take their respective supplement until after the blood draw on this day.

3.3.4 Blood Pressure and Heart Rate

Fasted, resting heart rate, systolic (SBP) and diastolic (DBP) blood pressures were measured in the supine position after five minutes of undisturbed supine rest in a quiet room. Heart rate was measured using the radial artery. Blood pressures was measured using the guidelines previously established (121). Briefly, the blood cuff was placed 2.5 cm above the elbow crease and inflated to about 30mmHg above estimated SBP. Cuff pressure was then be released at a consistent rate until the last Korotkoff sound is heard. Blood pressure was taken by the same researcher during the entirety of the study.

3.3.5 Anthropometrics and Body Composition

Measurements of height (Seca, Chino, CA) were recorded without shoes and rounded to the closest 0.1cm. Body mass was also recorded without shoes using the scale associated with the Bod Pod (COSMED, Chicago, IL). Body composition was measured using the Bod Pod (COSMED, Chicago, IL) with subjects seated in the pod in accordance with manufacturer's instructions. Circumference measurements was taken via TC2-19 three dimensional body scanner ($[TC]^2$, Cary, NC). In accordance to instructions set forth by the manufacturer, subjects were asked to wear light colored tight fitting underwear. Subjects did not be fasted for this measurement

3.3.6 Blood Sampling and Analysis

Fasted venous blood samples were collected (20 ml) from an antecubital vein and then allowed to clot at − 4 °C for 20 minutes. Samples collected in EDTA were then be centrifuged (Thermo Fischer Scientific, Waltham, MA) for 15 minutes at 3,500 rpm at four degrees Celsius, with the resultant supernatant aliquoted into multiple microtubes and stored at -80 degrees Celsius until analysis. Serum was analyzed for total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL) and glucose (Cholestech LDX, Hayward, CA). Additionally, serum was analyzed for total (TT) and free (FT) testosterone, estrogen, cortisol, insulin, insulin-like growth factor-I (IGF-I), and creatine kinase (CK). All of which will be analyzed using commercially available ELISA kits (VWR International, Radnor, PA).

3.3.7 Strength Testing

Subjects reported to the ISSM to complete maximal strength tests for squat and bench press in a fasted state, only having taken their supplement 45 minutes prior to testing. One

repetition maximum (1RM) was defined as the maximum amount of weight lifted one time through the full range of motion using proper form, according to the National Strength and Conditioning Association (NSCA) (20). Participants followed a warm-up specific to each lift as designated by the NSCA (20). Participants first completed the squat protocol, rest five minutes, and then completed the bench press protocol. For the squat exercise, participants performed five, three, two and one repetition at 50%, 70%, 90% and 100% of their most recently recorded 1RM (either during familiarization or previous testing period). Participants were given one, two, and four minutes of rest between each set, respectively. Likewise, participants completed five, three, two, one and one repetitions with 50%, 60%, 80%, 90% and 100% of previously recorded 1RM. Sets were separated by one, two, four and four minutes of rest. Upon successfully achieving 100% of most recently recorded 1RM, participants attempted higher weight after four minutes of rest. This process continued until participants failed to successfully complete the movement. Proper execution of the squat required the participant's hip crease will be required to be lower than that of the level of the knee (557). Similarly, proper execution of the bench required the participant's feet to remain on the floor, while hips, shoulders and head must remain flat on the bench (557).

Participants were allowed to use lifting equipment (i.e. shoes, belts, and wrist wraps); however, the equipment was required for training and all strength tests for the duration of the study. Participants were allowed to choose their personal lifting style for each of the tested lifts as long as each technique followed the USA Power Lifting (USAPL) rules (557). In addition, if the requirements for proper lift movement were not met, the lift was not accepted. Each lift was assessed by a certified strength and conditioning specialist (CSCS). If a maximal lift was unsuccessful, subjects were given the option to lower the weight or attempt the same weight again. Outside influences were controlled, such as music, which were prohibited during testing. Each participant was given equal verbal encouragement by researchers. Testing sessions occurred 72 to 96 hours after the final training session in order to reduce the effect of the last training session at mid-point and post-training testing, though supplementation continued as prescribed.

For each lift, after unracking the bar, the subject were unable to begin the lift until the CSCS gave a verbal "start" command. Upon hearing this command, participants completed the

movement. The participants were then be able to rerack the bar after a verbal "rack" command. The lift was not accepted until the final command is provided and the required protocol was followed.

3.3.8 Power Testing

Power output was tested in both strength movements and during a Wingate test. For power to be tested during the strength tests, a Tendo unit (Tendo, IRMO, SC) was attached to the barbell. Peak power and average power were recorded for each maximal lift.

Five minutes after strength testing, participants performed a Wingate test on a Velotron cycle ergometer (Racermate, Seattle, WA). Participants were fitted to the cycle ensuring that the seat height was lined up with the hip. After mounting the Velotron, the seat and handle bar height were further moved to ensure that the participant is comfortable and there is a 25-35 degree bend in their knee (390). Once comfortable, participants were given 20 seconds of warm up followed by a six second acceleration phase, during which they attempted to pedal as fast as possible to attain peak cadence. Immediately following the acceleration phase, a load equivalent to 7.5% of the participant's body mass was added to the fly wheel. Participants continued to pedal as fast as possible for the remaining 30 seconds (14). Upon completion of this test, peak, minimum and average power and fatigue index were recorded.

3.3.9 Lactate Threshold and VO$_2$max Testing

Participants arrived to the ISSM building in a fasted state, only having taken their supplement 45 minutes prior to their testing session. First, they performed three minutes of walking on the treadmill at three miles per hour (4.8km/hr). Upon completion, the treadmill was then fixed at a speed equivalent to the participants' 10 on the Borg rate of perceived effort (RPE) scale for the duration for the lactate threshold and VO$_2$max test. This speed was determined during the familiarization session. For the lactate threshold test, the percent grade was increased one percent every three minutes. After the sixth stage, inclines were increased two percent every three minutes for the remaining stages of the test (stages: 0%, 1%, 2%, 3%, 4%, 5%, 7%, 9%...).After each stage, the participants were instructed to straddle the treadmill to allow for blood collection via finger prick. Before each finger prick, the finger was cleaned with an alcohol swab and gauze. Lactate levels were assessed by Lactate Plus (Nova Biomedical, Waltham, MA). Participants returned to running at the next stage immediately after blood was

collected. A fixed marker of 4.0mmol/l was used to define the onset of blood lactate accumulation (OBLA) as it has been shown to be a valid marker for physiological changes in regards to endurance performance (363). Upon reaching this value, the test was terminated and participants resumed walking at three miles per hour (4.8km/hr) for six minutes to allow for active recovery.

After the six minutes of active recovery, the treadmill was returned to the given speed and grade associated with OBLA and the timer was started to measure time to exhaustion. Every minute the treadmill grade was increased two percent. Likewise, heart rate, VO_2, and respiratory exchange ratio (RER) was measured by a metabolic analysis system (PARVO, Sandy, UT). Additionally, participants reported their RPE in accordance to the Borg Scale of RPE. Before increasing the grade, the subject was asked if they thought they could run at the next stage. If so, the percent grade increased. If not, they were instructed to continue to run at the current stage. The test was completed once the participant reached volitional fatigue.

VO_2max was determined by attainment of at least two of the following: 1) reaching a plateau in VO_2 (<2.1ml/kg/min increase) in the final stages of the test, 2) Achieving a RER ≥1.10, 3) reaching an heart rate within five beats per minute of predicted maximal value (220-age), or 4) reporting an RPE of ≥18 (223).

Upon achieving VO_2max, the time to exhaustion was recorded. Likewise, the participant was sat down for immediate blood collection via finger prick for blood lactate measurements. Again, the finger was cleaned with an alcohol swab and gauze before the finger is lanced. This process was repeated at five and 10 minutes.

After the completion of all measures, treadmill speed and gradient were used to calculate maximal flat ground running speed. The equation used for this conversion was $S=S_r +(S_r$ x $0.045)$ x i: where S is the calculated flat ground peak speed, S_r is the peak treadmill speed and i is the treadmill inclination (22).

3.3.10 Dietary Analysis

Three-day food records (two weekdays and one weekend day) were completed during each testing period. Participants were asked to maintain a normal dietary intake during the study.

Dietary analysis using The Food Processor Version 10.13.1 dietary software (ESHA Research, Salem, OR) was performed by the same research technician for all participants.

3.3.11 Training Protocol

Participants were closely monitored by either a CSCS or by individuals who had been thoroughly trained in training session requirements for all training sessions and four days per week (Table 2). Participants trained either individually or in groups of no more than three during designated times throughout the day at the local Gold's Gym. Before each workout, participants confirmed that they had ingested their supplement 45 minutes prior to the training session. Further, before each workout, participants were allowed to perform their own individual warm ups to ensure that they are mentally and physically prepared for each training session. However, these warm-ups were kept constant throughout all training and testing.

Table 2. Weekly Training Timeline

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
Rest	Resistance	HIIT	Rest	Resistance	HIIT	Rest*

*; Reserved for a make-up session if required.

During each lifting session, participants completed the designated workout for the given day. The final set of each exercise was performed as a "plus" set, where the participant completed the maximal amount of repetitions to volitional fatigue (Table 3). This allowed the participants to increase repetition volume while working towards exhaustion. These extra repetitions were recorded and used for calculation of total workload (weight x reps)$_{set1}$+(weight x reps)$_{set2}$+(weight x reps)$_{set3}$ for all lifts. Music was permitted during training and all participants received verbal encouragement by all researchers and other subjects. Each lifting session lasted about an hour.

During each running session, participants completed the designated workout for the given day (Table 4). All running intensities were based off calculated flat ground running speed found at the end of each VO$_2$max test. All running time was recorded for total running time during each training session. Running volume was assessed as time (s) x intensity (percent of calculated flat ground speed at VO$_2$max). The acceptable compliance margin was $\geq 80\%$ for both training modalities during each of the six week training periods.

Table 3. Resistance Training Protocol

		Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 8	Week 9	Week 10	Week 11	Week 12	Week 13
DAY 1	Squat	3x12@ 65%	3x12@ 67.5%	3x10@ 70%	3x10@ 72.5%	3x10 @ 75%	3x10 @ 77.5%	3x6@ 80%	3x6@ 80%	3x6@ 82.5%	3x4 @ 87.5%	3x2 @ 90%	3x2 @ 92.5%
	Leg Extension	3x12	3x12	3x12	3x12	3x10	3x10	3x10	3x10	3x8	3x8	3x8	3x8
	Military Press	3x12	3x12	3x12	3x12	3x10	3x10	3x8	3x8	3x6	3x6	3x4	3x4
	Upright Row	3x12	3x12	3x12	3x12	3x10	3x10	3x10	3x10	3x8	3x8	3x8	3x8
	EZ Bar Curl	3x12	3x12	3x12	3x12	3x10	3x10	3x10	3x10	3x8	3x8	3x8	3x8
	Cable Push Down	3x12	3x12	3x12	3x12	3x10	3x10	3x10	3x10	3x8	3x8	3x8	3x8
	Crunches	50	50	50	50	75	75	75	75	100	100	100	100
Day 2	RDL	3x12	3x12	3x12	3x12	3x10	3x10	3x10	3x10	3x8	3x8	3x8	3x8
	Bench Press	3x12@ 65%	3x12@ 67.5%	3x10@ 70%	3x10@ 72.5%	3x10 @ 75%	3x10 @ 77.5%	3x6@ 80%	3x6@ 82.5%	3x6@ 85%	3x4 @ 87.5%	3x2 @ 90%	3x2 @ 92.5%
	UH Pull Down	3x12	3x12	3x12	3x12	3x10	3x10	3x10	3x10	3x8	3x8	3x8	3x8
	Incline Bench Press	3x12	3x12	3x12	3x12	3x10	3x10	3x10	3x10	3x8	3x8	3x8	3x8
	Seated Row	3x12	3x12	3x12	3x12	3x10	3x10	3x10	3x10	3x8	3x8	3x8	3x8

The first number under each week is the set number and the second number is the number of repetitions. The final set for each exercise is done to volitional fatigue. UH: underhand, RDL: Romanian deadlift. Seated Rows are performed with a neutral grip.

Table 4. HIIT Protocol

	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 8	Week 9	Week 10	Week 11	Week 12	Week 13
Day 1	1:01	2:01	2:01	2:01	2:01	2:01	2:01	2:01	2:01	2:01	2:01	2:01
	@85	@85	@85	@85	@85	@85	@85	@85	@85	@85	@85	@85
Day 2	1:01	2:01	2:01	2:01	2:01	2:01	2:01	2:01	2:01	2:01	2:01	2:01
	@90	@90	@95	@100	@105	@110	@115	@120	@120	@120	@120	@120

Ratios are work: rest in minutes. Intensity is set at percent of maximal flat ground speed calculated from intensity eliciting VO_2max. Each bout will be repeated 10 times.

3.3.12 Supplementation Protocol

Following baseline testing, all participants were stratified by the sum of total weight lifted (squat + bench), VO_2max, percent body fat, and years of training experience and randomly assigned to one of two groups that consumed either the supplement (SUP; Shroom Tech Sport, Onnit Labs, Austin, TX) or an isocaloric placebo (PL; dextrose, Onnit labs, Austin, TX) (Table 5). Supplements were dispersed in containers of 90 pills. Participants were required to return the empty bottles, in order to ensure compliance. Further, subjects were asked before each training session if and when they ingested the pills. Both groups will follow the dosing recommendations daily as prescribed by the manufacturer: >68.2 kg will consume three pills, ≥68.2kg to ≤90.9kg will consume four pills, and >90.9kg will consume five pills. All pills were consumed 45 minutes before each training session on an empty stomach, which is determined to be at least one hour after the participants' last meal. On non-training days, subjects were instructed to consume their given doses at breakfast. Finally, SUP will also be consumed before mid-point and post-training testing sessions. The acceptable compliance margin for supplementation was ≥ 80% for supplementation. SUP was third party tested for validity of contents and anabolic steroids by Chromadex, Inc (Irving, CA).

Table 5: The Contents of Shroom Tech Sport^{tm} and the Placebo

Shroom Tech Sport^{tm} (3 capsules)	
Ingredients	Amount (mg)
Cordyceps Sinensis	1500
Green Tea Leaf	525
Rhodiola Rosea	150
Ashwagandha	150
Astragalus	50
Vitamin B-12	3
Placebo (3 capsules)	
Dextrose	2375

3.4 Statistical Analysis

Based on an prior CT study (55) and an anticipated mean difference in strength performance measures of 33kg, power analysis indicated 10 subjects per group would be required to yield a power of 0.8 with a significance level of $p < 0.05$. However, because of the multitude of variables examined in the current study, 34 participants were recruited for the present study to ensure that small changes could be detected in all of the measured variables, as well as to account for subject attrition.

JMP software (Cary, NC) was used for all statistical analysis. POMS records was compared using two-tailed t-tests. Hormone and blood profiles, performance measures, body composition, and circumference measures was compared across all testing time points (baseline, mid-point and post-testing) using two-way ANOVAs to measure main. All ANOVAs were confirmed with a Student's T post-hoc analysis. Statistical significance was set at $p < 0.05$.

CHAPTER 4

RESULTS

4.1 Participants and Compliance

There were no statistical differences in baseline subject characteristics (Table 6). Of the 34 volunteers that were recruited, two volunteers did not meet the strength requirements for participation. Of those that did meet the performance requirements, four dropped out due to reasons of time commitment before beginning the study. In addition, seven were removed from the study (SUP: n= 5; PLA: n=2) and excluded from data analysis due to the inability to meet time requirement (n=3), injuries sustained outside of the research study (n=1), hormonal deficiencies (hypogonadism) (n=1), and inability to complete 80% of the scheduled training sessions (n=2). Additionally, one subject (SUP) did not complete the mid-point testing protocol due to personal scheduling conflicts. Finally, data points that were greater than three standard deviations from the mean were removed before analysis.

Table 6. Subject Characteristics*

	SUP (n=10)	PLA (n=11)	P-value
Age	21.5 ± 1.2	22.5 ± 2.7	0.315
Total Strength (kg)	223 ± 30	218 ± 30	0.640
VO2max (ml/kg/min)	54.2 ± 6.1	54.3 ± 6.7	0.801
Body Fat (%)	15.4 ± 6.7	15.1 ± 7.1	0.907
Training Years	6.4 ± 2.8	5.8 ± 2.7	0.562

*There were no statistical differences between groups or
categories SUP: supplement; PLA: placebo

4.2 Mood State Questionnaire

No group x time interactions were observed for the POMS variables. However, both groups reported increased fatigue from pre to post testing (SUP: Pre 2.6 ± 2.59 to Post 4.90 ±

3.96 v PLA: Pre 3.63± 3.53 v post 5.45 ± 4.61; p=0.045). Additionally, there was a main group effect for tension (p=0.039) (SUP: pre 4.8 ± 4.23 to post 6.3 ± 6.21 v PLA: pre 3.09 ± 2.00 v post 4.09 ± 3.65) with SUP demonstrating higher values.

4.3 Anthropometrics

There were no group, time, or group x time interactions for body mass index, fat free mass, or percent fat free mass. However, despite no significant time or group x time interactions, there was a main group effect for body mass (p=0.040) with SUP exhibiting lower values (SUP: pre 76.17 ± 8.74kg v mid 77.01 ± 9.27kg v post 76.82 ± 9.03kg; PLA: pre 77.32 ± 8.36kg v mid 77.54 ± 8.47kg v post 76.63kg). There was a significant effect of time for percent body fat (%BF) as both groups exhibited decreases (SUP: pre 15.5 ± 5.8% v mid 14.8 ± 7.2% v post 14.2 ± 6.6%; PLA: pre 16.2 ± 6.7% v mid 15.3 ± 6.5% v post 14.3 ± 6.4%; p=0.0065), with no differences between groups. There were main group (p= 0.042) and time (p=0.016) effects for fat mass but no group x time interactions (SUP: pre 11.92 ± 5.28kg v mid 11.51 ± 6.22kg v post 11.10 ± 6.96 kg; PLA: pre 12.83 ± 6.55kg v mid 12.23 ± 6.61kg v post 11.32 ± 6.49kg).

Main group effects were demonstrated in shoulder, average biceps, waist, abdominal, and hip circumferences. PLA exhibited greater circumferences in shoulder, waist full, abdominal and hip measures, while SUP exhibited greater measures in the average biceps circumference. There were no group, time, or group x time effects for average thigh or chest circumferences (Table 7).

There were no statistically significant differences between groups for change in lean mass index (Figure 5).

Table 7. Body Segment Circumferences

	SUP			PLA			P-value		
	Pre	Mid	Post	Pre	Mid	Post	Group	Time	Group x Time
Shoulder (cm)	40.9 ± 1.6	40.9 ± 1.7	41.3 ± 1.9	42.0 ± 2.8	42 ± 2.9	41.4 ± 2.7	0.005	0.763	0.213
Chest (cm)	104.3 3.3	104.4 ± 2.9	108.6 ± 8.7	106.8 ± 6.6	107.6 ± 7.0	106.9 ± 7.6	0.163	0.122	0.074
Average Biceps (cm)	34.9 ± 2.0	34.7 ± 2.3	35.1 ± 2.4	34.6 ± 1.9	34.8 ± 2.2	34.2 ± 2.0	0.004	0.521	0.149
Waist Full (cm)	83.3 ± 6.4	82.8 ± 7.5	83.0 ± 6.5	85.2 ± 6.3	84.5 ± 7.7	83.3 ± 7.5	0.003	0.118	0.242
Abdomen Full (cm)	84.9 ± 5.6	85.6 ± 8.2	87.2 ± 9.3	89.9 ± 9.2	94.5 ± 9.7	89.2 ± 8.9	<0.001	0.306	0.101
Hips (cm)	101.4 ± 5.3	101.7 ± 5.0	100.8 ± 5.5	103.4 ± 4.6	104.2 ± 4.9	102.6 ± 5.6	<0.001	0.219	0.71
Average Thigh (cm)	59.7 ± 5.3	60.3 ± 5.2	60.1 ± 5.1	59.2 ± 2.4	59.8 ± 3.5	59.0 ± 3.0	0.509	0.894	0.9263

*: Significant different than pre in the same group; ^: significant different between groups in same time point. SUP: supplement; PLA: placebo
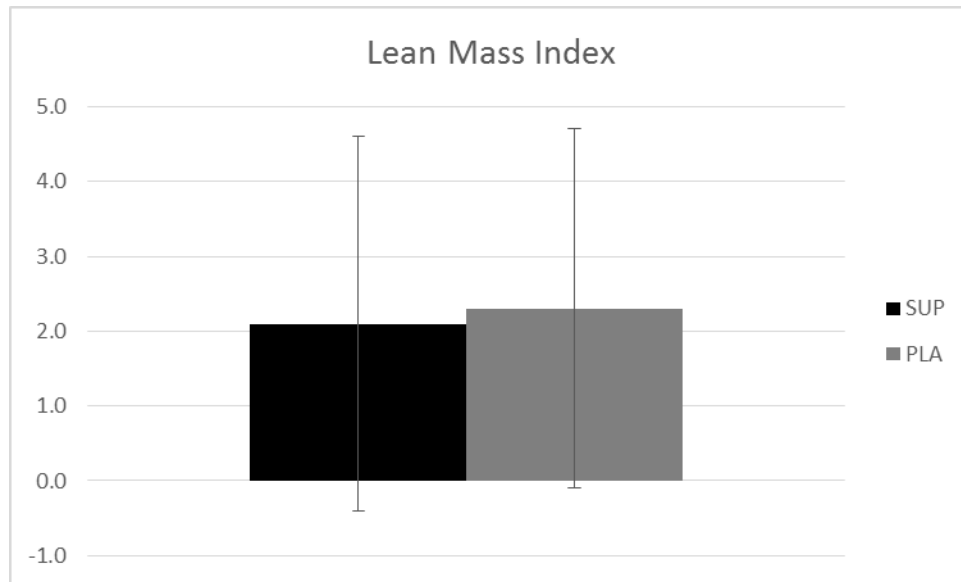
Figure 5. Lean Mass Index No statistical differences between groups after 12 weeks of training. SUP: supplement; PLA placebo

4.4 Testing Performance

4.4.1 Strength and Power Performance.

There were no group x time interactions for any of the strength variables. However, there was a main time ($p<0.0001$) and group ($p<0.0001$) effect for squat, with both groups increasing over time and SUP exhibiting higher values. Likewise, total strength demonstrated main effects for time ($p<0.0001$) and group ($p=0.0439$) with both groups increasing over time and SUP having greater values. Conversely, bench only demonstrated main effects for time ($p<0.0001$), with both groups increasing (Table 8).

There were no group, time, or group x time effects for average or peak power for either squat or bench.

4.4.2 VO$_2$max.

There were no time, group, or group x time interactions for relative VO$_2$max. Nonetheless, absolute VO$_2$max displayed a main group effect ($p=0.008$) (SUP: pre 4.1 ± 0.6L/min to mid: 4.1 ± 0.6L/min to post 4.2 ± 0.6L/min v PLA: pre 4.2 ± 0.5L/min to mid: 4.3 ± 0.5L/min to post 4.1 ± 0.4L/min) with PLA exhibiting greater values.

4.4.3 Wingate Power Output.

There were no main group or group x time interactions for any of the Wingate performance variables. However, max (p=0.007) and average power (p=0.004) increased over time regardless of group. Interestingly, fatigue index increased at midpoint (p=0.006) testing then returned to pre-training values. (Table 9)

Table 8. Strength Performance

	SUP			PLA			P-value		
	Pre	Mid	Post	Pre	Mid	Post	Group	Time	Group x Time
Squat (kg)	123 ± 16*	128 ± 16*^	132 ± 15*^†	118 ± 22	123 ± 22	128 ± 24^	<0.0001	<0.0001	0.759
Bench (kg)	100 ± 14	98 ± 12	102 ± 14†	100 ± 20	100 ± 19	105 ± 18^†	0.059	<0.0001	0.382
Total (kg)	223 ± 29*	222 ± 24	234 ± 28^†	218 ± 40	222 ± 39	232 ± 40^†	0.044	<0.0001	0.512

*: Significantly different than PLA at same time point, ^: Significantly different than pre
†: Significant different than mid

Table 9. Wingate Power Performance

	SUP			PLA			P-value		
	Pre	Mid	Post	Pre	Mid	Post	Group	Time	Group x Time
Max Power (W)	924 ± 192	1025 ± 221^	959 ± 207	916 ± 211	982 ± 118	915 ± 156	0.783	0.007	0.626
Average Power (W)	686 ± 109	739 ± 126^	714 ± 116	668 ± 121	714 ± 106	686 ± 105	0.537	0.004	0.81
Fatigue Index (W/s)	16 ± 6	20 ± 7^	17 ± 6*	17 ± 7	18 ± 5	15 ± 4*	0.542	0.006	0.078

^: Significantly different than pre *: Significant different than mid; SUP: supplement; PLA: placebo

4.4.4 Performance during Training

4.4.4.1 Bench, Squat, and Total Volume. Training volume was assessed as the total amount of recorded repetitions for squat and bench exercises. There were no group x time interactions for training volume for any of the main lifts (bench or squat) or the combination of the two (total). However, training volume decreased over time for bench, squat, and total as

intensity increased (p<0.001). Interestingly, there was a main group effect in bench (p<0.001) and total (p=0.019) training volumes with SUP demonstrating greater total volume. After consolidating the lifting intensities into four categories ("low": 65-70%, "moderate": 72.5-77.5%, "high": 80-85%, and "maximal":87.5-92.5 significant differences in average repetitions completed at "moderate" intensity for bench (SUP: 29 ± 1reps v PLA: 25 ± 3reps; p=0.02) (Figure 6) and total (SUP: 62 ± 4reps v PLA: 57 ± 4; p=0.04) (Figure 7) training volumes were noted. There were no significant differences between groups in any squat training volumes.

4.4.4.2 Workload. Workload (total weight moved x total repetitions completed) was analyzed for each individual resistance training day and the combination thereof (total). There was a main group effect for day one (p<0.001), day two (p=0.002), and total (p=0.002) workloads, with SUP performing greater workloads than PLA. Main time effects also exist for squat, bench, and total (p<0.001, p<0.001, and p=0.002, respectfully), with increases in workload to week five and subsequent decreases in workload. Depsite these findings, there were no group x time effects for any of the any of the workloads analyzed. Upon further analysis, two tailed Ttest revealed significant differences in week five day two (SUP: 279,342 ± 26,689kg v PLA: 251,866 ± 23,985kg; p=0.04) and total (SUP: 464,197 ± 44,325kg v PLA: 412,337 ± 38,988kg; p=0.02) workloads (Figure 8). Additionally, week five day one exhibited a trend towards a difference in workloads (SUP: 177,864 ± 22,383kg v PLA: 160,470 ± 18,229kg; p=0.07). There were no other significant differences between the two groups in daily or total workloads for the remaining weeks.

4.4.4.3 Running Volume. Weekly running volume was first compared across each week by day (day one: constant 80% of calculated max flat ground running speed; day two: progressed "fast" running day) and the combination thereof (total). There were main time effects for day one (p<0.001), day two (p<0.001), and total running volume (p<0.001). There was also a main group effect for the progressed running day (p=0.003) across the entirty of the training program, with SUP displaying greating running volumes compared to PLA. Despite these findings, there were no group x time interactions for either day or total running volume .

Due to the repetition of some intensities through the training cycle, running volume was further analyzed as average running time at each intensity (total running time at a given intensity/ number days programed to that intensity). Again, there were no statistically significant group x

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time interactions. In spite of this finding, further analysis revealed a main group effect (p=0.03), with SUP performing a greater amount of running volume (SUP: 891 ± 41sec v PLA: 863 ± 36sec). There was also a main time effect (p<0.001) as training volume decreased for both groups with increases in intensity. Interestingly, when average running times were compared to those of 90% max calculated flat ground speed, post hoc anaylisis revealed a significant differences in running volume starting at 100% max for PLA. Conversely, this difference was first observed at 105% for SUP (Figure 9).

Upon further analysis, two tailed Ttest revealed a significant difference at 100% max (SUP: -41 ± 83sec v PLA: -147 ± 115sec; p=0.028) in the changes in total running volume relative to those at 90% of calculated max flat ground running speed (Figure 10).
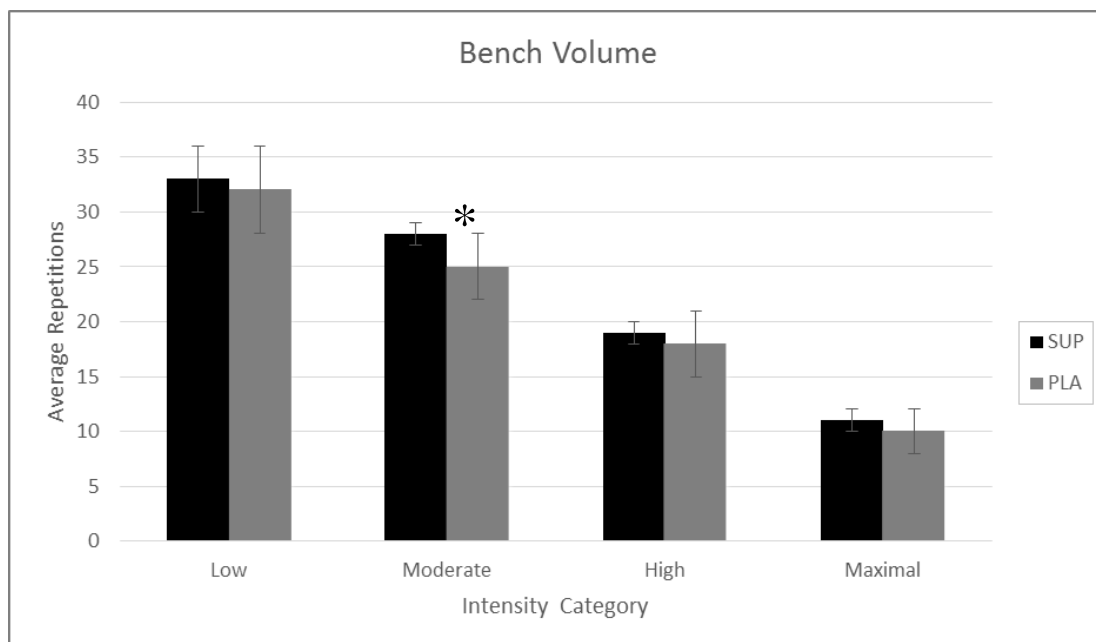
Figure 6. Average Training Volume for Bench*: Significant difference between group (p<0.05); ("low": 65-70%, "moderate": 72.5-77.5%, "high": 80-85%, and "maximal":87.5-92.5%); SUP: supplement; PLA: placebo
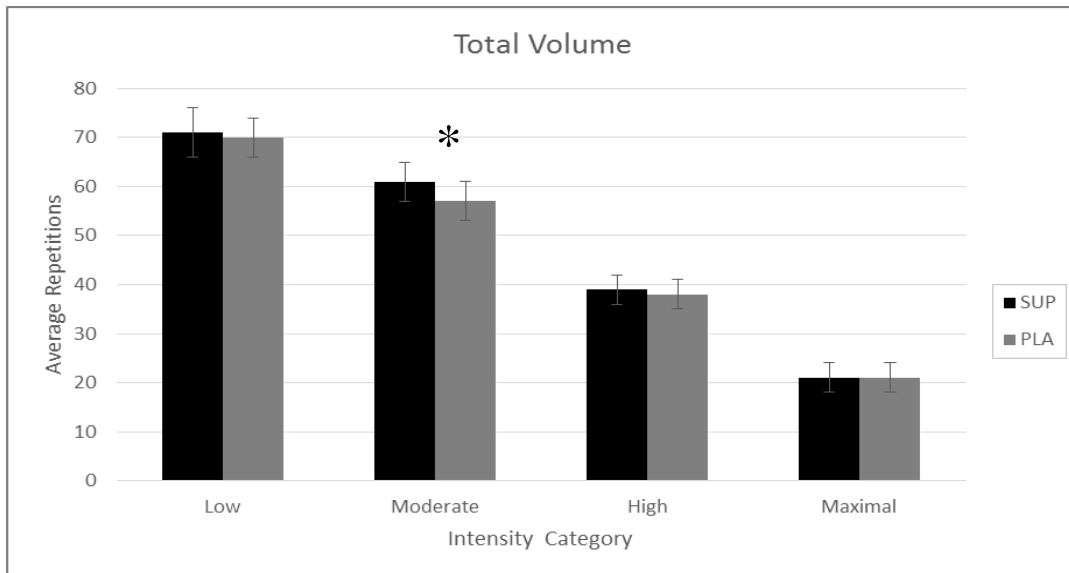
Figure 7. Average Training Volume for Bench and Squat. *: Significant
difference between group (p<0.05); "low": 65-70%, "moderate": 72.5-77.5%,
"high": 80-85%, and "maximal":87.5-92.5%; SUP: supplement; PLA: placebo
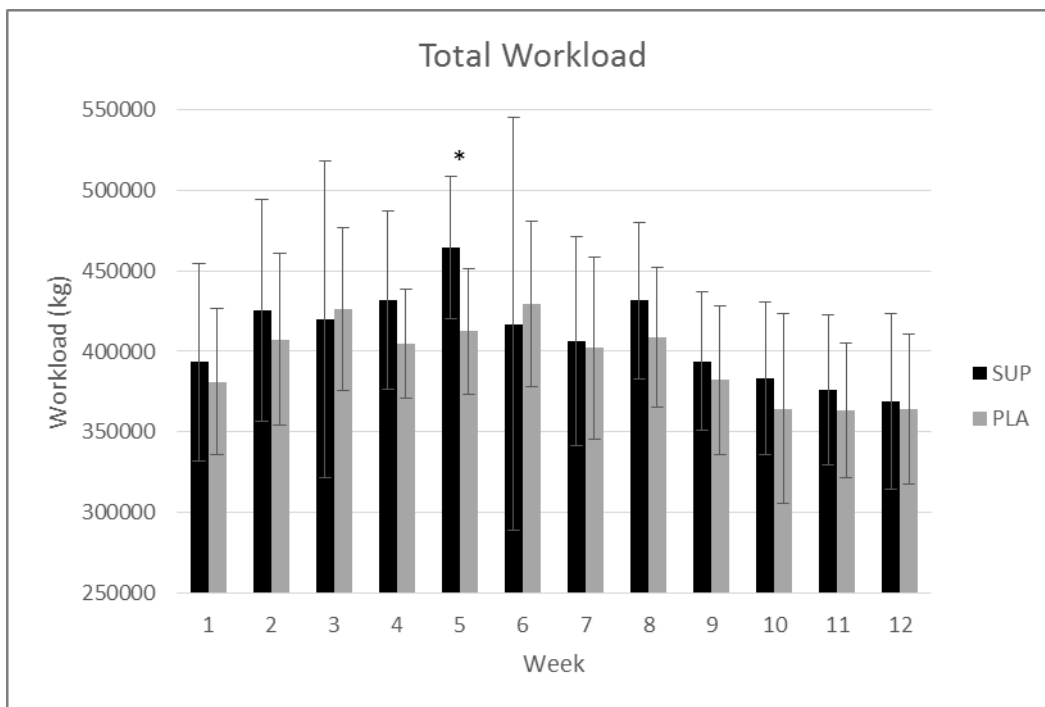
Figure 8. Total Training Workload *: Significant difference (p<0.05)
between groups at given intensities. SUP: supplement; PLA: placebo
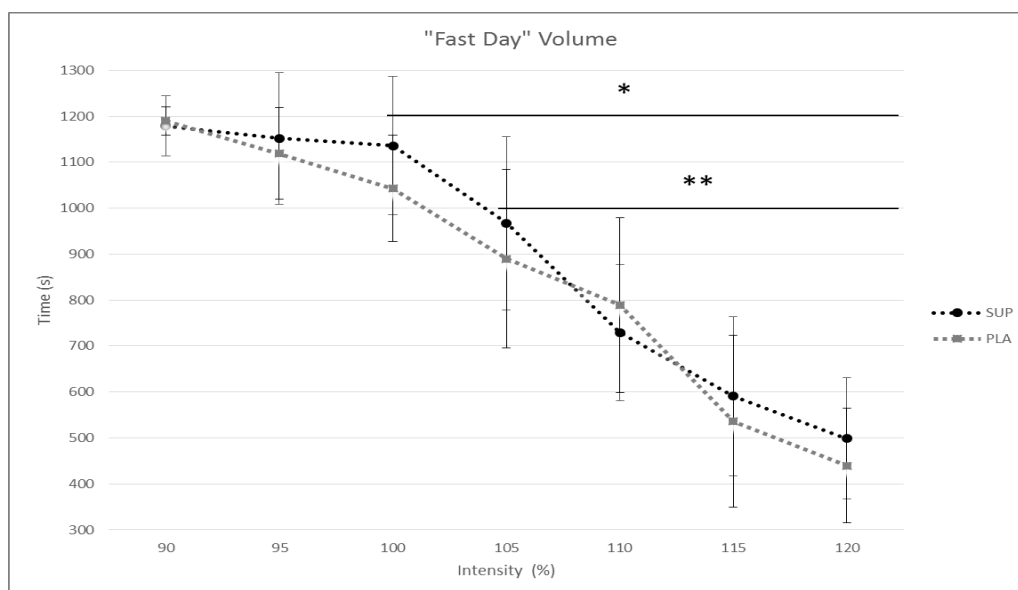
Figure 9. Total "Fast" Day Running Volume *: Significant difference (p<0.05) from 90% max flat ground speed (PLA). **: Significant difference from 90% max flat ground speed (SUP). SUP: supplement; PLA: placebo
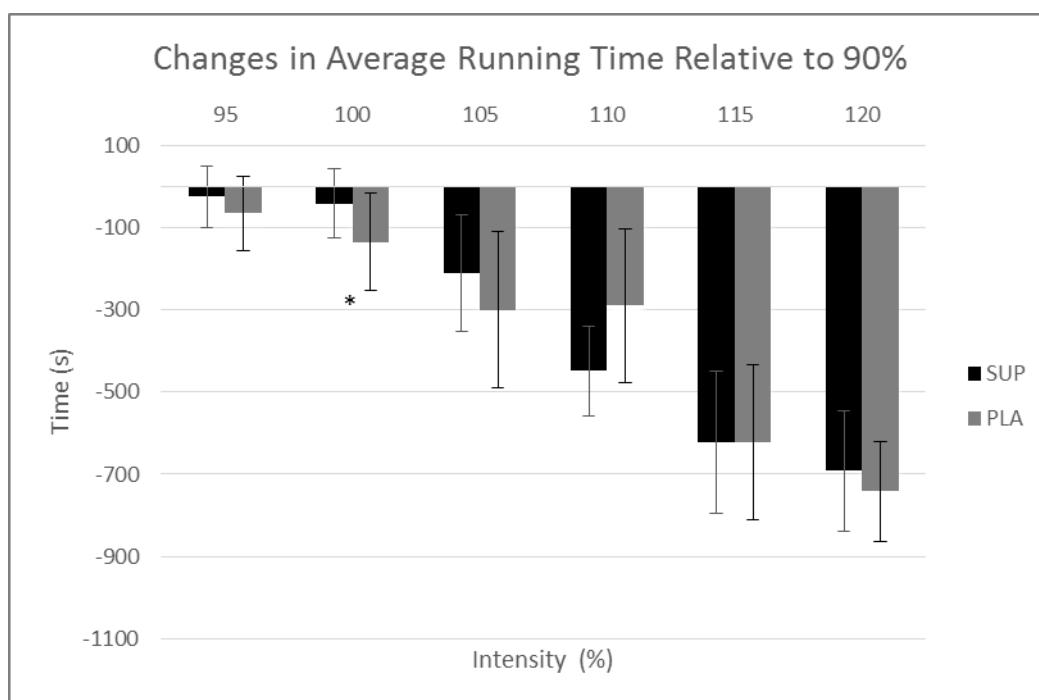
Figure 10. Changes in Average Running Time Relative to 90% *
Significant difference (p<0.05) between groups at given intensities. SUP: supplement; PLA: placebo

4.5 Blood Profiles and Dietary Intake

4.5.1 Hormones Profiles and Blood Markers

Of the blood variables measured, only dihydrotestosterone (DHT) demonstrated a main group effect (p<0.001), with PLA exhibiting higher concentraions compared to SUP. Cortisol was the only variable that showed a main time effect (p= 0.018) with both groups decreasing over time. Post hoc analysis revealed a significant difference between pre and post cortisol concentrations in the SUP (pre: $19.7 \pm 5.2\mu g/dl$ v post: $16.4 \pm 4.5\mu g/dl$; p= 0.01) but not PLA (pre: $17.6 \pm 4.6\mu g/dl$ v post: $16.6 \pm 4.3\mu g/dl$; p=0.34). Despite these findings, there were no statistically significant group x time interactions among any of the hormones and damage makers (Table 10).

Table 10. Hormone and Damage Markers

	SUP			PLA			P-value		
	Pre	Mid	Post	Pre	Mid	Post	Group	Time	Group x Time
Testosterone (ng/mL)	5.9 ± 1.1	5.2 ± 1.1	5.0 ± 1.8	5.8 ± 1.2	5.7 ± 1.6	5.7 ± 1.4	0.081	0.113	0.281
Cortisol (ug/dL)	19.7 ± 5.2	18.7 ± 4.2	16.4 ± 4.5*	17.6 ± 4.6	17.9 ± 6.1	16.6 ± 4.3	0.16	0.018	0.342
SHBG (nmol/L)	27.0 ± 6.7	29.0 ± 11.8	28.5 ± 7.7	29.0 ± 14.2	30.6 ± 17.3	29.2 ± 14.2	0.299	0.47	0.907
Free Testosterone (pg/mL)	13.9 ± 4.9	14.3 ± 5.8	13.6 ± 4.7	14.0 ± 4.4	14.2 ± 3.9	15.5 ± 4.7	0.9	0.993	0.211
DHT (pg/mL)	917.3 ± 424	718.4 ± 210.1^	748.3 ± 150.4*^	1062.9 ± 421.3	939.9 ± 390.8	946.3 ± 748.3	<0.001	0.111	0.373
DHEA (pg/mL)	11.6 ± 4.1	12.2 ± 6.4	11.2 ± 4.8	11.6 ± 5.7	14.6 ± 6.6	10.1 ± 3.4	0.753	0.085	0.293
Insulin (pmol/L)	26.3 ± 6.6	28.9 ± 9.4	27.6 ± 9.1	28.9 ± 11.1	32.4 ± 12.6	27.6 ± 14.1	0.443	0.254	0.965
IGF-I (ng/mL)	87.3 ± 22.8	92.4 ± 15.5^	94.1 ± 27.1^	83.9 ± 19.1	82.6 ± 21.4	80.3 ± 20.8	0.004	0.719	0.376
CK (µ/L)	14.4 ± 16.6	11.7 ± 11.2	10.7 ± 6.9	16.4 ± 21.3	8.7 ± 6.5	9.3 ± 7.3	0.859	0.498	0.655

*: Significantly different than mid; ^: Significantly different than PLA at same time point.
SUP: supplement; PLA: placebo; SHBG: Sex hormone binding globulin; DHT: Dihydrotestosterone; DHEA: Dehydroepiandrosterone IGF-I: Insulin-like growth factor-I;

4.5.2 Cardiovascular and Cardiometabolic Profiles

Main group effects were found for heart rate (p<0.001), systolic blood pressure (p=0.039) and HDL levels (p<0.001) with SUP exhibiting greater values that PLA for heart rate and systolic blood pressure and lower values for HDL. Further, there were main time effects for systolic blood pressure, total cholesterol, LDL, and HDL, with decreases in total cholesterol (SUP: Pre: 152 ± 22mg/dL to Mid: 142 ± 23mg/dl to Post: 147 ± 23mg/dl v PLA: Pre: 154 ±

29mg/dl to Mid: 142 ± 22mg/dl to Post: 143 ± 22mg/dl; p=0.009), LDL (SUP: Pre: 83 ± 26mg/dL to Mid: 74 ± 14mg/dl to Post: 80 ± 26mg/dl v PLA: Pre: 82 ± 24mg/dl to Mid: 70 ± 13mg/dl to Post: 76 ± 18mg/dl; p=0.047) and HDL (SUP: Pre: 48 ± 11mg/dL to Mid: 45 ± 10mg/dl to Post: 44 ± 7mg/dl v PLA: Pre: 60 ± 12mg/dl to Mid: 55 ± 12mg/dl to Post: 54 ± 10mg/dl; p=0.013) and increases in systolic blood pressure (SUP: Pre: 128 ± 10BPM to Mid: 132 ± 16 BPM to Post: 138 ± 16 v PLA: Pre: 120 ± 10BPM to Mid: 126 ± 12BPM to Post: 132 ± 16BPM; p=0.025). Despite these findings, there were no group x time interactions for any of the variables (Table 11).

Table 11. Cardiovascular and Cardiometabolic Markers

	SUP			PLA			P-value		
	Pre	Mid	Post	Pre	Mid	Post	Group	Time	Group x Time
Heart Rate (BPM)	57 ± 14†	55 ± 11†	53 ± 7	49 ± 8	50 ± 9	49 ± 10	<0.001	0.54	0.361
Systolic (mmHg)	128 ± 10	132 ± 16*	138 ± 16*†	120 ± 10	126 ± 12	132 ± 16*	0.039	0.025	0.999
Diastolic (mmHG)	70 ± 10	68 ± 14	70 ± 10	70 ± 12	74 ± 12	76 ± 14	0.14	0.808	0.369
Total Cholesterol (mg/dL)	152 ± 22	142 ± 23*	147 ± 23	154 ± 29	142 ± 22*	143 ± 22*	0.863	0.009	0.706
LDL (mg/dL)	83 ± 26	74 ± 17	80 ± 26	82 ± 24	70 ± 13*	76 ± 18*	0.272	0.047	0.843
HDL (mg/dL)	48 ± 11†	45 ± 10†	44 ± 7†	60 ± 12	55 ± 12*	54 ± 10*	<0.001	0.013	0.505
Glucose (mg/dL)	86 ± 6	88 ± 7	86 ± 6	86 ± 7	88 ± 3	87 ± 9	0.964	0.452	0.977
Triglycerides (mg/dL)	98 ± 45	85 ± 38	96 ± 46	82 ± 22	86 ± 23	88 ± 36	0.156	0.991	0.75

* Significantly different than pre; † Significantly different than PLA at same time point SUP: supplement; PLA: placebo; LDL: low density lipids; HDL: high density lipids

4.6 Dietary Intake

There were no statisistcally significant group x time interactions for any of the variables assessed through dietary food logs. Despite this finding, there were main time effects for total kcals (p=0.001), total protein (p=0.015), and total carbohydrate (p=0.002) ingested, with increases in total kcals and total carbohydrate. Interestingly, total protein seemed to increase from pre-training to midpoint then return to baseline levels. Further, a main group effect was found in caffeine ingestion (0.014), with SUP ingesting more than the PLA (Table 12).

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Table 12. Dietary Intake

	SUP			PLA			P-value		
	Pre	Mid	Post	Pre	Mid	Post	Group	Time	Group x Time
Total Kcals	2643 ± 713	3285 ± 934 ^	2955 ± 785*^	2532 ± 795	2921 ± 838	2965 ± 783	0.198	0.001	0.377
Total Protein (g)	147 ± 45	180 ± 59*^	134 ± 61	124 ± 57	161 ± 56	144 ± 55	0.21	0.015	0.399
% Protein	22.5 ± 5.3	22.2 ± 5.6	19.2 ± 9.9	20.3 ± 7.3	23.5 ± 9	20.7 ± 9	0.836	0.283	0.478
Total Carbohydrate (g)	272 ± 66	346 ± 116^	315 ± 129^	262 ± 120	321.4 ± 130^	331 ± 154^	0.861	0.002	0.569
% Carbohydrate	41.9 ± 6.2	41.9 ± 7.2	41.7 ± 8.3	41 ± 10.5	43.4 ± 8.2	43.4 ± 12	0.246	0.44	0.927
Fat (g)	99± 33	126 ± 53	112 ± 31	100 ± 44	107 ± 29	115 ± 34	0.476	0.136	0.264
% Fat	33.4 ± 5.9	339 ± 6	34 ± 4	34.3 ± 7.7	33.4 ± 4.8	35 ± 7	0.699	0.811	0.752
Alcohol (g)	12 ± 19	10 ± 15	10 ± 19	9 ± 13	10 ± 23	1 ± 2	0.426	0.834	0.601
Caffeine (mg)	89 ± 105*	72 ± 141*	67 ± 51	39 ± 39	42 ± 66	17 ± 23	0.014	0.573	0.912

*: Significantly different than PLA at same time point; ^: Significantly different than Pre;
SUP: supplement; PLA: placebo

CHAPTER 5

DISCUSSION

The primary finding of the present study was that SUP demonstrated greater bench and total training volumes at "moderate" intensities (72.5 to 77.5% 1RM) and exhibited smaller decrements in running volumes at 100% max speed when compared to those achieved at baseline (90%). Despite these findings, there were no significant differences between groups in total resistance training (65 to 92.5% 1RM) or total running (90 to120%) volumes or workload over the entirety of the 12-week training program. Moreover, SUP and PLA demonstrated significant increases in strength and decreases in percent body fat, after 12 weeks of CT. Despite these findings, there were no statistically significant differences between the two groups in any of the strength, power, or aerobic performance tests, body composition, or cardiometabolic markers after 12 weeks of training and supplementation.

5.1 Strength and Power Outcome Performance

Both groups exhibited increases in all strength performances and max and average power output, without differences between the two groups. These findings support earlier data suggesting that resistance training in combination with HIIT (55, 432, 471) and separation of at least 24 hours between resistance and aerobic training sessions (26, 55, 153, 315) do not hinder increases in strength. Indeed, the present study found similar results with significant increases in all strength performance variables with a protocol that consisted of HIIT occurring 24 hours after RT. The reported similarities in strength performance between SUP and PLA supports literature questioning the efficacy of multi-ingredient performance supplements (MIPS) on strength performance (377, 537). Indeed, Ormsbee et al. (377) reported no differences in strength between MIPS (whey protein, casein protein, branch chain amino acids, creatine, beta-alanine, and caffeine) and PLA, albeit with different primary active ingredients compared to the present study, after six weeks of resistance training. Conversely, there have been multiple studies that demonstrate the positive effects of MIPS supplementation on strength (282, 283, 457, 481) and power (377) performance. Though the literature is more supportive of MIPS efficacy, direct comparison of these interventions is difficult as the type and dosage of ingredients often varies from product to product in each study. Despite this limitation, comparison to work conducted

with individual ingredients has demonstrated no differences between groups, similar to the results in strength performance to the current study. Indeed, De Bock et al. (33) reported supplementation with 200mg of rhodiola rosea (RR) extract did not elicit increases in max isometric knee extension or maximal limb velocity in acute (60 minutes prior to exercise) supplementation in men and women. Moreover, the same study demonstrated four weeks of continual supplementation with 200mg of RR without exercise intervention also resulted in no change to performance. Notably, research concerning cordyceps sinensis (CS) in combination with resistance training is scarce. Nonetheless, Hsu et al. (199) demonstrated no significant differences in bench press, leg press, or seated row strength between young men who supplemented with CS (2.4g daily for eight weeks) and those who supplemented with PLA in combination with eight weeks of resistance training. Again, these data reflect the findings of the current study. Nevertheless, the wide variety of supplementation and RT protocols warrant further investigation before true conclusions about the effects of cordyceps on strength performance can be made.

5.2 VO$_2$max Outcome Performance

There were no significant changes from baseline testing in either relative or absolute VO$_2$max among or between groups. This lack in change may be attributed to the subjects' baseline aerobic characteristics. Notably, many of the CT studies using HIIT as the mode of aerobic training that demonstrated increases in VO$_2$max exhibited lower baseline values (~ 40ml/kg/min) (55, 432) than those of the present study (~54ml/kg/min). Previous research suggests training status mediates protein expression and, thus, is linked to performance responses to different modes of exercise. Indeed, Coffey et al. (68) demonstrated molecular responses to aerobic training in experienced strength-trained individuals but not in those who were aerobically-trained. Notably, subjects in the current study experienced an average of 30 minutes of HIIT per week for 12 weeks with no change in max aerobic performance. In contrast, subjects completing a similar model of concurrent training consisting of HIIT (five rounds of three minute of cycling at 90-100% VO$_2$max) and RT (432) demonstrated increases in VO$_2$max, albeit from lower baseline VO$_2$max levels, after completing 45 minutes of HIIT per week for 22 weeks. Further, 10 weeks of continuous running for an average of 110 minutes per week has been shown to significantly increase max aerobic capacity (pre:50.7±5.8ml/kg/min to post: 57.1±5.0ml/kg/min; p<0.05) in healthy men with a VO$_2$max of ≥50ml/kg/min. Although not

significant, the same study demonstrated that concurrent training, consisting of the same aerobic program and resistance training, elicited similar increases (pre: 52.3±4.4ml/kg/min to post: 55.8±5.2ml/kg/min; p>0.05) in healthy men (92). Together, it could be suggested that the elevated max aerobic ability in the current subjects may require a greater training stimulus to elicit increases in VO_2max. Additionally, the present results support earlier reports demonstrating no changes in VO_2max when utilizing chronic supplementation of combinations of CS and RR supplementation in young competitive adult cyclist without an exercise intervention and no mention of alterations to exercise habits (71, 103). Interestingly, supplementation with rhodiola crenulata (RC) did not further enhance VO_2max when combined with programmed high altitude aerobic training in young men (59). Of note, RC is a plant of the same genus as RR. Further, both roots have been shown to be made of the same phytochemical and pharmacological characteristics (specifically rosavine and salidroside) with the exception of rosarine, which only seems to be a component of RR (1). Interestingly, Chen et al. (59) demonstrated that two weeks of chronic supplementation with CS (600mg) and RC (1400mg) per day in combination with a structured high altitude aerobic training consisting of multiple training modalities (mountain running, fartlek runs, resistance training, HIIT, and speed training) did not elicit changes in sea level VO_2max in either group in young long-distance track and field athletes. Similar results were found in a trained cyclists chronically supplementing with CS for five weeks without a programmed exercise intervention (381). Further, 12 weeks of chronic supplementation of only CS and without a programmed exercise intervention did not elicit changes in VO_2peak in healthy elderly men (60). Together, these findings would suggest that the active ingredients, CS and RR, do not have any effect on maximal aerobic capacity. Conversely, De Bock and colleagues (33) demonstrated that acute supplementation of RR (200mg) elicited significant differences in VO_2peak compared to PLA (52.9 ± 2.7 ml/kg/min v 50.9 ± 1.8 ml/kg/min; p<0.05, respectively). Of note, there were no changes in VO_2peak in groups after four weeks of supplementation with either a RR or PLA in the same study. Though the results of the current literature seem equivocal, the current study and the majority of literature suggest that while acute supplementation may elicit increases in VO_2max, chronic supplementation with CS and RR, individually or in combination, does not enhance VO_2max.

5.3 Training Performance

In the present study, there were no statistically significant differences between groups in total resistance training volume or workload over the entirety of the 12-week training program consisting of four total training days, two allocated to RT and two to HIIT. Despite these findings, there were portions of the training program in which SUP outperformed PLA. Notably, during RT, SUP performed more repetitions than PLA at prescribed weight considered to be "moderate" (72.5-77.5% 1RM) intensities in both bench and total volume (the combination of bench and squat). These findings are further supported within the current study with SUP performing greater workloads on day two and in total (the combination of day one and two) than PLA during week five, which consisted of high volumes of moderate intensities for all lifts programmed. Notably, although not significant, SUP trended to have greater a workload on day one during the same week. Moreover, during HIIT, supplementation with SUP attenuated decrements in "fast day" running volume relative to 90% max. Indeed, PLA displayed significant differences from 90% max at 100% max while SUP did not exhibit these differences until 105% max. These findings were supported by significant differences between groups at 100% max in change in running volume relative to baseline (90%).

When taken together, these reported differences in RT and HIIT volumes maybe the result of the active ingredients RR and CS in SUP. One plausible mechanism is CS's reported ability to aid in the buffering of hydrogen ions that associate with lactate to form lactic acid through increased MCT1 expression (287). Markedly, RT with high volumes of moderate intensity (551) and running at max intensities (467) have been shown to elicit elevated blood lactate levels. Further, it is well documented that as lactate accumulates, associated hydrogen ions, which lower intracellular and blood pH, negatively affect exercise performance (85, 117). While the true relationship between lactate and cellular acidosis still unclear (165), there is evidence demonstrating MCT1's ability to transport lactic acid (lactate + hydrogen ion) across the cellular membrane (414). Though the present findings cannot directly support MCT1 upregulation with SUP use, when taken in consideration with previous research demonstrating increases in metabolic threshold with chronic supplementation ($\geq$6 weeks) in elderly populations (60, 547) and time to exhaustion in animal swimming (258, 287), upregulation of MCT1 expression due to CS supplementation seems to be one plausible mechanism of the extended running times.

Notably, RR has also been shown to extend time to exhaustion in animal swimming (294, 388) and human running models (33). De Bock et al. (33) demonstrated significant increases in running time (RR: 17.2 ± 0.8min v PLA: 16.8 ± 0.7min; $p<0.05$) after one acute supplementation (200mg) with RR 60 minutes prior to VO_2max testing on a motorized treadmill. Additionally, RR may influence perception of exercise intensity. Two studies (101, 370) have demonstrated that acute supplementation of RR (3mg/kg (~200mg)) elicited lowered rating of perceived exertion (RPE) during continuous exercise on a bicycle ergometer. Indeed, Duncan et al. (101) demonstrated decreases in RPE at the conclusion of a 30 minute cycling trial at 70% VO_2max in young men. Similarly, Noreen et al. (370) demonstrated decreased RPE in a six-mile cycling time trial in young active women. Further, the same study demonstrated that RR elicited faster trial times (RR: 25.4 ± 2.7min v PLA: 25.8 ± 3.0min; $p=0.037$). Conversely, Walker et al. (517) demonstrated that supplementation with 1500mg of RR over three days did not elicit significant changes in duration of exhaustive wrist flexion exercise in trained men (RR: 10.60 ± 0.36 minutes v PLA: 10.48 ± 0.68 minutes, $p<0.05$) or RPE. Originally, De Bock et al. (33) proposed that the RR's effects on endurance exercise lie in its high concentrations of chemical phenolic compounds phenylpropanoids and phenthylethane derivatives, which have been shown to be structurally similar to catecholamines. Specifically, RR contains monoterpene glucoside, which has been shown to inhibit monoamine oxidases A and B (91), which have been shown to deactivate neurotransmitters (438). Further, these compounds have been shown to increase opioid receptors and peptides such as β-endorphins in animal models (304, 305). More recently, Chen et al. (59) suggested that two weeks of chronic supplementation with RC (1400mg) and CS (600mg) may be acting through alterations in autonomic nervous system. The authors go credit the supplementation of RC for the attenuation of in reduction of parasympathetic nervous system activity, compared to PLA (RC: -41.30 ± 4.37 % v PLA: $-51.76 - 3.97\%$; $p<0.05$) after two weeks of altitude training. These findings are further supported by work by De Bock et al. (33) and Noreen et al. (370) that demonstrated lower heart rates with the supplementation of RR during the first six minutes of exhaustive running exercise (33) and during warm-up before a six mile running time trial (370) in active young men and women. Notably, there is a very close linear relationship between heart rate and RPE (38). It is plausible to suggest that if supplementation with RR can attenuate increases in heart rate, even during the first minutes of exercise, it would result lower RPE. Though training RPE was not measured in the current study,

lowered perception of exercise intensity may account for the attenuated decrements in running volume at 100%.

Finally, when taken in combination, CS and RR have demonstrated conflicting results in exhaustive exercise performance (59, 71, 103). Chen et al. (59) demonstrated significant increases in time to exhaustion during sea-level Bruce VO_2max testing protocol in young track athletes supplementing with CS (600mg) and RC (1400mg) per day in combination with two weeks of high altitude aerobic training (863.44 ± 40.34sec to 908.89 ± 34.74sec; p<0.05) while the PLA did not (852.22 ± 39.7sec to 870.67 ± 40.05sec). Conversely, Earnest et al. (103) demonstrated that four days of preloading with CS (2000mg) and RR (600mg) followed by an 11-day maintenance phase (CS: 1000mg; RR 300mg) did not elicit any changes in time in cycling to exhaustion between groups or compared to baseline testing (treatment 38.47 ± 1.7min; PLA 36.95 ±1.8min; p>0.05). Likewise, Colson et al. (71) found similar results in trained cyclist (18 to 50 years old) reporting no significant differences between the two groups after supplementing with the same blend and dose of ingredients. Interestingly, of the three studies, Chen et al. (59) is the only study that controlled for physical activity by having a structured exercise program. The other studies instructed their participants to maintain exercise training and dietary patterns (103) or to simply refrain from strenuous activity 24 hours prior to the cycle ergometer testing (71). These methodological differences could be confounding factors that may lead to discontinuity in the literature.

Interestingly, these methodological differences in supplement ingestion may call attention to supplementation protocol of the active ingredients in SUP. Indeed, the aforementioned studies demonstrated supplementation within an hour prior to the testing protocol demonstrated significant impacts on aerobic performance (33, 370), heart rate (33, 370), and RPE (101, 370), while those that made mention of a chronic "loading phase" but no mention of supplementation prior to exercise or testing did not report any significant changes in performance (71, 103, 517). Additionally, supplementation varied between each of the studies as subjects were instructed to ingest their supplement during the morning hours (71), made no mention of specific chronic supplementation instructions (103, 517) or instructed subjects to ingest their supplement the morning of testing with no mention of chronological proximity to testing (517). These differences must be considered when interpreting the results. The present study was highly

regulated in every aspect, strictly controlling for supplementation and supervised exercise training. Subjects in the current study ingested the supplement daily, 45 minutes prior to exercise and testing sessions and during breakfast on non-training days which elicited increases in relative muscular endurance at "moderate" intensities during RT and attenuated decrements in running volume when running at max intensities. Albeit small, these data strengthen support for pre-exercise consumption of the active ingredients found in SUP. Notably, supplementation occurred daily over the course of 12 week training program in the current study, which may lend support to "loading" protocols of the active ingredients. However, the reported significant differences between supplementation with active ingredients and PLA in protocols with supplementation occurring within 60 minutes of exercise (33, 101, 370), combined with specific time points in training in the current study at which SUP out performed PLA without differences in aerobic, strength or power test performances may advocate that the active ingredients of SUP do not "load" like beta-alanine (170) and creatine (202), which would suggest that changes in performance may be strictly based in acute responses.

5.4 Body Composition

Regardless of group, subjects in the present study had a significant decrease in percent body fat with no difference between SUP and PLA. This suggests that CT consisting of RT and HIIT reduces fat mass and improves body composition. Despite lack of evidence of CT's effects on body fat, many of these studies report increases in lean (55) and muscle mass (432, 471) and leg circumferences (432), which were not demonstrated in the current study. These differences may be attributed to the differences in training programs. For example, De Souza et al. (471) had subjects complete eight weeks of hypertrophy-focused strength training that emphasized high training volumes (6-12RM) and lean mass increased as anticipated. Conversely, the present study consisted of a progressive resistance training protocol with a focus in strength performance with a decrease in workload over the last six weeks; again, no change was observed in lean mass. Indeed, a recent review by Schoenfeld et al. (447) demonstrated a dose-relationship between training volume and increases in muscle hypertrophy, suggesting that the greater training volume in De Souza et al. (471) would elicit greater increases in lean mass than the present study. Despite these findings, our CT model still elicited significant decreases in percent body fat and fat mass without significant differences between the two groups. These findings support earlier work by De Bock et al. (33) who demonstrated no significant changes in body mass after four

weeks of RR supplementation (200mg) without exercise intervention. Further, despite differences at specific time points in RT ("moderate" intensities) and HIIT (100% max), there were no significant differences among groups for total training workloads or total running volume across the entirety of the 12-week study. This could further contribute to the lack of changes in body composition between SUP and PLA. Indeed, when comparing creatine supplementation to PLA in division 1A football players, Kreider et al. (282) demonstrated significant increases in total working volume for bench, squat, and power clean exercises in those that supplemented with creatine that coincided with significantly different increases in lean mass (Creatine: 71.5 ± 12 to 73.9 ± 11.9kg v PLA: 69.8 ± 8.7 to 71.2 ± 9.9kg, p=0.04). These findings were not replicated in the current study, albeit creatine was not an active ingredient in SUP. Additionally, despite differences at 100% max, when observed over the entirety of the 12-week training protocol, no differences were observed in total running volume. This may also factor into the lack of change in body fat between groups as it has been shown that greater running duration at comparable intensity elicits increased energy expenditure (453). Further, no significant differences were observed between groups in macro nutrient or caloric intake. It is plausible that alterations in energy expenditure or energy intake would lead to alterations in fat or lean mass, although not necessarily. Thus, the lack of differences in changes in body fat and percent body fat may be due to no differences in running volumes or macronutrient selection and caloric intake.

5.5 Resting Hormone Responses

The resting hormonal responses to the training reflect those of the literature (4, 27, 52). Indeed, Bell et al. (27) reported on changes in testosterone, sex hormone binding globulin and growth hormone in both young men and women after 12 weeks of concurrent training consisting of three continuous exercise sessions and three progressive RT sessions. Interestingly, Bell et al. (27) reported that concurrent training did not elicit changes in urinary cortisol levels in young men, despite changes in young females (45.32 ± 14.32 nmol/24hours to 38.75 ± 6.79nmol/24hours to 83.13 ± 15.35 nmol/24hours; p<0.05). The lack of a time effect in the present study for free testosterone, testosterone, SHBG, DHT, DHEA, insulin, or IGF-I indicates that our concurrent training model did not have any effects on these resting concentrations. Despite different aerobic training modalities, the current study supports the current literature suggesting that CT does not affect resting hormonal concentrations. Interestingly, post hoc

analysis revealed a significant differences in final resting cortisol levels compared to baseline (pre: 19.7 ± 5.2µg/dl to mid: 18.7 ± 4.2µg/dl to post: 16.4 ± 4.5µg/dl; p<0.05). This may be due to another active ingredient in SUP, ashwagandha. Indeed, chronic supplementation with ashwagandha (500mg/day and 1000mg/day) elicited significant decreases in serum cortisol concentrations (-14.5%, -24.2%, and 30.5%, respectively) in men and women (18 to 60 years old) demonstrating a chronically stressful lifestyle with a mHAM-A score of 24 to 42 (17). Together, these results support possible benefits to ashwagandha supplementation on decreasing resting cortisol concentrations, which may blunt the effects of catabolic environments and aid in recovery techniques.

5.6 Resting Health Markers

Neither SUP nor PLA influenced triglyceride or glucose concentrations. While studies concerning RR and CS effects on blood lipid profiles are scarce, these results reflect previous work conducted with herbal based MIPS (283) and more traditional MIPS (445, 456). Indeed, the present study showed decreases in total cholesterol, LDL, and HDL (though remaining among healthy recommendations). Interestingly, a recent meta-analysis surveyed eight studies regarding CT's effects on blood profiles revealing improvements in LDL, total cholesterol, triglyceride, and HDL concentrations in men and women (487). Of those studies examined, one (507) demonstrated that 12 weeks of HIIT (one minute 80-95% max heart rate) combined with active recovery (four minutes 75-85% max heart rate) and upper-body resistance training did not elicit significant changes in triglycerides, total cholesterol, HDL and LDL in healthy elderly men. Interestingly, these findings do not support those of the current study or the rest of literature. Overall, the results of the current study and the majority of literature suggest that concurrent training may elicit positive outcomes on blood lipid profiles.

Finally, there was an increase in systolic blood pressure over the 12-week training protocol, with no significant differences between SUP (138 ± 16mmHg) and PLA (132 ± 16mmHg). Interestingly, research concerning concurrent training's effects on resting blood pressure is limited, especially in CT models utilizing high intensity running and progressive resistance training. Nevertheless, Sillanpää et al. (462) demonstrated that 21 weeks of CT (two days of progressed continuous cycling and two days of resistance training) did not exert any effects on systolic blood pressure in middle-aged and older women. As independent factors,

resistance training (78) and high intensity interval training (247) have been shown to reduce systolic blood pressure. These findings were not reflected in the current study. Regardless of these contradictions, it should be noted that midpoint and post-training resting blood pressure was attained during two high stress periods in the academic calendar (mid-terms and finals). Notably, mental stress has been shown to increase systolic blood pressure (185) which may stem from a state of excess sympathoadrenal activation (491). Ultimately, these findings suggest that the tested supplement does not affect disease factors differently than concurrent training alone.

5.7 Profile of Mood States

In regards to psychological profiles, there were no differences between the two groups. However, there was an increase in ratings of fatigue in both groups. This change may be due to the high intensity of which the study consisted. These findings support previous work showing that high intensity exercise significantly increases POMS scores of fatigue (166, 476). Notably when comparing the dietary intake on fat oxidation in competitive endurance athletes, Stepto et al. (476) demonstrated increased POMS scores after eight rounds of five minutes of cycling at 86 $\pm$ 2% VO$_2$peak in both high carbohydrate (42 $\pm$ 21) and high fat (35 $\pm$ 20) groups immediately after high intensity bouts. Notably, the increase in fatigue scores for both groups would suggest that HIIT elicits elevated levels of fatigue. Thus, it is reasonable to suggest that the 12-week training protocol in the current consisting of two RT sessions and two HIIT sessions would also elicit elevated fatigue scores in both groups.

5.8 Adverse Effects

Of note, headache (PLA: n=1), dry-mouth (PLA: n=1) and difficulty sleeping (SUP: n=1) were reported over the 12-week study. Though side effects are rare, when supplementing with RR (1.5g to 2g) insomnia and irritability have been reported in previous review (242), which is much higher the average consumption of the current study (~200mg).

5.9 Limitations

There were several limitations to this study that must be addressed. Primarily, the amounts of individual ingredients in SUP were combined into a proprietary blend, and thus were not able to be adjusted to accommodate for the differing body masses among individuals. Further, dosing was dependent upon the body mass of each subject, suggesting that subjects took varying amounts of ingredients, which may have resulted in differences in outcomes for differing

weight groups. As previously mentioned, RR supplementation with 3mg/kg of body weight elicited significant improvements in cycle ergometer time trial performance (370). Nonetheless, these groups were too small to make accurate assessments. Additionally, the varying amounts and ingredients in MIPS make direct comparison quite difficult. Moreover, the variation in concurrent training models, even those utilizing HIIT protocols, is quite broad, which makes even direct comparison to training models challenging. Compared to the literature, the current study demonstrated extreme lengths to ensure training and supplementary compliance, through supervised training and monitored supplement consumption. Despite these efforts, dietary intake may have been another limitation to the current study. Dietary intake was monitored through food logs and there may have been some discrepancies between recorded and actual caloric and macronutrient intake as has been reported previously (301). Finally, though the current study successfully stratified subjects by percent body fat, the range within groups to achieve similar means between groups may have affected the outcomes of this study. Indeed, though the average percent body fat of each group was considered to be "lean", subject's percent body fat ranged from "very lean" to "obese" in each group, which, when combined with dietary recall data, is indicative of a wide array of lifestyles which may have affected this study.

5.10 Conclusion

In conclusion, supplementation with SUP, 45 minutes prior to exercise, enhanced moderate intensity resistance exercise performance and max intensity HIIT performance in recreationally trained men. Additionally, 12 weeks of CT protocol consisting of progressive RT and HIIT improved strength and power performance while decreasing fat mass; however there were no differences between groups. Therefore, use of SUP (792mg per 23kg of body weight) for 12 weeks may be beneficial for resistance training at moderate intensities and aerobic training at maximal intensity may be beneficial for recreationally active men.

APPENDIX A

IRB LETTERS OF APPROVAL

Florida State
U N I V E R S I T Y

Office of the Vice President For Research
Human Subjects Committee
Tallahassee, Florida 32306-2742
(850) 644-8673 · FAX (850) 644-4392

APPROVAL MEMORANDUM

Date: 12/11/2014

To: Vince Kreipke ███████████

Address: 1493   ███████████

Dept.:   NUTRITION FOOD AND EXERCISE SCIENCES

From: Thomas L. Jacobson, Chair

Re: Use of Human Subjects in Research
Effects of STS Supplementation and Concurrent Training on Body Composition, Performance and Health in Collegiate-aged Men

The application that you submitted to this office in regard to the use of human subjects in the research proposal referenced above has been reviewed by the Human Subjects Committee at its meeting on 12/10/2014
Your project was approved by the Committee.

The Human Subjects Committee has not evaluated your proposal for scientific merit, except to weigh the risk to the human participants and the aspects of the proposal related to potential risk and benefit. This approval does not replace any departmental or other approvals which may be required.

If you submitted a proposed consent form with your application, the approved stamped consent form is attached to this approval notice. Only the stamped version of the consent form may be used in recruiting research subjects.

If the project has not been completed by 12/09/2015 you must request a renewal of approval for continuation of the project. As a courtesy, a renewal notice will be sent to you prior to your expiration date; however, it is your responsibility as the Principal Investigator to timely request renewal of your approval from the Committee.

You are advised that any change in protocol for this project must be reviewed and approved by the Committee prior to implementation of the proposed change in the protocol. A protocol change/amendment form is required to be submitted for approval by the Committee. In addition, federal regulations require that the Principal Investigator promptly report, in writing, any unanticipated problems or adverse events involving risks to research subjects or others.

By copy of this memorandum, the chairman of your department and/or your major professor is reminded that he/she is responsible for being informed concerning research projects involving human subjects in the department, and should review protocols as often as needed to insure that the project is being conducted in compliance with our institution and with DHHS regulations.

This institution has an Assurance on file with the Office for Human Research Protection. The Assurance Number is IRB00000446.

Cc: Robert Moffatt ███████████ Advisor
HSC No. 2014.14229

The Florida State University
Office of the Vice President For Research
Human Subjects Committee
Tallahassee, Florida 32306-2742
(850) 644-8673, FAX (850) 644-4392

RE-APPROVAL MEMORANDUM

Date: 10/15/2015

To: Vince Kreipke █████████████

Address: 1493
Dept.: NUTRITION FOOD AND EXERCISE SCIENCES

From: Thomas L. Jacobson, Chair

Re: Re-approval of Use of Human subjects in Research
Effects of STS Supplementation and Concurrent Training on Body Composition, Performance
and Health in Collegiate-aged Men

Your request to continue the research project listed above involving human subjects has been
approved by the Human Subjects Committee. If your project has not been completed by
10/12/2016, you must request renewed approval by the Committee.

If you submitted a proposed consent form with your renewal request, the approved stamped
consent form is attached to this re-approval notice. Only the stamped version of the consent form
may be used in recruiting of research subjects. You are reminded that any change in protocol for
this project must be reviewed and approved by the Committee prior to implementation of the
proposed change in the protocol. A protocol change/amendment form is required to be submitted
for approval by the Committee. In addition, federal regulations require that the Principal
Investigator promptly report in writing, any unanticipated problems or adverse events involving
risks to research subjects or others.

By copy of this memorandum, the Chair of your department and/or your major professor are
reminded of their responsibility for being informed concerning research projects involving
human subjects in their department. They are advised to review the protocols as often as
necessary to insure that the project is being conducted in compliance with our institution and
with DHHS regulations.

Cc: Robert Moffatt, Advisor █████████████
HSC No. 2015.16393

APPENDIX B

INFORMED CONSENT

Effects of STS Supplementation and Concurrent Training on Body Composition, Performance and Health in Collegiate-aged Men

Informed Consent Form

1) I voluntarily, without element of force or coercion, consent to be a subject in the project titled, "Effects of STS Supplementation and Concurrent Training on Body Composition, Performance and Health in Collegiate-aged Men." This study is being conducted by Vince Kreipke, Dr. Michael Ormsbee and Dr. Robert Moffatt through the Department of Nutrition, Food and Exercise Sciences and the Institute of Sports Sciences and Medicine (ISSM) at Florida State University.

2) This study will examine the effect of Shroom Tech Sport (STS) supplementation and concurrent training on body composition, limb segment girths, and anthropometric measurements (height and body mass).

   This study will also examine the effect of STS supplementation and concurrent training on human performance: anaerobic power output and fatigue (30 second Wingate test), one repetition maximum (1RM) strength (bench press and squat), lactate threshold, maximal oxygen consumption (VO_2max), and total training volume ((weight x reps)$_{set 1}$+(weight x reps)$_{set 2}$+ (weight x reps)$_{set 3}$).

   Finally, this study will investigate the effects of STS supplementation and 12 weeks of concurrent training on serum concentrations of insulin, cortisol, estrogen, testosterone, insulin-like growth factor I, creatine kinase, inerleukin-6, dihydrotestosterone, erythropoietin and dehydroepiandrosterone and cardiometabolic markers of health (glucose and blood lipids).

3) Participation in this study will require me to come to the gym on 48 separate occasions (4x/week for 12 weeks: 2 strength training sessions and 2 high-intensity interval training (HIIT) sessions) and the Institute of Sport Science and Medicine (ISSM) on 11 separate occasions (visits 1-11) over the course of 14 weeks for laboratory testing. These visits are described below:

   Visit 1 (Familiarization) (120 minutes): I will be given a medical history questionnaire to complete and sign. They will not be able to participate in this study if they have medical issues preventing my full participation or that interfere with nutrient metabolism, or meet any of the other exclusion criteria: prior steroid use, a history of tumors, less than one year of experience with exercise training, pre-existing musculoskeletal disorders and not participated in the three week wash out period.

   Strength and Power Test Familiarization: I will first report to the ISSM two weeks prior to baseline testing in order to become familiar with the strength and power output and fatigue testing techniques. I will first be briefed on the 1RM strength testing protocol. I will then warm-up for 1 repetition maximal (1RM) squat testing, which will consist of three sets at 50, 75, 85, and 90 percent of my estimated 1-RM for the following repetitions: 5, 3, 1, and 1, respectively. All sets will be separated by three minutes of rest. After completing the squat 1RM, I will start the bench press warm up, in identical fashion to that of the squat. I will then be instructed on the protocol for the 30 second Wingate test (anaerobic power output and fatigue). After this instruction, I will perform a maximal effort on a cycle ergometer for 30 seconds. I will also be given a three-day food and fluid intake journal to complete and return at visit 3.

Visit 2 (VO₂max and Lactate Threshold Test Familiarization) (60 minutes): (No more than 3 days after Visit 1): I will report again to the ISSM in order to test my VO₂max and lactate threshold. I will first be briefed on the testing protocol for VO₂max test and lactate threshold testing. First, I will perform a 5 minute warm-up at half my selected pace. Then, I will perform a graded treadmill run at a speed at which I feel comfortable (able to maintain for a 30-minute run). The treadmill grade will be increased by two percent very two minutes until I can no longer keep pace (volitional fatigue). I will also have a sham finger prick performed every two minutes, which will mimic the finger pricks for the actual lactate threshold test (Visit 5). Following the run, I will rest for 10 minutes in a seated position, during which sham blood collections will be taken at five and 10 minutes.

Visit 3 (2 weeks after Visit 1) (45 minutes): I will report to the ISSM in the morning, between the hours of 0700 and 1000 to measure my body composition, resting heart rate and blood pressure, anthropometrics, and to provide a blood sample after an eight hour fasting period. Blood (20 mL) will be collected under sterile conditions from a forearm vein by an experienced and trained phlebotomist. These test results will serve as a baseline to be compared to later in the study. I will also fill out a mood state questionnaire and return my completed three-day food and fluid intake journal. I will then report to the William Johnson Building to have my body segment girths measured non-invasively using imaging software (TC2-18 3d Body scanner). These results will also serve as baselines for later comparison.

Visit 4 (within 3 days of Visit 3) (90 minutes): I will return to the ISSM between the hours of 0700 and 1000 to have my maximum strength (1RM for squat and bench), power output and fatigue measured in the same fashion as the familiarization visits. These results will also act as a baseline to be compared to later in the study.

Visit 5 (between 3-5 days of Visit 4) (45 minutes): I will report to the ISSM between the hours of 0700 and 1000 to test my VO₂max and lactate threshold. VO₂max will be measured via graded treadmill running test in the same fashion as the familiarization test. Lactate threshold will also be measured during this test (finger prick) in the same fashion as the familiarization test.

Supplementation: After these tests have been completed, I will be placed into one of two groups: STS supplementation or an isocaloric placebo (PL). Supplements will be taken (capsules; 1 pill for every 22.7kg of body weight) on an empty stomach (≥1 hour past eating the last meal) 30-60 minutes prior to working out. These supplements will also be taken on non-training days (2 capsules) on an empty stomach. All supplementation doses are based upon manufacturer's instruction.

STS is a multi-ingredient performance supplement composed of two main ingredients, cordyceps sinensis and rhodiola rose. STS also contains green tea leaf extract, ashwagandha root, astragalus root, vitamin B-12, and chromium. The placebo is a non-caloric cellulose.

I will bring back all empty supplement containers in order to verify compliance with the research staff.

Training: I will come to the gym to perform the prescribed workout for each training day. These workouts will occur four days per week for 12 weeks, totaling 48 workouts. Each week will consist of two resistance training days (Monday and Thursday) and two HIIT days (Tuesday and Friday). Each of these sessions will be monitored by a certified personal trainer and progressed by a certified strength and conditioning specialist. The resistance training sessions consist of a total body, hypertrophy-focused training program. The HIIT protocol is will consist of rest to work ratios progressed in both duration and percentage of maximum heart rate, measured during the VO_2max test (Visit 5). Training volume for each lift and running durations for HIIT will be recorded.

Visit 6 (45 minutes): Halfway through exercise training (following week six and during week seven), I will return back to the ISSM, eight hours fasted (between the hours of 0700 and 1000), to have my blood drawn in the same fashion as the baseline draw. I will also have my body composition, limb segments, resting heart rate and blood pressure, and anthropometrics measured during this visit. I will also be given a three-day food and fluid intake journal to complete and return the next week of training.

Visit 7 (within 3 days of visit 6) (120 minutes): The next laboratory visit I will return to the ISSM between the hours of 0700 and 1000 to have 1RM strength and power output and fatigue measured in the same fashion as visit 4.

Visit 8 (within 3 days of visit 7) (45 minutes): I will report to the ISSM between the hours of 0700 and 1000 to test my VO_2max and lactate threshold in the same fashion as visit 5.

Training and supplementation will then continue for six more weeks in the same fashion as the first six weeks and progressed accordingly.

Visit 9 (45 minutes): After 12 weeks of exercise training, during week 14 of the study, I will return back to the ISSM to have my blood drawn in the same fashion as visit 6. I will once again report in the morning between the hours of 0700 and 1000 after a fasting time of at least eight hours and I will complete a 3-day food and fluid journal. I will also have my body composition, limb segments, resting heart rate and blood pressure, and anthropometrics measured during this visit. I will also return a completed three-day food journal, given during the last week of training.

Visit 10 (within 3 days of visit 9) (120 minutes): The next laboratory visit I will return to the ISSM between the hours of 0700 and 1000 to have my 1RM strength and power output and fatigue measured in the same fashion as visit 4.

Visit 11 (between 3-5 days of visit 10) (45 minute): I will report to the ISSM between the hours of 0700 and 1000 to test my VO_2max and lactate threshold in the same fashion as visit 5.

4) I understand the risks of this study and the levels thereof. I may experience muscle sprain, strain, soreness, and fatigue to the high level of training and testing procedures that I will be enduring. Although not anticipated, due to the addition of a supplement to my diet I may experience gastrointestinal discomfort. I understand that there is a chance that the ingredient rhodiola rosea, can cause me to experience jitteriness and may interfere with my sleep, though

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unlikely. I also understand that due to the nature of blood draws, I will be subjected to venous puncture which could result in pain and possible infection, though highly unlikely.

5) The benefits of participating in this study include a coached 12 week training program that is designed to increase my strength and aerobic capacity. I will also be given information readings about my body composition. I also have the chance of receiving free supplement STS. $50 upon seven week completion and $150 upon completion of final testing (Week 14).

6) The results of this study may be published but my name and/or identity will not be released. Information obtained during the course of the study will remain confidential, to the extent allowed by law. My name will not appear on any of the results. No individual responses will be reported, only group responses will be published. My identity will be kept confidential by assigning each participant a code. Data will be kept on a password locked computer in a locked office for five years and then destroyed.

7) In the case of injury, first aid (free of charge) will be provided by the laboratory personnel working on the project. However, any other treatment or care will be provided at my own expense.

8) Any questions I have concerning the research study or my participation in it, before or after my consent, will be answered by the investigators or they will refer me to knowledgeable sources. I understand that I may contact Dr. Michael Ormsbee at 85████████████████████ or Vince Kreipke at ████████████████████ or questions about the research study or my rights. Group results will be sent to me upon my request.

9) The nature, demands, benefits, and risks of this study have been explained to me. I knowingly assume any risk involved.

10) I have read the informed consent form. I understand that I may withdraw my consent and discontinue participation at any time without penalty or loss of the benefits to which I may otherwise be entitled. In signing this consent form, I am not waiving my legal claims, rights or remedies. A copy of this consent form will be given to me.

_____
Print name

_____   _____
Signature   Date

MEDICAL HISTORY FORM

Strength and Conditioning Laboratory
Florida State University
Nutrition, Food and Exercise Sciences
Medical History Questionaire

This is your medical history form, to be completed prior to your first training session. All information will be kept confidential. This information will be used for the evaluation of your health and readiness to begin our exercise program. The form is extensive, but please try to make it as accurate and complete as possible. Please take your time and complete it carefully and thoroughly, and then review it to be certain you have not left anything out. Your answers will help us design a comprehensive program that meets your individual needs.

If you have questions or concerns, we will help you with those after this form is completed. We realize that some parts of the form will be unclear to you. Do your best to complete the form. Your questions will be thoroughly addressed afterwards. It might be helpful for you to keep a written list of questions or concerns as you complete the medical history form.

Name: _____

Date: _____

MEDICAL HISTORY AND SCREENING FORM

General Information

Participant:

Name _____

Address _____

Contact phone numbers _____

Birth date / Age _____

Phone Number_____

Personal Physician' Name _____ Phone Number_____

　　　　　Address: _____

　　　　　_____

Marital Status:

☐ Single　　　　☐ Married　　　　☐ Divorced　　　　☐ Widowed

Sex:

☐ Male　　　　☐ Female

Height _____ in. _____cm　Weight_____lbs_____kg

Race_____

Education:

☐ Grade School　　☐ Jr. High School　　☐ High School

☐ College (2-4 years)　☐ Graduate School　　☐ Degree _____

Occupation:

Position _____ Employer _____

Address _____

Phone _____

What is (are) your purpose (s) for participation in this Fitness Program?

☐ To determine my current level of physical fitness and to receive recommendations for an exercise program.

☐ Other (please explain) _____
　_____
　_____
　_____
　_____

Nutritional Supplements and Medications

Please list all vitamins, minerals and herbs and other nutritional (performance) supplements as well as medications you are currently taking. (examples: creatine monohydrate, nitric oxide, hydroxy-beta-methylbutyrate (HMB), androsterone derivatives, pharmacological agents including steroids)

_____
_____
_____
_____

How frequently? _____

If you are currently taking any of these supplements are you willing to stop taking them for a period of one month and through the duration of the six-week study and through pre and post testing? Yes No

Exercise

How often do you participate in resistance training a week? _____x week

How many years have you been participating in resistance training? _____years

Present Medical History

Check those questions to which you answer yes (leave the others blank).

Has a doctor ever said your blood pressure was too high?
Do you ever have pain in your chest or heart?
Are you often bothered by a thumping of the heart?
Does your heart often race?
Do you ever notice extra heartbeats or skipped beats?
Are your ankles often badly swollen?
Do cold hands or feet trouble you even in hot weather?
Has a doctor ever said that you have or have had heart trouble, an abnormal electrocardiogram (ECG or EKG), heart attack or coronary?
Do you suffer from frequent cramps in your legs?
Do you often have difficulty breathing?

Do you get out of breath long before anyone else?

Do you sometimes get out of breath when sitting still or sleeping?

Has a doctor ever told you your cholesterol level was high?

Has a doctor ever told you that you have an abdominal aortic aneurysm?

Has a doctor ever told you that you have critical aortic stenosis?

Comments: _____
_____
_____
_____

Do you now have or have you recently experienced:

Chronic, recurrent or morning cough?

Episode of coughing up blood?

Increased anxiety or depression?

Problems with recurrent fatigue, trouble sleeping or increased irritability?

Migraine or recurrent headaches?

Swollen or painful knees or ankles?

Swollen, stiff or painful joints?

Pain in your legs after walking short distances?

Foot problems?

Back problems?

Stomach or intestinal problems, such as recurrent heartburn, ulcers, constipation or diarrhea?

Significant vision or hearing problems?

Recent change in a wart or a mole?

Glaucoma or increased pressure in the eyes?

Exposure to loud noises for long periods?

An infection such as pneumonia accompanied by a fever?

Significant unexplained weight loss?

A fever, which can cause dehydration and rapid heart beat?

A deep vein thrombosis (blood clot)?

A hernia that is causing symptoms?

Foot or ankle sores that won't heal?

Persistent pain or problems walking after you have fallen?

Eye conditions such as bleeding in the retina or detached retina?

Cataract or lens transplant?

Laser treatment or other eye surgery?

Comments: _____
_____
_____
_____

Women only answer the following. Do you have:

Menstrual period problems?

Significant childbirth - related problems?

Urine loss when you cough, sneeze or laugh?

Date of the last pelvic exam and / or Pap smear _____

Comments: _____
_____
_____
_____

Are you on any type of hormone replacement therapy?_____

Men and women answer the following:

List any prescription medications you are now taking: _____
_____
_____

List any self-prescribed medications, dietary supplements, or vitamins you are now taking: _____
_____
_____

List any other medical or diagnostic test you have had in the past two years: _____
_____
_____

List hospitalizations, including dates of and reasons for hospitalization:_____
_____
_____

List any drug allergies: _____
_____
_____

Past Medical History

Check those questions to which your answer is yes (leave others blank).

    Heart attack if so, how many years ago? _____
    Rheumatic Fever
    Heart murmur
    Liver complications _____
    Kidney complications_____
    Diseases of the arteries
    Varicose veins
    Arthritis of legs or arms
    Diabetes or abnormal blood-sugar tests
    Phlebitis (inflammation of a vein)
    Dizziness or fainting spells
    Epilepsy or seizures
    Stroke
    Diphtheria
    Scarlet Fever

Infectious mononucleosis
Nervous or emotional problems
Anemia
Thyroid problems
Pneumonia
Bronchitis
Asthma
Abnormal chest X-ray
Other lung disease
Injuries to back, arms, legs or joint
Broken bones
Jaundice or gall bladder problems

Comments: _____
_____
_____
_____

Have you ever been Hospitalized? Yes   No, if yes please explain
_____
_____
_____
_____

Family Medical History

Father:

☐ Alive   Current age _____

My father's general health is:

☐ Excellent   ☐ Good   ☐ Fair   ☐   Poor

Reason for poor health: _____

☐ Deceased   ☐ Age at death _____

Cause of death: _____

Mother:

☐ Alive   Current age _____

My mother's general health is:

☐ Excellent   ☐ Good   ☐ Fair   ☐   Poor

Reason for poor health:_____

☐ Deceased   ☐ Age at death _____

Cause of death: _____

Siblings:

Number of brothers _____ Number of sisters _____ Age range _____

Health problems _____

Familial Diseases

Have you or your blood relatives had any of the following (include grandparents, aunts and uncles, but exclude cousins, relatives by marriage and half-relatives)?

Check those to which the answer is yes (leave other blank).

Heart attacks under age 50
Strokes under age 50
High blood pressure
Elevated cholesterol
Diabetes
Asthma or hay fever
Congenital heart disease (existing at birth but not hereditary)
Heart operations
Glaucoma
Obesity (20 or more pounds overweight)
Leukemia or cancer under age 60

Comments: _____
_____
_____
_____

Other Heart Disease Risk Factors

Smoking

Have you ever smoked cigarettes, cigars or a pipe?
☐ Yes   ☐ No

 (If no, skip to diet section)

If you did or now smoke cigarettes, how many per day?   _____   Age started _____

If you did or now smoke cigars, how many per day?   _____ Age started

If you did or now smoke a pipe, how many pipefuls a day? _____   Age started _____

If you have stopped smoking, when was it? _____

If you now smoke, how long ago did you start? _____

Diet

What do you consider a good weight for yourself? _____

What is the most you have ever weighed (including when pregnant)? _____

How old were you? _____

My current weight is: _____

One year ago my weight was:_____

Number of meals you usually eat per day: _____

Do you ever drink alcoholic beverages?

☐ Yes   ☐ No

If yes, what is your approximate intake of these beverages?

Beer:

☐ None   ☐ Occasional   ☐ Often   If often, ____ per week

Wine:

☐ None   ☐ Occasional   ☐ Often   If often, ____ per week

Hard Liquor:

☐ None   ☐ Occasional   ☐ Often   If often, ____ per week

Comments: _____
_____
_____
_____

By signing this document I agree that the above information is accurate to the best of my knowledge.

Participant's Signature_____Date_____

Participant's Printed Name _____

APPENDIX D

PROFILE OF MOOD STATES

PROFILE OF MOOD STATES

ID#: _____.

DATE: _____.

Below is a list of words that describe feelings people have. Please read each one carefully. Then check ONE space to the right of each feeling that best describes how you have felt DURING THE PAST WEEK.

0 = NOT AT ALL   1 = A LITTLE   2 = MODERATELY   3 = QUITE A BIT   4 = EXTREMELY

	0	1	2	3	4		0	1	2	3	4
1. Friendly						34. Nervous					
2. Tense						35. Lonely					
3. Angry						36. Miserable					
4. Worn-out						37. Muddled					
5. Unhappy						38. Cheerful					
6. Clear-headed						39. Bitter					
7. Lively						40. Exhausted					
8. Confused						41. Anxious					
9. Sorry for things done						42. Ready to Fight					
10. Shaky						43. Good Natured					
11. Listless						44. Gloomy					
12. Peeved						45. Desperate					
13. Considerate						46. Sluggish					
14. Sad						47. Rebellious					
15. Active						48. Helpless					
16. On Edge						49. Weary					
17. Grouchy						50. Bewildered					
18. Blue						51. Alert					
19. Energetic						52. Deceived					
20. Panicky						53. Furious					
21. Hopeless						54. Efficient					
22. Relaxed						55. Trusting					
23. Unworthy						56. Full of Pep					
24. Spiteful						57. Bad Tempered					
25. Sympathetic						58. Worthless					
26. Uneasy						59. Forgetful					
27. Restless						60. Carefree					
28. Unable to concentrate						61. Terrified					
29. Fatigued						62. Guilty					
30. Helpful						63. Vigorous					
31. Annoyed						64. Uncertain					
32. Discouraged						65. Bushed					
33. Resentful											

THREE DAY FOOD LOG

3 Day Food and Activity Record

Directions for 3-Day Food and Activity Record

1. Keep your 3-day food record on three consecutive days. Try to have at least one of those days be on the weekend.

2. Please record each food you eat immediately after you eat it.

3. Record only one food item per line.

3. Be as specific as possible when describing a food eaten: how it was cooked and the amount you ate. Don't forget to include all beverages you drink. For example: Coffee with 1 tsp. Cream, 12 oz. Regular Coke, or 8 oz. Sweetened Tea.

4. Include brand names or labels from food items whenever possible.

5. Record amounts eaten in household measures. For example: one cup nonfat milk, 3 ounces grilled chicken, 2 tablespoons ranch dressing, 1 medium fruit, 2 slices cheese.

6. Include the method used to prepare the food item. For example: fresh, frozen, stewed, fried, baked, canned, broiled, raw, braised.

7. For canned foods, include the liquid in which it was canned. For example: Sliced peaches in heavy syrup or Fruit cocktail in light syrup.

8. If you eat at a restaurant, do your best to estimate portion size and list the restaurant you ate at. List any visible fat, oil, or sauces added to your food.

9. List amount and type of oil or butter you use in the preparation of your food.

10. Do not alter your diet while you are keeping a food record.

11. Please indicate the activities you participated in during each of the days that you record your diet along with the duration of activity.

3 Day Food and Activity Record

Date   October 2, 2010   Participant ID #   035

Day of the Week   Wednesday

Time of day	Serving Size	Food Item	Specific Activity
7:30 am	1 cup	Cheerios	Sat still on couch
	½ cup	2% milk	
	1 cup	Apple juice	
10:00 am	1 medium	Banana	Chores in house
	1 cup	water	
12:00 pm	2 slices	Bread – hamburger bun	Walked short
	1 slice	Cheddar cheese	Distances. To and from car
	1 patty	Hamburger	
	1 supersized	French fries	
	1 16 ounce	Regular coke	
3:30 pm	15	Crackers - Sociables	Worked at desk.
	2 Tbsp	Peanut butter	Seated.
	1 8 ounce	Juice box	
6:30 pm	5 ounces	Chicken –thigh - baked	Watched TV
	1 ½ cups	rice	
	½ cup	Broccoli	
	1 cup	2% milk	
	½ cup	Mixed fruit – fruit cocktail with sauce	
7:45 pm	1 ½ cups	Vanilla ice cream	Watched TV
	3 Tbsp	Chocolate sauce	

Did you consume your supplement? (Y/N) _____

Was this a typical day's intake? (Y/N. If no, please explain).
  No, this was not a typical day's intake because I had a doctor's appointment and we went to McDonald's afterwards for lunch.

3 Day Food and Activity Record

Date _____   Participant ID # _____

Day of the Week _____

Time of day	Serving Size	Food Item	Specific Activity

Did you consume your supplement? (Y/N) _____

Was this a typical day's intake? (Y/N. If no, please explain).

_____

_____

_____

3 Day Food and Activity Record

Date _____   Participant ID # _____

Day of the Week _____

Time of day	Serving Size	Food Item	Specific Activity

Did you consume your supplement? (Y/N) _____

Was this a typical day's intake? (Y/N. If no, please explain).

_____

_____

_____

3 Day Food and Activity Record

Date _____   Participant ID # _____

Day of the Week _____

Time of day	Serving Size	Food Item	Specific Activity

Did you consume your supplement? (Y/N) _____

Was this a typical day's intake? (Y/N. If no, please explain).

_____

_____

_____

APPENDIX F

DATA COLLECTION SHEET

Shroom Tech Sport Data Tracking Sheet

Subject Number:_____

Baseline Testing

Height (cm): _____

Body Mass (Kg):_____

BMI (kg/cm^2):_____

Blood Pressure   Systolic (mmHg): _____   Diastolic (mmHg):_____

Max Strength   Bench: _____lbs _____Kg   Squat: _____lbs _____Kg

Wingate   Max Power Output:_____ Min. Power Output_____   Fatigue Rate:_____

VO$_2$max (ml/kg/min):_____   Lactate Stage: _____   Lactate (mmol):_____

Lactate 5min:_____   Lactate 10min:_____

Time to Exhaustion (Sec) : _____

Total Cholesterol: _____   LDL:_____ HDL:_____ Glucose:_____ Triglycerides:_____

Mid-training Testing

Height (cm): _____

Body Mass (Kg):_____

BMI (kg/cm^2):_____

Blood Pressure   Systolic (mmHg): _____   Diastolic (mmHg):_____

Max Strength   Bench: _____lbs _____Kg   Squat: _____lbs _____Kg

Wingate   Max Power Output:_____ Min. Power Output_____   Fatigue Rate:_____

VO$_2$max (ml/kg/min):_____   Lactate Stage: _____   Lactate (mmol):_____

Lactate 5min:_____   Lactate 10min:_____

Total Cholesterol: _____   LDL:_____ HDL:_____ Glucose:_____ Triglycerides:_____

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Post-training Testing

Height (cm): _____

Body Mass (Kg):_____

BMI (kg/cm^2):_____

Blood Pressure   Systolic (mmHg): _____   Diastolic (mmHg):_____

Max Strength   Bench: _____lbs _____Kg   Squat: _____lbs _____Kg

Wingate   Max Power Output:_____ Min. Power Output_____   Fatigue Rate:_____

VO$_2$max (ml/kg/min):_____   Lactate Stage: _____   Lactate (mmol):_____

                                        Lactate 5min:_____   Lactate 10min:_____

Total Cholesterol: _____   LDL:_____ HDL:_____ Glucose:_____ Triglycerides:_____

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BIOGRAPHICAL SKETCH
Vince C Kreipke

Florida State University

EDUCATION

Florida State University, Tallahassee, FL   **Current**
PhD Exercise Physiology

Indiana University, Bloomington, IN   **Dec. 2010**
M.S. Applied Sport Science

DePauw University, Greencastle, IN   **May 2009**
B.A. Kinesiology

MEMBERSHIPS AND CERTIFICATIONS

Memberships

National Strength and Conditioning Association (NSCA)   **2010 - Current**

American College of Sports Medicine (ACSM)   **2012 - Current**

International Society of Sports Nutrition (ISSN)   **2015 - Current**

Certifications

Certified Strength and Conditioning Specialist   **2010 - Current**
NSCA

USAW-L1SP   **2010 - Current**
USA Weightlifting

Certified Sports Nutritionist   **2015 - Current**
ISSN

LAB SKILLS

- Maximal Oxygen Consumption Testing
- Sub-Maximal Oxygen Consumption Testing
- Resting Metabolic Rate
- Diet Analysis
- Blood Lactate Analysis
- Maximal Strength Testing

- Body Composition Testing:
  - Skin-Fold
  - Air Displacement Plethysmography (Bodpod)
  - Under-water Weighing
- Blood Pressure
- Electrocardiogram (EKG)
- Flexibility Testing

PROFESSIONAL EXPERIENCE

Visiting Assistant Lecturer   **Sept. 2016-Current**
Wingate University
- **EXSC 101 Introduction to Exercise Science**
- **EXSC 205 Principles of Resistance Training**
- **EXSC 312 Structure and Function**
  - **Lab**
- **EXSC 410 Exercise Prescription: Special Populations**

Research Assistant   **Aug. 2013 - Aug. 2016**
Florida State University
Managed successful research projects while maintaining high scientific standards
Attained over $200,000 in private funding
Relayed scientific principles across multiple communication mediums

Teaching Assistant
Florida State University
- **APK3110 Applied Exercise Physiology**   **Aug. 2012 - Aug. 2016**
- **PET3361 Nutrition and Sport (Online)**   **Jan. 2014 - May 2014**

Research and Development Intern   **July 2014 - Aug. 2014**
Dymatize Nutrition
Evaluated shelf life and sensory comparison of products
Developed alternative products to meet changing demands
Produced placebos and treatments for nutrition studies

Strength and Conditioning Assistant   **Aug. 2011 - Feb. 2012**
Indiana University
Assisted in programming and implementing the wrestling
team's work outs

Intern Coach
Mountain Athlete/ MilitaryAthlete   **Jan 2011 - Mar 2011**
Developed and supervised training regimes specific to
individual athlete needs

MENTOR EXPERIENCE

Graduate Mentor, Florida State University
    Demonstrated: Project Design, IRB submission, Subject Interaction, and Performance
    Assessment
    Students: Kyle Cesareo, Sam Leyh, Josh D'Alessandro

Under-graduate Mentor, Florida State University
    Demonstrated: Subject Interaction, Data Collection, and Project Organization
    Students: Xander Green, Andrew Simmerling, Lia Liberatore, Matthew Boone, Monica
    Shevock, Shemar Crawford, Zanrha Esteban, Johnny Silvers, Kaycee Villane, Rachel
    Blakeley

RESEARCH AND CREATIVE WORKS

REFEREED JOURNAL ARTICLES

In Print

Kreipke VC, Allman BR, Kinsey AW, Moffatt RJ, Hickner RC, Ormsbee MJ. (2015). Impact
    of Four Weeks of a Multi-Ingredient Performance Supplement on Muscular Strength,
    Body Composition, and Anabolic Hormones in Resistance-Trained Young Men. J
    Strength Cond Res. 29(12): 3453-65

Allman BR, **Kreipke VC**, Ormsbee MJ. (2015). What Else Is in Your Supplement? A Review
    of the Effectiveness of the Supportive Ingredients in Multi-Ingredient Performance
    Supplements to Improve Strength, Power, and Recovery. *Strength and Conditioning
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In Review

Moffatt RJ, Stamford BA, **Kreipke VC**. (2016). Immediate Effects of Cigarette Smoking on
    Metabolic Efficiency during Light Exercise. Metabolism

NONREFEREED JOURNAL ARTICLES

Kreipke VC. (2015). 4 Key Ingredients for Your Pre-Workout! *Bodybuilding.com,* online

Kreipke VC. (2015). 4 Essential Post-Workout Ingredients. *Bodybuilding.com,* online

Kreipke, VC. & Ormsbee, MJ. (2014). Longjack root: the new T booster? *Sports Nutrition Insider*, online, 1-3.

PRESENTATIONS

INVITED PRESENTATIONS

Oral

Kreipke VC. (2014). *Possibilities of Long Jack Root Supplementation*. Delivered at 3 Minute Thesis. Tallahassee, FL

Kreipke VC, Alman BR, Kinsey AW, Hickner RC, Dubis GS, Tanner CJ, Moffat RJ, Ormsbee MJ. (2014). *The Impact of Four Weeks of T+ Supplementation on Strength and Endocrine Markers of Anabolism in Power Athletes.* Delivered at NSCA National Conference. Las Vegas, NV

Kreipke VC. (2015). Options at the Fork in the Road. Health Occupations Students of America. Tallahassee, FL

Poster

Kreipke VC, Stamford BA, Moffatt RJ. (2014). *Influence of Cigarette Smoking and the Attainment of Steady State during Light Exercise* .Delivered at National ACSM Conference Orlando, FL

INVITED LECTURES

Kreipke, VC. (2014). *Options and the Rabbit Hole.* Delivered at Florida Atlantic University, Boca Raton, FL

GRANTS FUNDED

Ormsbee, M. J., **Kreipke, VC**. (Aug 2013–Aug 2015). *The Impact of T+^{Tm} Supplementation on Anabolic Hormone Profile, Performance, and Safety in Power Athletes*. Funded by Onnit Labs, Inc. Total award $81,630; supplement and placebo gifted

Ormsbee, M. J., **Kreipke, VC**. (Aug 2015–May 2016*). Effects of STS Supplementation and Concurrent Training on Body Composition, Performance and Health in Collegiate-aged Men*. Funded by Onnit Labs, Inc. Total award $137,860; supplement and placebo gifted

SERVICE

INTERVIEWS

Gelger, B. (2015). How to Build Monster Traps! *Bodybuilding.com* [Online]. http://www.bodybuilding.com/fun/how-to-build-monster-traps.html

Gelger, B. (2015) How to Build Monster Forearms. *Bodybuilding.com* [Online]. http://www.bodybuilding.com/fun/how-to-build-monster-forearms.html

AWARDS

3rd Place Poster Presentation CHS Creativity Day   **Feb. 2014**
Florida State University

Jean A. Reutlinger and Lillian H. Munn Scholarship   **Aug. 2013 - Dec. 2013**
Florida State University