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The Effect of Training Volume and Intensity on Improvements in Muscular Strength and Size in Resistance-trained Men

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THE EFFECT OF TRAINING VOLUME AND INTENSITY ON IMPROVEMENTS IN MUSCULAR STRENGTH AND SIZE IN RESISTANCE-TRAINED MEN

by

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ABSTRACT

The magnitude of improvements in muscular strength and size are influenced by the volume and intensity of a resistance training program. While it is clearly advantageous for resistance-trained individuals to utilize programming specific to these goals, it not clear which is more important. Therefore the purpose of the present investigation was to determine the effect of focusing on training volume versus intensity on changes in muscle size and strength. Changes in muscular strength and size were examined in 29 resistance-trained men following 8 weeks of resistance training. Participants were randomly assigned to either a high volume (VOL, n = 14, 4 x 10 – 12RM, 1min rest) or high intensity (INT, n = 15, 4 x 3 – 5RM, 3min rest) resistance training program. Lean body mass, lean arm and leg mass, were assessed by dual energy X-ray absorptiometry, while ultrasound images (VL-vastus lateralis, RF-rectus femoris, PM-pectoralis major, and TB-triceps brachii) were used to assess changes in muscle cross-sectional area (CSA) and thickness (MT). Strength was measured by one repetition-maximum (1RM) squat (SQ) and bench press (BP). Changes in muscular (RF & VL) activation in response to increases in submaximal SQ intensity (40-, 60-, 80-, & 100%-1RM) were assessed via surface electromyography. Blood samples were collected at baseline, immediately post, 30min post, and 60min post-exercise at week 3 (WK3) and week 10 (WK10), to assess plasma/serum testosterone, growth hormone (GH), insulin-like growth factor-1 (IGF1), cortisol (CORT), and insulin. Area under the curve analysis revealed a greater ($p < 0.05$) increase for VOL (WK3: GH & CORT; WK10: CORT) compared to INT. Compared to

WK3, WK10 showed reduced responses for VOL (GH and CORT) and INT (IGF1). Significant group differences were observed for changes in lean arm mass (INT: 5.2 ± 2.9%, VOL: 2.2 ± 5.6%) and BP 1RM (INT: 14.8 ± 9.7%, VOL: 6.9 ± 9.0%). Over the course of 8 weeks, our data indicate that trained men would benefit more when focusing on training intensity, rather than volume, for strength and size improvements.

I dedicate my dissertation work to my mentors, friends, and family.

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TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

CHAPTER 1: INTRODUCTION

Resistance training is an effective tool for stimulating muscle growth and improving maximal strength. By manipulating acute training variables (i.e. mode, intensity, volume, duration, frequency, and rest intervals), differences in both mechanical and metabolic stresses can be imposed (Paul & Rosenthal, 2002; Ratamess et al., 2009; Tesch & Larsson, 1982; Toigo & Boutellier, 2006). As intensity of resistance exercise is elevated, a greater emphasis on mechanical stress is observed, which results in a greater activation of a large percentage of fast-twitch fibers within the muscle (Abbott, Bigland, & Ritchie, 1952; Henneman, Somjen, & Carpenter, 1965; Katz, 1939). In contrast, when the focus of the resistance training protocol is of high volume (i.e., greater number of repetitions performed with short rest intervals), a greater metabolic stress appears to occur (Nicholson, Mcloughlin, Bissas, & Ispoglou, 2014; Ratamess et al., 2009). When the focus shifts towards a greater metabolic stress, a minimum intensity threshold still needs to be achieved to stimulate muscle activation (Evans, 2002; Jones & Rutherford, 1987; W. J. Kraemer & Ratamess, 2004, 2005; Ratamess et al., 2009). Beyond that threshold, metabolic stress is increased by elevating volume (sets x repetitions) and reducing rest between sets (Evans, 2002; Jones & Rutherford, 1987; W. J. Kraemer & Ratamess, 2004, 2005; Ratamess et al., 2009). In both training scenarios, if the stimulus is at a level that the muscle is not accustomed to, there is a greater likelihood for damage to occur to the activated muscle. The resulting repair process may stimulate adaptation leading to increases in muscle strength and/or muscle growth (Anderson & Kearney,

1982; Carosio, Berardinelli, Aucello, & Musarò, 2011; Clarkson & Hubal, 2002; Clarkson, Nosaka, & Braun, 1992; Tesch & Larsson, 1982; Toigo & Boutellier, 2006). Present understanding suggests that high volume, short rest resistance training programs primarily target muscle growth, while high intensity and long rest resistance training programs primarily target adaptations in muscle strength (Baechle, Earle, & Wathen, 2008; Ratamess et al., 2009). However, recent studies have begun to question these training paradigms (Schoenfeld, 2013; Schroeder, Villanueva, West, & Phillips, 2013).

The general recommendation that high volume, low rest training programs are optimal for stimulating muscle growth is based to a large extent on empirical evidence suggesting that this training paradigm is generally seen among bodybuilders (Hackett, Johnson, & Chow, 2013), and by scientific investigations that provide evidence indicating greater changes in muscle hypertrophy as the volume of the workout increases (i.e., number of sets performed) (Goto et al., 2004; W. J. Kraemer, 1997; W. J. Kraemer et al., 2000; Marx et al., 2001). A higher training volume is associated with a greater anabolic hormone response to exercise (Crewther, Cronin, Keogh, & Cook, 2008; W. J. Kraemer et al., 1991; W. J. Kraemer et al., 1990; McCaulley et al., 2009), which has been related to changes in muscle fiber size (McCall, Byrnes, Fleck, Dickinson, & Kraemer, 1999; West & Phillips, 2012). However, these studies extrapolated the acute endocrine response to a single bout of exercise to changes in skeletal muscle that occur over time. Although exogenously administered anabolic hormones (i.e. testosterone) have been shown to linearly increase lean tissue accruement (Bhasin et al., 1996; Bhasin, Woodhouse, Casaburi, et al., 2001), no studies are known to have demonstrated a

relationship between increases in the anabolic hormone response during a typical resistance training program using multi-joint structural exercises and increases in muscle mass. Furthermore, investigations comparing the acute anabolic hormone response in different resistance exercise protocols have been unable to demonstrate that a greater metabolic stress, generally associated with high volume training programs, is more advantageous for stimulating greater testosterone and IGF-1 responses than training programs focusing on high intensity training (Hasani-Ranjbar, Far, Heshmat, Rajabi, & Kosari, 2012; W. J. Kraemer et al., 1990; McCaulley et al., 2009; McKay, O'Reilly, Phillips, Tarnopolsky, & Parise, 2008; Schwab, Johnson, Housh, Kinder, & Weir, 1993; West et al., 2010; West et al., 2012; West et al., 2009). Interestingly, the high volume training programs do appear to be consistent in stimulating a greater cortisol response to the training stress (Buresh, Berg, & French, 2009; Hakkinen & Pakarinen, 1993; W. J. Kraemer et al., 1996; McCaulley et al., 2009; Smilios, Pilianidis, Karamouzis, & Tokmakidis, 2003; West et al., 2010; Zafeiridis, Smilios, Considine, & Tokmakidis, 2003). Chronically high levels of cortisol are associated with decreases in lean mass as well as total body mass (Barton, Schreck, & Barton, 1987; Crowley & Matt, 1996; Darmaun, Matthews, & Bier, 1988; Simmons, Miles, Gerich, & Haymond, 1984). However, whether transient elevations in cortisol, which may accompany metabolically stressful training programs, impair muscle growth is not well understood. In consideration of the lack of any strong relationship demonstrated in the anabolic hormonal response to resistance exercise and muscle growth, several investigators have begun to question the theoretical basis of high volume, low rest resistance training

programs for maximizing muscle hypertrophy (Schoenfeld, 2013; Schroeder et al., 2013). An alternative argument being raised is based upon the suggestion that a greater mechanical stress, associated with higher intensity training programs, may activate more fibers and provide a greater stimulus to muscle growth than the greater metabolic stress associated with high volume training (Barash, Mathew, Ryan, Chen, & Lieber, 2004; Brentano & Martins, 2011; Clarkson et al., 1992; Ratamess et al., 2009).

A potential caveat observed in the studies questioning the benefits associated with high volume training paradigms and the muscle hypertrophy response is that they have primarily examined recreational or previously untrained individuals. Differences in the physiological response to resistance exercise between trained and untrained individuals have resulted in training recommendations for maximizing the strength and hypertrophy gains to be specific to training status (Ratamess et al., 2009). However, studies comparing high intensity to high volume resistance training program paradigms in resistance-trained individuals are limited. Generally, these investigations have suggested that high intensity training is more beneficial for strength enhancement, but similar to high volume training protocols for enhancing muscle hypertrophy (Brandenburg & Docherty, 2002; Schoenfeld et al., 2014). However, several methodological limitations are associated with these studies. Both investigations employed training programs that would not be typically used by experienced, resistance-trained individuals. Brandenburg and Docherty (2002) only used two single-joint exercises, while the hypertrophy workout from the study by Schoenfeld and colleagues (2014) only lasted 17 minutes. In addition, neither investigation examined endocrine responses or the magnitude of muscle

activation. In consideration of the lack of research comparing commonly used training programs by experienced resistance trained individuals, the purpose of this study was to compare typical high volume, short rest and high intensity, long rest resistance training programs in experienced resistance-trained individuals on endocrine, muscle strength and hypertrophy changes during an 8-week training period.

CHAPTER 2: LITERATURE REVIEW

Increases in muscle mass and strength are desired by most competitive athletes (W. J. Kraemer, Ratamess, & French, 2002; Young, 2006) and non-athletes (Brown, McCartney, & Sale, 1990; Häkkinen, Kallinen, et al., 1998; Häkkinen, Newton, et al., 1998) for enhancing sports performance or quality of life, respectively. Resistance training is often the primary method utilized to elicit such adaptations because it imposes both mechanical and metabolic stresses that are believed to influence muscle growth and strength development (deVries, 1968; Evans, 2002; Jones & Rutherford, 1987; Moritani, 1993; Moritani & deVries, 1979; Thomsen & Luco, 1944; Vandenburgh, 1987). The severity of mechanical and/or metabolic stress is based upon the manipulation of the acute program variables of exercise (i.e. modality, training intensity load, time under tension, training volume, training frequency, and rest between sets and workouts) (Paul & Rosenthal, 2002; Ratamess et al., 2009; Tesch & Larsson, 1982; Toigo & Boutellier, 2006). However, considering that variable manipulation has infinite possibilities, determining the most appropriate combinations for imposing these stresses and maximizing strength gains and muscle growth appears to be an important endeavor.

Mechanical Stress

Mechanical stress is characterized by the tension created when activated muscle moves through a range of motion against an external force (i.e. intensity load) (Adams & Bamman, 2012; Jones & Rutherford, 1987; Vandenburgh, 1987). The application (or lack of application) of tension, through passive (e.g. shortening or lengthening) or active

(e.g. voluntary contraction) means has been demonstrated to affect the size of skeletal muscle (Goldberg, Etlinger, Goldspink, & Jablecki, 1975; Goldspink, 2002; Roy, Baldwin, & Edgerton, 1991), with the change in size being dependent upon how the tension is applied. Chronically applied passive tension results in the addition of new sarcomeres to the length of a muscle fiber, whereas forcibly applied tension increases the diameter of existing sarcomeres (Paul & Rosenthal, 2002; Tesch & Larsson, 1982; Toigo & Boutellier, 2006; P. E. Williams & Goldspink, 1971). Further, skeletal muscle has the ability to differentiate the type of mechanical stress and convert that information into a biochemical process (i.e. mechano-transduction) that results in either protein synthesis or breakdown (Hornberger, 2011; Hornberger & Esser, 2004; Martineau & Gardiner, 2001; Toigo & Boutellier, 2006; Vandenburgh, 1987). The manner in which this occurs is not well understood, though it is believed that deformation to the structure of the muscle is the primary stimulus. It has been suggested that mechanically-induced changes (in length or rupture) to the lipid bilayer of skeletal muscle may serve as a receptor to the mechanical stimulus, which in turn may stimulate the release of growth factors that result in protein synthesis (Hamill & Martinac, 2001; Kimball, Farrell, & Jefferson, 2002). Similarly, changes in the spatial organization of non-contractile proteins within the skeletal muscle cell may also stimulate protein synthesis (Rando, 2001; Wang, Butler, & Ingber, 1993). If sufficient tension is applied (i.e. greater than what the muscle is generally accustomed), damage to the contractile proteins within the activated musculature may also occur (Allen, Whitehead, & Yeung, 2005; Clarkson et al., 1992; Enoka, 1996; Evans & Cannon, 1991; Paul & Rosenthal, 2002; Tesch & Larsson, 1982;

Toigo & Boutellier, 2006). In this case, an inflammatory response is initiated for the purpose of removing damaged tissue (Clarkson & Hubal, 2002; Tidball, 2005). Once cleared, the previously injured site is inhabited by stem cells (i.e. satellite cells), sourcing from the periphery of the muscle fiber, which fuse to the existing muscle tissue (Carosio et al., 2011) increasing its size. Consequently, the associated musculature becomes stronger and more durable against future damage brought on by the particular stimulus (Anderson & Kearney, 1982).

Providing for adequate recovery, systematic exposure to mechanical stimulation will result in muscular enhancements (Barash et al., 2004; Brentano & Martins, 2011; Clarkson et al., 1992; Ratamess et al., 2009; Tee, Bosch, & Lambert, 2007). The nature of this response has been likened to the General Adaptation Syndrome (GAS), first introduced by Sir Hans Selye, which describes an organism's effort to adapt to an unknown stress (Selye, 1936). In brief, when the organism is presented with an unfamiliar stress (e.g. mechanical, metabolic, environmental, psychological, etc.), an initial "Alert" phase occurs which is characterized by a series of reductions in normal physiological function. If the stress continues for only a short period of time, or is followed by series of similar but smaller stressors, the diminished functions will return to normal status and eventually surpass their previous limitations. However, if these stressors were to continue for an extended period of time, more severe diminishment in function will occur. The former concept has since been applied to resistance training, where skeletal muscle is presented with repetitive, submaximal mechanical stress in order to elicit improved function.

Resistance training is an efficient tool for applying mechanical stress because the movements typically involve both passive and active components. That is, eccentric lengthening and voluntary activation satisfy the requirements for inducing longitudinal and cross-sectional fiber growth, respectively (Paul & Rosenthal, 2002; Tesch & Larsson, 1982; Toigo & Boutellier, 2006). Further, because muscle activation is proportional to the intensity of exercise (Abbott et al., 1952; Henneman et al., 1965; Katz, 1939), greater mechanical stress theoretically stimulates growth in a large percentage of muscle fibers and it also encourages a faster and more coordinated response from the activated fibers when presented with heavy loads (Barash et al., 2004; Brentano & Martins, 2011; Clarkson et al., 1992; Ratamess et al., 2009; Tee et al., 2007). During resistance training, the severity of mechanical stress is related to the magnitude and/or duration of the applied tension (Nosaka, Newton, & Sacco, 2002; Kazunori Nosaka, Kei Sakamoto, Mike Newton, & Paul Sacco, 2001; Kazunori Nosaka, K Sakamoto, Michael Newton, & Paul Sacco, 2001). Typically, it is maximized by using heavy loads (1 – 6 RM) with long rest periods (3 – 5 minutes) (Baker, 2001; Gonzalez-Badillo, Izquierdo, & Gorostiaga, 2006; Peterson, Rhea, & Alvar, 2004; Ratamess et al., 2009), which enables maximal fiber activation to occur across each set due to adequate time for phosphocreatine (PCr) replenishment between sets (de Salles et al., 2009; Harris et al., 1976). Consequently, emphasizing mechanical stress during resistance training may maximize strength improvements by enabling muscle growth and improved fiber activation.

Metabolic Stress

Metabolic stress reflects the ability to provide energy, in the form of adenosine triphosphate (ATP), at a pace concomitant with the demands of exercise. During resistance training, ATP is made available from all three energy systems (i.e. phosphagen, glycolytic, and oxidative). Initially, the phosphagen system is primarily recruited to meet energy requirements, because of how rapidly it can convert PCr to ATP and supply it to contractile proteins (Harris et al., 1976; Harris, Hultman, & Nordesjö, 1974). However, as PCr supply is depleted, ATP production shifts towards the glycolytic system as the primary provider (Essen-Gustavsson & Tesch, 1990; Tesch, Colliander, & Kaiser, 1986), which is a slower process that also results in the production of lactate. By itself, the production of lactate is not the metabolic stress that stimulates muscle growth. Rather, the hypoxia and associated hydrogen ions that dissociate from lactate, prior to its release into the blood, lower intracellular pH and impair glycolytic enzyme activity and ATP production (Cairns, 2006; W. J. Kraemer, Noble, Clark, & Culver, 1987) contribute to the metabolic stress. The fatiguing nature of this process has been suggested to positively influence muscle fiber activation (Houtman, Stegeman, Van Dijk, & Zwarts, 2003; K. Miller, Garland, Ivanova, & Ohtsuki, 1996; Takarada, Takazawa, et al., 2000). That is, as low intensity threshold fibers (i.e. type I fibers) fatigue, higher intensity threshold fibers (i.e. type II fibers) are activated. Though activation may not be comparable to when mechanical stress is the focus (Abbott et al., 1952; Henneman et al., 1965; Katz, 1939; Suga et al., 2009), as metabolic stress becomes more severe, adaptation across a larger percentage of fibers might be stimulated.

During resistance training, metabolic stress might be maximized through a wide variety of training variable combinations that emphasize energy restriction. Training programs that focus on meeting this criteria generally employ high training volumes (8 – 12RM) with short rest intervals (30 – 90 seconds) (Ratamess et al., 2009). The demanding nature from longer set durations on short rest is exacerbated by repeated muscular contractions that limit blood flow and oxygen delivery to the exercising musculature (Tamaki, Uchiyama, Tamura, & Nakano, 1994). The acute hypoxia induced by this training scheme has the potential for promoting the accumulation of metabolites (e.g. lactate and hydrogen ions) (Nicholson et al., 2014; Suga et al., 2009) and free radicals (Goldfarb et al., 2008), which are believed to be advantageous for muscle growth (C. S. Fry et al., 2010; Takarada, Takazawa, et al., 2000). In support, induced hypoxia through occlusion of the exercising musculature has produced comparable muscle growth when using low training intensities (20 - 50% 1RM) in comparison to moderate-heavy training loads without occlusion (50 – 85% 1RM) (Barcelos et al., 2015; Martín-Hernández et al., 2013; Vechin et al., 2014). Further, at higher intensities (i.e. 70% 1RM), resistance training with occlusion has induced greater hypertrophy in comparison to the same intensity under normal blood flow conditions (Nishimura et al., 2010). Though growth from this manner of training may in part be the consequence of increased intracellular hydration, as Martin-Hernandez and colleagues (2013) observed changes in muscle size without changes in architecture (i.e. pennation angle), these findings illustrate the effectiveness of stimulating hypoxic conditions to facilitate muscle growth. Moreover, attempting to inhibit metabolite production and reduce the associated pain

during recovery by taking anti-inflammatory medications (i.e. ibuprofen, indomethacin, and acetaminophen) has been demonstrated to also reduce satellite cell proliferation and protein synthesis (Mikkelsen et al., 2009; Trappe et al., 2002).

In addition to the aforementioned mechanisms, a prominent feature of high volume resistance training is the associated endocrine response. Resistance training programs that focus on metabolic stress when using moderate intensity loads has been associated with elevations in the circulating concentrations of anabolic hormones (e.g. growth hormone, testosterone, and insulin-like growth factor 1) (W. J. Kraemer & Ratamess, 2005). For example, a greater lactate response is associated with elevations in circulating concentrations of growth hormone (Hakkinen & Pakarinen, 1993; Hoffman et al., 2003; W. J. Kraemer et al., 1990; Vanhelder, Radomski, & Goode, 1984; West et al., 2010). Elevations in growth hormone concentrations, in addition to the mechanical stress of training, stimulates the production of insulin-like growth factor-1 (Clemmons, Underwood, & Van Wyk, 1981; D'Ercole & Underwood, 1987; Devol, Rotwein, Sadow, Novakofski, & Bechtel, 1990; Gregory et al., 2013; Hameed et al., 2004; McKay et al., 2008), while testosterone seems to be affected by a variety of resistance training paradigms (Hakkinen, Pakarinen, Kraemer, Newton, & Alen, 2000; W. J. Kraemer et al., 1990; McCaulley et al., 2009; Schwab et al., 1993; Smilios et al., 2003; West et al., 2009). The elevation of these hormones (discussed below), in addition to others (e.g. insulin), may be crucial for enhancing muscle growth when in combination with sufficient muscle fiber recruitment (Evans, 2002; Jones & Rutherford, 1987; W. J. Kraemer & Ratamess, 2004, 2005; Ratamess et al., 2009).

Growth Hormone

The superfamily of growth hormone (GH) proteins refers to over one hundred heterogeneous polypeptide isoforms (Baumann, 1990; Rigamonti et al., 2012; Romero-Prado & Martin-Cofreces, 2011) that are controlled by the anterior pituitary gland and primarily stimulated for release during sleep and exercise (Godfrey, Madgwick, & Whyte, 2003). GH's (the 22 kD primary form) role in muscle development may be dependent upon several factors. Generally, its direct effect on muscle growth is observed prior to adulthood (Lissett & Shalet, 2000; Pell & Bates, 1990), whereas later on, this is likely accomplished through indirect means. During adulthood, GH appears to stimulate muscle growth by influencing the production of Insulin-Like Growth Factor-1 (IGF-1) (Le Roith, Bondy, Yakar, Liu, & Butler, 2001; Mauras & Haymond, 2005; Walenkamp & Wit, 2007), a potent anabolic agent. Several investigations have reported increases in both circulating and intramuscular concentrations of IGF-1 in response to increased concentrations of GH (Clemmons et al., 1981; D'Ercole & Underwood, 1987; Devol et al., 1990; Iida et al., 2004; Yang & Goldspink, 2002). However, the anabolic effect of GH does not appear to be limited to its stimulation of IGF-1.

GH appears to influence growth by another mechanism that is independent from IGF-1. For example, severe growth retardation occurs in mice bred without IGF-1 and GH receptors. However, this effect is blunted in mice who are only missing their IGF-1 receptors (Lupu, Terwilliger, Lee, Segre, & Efstratiadis, 2001). In this capacity, GH may positively influence muscle growth by promoting amino acid transport into skeletal muscle (Cameron et al., 1988; Fryburg, Gelfand, & Barrett, 1991), in a manner unrelated

to the functions of insulin or IGF-1 (Fryburg et al., 1991). During resistance exercise this function may work in combination with GH's ability to promote the usage of free fatty-acids and glucose (Gravholt et al., 1999; Moller et al., 1995), and spare amino acids from catabolism. Thus it appears that GH has an important role in stimulating muscle growth.

In relation to exercise, the magnitude of the GH response appears to be predicated upon the degree of metabolic stress imposed by the workout. Vanhelder and colleagues (1984) reported significant correlations (r = 0.99) between GH and blood lactate concentrations in response to heavy (85% 1RM) resistance training (Vanhelder et al., 1984). Similar responses were found following very heavy (20 x 1 RM, 100% 1RM) and moderate (10 x 10RM, 70% 1RM) resistance training designs (Hakkinen & Pakarinen, 1993). In support of these relationships, several investigations have reported a greater GH response to training protocols that also produced higher blood lactate responses (Hoffman et al., 2003; W. J. Kraemer et al., 1991; W. J. Kraemer et al., 1990; Smilios et al., 2003; Spiering et al., 2008; West et al., 2010; Zafeiridis et al., 2003). Further, elevations in GH appear to persist despite correcting for plasma volume shifts (McCall et al., 1999) which if left unaccounted for, might result in a misleading interpretation (R. Kraemer, Kilgore, & Kraemer, 1993). Although the majority of these studies indicate that a higher training volume is optimal for eliciting a GH response, it is likely related to training intensity and muscle recruitment. For example, very high training volume (7 x 21RM) was not capable of producing a significant rise in GH or blood lactate when the intensity of training was only 30% of the 1 RM (Vanhelder et al., 1984). Similarly, 3 – 4 sets at 8 – 10 RM did not produce a significant GH or blood lactate response when the

exercise regimen only included unilateral leg extension and leg press (Wilkinson, Tarnopolsky, Grant, Correia, & Phillips, 2006). This has been consistently demonstrated in several studies that have reported similar results following 2.5 – 6 months of resistance training (Buresh et al., 2009; Hakkinen et al., 2000; McCall et al., 1999; Mitchell et al., 2013). Thus, a reduction in pH common during a metabolically stressful training regimen appears to be the most influential factor in stimulating elevations in the GH response to exercise (W. J. Kraemer et al., 1993; W. J. Kraemer & Ratamess, 2005).

Testosterone

The influential role of testosterone on skeletal muscle hypertrophy has been well documented (Bhasin, Woodhouse, & Storer, 2001; Deschenes, Kraemer, Maresh, & Crivello, 1991; Kadi, 2008; Loebel & Kraemer, 1998; Sipilä et al., 2013). Testosterone is a steroid hormone that binds to its receptor within target tissues (e.g. skeletal muscle) and is then transported to the cell nucleus where it exerts its primary physiological effect (Sinha-Hikim, Taylor, Gonzalez-Cadavid, Zheng, & Bhasin, 2004; Vingren et al., 2010). As an anabolic hormone, its primary physiological role is to increase protein synthesis through a variety of mechanisms (Ferrando et al., 1998; Sheffield-Moore et al., 1999; Urban et al., 1995). For instance, testosterone directly influences protein synthesis by promoting the replication and activation of satellite cells and myonuclei, thus stimulating an increase in the number of myogenically committed cells (Herbst & Bhasin, 2004; Sinha-Hikim, Cornford, Gaytan, Lee, & Bhasin, 2006; Sinha-Hikim, Roth, Lee, & Bhasin, 2003). It also may support protein synthesis by facilitating the reutilization of intracellular amino acids from protein breakdown (Ferrando et al., 1998; Sheffield-Moore

et al., 1999) and has been associated with the release of other hormones (i.e. growth hormone and IGF-1) with anabolic functions (Crewther, Keogh, Cronin, & Cook, 2006; Sculthorpe et al., 2012; Sheffield-Moore et al., 1999; Urban et al., 1995). It may also assist growth by counteracting the catabolic actions of cortisol (S.-y. Chen, Wang, Yu, Liu, & Pearce, 1997; Mayer, Shafrir, Kaiser, Milholland, & Rosen, 1976; Syms, Nag, Norris, & Smith, 1987). Enhanced cortisol levels have been demonstrated to upregulate ubiquitin ligases (e.g. Muscle Atrophy F-Box) that culminate in muscle atrophy (Zhao et al., 2008). Elevations in circulating concentrations of testosterone enhances protein synthesis and inhibits protein breakdown within skeletal muscle (Crowley & Matt, 1996). Consistent with this, Zhao and colleagues (2008) reported that testosterone administration can suppress the catabolic effects of elevated cortisol concentrations. Furthermore, evidence suggests a non-genomic (i.e. independent of its receptor) role where testosterone stimulates transient increases in intracellular calcium (Estrada, Espinosa, Müller, & Jaimovich, 2003; Estrada, Liberona, Miranda, & Jaimovich, 2000), which may temporarily elevate maximal force production (Hamdi & Mutungi, 2010). Thus, it appears that elevating circulating testosterone concentrations has a significant impact on muscle growth.

Acute resistance exercise has been repeatedly shown to elevate circulating testosterone concentrations, though its responses to specific program variables have been inconsistent. In a classic study, Kraemer and colleagues (1990) reported significant elevations in serum testosterone during and following (up to 15 minutes post-exercise) resistance training protocols utilizing either high intensity loads (i.e. 5RM vs. 10RM) or

short rest periods (i.e. 1 min vs. 3 min). Though exceptions have been reported (McCall et al., 1999; McCaulley et al., 2009; Wilkinson et al., 2006), similar responses, regardless of the subject's training status, have been observed during resistance training protocols using low volume, heavy training loads (e.g. 5 – 6 RM, 85 – 95% 1RM) (Schwab et al., 1993), as well as from high volume, moderate intensity loads (i.e. 8 – 15 RM, 55 – 75% 1RM) (Ahtiainen, Pakarinen, Alen, Kraemer, & Häkkinen, 2003; Hakkinen et al., 2000; Hansen, Kvorning, Kjaer, & Sjøgaard, 2001; McCaulley et al., 2009; Schwab et al., 1993; Smilios et al., 2003; West et al., 2010; West et al., 2009). In regards to the rest interval, both shorter (< 2 min) (Hansen et al., 2001; McCaulley et al., 2009; Schwab et al., 1993; West et al., 2010; West et al., 2009) and longer (> 2min) (Ahtiainen, Pakarinen, Alen, et al., 2003; Hakkinen et al., 2000) rest periods have been demonstrated to cause an elevated response. In short, the evidence does not appear to provide any clear indication that one mode of training has any advantage in stimulating testosterone secretion. A potential confound influencing the variability in these findings is that several studies do not correct for the plasma volume shifts that may occur during resistance exercise (R. Kraemer et al., 1993). For instance, the significant testosterone response observed by McCall and colleagues (1999) disappeared after correcting for plasma volume shifts. With that in mind, it may be speculated that these data point towards testosterone responding best to when overload is accomplished by adding more weight (Ahtiainen, Pakarinen, Kraemer, & Häkkinen, 2003) or more exercises (Hansen et al., 2001; West et al., 2010; West et al., 2009). Therefore, it would seem that mechanical overload may be the primary influence for acute elevations of testosterone following resistance exercise.

The effect of prolonged resistance training on resting testosterone concentrations and its response to exercise is inconclusive. Elevations in resting concentrations have been observed following short- (i.e. 4 – 14 weeks) (Ahtiainen, Pakarinen, Alen, et al., 2003; W. J. Kraemer, Häkkinen, et al., 1999; Staron et al., 1994) and long-term (2 years) (Hakkinen, Pakarinen, Alen, Kauhanen, & Komi, 1988) resistance training, while others have reported no changes following one year of training (A. C. Fry et al., 1994). Interestingly, Fry and colleagues (1994) observed decreased resting levels during a week of high volume training indicating the potential effect of an overreaching week. However, the researchers also observed a diminished effect (from the high volume week) on resting concentrations following the year of training, which may indicate a proactive response to the stress of chronic exercise.

In regards to the testosterone response to exercise, the majority of research examining the effect of prolonged training (2 - 6 months) show either a similar or lower testosterone response (Alen, Pakarinen, Häkkinen, & Komi, 1988; Bell, Syrotuik, Martin, Burnham, & Quinney, 2000; Buresh et al., 2009; Hakkinen et al., 2000; Hansen et al., 2001; McCall et al., 1999; Mitchell et al., 2013; Reaburn, Logan, & Mackinnon, 1997; West et al., 2010; Wilkinson et al., 2006). Only Fry and colleagues (1994) observed an enhanced response during the overreaching week. Thus, it appears that resistance training has minimal effects on resting testosterone concentrations, while further evidence is necessary to make any definitive conclusions regarding the response to exercise.

Insulin-Like Growth Factor (IGF-1)

IGF-1 is a term applied to several variant forms of the peptide hormone, which can be found circulating in the blood, as well as being expressed within skeletal muscle (Goldspink, 2005). IGF-1 is believed to induce a potent anabolic effect by stimulating signaling pathways for protein synthesis within muscle (Dunn, Burns, & Michel, 1999; Dunn, Chin, & Michel, 2000; Michel, Dunn, & Chin, 2004; Musarò, McCullagh, Naya, Olson, & Rosenthal, 1999; Ochi, Ishii, & Nakazato, 2010) and suppressing transcription proteins that limit muscle growth (Sandri et al., 2004; Stitt et al., 2004). In response to damage, IGF-1 is believed to play an important role during the repair process. During the early stages of muscle repair, it has been suggested that IGF-1 is responsible for the activation and proliferation of satellite cells (Adams, 1998; Barton-Davis, Shoturma, & Sweeney, 1999; Hill & Goldspink, 2003). Later, IGF-1 may facilitate protein synthesis for an extended period of time (Barton-Davis et al., 1999; Hill & Goldspink, 2003; McKay et al., 2008), possibly by mediating the fusion of satellite cells to muscle fibers (Toigo & Boutellier, 2006). Consequently, changes in circulating levels of IGF-1 have been suggested to be related to changes in strength (Borst et al., 2001).

The presence of IGF-1 is believed to be regulated by GH and the occurrence of muscle damage induced by mechanical stress (Bamman et al., 2001; Clemmons et al., 1981; D'Ercole & Underwood, 1987; Devol et al., 1990; Gregory et al., 2013; Hameed et al., 2004; Iida et al., 2004; McKay et al., 2008; Yang & Goldspink, 2002). However, the studies examining the IGF-1 response to a high-volume, moderate-intensity resistance training protocol, known to induce an enhanced growth hormone response (W. J.

Kraemer et al., 1990), have offered conflicting results. For instance, IGF-1 circulating concentrations have been observed to increase during and following exercise (Gregory et al., 2013; West et al., 2010; West et al., 2012; West et al., 2009) with peak elevations generally occurring during exercise (Gregory et al., 2013) or within 15 – 30 minutes post-exercise (West et al., 2010; West et al., 2012; West et al., 2009), before returning to baseline. In contrast, significant reductions from baseline have been observed at six and nine hours following exercise without any increase seen during or immediately following the workout (Hasani-Ranjbar et al., 2012). Others, using different high-volume training variations (to 3 x 10 RM, 1 min rest) have not observed IGF-1 concentration changes over the course of 2 – 13 hours post-exercise (McKay et al., 2008; Nindl et al., 2001; Spiering et al., 2008; Wilkinson et al., 2006). Consequently, the expected IGF-1 response to exercise may be dependent upon the exact training stimulus as well as when samples are collected.

A possible explanation for the varied responses seen in circulating IGF-1 concentrations following exercise may involve the efficiency of IGF-1 uptake by activated tissue. Though information is limited, elevations in intramuscular IGF-1 have been observed 1 – 3 days following a high volume, high intensity isokinetic protocol (McKay et al., 2008). Further, high volume (8 – 12 RM) resistance training has been demonstrated to improve resting levels of IGF-1 within skeletal muscle (Hameed et al., 2004), while it seems to have no effect on its circulating concentrations (Gregory et al., 2013; Hameed et al., 2004; McCall et al., 1999; Mitchell et al., 2013; West et al., 2010;

Wilkinson et al., 2006). Thus, complete understanding of IGF-1's role in muscle growth following acute exercise or during prolonged resistance training is still unclear.

Insulin

Insulin is a peptide hormone that is primarily responsible for transporting glucose and amino acids into skeletal muscle (Lee & Pilch, 1994; White & Kahn, 1994). In this capacity, insulin provides muscle with valuable energy for activity and growth. However, it has also been suggested that insulin can affect protein synthesis in a manner that is distinct from its transporting function (Biolo, Fleming, & Wolfe, 1995). More specifically, insulin has been observed to be an upstream regulator of both glycolysis and mammalian target of rapamycin (mTOR), an intracellular protein involved in muscle cell growth (Manning & Cantley, 2007; Tixier et al., 2013). Upon binding with its receptor, the insulin-receptor complex activates phosphoinositide 3-kinase (PI3K) which activates protein kinase B (PKB), also known as AKT. The PI3K/AKT pathway in turn may stimulate glycolysis and mTOR or inhibit forkhead box (FOXO) transcription proteins that regulate growth (Manning & Cantley, 2007; Tixier et al., 2013). By stimulating glycolysis, insulin facilitates the production of energy (Lunt & Vander Heiden, 2011) that may be used to sustain growth. Indeed, Jepson and colleagues (1988) observed parallel stimulation of protein synthesis and breakdown in relation to insulin concentrations Further, its involvement in protein synthesis may be greater at lower concentrations (Jepson, Bates, & Millward, 1988), when adequate nutrient intake is not present (i.e. starvation); suggesting a pivotal role for sparing protein under such conditions (Goldberg, 1979; Millward & Waterlow, 1978). Nevertheless, its role for stimulating appreciable

muscle growth cannot be realized in the absence of an adequate amino acid supply (Koopman, 2007; Wolfe, 2000). Thus nutrient intake is recommended surrounding resistance training to maximize insulin's anabolic effect.

Training at least two hours post-prandial has been demonstrated to diminish circulating concentrations of insulin, that is likely related to the reductions reported in glucose concentrations (Raastad, Bjøro, & Hallen, 2000; Spiering et al., 2008; Thyfault, Carper, Richmond, Hulver, & Potteiger, 2004; Volek et al., 2004). However, when protein and carbohydrates are consumed immediately prior to or during exercise, significant elevations in insulin concentrations during and following (up to 2 hours) a high volume, moderate intensity resistance training protocol have been reported (Bird, Tarpenning, & Marino, 2006; Hulmi, Volek, Selänne, & Mero, 2005; Tipton et al., 2001). The post-workout response was nearly identical when participants only consumed the protein/carbohydrate drink post-workout (Tipton et al., 2001). Similarly, a follow-up investigation showed that timing of the supplement (pre-workout vs. post-workout) made no difference in the total insulin response when consuming an amino acid/carbohydrate beverage (Tipton et al., 2007). However, when protein is the only substrate consumed prior to exercise, the insulin response does not appear to be as strong (Chandler, Byrne, Patterson, & Ivy, 1994). Rather, a second feeding (protein only), post-exercise may be necessary to produce a more substantial response (Hulmi et al., 2005). This appears to be consistent with the insulin responses normally seen with a post-workout drink (Biolo, Tipton, Klein, & Wolfe, 1997; Børsheim et al., 2004; Chandler et al., 1994; Esmarck et al., 2001; Rasmussen, Tipton, Miller, Wolf, & Wolfe, 2000; Thyfault et al., 2004).

Adaptations to prolonged resistance training consistently show a reduced basal and total insulin response to exercise (Björntorp, de Jounge, Sjöström, & Sullivan, 1970; Krotkiewski et al., 1985; J. P. Miller et al., 1994; W. Miller, Sherman, & Ivy, 1984). It is likely that improvements in muscular mass, generally seen in response to resistance training, lead to greater insulin utilization and sensitivity by skeletal muscle.

Mechanical versus metabolic stress in resistance training

The exact training paradigm that provides the greatest stimulus for muscle growth and strength development is debatable. There is supporting information for emphasizing training intensity, as well as emphasizing training volume at moderate loads and short rest periods (Aagaard et al., 2001; Campos et al., 2002; Chestnut & Docherty, 1999; Erskine, Fletcher, & Folland, 2014; Schoenfeld et al., 2014; West & Phillips, 2012). Consequently, it has been suggested that the ideal range for stimulating strength and hypertrophy encompasses both of these strategies (A. C. Fry, Kraemer, & Ramsey, 1998; Ratamess et al., 2009). An advantage or potential disadvantage to having a wide-range of program recommendations is that it leaves a great deal of freedom for interpretation during program development. For example, strength and conditioning professionals may progress in linear fashion from a predominant focus on training volume towards training intensity over the course of several weeks or simply include both strategies within the same training cycle (Bradley-Popovich, 2001; Monteiro et al., 2009; Rhea, Ball, Phillips, & Burkett, 2002). However, it is not clear whether these practices are optimal or necessary for all individuals. Historical experience with resistance training, as well as current training status, are both known to significantly affect training outcomes (W. J.

Kraemer, Staron, et al., 1998; Ratamess et al., 2009). In untrained individuals, the introduction of resistance training alone, regardless of programming, may be sufficient to stimulate changes in strength and size. Whereas trained individuals may require more specific guidelines.

The Role of Training Status

Resistance training experience is an important determinant for the level of precision necessary to prescribe effective training programs. During the initial weeks of a new training regimen, novice lifters will experience several neurological adaptations that will assist them in correctly performing exercise movements (Moritani & deVries, 1979). These changes will in turn allow for a more effective and efficient recruitment of muscle (deVries, 1968; Moritani, 1993; Moritani & deVries, 1979; Ploutz, Tesch, Biro, & Dudley, 1994), which may be observed in rapid improvements in strength during this phase. The beginning stages of muscle hypertrophy will also take place during this time, but phenotypic changes in muscle size will not be apparent for a few weeks (Moritani & deVries, 1979; Phillips, 2000; Staron et al., 1994). Nevertheless, the lack of experience allows for the rapid development of muscle in the untrained subject from a variety of resistance training schemes. It has therefore been suggested that healthy, untrained individuals may experience improvements in muscular strength and size in response to general, non-specific resistance training (Ratamess et al., 2009), whereas those with several years of resistance training experience are limited in this capacity. Consequently, particular attention must be placed upon variable manipulation in order to induce changes in strength and size in resistance-trained adults (Ratamess et al., 2009).

Programming for Novice Lifting

For novice lifters, the current body of evidence comparing high volume to high intensity resistance training shows similar changes occurring in muscular strength and hypertrophy. In fact, the current training recommendation for stimulating hypertrophy (i.e. 1 – 3 sets, 70 – 85% 1RM, 8 – 12 RM) (Ratamess et al., 2009) may be too stringent, as similar increases in muscle size have also been observed across a much wider intensity load and volume combinations (i.e. 3 – 28 RM) (Alegre et al., 2014; Campos et al., 2002; Chestnut & Docherty, 1999; Lamon, Wallace, Leger, & Russell, 2009; Leger et al., 2006). In terms of strength improvement, the evidence generally supports heavier intensity load and volume combinations (i.e. > 75% 1RM, < 11RM) (Campos et al., 2002; Mitchell et al., 2012; Ogasawara, Loenneke, Thiebaud, & Abe, 2013) than the current recommendation for novice lifters (i.e. 1 – 3 sets, 60 – 70% 1RM, 8 – 12 RM) (Ratamess et al., 2009). However, lower intensity loads may still produce comparable hypertrophy and strength gains as heavier loads, if the activated musculature is overloaded in some capacity. For example, when utilizing resistances that are not generally considered to be sufficient for stimulating hypertrophy or maximal strength (i.e. <60% 1RM), similar gains, when compared to the use of heavier loads, have been reported when sets are performed to failure (Alegre et al., 2014; Campos et al., 2002; Chestnut & Docherty, 1999; Holm et al., 2008; Lamon et al., 2009; Leger et al., 2006; Mitchell et al., 2012; Ogasawara et al., 2013; Stone & Coulter, 1994; Tanimoto & Ishii, 2006) or when the time under tension (for each repetition) is increased (Tanimoto et al., 2008). In regards to training volume, specifically the number of sets per exercise (Abe,

DeHoyos, Pollock, & Garzarella, 2000; Mitchell et al., 2012; Rønnestad et al., 2007; Starkey et al., 1996) only appear to have a limited impact on strength gains and hypertrophy in the untrained individual. Novice lifters appear to respond more readily in response to less complex training programs (Ahtiainen, Pakarinen, Alen, et al., 2003).

Training Program Design for the Experienced Resistance Trained Individual

There appears to be only a limited number of studies examining the effect of training intensity versus training volume on experienced, resistance trained individuals (Brandenburg & Docherty, 2002; Schoenfeld et al., 2014). While the findings of those studies provide some direction regarding the merits of one training scheme over another, several methodological limitations within these studies prevent any definitive determination.

Brandenburg and colleagues (2002) reported greater strength increases from a supra-maximal eccentric loading (110 – 120% 1RM) scheme in comparison to high volume resistance training (3 – 4 sets at 10 RM, rest = 3 min), but failed to observe significant changes in muscle size over the course of a 9-week training intervention. Unfortunately, neither scheme accurately reflects the training habits of resistance-trained adults (Ebben, Carroll, & Simenz, 2004; Hackett et al., 2013; Swinton, Lloyd, Agouris, & Stewart, 2009). For example, both training protocols consisted of only two single-joint, open-chain exercises (i.e. preacher curl and supine elbow extension), which limits the potential for building strength and size because less muscle is activated in comparison to multi-joint, closed-chain exercises (Augustsson, Esko, Thomeé, & Svantesson, 1998; Gentil et al., 2013; Stensdotter, Hodges, Mellor, Sundelin, & Hager-Ross, 2003).

Therefore, while this outcome demonstrates the merits for the use of greater intensity for eliciting strength gains, it does not provide information for stimulating muscle growth.

More recently, Schoenfeld et al., (2014) investigated the effect of high intensity training design (7 x 3 RM, rest = 3 min) in comparison to a volume-equated, moderate intensity scheme (3 x 10 RM, rest = 90 sec) in resistance-trained men. Results indicated that the high intensity training group achieved greater upper-body strength improvements and equal size increases in comparison to the moderate intensity training program. Although this investigation appears to support training intensity as having a greater stimulus for strength gains than training volume, several methodological limitations question the validity and practicality of these findings. For instance, despite using a full-body training regimen, changes in muscle size were assessed by a single image of biceps brachii muscle thickness using B-mode ultrasound, which is unacceptable because it ignores adaptation variances that occur across the width of skeletal muscle (Wells et al., 2014). Instead, it would have been more informative to track changes in muscle growth via images of muscle thickness and cross-sectional area, obtained from a panoramic sweep. Similarly, it would have been more appropriate to collect images from the primary movers of both upper-body pressing motions (i.e. pectoralis major and triceps brachii) and lower body exercise (i.e. vastus lateralis and rectus femoris), since these muscles are commonly examined during ultrasonic assessment of muscle hypertrophy (Abe et al., 2000; Alegre et al., 2014; Farthing & Chilibeck, 2003; Reeves, Narici, & Maganaris, 2004; Starkey et al., 1996; Tanimoto et al., 2008). Therefore, the changes reported in muscle size by Schoenfeld et al. (2014), must be considered questionable.

More importantly, the training design of the study limits the practical application of these findings. Specifically, the volume-equated "hypertrophy" scheme, which lasted 17 minutes in total, does not accurately reflect a typical training duration for resistance-trained adults (Ebben et al., 2004; Hackett et al., 2013; Swinton et al., 2009). In this capacity, the study does not make an accurate comparison leaving much to be learned regarding the differences of the two training schemes.

An additional concern with both studies examining trained individuals is that neither performed biochemical analysis. As a result, it remains unknown whether the utilized training schemes sufficiently stimulated the anabolic hormone response. As previously mentioned, because Brandenburg et al., (2002) only used two single-joint, open-chain exercises, this is definitely a concern. However, it is also a concern with the investigation by Schoenfeld and colleagues (2014) because the desired anabolic hormone response has been shown to occur following much simpler training schemes (A. C. Fry et al., 1998; McCaulley et al., 2009; Nicholson et al., 2014; Schwab et al., 1993), as well as from more comprehensive designs (Beaven, Gill, & Cook, 2008; W. J. Kraemer et al., 1991; W. J. Kraemer et al., 1990). Furthermore, the exact response appears to be affected by individual responsiveness to resistance exercise (Beaven et al., 2008). Consequently, it cannot be assumed that the training programs provided the appropriate stimulus.

Shortcomings of the Hormone Hypothesis

As has been discussed, only a couple of studies (Brandenburg & Docherty, 2002; Schoenfeld et al., 2014) have directly compared high intensity to high volume resistance training for stimulating muscle growth. Consequently, the recommendation for

optimizing muscle hypertrophy in trained individuals is primarily based upon inferred data. For example, the suggestion that experienced lifters should devote the majority of training to higher volume loading is based upon data showing the benefit of using multiple sets over one set (W. J. Kraemer, 1997; W. J. Kraemer et al., 2000; Marx et al., 2001) or adding an extra set to an existing program (Goto et al., 2004). While this does imply a greater effect on muscle growth from increased training volume, it says nothing about exercise intensity. Rather, the concept that high volume, short rest interval resistance training may be superior to using higher intensity loads for stimulating growth is based upon, in part, the enhanced anabolic hormone response to exercise. More specifically, it is based upon the finding that a high volume (3 x 10RM vs. 3 – 5 x 5 RM) resistance training scheme with shorter rest periods (1 min vs. 3 min) produces the greatest growth hormone response to exercise (W. J. Kraemer et al., 1990). Subsequent investigations have reported similar results in regards to GH, but also suggested that high volume resistance exercise will also stimulate elevations in the concentrations of other anabolic hormones (i.e., testosterone and IGF-1) (Ahtiainen, Pakarinen, Alen, et al., 2003; Beaven et al., 2008; Gregory et al., 2013; Hakkinen et al., 2000; Hansen et al., 2001; Hoffman et al., 2003; W. J. Kraemer et al., 1991; Linnamo, Pakarinen, Komi, Kraemer, & Häkkinen, 2005; McCaulley et al., 2009; McKay et al., 2008; Schwab et al., 1993; Smilios et al., 2003; Spiering et al., 2008; West et al., 2010; West et al., 2012; West et al., 2009; Zafeiridis et al., 2003). The compelling argument is centered around the idea that elevated concentrations of these anabolic hormones can improve their chances of binding to their receptor and initiate a cascade of intracellular reactions that

stimulate muscle protein synthesis leading to muscle growth (Baar & Esser, 1999; Baar, Nader, & Bodine, 2006; Bush et al., 2003; Clemmons et al., 1981; Kumar et al., 2009; Mitchell et al., 2013; Nader, 2005; Reynolds, Bodine, & Lawrence, 2002; Terzis et al., 2008; Welle, Bhatt, & Thornton, 1999). However, concerns regarding the post-exercise hormone response's influence on muscle growth has led some to discuss its importance (Schoenfeld, 2013; Schroeder et al., 2013).

Cortisol responds to high-volume resistance training

Cortisol is a steroid hormone that responds to stress (e.g. physical, psychological, social, etc.) by mobilizing energy. In particular, cortisol mobilizes fatty acids and amino acids via lipolysis and proteolysis, respectively (Goldberg, Tischler, DeMartino, & Griffin, 1980; W. J. Kraemer & Ratamess, 2005; Schakman, Kalista, Barbe, Loumaye, & Thissen, 2013). It also minimizes energy storage by reducing muscular sensitivity to insulin (Short, Bigelow, & Nair, 2009). Most importantly though in regards to stimulating muscle growth, is the potential competition between cortisol and testosterone within the cell nucleus to exert its effect at the cellular level (S.-y. Chen et al., 1997; Crowley & Matt, 1996; Mayer et al., 1976; Syms et al., 1987). Cortisol at elevated concentrations can inhibit the anabolic effect of testosterone. Consequently, elevations in cortisol have the potential to limit muscle growth.

Acute elevations in cortisol are often seen following resistance exercise (Buresh et al., 2009; Hakkinen & Pakarinen, 1993; W. J. Kraemer et al., 1996; McCaulley et al., 2009; Smilios et al., 2003; Uchida et al., 2009; Zafeiridis et al., 2003). However, this likely has a minimal effect on inhibiting the muscle remodeling process. Like GH,

cortisol appears to respond to the metabolic demand of activity. That is, resistance training protocols that stimulate an increase in blood lactate concentrations also produce the greatest elevations in cortisol (Ahtiainen, Pakarinen, Kraemer, et al., 2003; Buresh et al., 2009; Hakkinen & Pakarinen, 1993; Hansen et al., 2001; W. J. Kraemer et al., 1996; W. J. Kraemer et al., 1993; W. J. Kraemer et al., 1987; McCaulley et al., 2009; Ratamess et al., 2005; Smilios et al., 2003; Spiering et al., 2008; Uchida et al., 2009; West et al., 2010; Zafeiridis et al., 2003). In response to this type of training, cortisol concentrations peak during exercise and eventually return to (or drop below) normal within 1 – 2 hours (Ahtiainen, Pakarinen, Kraemer, et al., 2003; Guezennec, Leger, Lhoste, Aymonod, & Pesquies, 1986; Hakkinen & Pakarinen, 1993; Hakkinen et al., 1988; W. J. Kraemer et al., 1996; W. J. Kraemer et al., 1993; W. J. Kraemer, Fleck, et al., 1999; W. J. Kraemer et al., 1992; W. J. Kraemer, Häkkinen, et al., 1999; W. J. Kraemer et al., 1987; Ratamess et al., 2005; Smilios et al., 2003; Zafeiridis et al., 2003). However, because acute elevations are transitory, it is not likely to have any significant effect on muscle repair and remodeling. Furthermore, acute elevations in cortisol have not been shown to impact muscle protein synthesis (Short et al., 2009).

During prolonged, stressful periods of training, elevations in cortisol may have a negative effect on skeletal muscle and body mass (Barton et al., 1987; Crowley & Matt, 1996; Darmaun et al., 1988; Simmons et al., 1984). Little is known in regards to whether consistent moderate-intensity, high-volume resistance training, known to elevate cortisol (Ahtiainen, Pakarinen, Alen, et al., 2003; Buresh et al., 2009; Hansen et al., 2001; W. J. Kraemer, Staron, et al., 1998; McCall et al., 1999), has a negative influence on muscle

growth in experience, resistance trained individuals. This is likely related to the limited studies that have compared different resistance training paradigms on the hormonal response in experienced, resistance trained individuals.

In untrained adults, several studies suggest that high volume resistance training will either reduce (W. J. Kraemer, Staron, et al., 1998) or maintain (Ahtiainen, Pakarinen, Alen, et al., 2003; Hansen et al., 2001) basal cortisol concentrations. Although this might imply that regular high volume training does not impose chronic stress, these findings cannot be applied to trained adults. In these studies, participants only trained twice per week and rest times were slightly greater (1.5 – 3 minutes) than what is generally recommended to maximize the hormonal response. Similarly, because the cortisol response to training was either reduced (Hansen et al., 2001) or maintained (Ahtiainen, Pakarinen, Alen, et al., 2003; W. J. Kraemer, Staron, et al., 1998), it would appear that the lower training frequency allowed for sufficient adaptation to the metabolic stress imposed by exercise. Using a greater training frequency (3 days $\cdot$ wk^{-1}), McCall and colleagues (1999) observed similar cortisol elevations in response to exercise after 4 and 8 weeks into a 12-wk, high volume training (3 x 10 RM, 1 min rest) program. Nevertheless, the ~22% drop in basal cortisol concentrations in addition to a 12.7% increase in muscle size, provides evidence that exercise-induced elevations in cortisol do not impair the muscle growth processes. However, it remains to be seen whether greater training frequency (> 3 days $\cdot$ wk^{-1}) using a high volume scheme has a negative impact on muscle growth in comparison to training schemes that typically produce a lower cortisol response.

Relationships to muscle growth

It is clear that the physiological role of testosterone, GH, and IGF-1 includes enhancing the anabolic processes within tissue that lead to skeletal muscle growth. However, it is not clear whether stimulating these hormones during exercise actually influences muscle growth. For example, a pair of studies observed significant muscle growth without significant elevations in anabolic hormones (West et al., 2010; Wilkinson et al., 2006). Wilkinson and colleagues (2006) demonstrated improvements in maximal dynamic and isometric strength (12 – 44%) and quadriceps cross-sectional area (5%) in response to resistance training without elevating testosterone, GH, or IGF-1 concentrations. A subsequent study reported similar improvements in size and strength following 15 weeks of training using protocols designed to elicit either a "high hormonal" or "low hormonal" response to exercise (West et al., 2010). Although these studies certainly question whether acute elevations in anabolic hormone are necessary for stimulating growth, they do not dispel their importance. The study by Wilkinson and colleagues (2006) did not include a comparison to programming that significantly elevated anabolic hormones, while the within-subject design employed by West and colleagues (2010) cannot rule out an influence on growth.

Studies demonstrating large acute hormonal (testosterone and GH) responses as being beneficial for strength (Hansen et al., 2001) or muscle growth (Rønnestad, Nygaard, & Raastad, 2011) also suffer from several confounding methodological issues. One study did not control for strength differences (20 – 25%) in their subjects at baseline (Hansen et al., 2001), which have been demonstrated to affect the testosterone response

to exercise (Ahtiainen, Pakarinen, Kraemer, & Hakkinen, 2004). Thus, the large variability in baseline strength measures may have contributed to a large variability in the hormonal and muscle response patterns. Issues have also been raised from the study of Rønnestad and colleagues (2011) who examined the effect of exercise order (training lower-body musculature prior to unilateral, upper-body resistance training or unilateral, upper-body resistance training alone). They reported a significantly greater growth in upper-body muscle in the group exercising the lower-body prior to the upper body workout, compared to upper-body alone. They suggested that the large muscle mass exercises that preceded exercises using a smaller muscle mass stimulated a greater GH and testosterone response and provided a greater stimulus for muscle growth. However, it has been argued that the authors' suggestion that improvements in muscle cross-sectional area occurred without any changes in muscle volume is implausible (Phillips, 2012). Rather, it is more likely that the observed differences between conditions were the consequence of a misalignment (between limbs) during the magnetic resonance imaging (MRI) assessment. Furthermore, the researchers based their assertion upon pairwise comparisons, not on an analysis of variance. Thus, these results provide no clear evidence that post-exercise elevations in anabolic hormones is more beneficial for promoting muscle growth.

Studies using correlational designs have not produced compelling evidence demonstrating a relationship between the hormonal response and muscle adaptation. This may be a function of inappropriately measured relationships, but may also be due to other confounding factors. Some investigators have used the hormonal response from a single

time point (e.g. pre-training) and related it to changes in muscle size at the end of the study (McCall et al., 1999; West & Phillips, 2012). The problem with relating a hormonal response from a single time point is that it assumes a similar response across the entire duration of training, which cannot be assumed. Several investigations have reported changes in the hormonal response to exercise following prolonged training (Ahtiainen, Pakarinen, Alen, et al., 2003; Hakkinen et al., 1988; Hameed et al., 2004; W. J. Kraemer, Häkkinen, et al., 1999; McCall et al., 1999; Staron et al., 1994). Others have compared the percent change in the endocrine response to percent change in muscle growth (Ahtiainen, Pakarinen, Alen, et al., 2003). The validity of this approach is questionable. For example, Ahtiainen, and colleagues (2003) reported percent changes using positive and negative values for the hormone response, but only positive values for muscle size changes. This resulted in a positive relationship where more than half of the participants experienced a reduced hormone response though they gained muscle. An alternative approach might be to perform a partial correlation, where multiple time points are taken into account, including baseline values. This would potentially negate the influence of a varied hormone response throughout training.

To date, investigations examining the relationship in the hormonal response to muscle growth have not provided convincing evidence. The significant relationship reported between the testosterone response and muscle growth ($r = 0.76$), reported by Ahtiainen, and colleagues (2003), was from an investigation of only eight physically active men. In contrast, others have reported no relationships ($r = 0.06 – 0.14$; $p > 0.05$) using similar but larger sample populations (10 – 56 participants) (McCall et al., 1999;

West & Phillips, 2012). In regards to GH, investigations have shown weak to strong (r = 0.28 – 0.74) relationships to changes in biopsied samples of muscle fiber (McCall et al., 1999; West & Phillips, 2012), but not to changes in total muscle cross-sectional area (MRI) or lean body mass. The important distinction here is that changes in total muscle size cannot be extrapolated from changes in a microscopic sample of that muscle's fibers. Finally, no study examining the IGF-1 response to exercise (McCall et al., 1999; West & Phillips, 2012) has observed a relationship of that response to muscle growth. Therefore, without direct evidence showing that exercise-induced elevations in anabolic hormones are influencing muscle growth, their role in stimulating muscle growth remains hypothetical. Further, as research continues in this area the mechanism of action associated with the endocrine stimulus on muscle growth still needs to be clearly defined.

Individual variability in the hormonal training response

Individual variability is a possible confound for relying on an elevated anabolic hormone response to training for inducing muscular hypertrophy. Beaven and colleagues (2008) examined the testosterone response to four separate resistance training protocols that varied in both volume (5RM – 15RM) and intensity (40 – 85% 1RM). Although the mean response was similar between the training protocols, a great deal of variability existed among the participants, and between the protocols regarding differences in the testosterone response (Beaven et al., 2008). Other investigations, using similar resistance training protocol designs have reported the testosterone response to have either decreased (Bosco, Colli, Bonomi, von Duvillard, & Viru, 2000) or increased by 11 – 72% (Beaven et al., 2008; Gotshalk et al., 1997; Hakkinen & Pakarinen, 1993; W. J. Kraemer et al.,

1990; Smilios et al., 2003). The variability in the endocrine response can have a significant impact on an individual's response to a training protocol (Alen et al., 1988; Jensen et al., 1991) and potentially the outcome from a given intervention. While using homogenous population samples that are controlled for age, gender, and training backgrounds may help towards regulating observed hormone concentrations across participants, it is only the first step. There are several lifestyle factors that must also be considered. For example, Cook & Crewther (2012) observed that changes in testosterone concentrations were different depending upon the visual stimulus set to induce an emotional response (e.g. happy, angry, sad, etc.). Further, when presenting the various stimuli prior to exercise, there was a strong, positive within-individual correlation (r = 0.85) between the relative testosterone response and voluntary strength (Cook & Crewther, 2012). Likewise, basal concentrations, as well as the response to exercise, of several hormones are also subject to external influence (e.g. psychological and social stress, genetics, sleeping habits, nutrition, etc…) (Hulmi et al., 2005; W. J. Kraemer & Ratamess, 2005; W. J. Kraemer, Volek, Bush, Putukian, & Sebastianelli, 1998; A. G. Williams, Ismail, Sharma, & Jones, 2002). Thus, it becomes imperative that as much of the external environment be controlled to minimize variability.

Conclusion

The importance of mechanical versus metabolic stress for inducing improvements in muscular strength and size is not well-understood in trained individuals. The current recommendation calls for training to focus primarily on volume at moderate intensity with short rest breaks. The metabolic stress imposed by this manner of training is

thought to be capable of producing a greater anabolic hormone response in comparison to training at greater intensities and lower volume. However, the actual importance of this greater anabolic response has not been established. On the other hand, a training program utilizing a high intensity of training may activate a greater muscle mass, and therefore cause greater mechanical stress or tension. Since activation is necessary for stimulating adaptation, it would seem that maximizing mechanical stress would induce the greatest improvements to muscle. Nevertheless, the evidence comparing mechanical versus metabolic stress is limited. Thus, the purpose of the present investigation was to compare a high intensity, low volume training program (e.g., similar to a strength/power phase in a periodized training program) to a low-moderate intensity, high volume training program (e.g. similar to a hypertrophy phase in a periodized training program) on changes in muscle growth and strength. We expect both training programs will improve muscular size and strength. However, greater muscular activation improvements in the high intensity group will result in a greater degree of muscular hypertrophy and strength in comparison to the higher volume group.

CHAPTER 3: METHODOLOGY

Participants

Thirty-three physically-active, resistance-trained men agreed to participate in this study. Following an explanation of all procedures, risks and benefits, each participant provided his informed consent to participate in the study. This investigation was approved by the New England Institutional Review Board. All participants were free of any physical limitations (determined by medical history questionnaire and PAR-Q) and had been regularly participating (at the time of recruitment) in resistance training for a minimum of 2 years (5.7 ± 2.2). Prior to the investigation, all of the participants described their training habits to be different from the investigation's training regimen in terms of exercise order and groupings. Approximately 82% of the participants described their normal repetition range to be either lower (VOL = 77%) or higher (INT = 87%) than what they were assigned in the study, with about 43% typically using a 6 – 10 RM range and another 21% using an alternating (or pyramid) structure for specific multi-joint, structural and assistance exercises. Additionally, 50% of the participants reported using either longer (VOL = 54%) or shorter (INT = 47%) rest periods, while approximately 29% did not track their rest times previously. The remaining participants employed a similar training scheme (i.e. intensity, volume, and rest) to what they were assigned in the study.

Experimental Design

Prior to the onset of the actual training program all participants were required to complete a 2-wk training program as a preparatory phase of the actual study. During the preparatory period four participants removed themselves from the study for reasons unrelated to the investigation. Following the preparatory period, assessments of body composition, muscle morphology, maximal strength, and muscle activation occurred. Following these pre-training (PRE) assessments, participants were randomly assigned to one of two training groups: a high-intensity, low volume training group (INT; n = 15; 24.7 ± 3.4 y; 90.0 ± 15.3 kg; 179.5 ± 5.6 cm) or a high-volume, moderate intensity training group (VOL; n = 14; 24.0 ± 2.7 y; 90.1 ± 11.7 kg; 169.9 ± 29.0 cm). No group differences in absolute strength (1RM; squat: $p = 0.653$; bench press: $p = 0.661$) or relative strength (1RM · body mass^{-1}; squat: $p = 0.308$; bench press: $p = 0.843$) were observed prior to the training intervention. Participants completed at least 90% of their respective resistance training sessions over the course of the 8-week training study. No differences ($p = 0.547$) in the number of workouts completed were observed between groups. To compare changes in strength and muscle hypertrophy between groups, each group completed an 8-wk resistance-training program (4 sessions · wk^{-1}) under the direct supervision of certified strength and conditioning specialists (CSCS). Post-testing (POST) occurred following the completion of the 8-wk training program. The study design is illustrated in Figure 1.

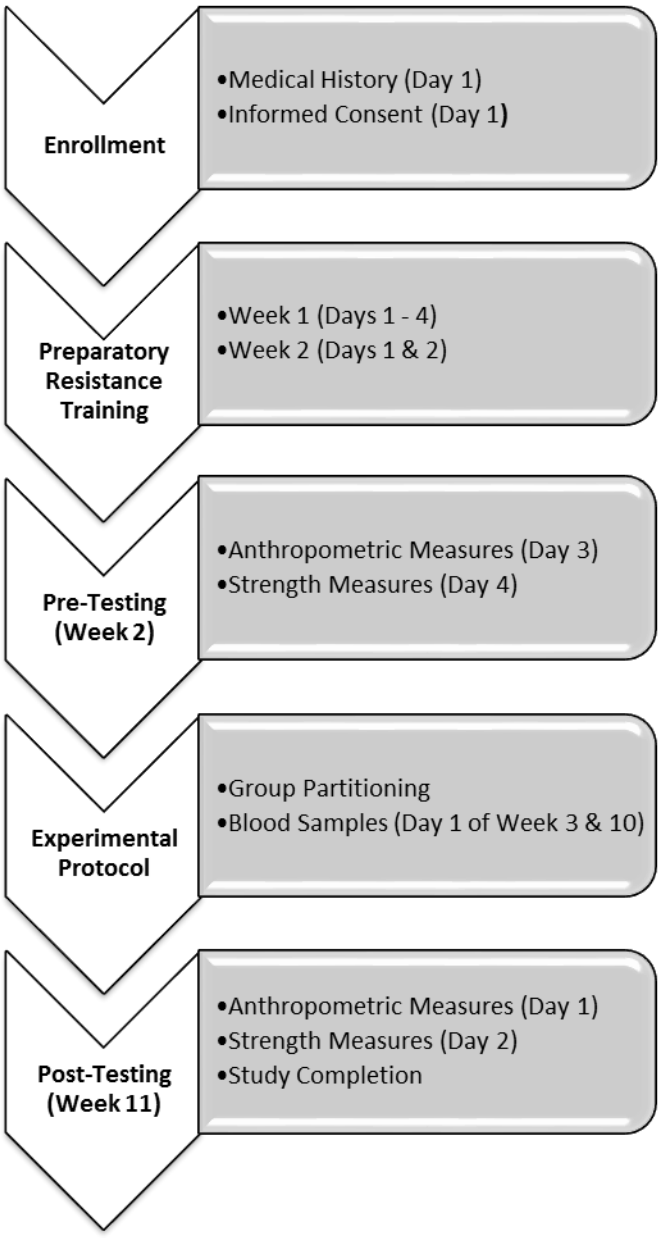


Figure 1. Study Design

Preparatory phase of training

All participants completed the identical base resistance training protocol during the two weeks prior to the training intervention (see Table 1). This phase encompassed a total of six workouts: four workouts (Monday, Tuesday, Thursday, and Friday) during the first week and two workouts (Monday and Tuesday) during the second week. The purpose of the base training program was to instruct proper lifting technique, familiarize participants with all exercises and ensure the participants initiated the study in a trained state. In comparison to the training intervention groups, the exercises (and their order) were identical but the volume (6 – 8 RM) and rest time (1 – 2 minutes) differed.

Table 1. Resistance training program

Exercise Prescription			
Program Variable	Preparatory Phase	VOLUME	INTENSITY
Training Intensity	80 – 85% 1RM	70% 1RM	90% 1RM
Training Volume	4 X 6 – 8 repetitions	4 X 10 – 12 repetitions	4 X 3 – 5 repetitions
Rest Time	1 – 2 minutes	1 minute	3 minutes

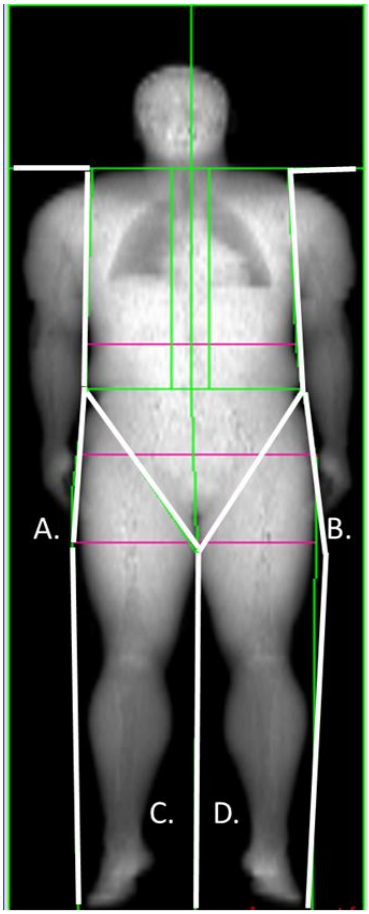
Specific Exercises			
Day 1	Day 2	Day 3	Day 4
Back Squats	Bench Press	Barbell Squats	Bench Press
Deadlifts	Incline Bench Press	Deadlifts	Incline Bench Press
Leg Press	Dumbbell Flys	Barbell Lunge	Dumbbell Flys
Lat Pull Downs	Seated Shoulder Press	Seated Row	Seated Shoulder Press
Barbell Bent-Over Rows	Lateral Dumbbell Raise	Dumbbell Pullover	Lateral Dumbbell Raise
Barbell Biceps Curls	Triceps Extension	Barbell Biceps Curls	Triceps Extension

Note. Volume = Sets X Repetitions

Anthropometric and morphologic assessments

Anthropometric and morphologic measurements for all participants were conducted approximately 24 hours prior to all strength measures and in the following sequence: height, body mass, body composition, and muscle morphology. Height (±0.1 cm) and body mass (±0.1 kg) were determined using a Health-o-meter Professional (Patient Weighing Scale, Model 500 KL, Pelstar, Alsip, IL, USA) with the participants standing barefoot, with feet together, in their normal daily attire. Body composition, total body muscular mass, and muscular mass of the limbs (Figure 2) were determined using whole body-dual energy x-ray absorptiometry (DEXA) scans (Prodigy^{TM}; Lunar Corporation, Madison, WI). Total body estimates of percent fat (%FAT) and non-bone lean body mass (LBM; ±0.1 kg) were determined using company's recommended procedures and supplied algorithms. For the upper-body, lean arm mass (ARM; ±0.1 kg) was the sum of lean arm mass from both arms (see Figure 2A and 2B), while lean leg mass (LEG; ±0.1 kg) was similarly calculated (see Figure 2C and 2D). Quality assurance were assessed by daily calibrations performed prior to all scans using a calibration block provided by the manufacturer. All DEXA measurements were performed by the same certified radiological technician. Previously, intraclass correlation coefficients ($ICC_{3,1}$), standard error of the measurement (SEM), and minimal difference (MD) values for the ARM ($ICC_{3,1}$ = 0.99, $SEM_{3,1}$ = 0.11 kg, MD = 0.23 kg), LEG ($ICC_{3,1}$ = 0.99, $SEM_{3,1}$ = 0.46 kg, MD = 0.91 kg), LBM ($ICC_{3,1}$ = 0.99, $SEM_{3,1}$ = 0.78 kg, MD = 1.53 kg), and

%FAT ($ICC_{3,1}$ = 0.99, $SEM_{3,1}$ = 0.73%, MD = 1.44%) had been determined as previously recommended (Weir, 2005) on ten healthy adults (35.9 ± 13.7y; 96.7 ± 15.0kg; 168.0 ± 9.7cm) using the methodology described above.



Note. A. Upper limb – right; B. Upper limb – left; C. Lower limb – right; and D. Lower limb – left

Figure 2. Regions of interest for dual energy X-ray absorptiometry measurement of lean mass

Ultrasonography measurements

Non-invasive skeletal muscle ultrasound images were collected from the dominant thigh, arm, and chest of all participants. This technique uses sound waves at fixed frequencies to create in vivo, real time images of the limb musculature. Prior to image collection, all anatomical locations of interest were identified using standardized landmarks for the rectus femoris (RF), vastus lateralis (VL), pectoralis major (PM), and triceps brachii (TB) muscles. The landmarks for the RF and VL were identified along the longitudinal distance over the femur at 50% of the length of each muscle, respectively. The length of the RF was defined as the length between the anterior, inferior suprailiac crest and the proximal border of the patella, while the length of the VL encompassed the distance from the lateral condyle of the tibia to the most prominent point of the greater trochanter of the femur; VL measurement require the participant to lay on their side. For landmark identification (and ultrasound measurement) of the PM, the participant was required to continue lying supine but with their dominant shoulder abducted and elbow flexed so that the dominant hand was positioned behind their head. Initially, 50% of the distance between the suprasternal notch and the most inferior point of the body of the sternum was identified. Subsequently, the cross-sectional distance from this point to the lateral-most border of the muscle (approximately level with the 2nd rib) was used for measurement. Finally, landmark identification of the TB required the participant to straddle the examination table and internally rotate their dominant shoulder, flex the elbow and rest their dominant hand upon their thigh. The specific landmark for the TB was identified along the longitudinal distance over the humerus at a position 40% of the distance from the lateral epicondyle to the

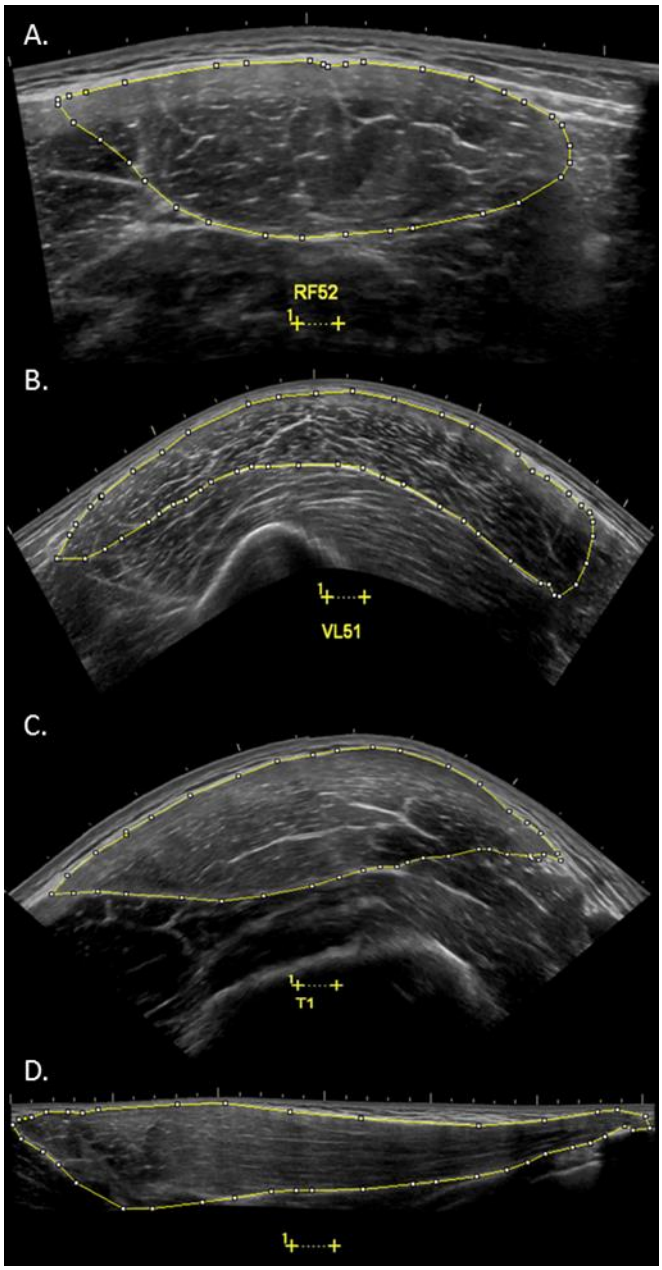
acromion process of the scapula (Ichinose, Kanehisa, Ito, Kawakami, & Fukunaga, 1998). Subsequently, the participant resumed laying supine on the examination table for a minimum of 15 minutes to allow fluid shifts to occur before images were collected (Berg, Tedner, & Tesch, 1993). The same investigator performed all landmark measurements for each participant.

A 12 MHz linear probe scanning head (General Electric LOGIQ P5, Wauwatosa, WI, USA) was coated with water soluble transmission gel to optimize spatial resolution and used to collect all ultrasound images. Collection of each image began with the probe being positioned on (and perpendicular to) the surface of the skin to provide acoustic contact without depressing the dermal layer. Subsequently, the extended field of view mode (Gain = 50 dB; Image Depth = 5cm) was used to capture panoramic images of the muscular regions of interest. For each region, two consecutive images were collected. Each of these images included a horizontal line (approximately 1cm), located above the image, which was used for calibration purposes when analyzing the images offline (Chapman, Newton, McGuigan, & Nosaka, 2008). To capture images of the RF, the participant remained in the supine position, with their legs extended but relaxed. A rolled towel was placed beneath the popliteal fossa of the dominant leg, allowing for a 10° bend in the knee as measured by a goniometer, and the dominant foot secured (Bemben, 2002). For the VL, the participant was placed on their side with their legs together and the rolled towel between their needs. Once again, the legs were positioned to allow a 10° bend in the knees, as measured by a goniometer (Bemben, 2002). Measurement of the PM required the participant to lay supine, in the fashion described above, while TB measurement

required the participant to lay prone with their arms extended, resting at their side. For all muscles of interest, muscle cross-sectional area (CSA) was obtained using a cross-sectional sweep in the axial plane at each location across the muscle. In addition to these measures, a longitudinal images at 50% of the muscle length were used to determine muscle thickness (MT) in the RF and VL muscles (Cadore et al., 2012). The same investigator positioned each participant and collected all images.

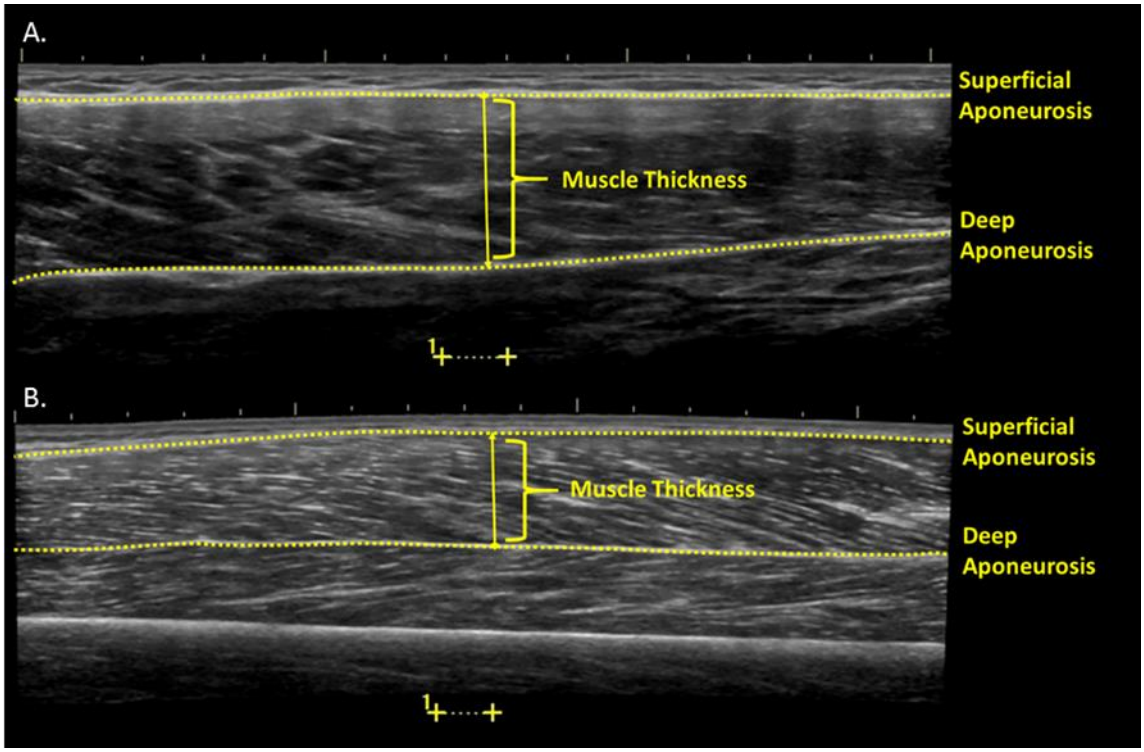
After all images were collected, the ultrasound data was transferred to a personal computer for analysis via Image J (National Institutes of Health, Bethesda, MD, USA, version 1.45s) by the same technician. To measure CSA, the polygon tracking tool in the ImageJ software was used to isolate as much lean muscle as possible without any surrounding bone or fascia in the RF (Figure 3A), VL (Figure 3B), TB (Figure 3C), and PM (Figure 3D) (Cadore et al., 2012). Subsequently, Image J calculated the area contained within the traced muscular image and reported this value in centimeters squared ($\pm 0.1 cm^2$). The distance (±0.1cm) between the superficial aponeurosis to the deep aponeurosis was used to determine MT in the RF (Figure 4A) and VL (Figure 4B) muscles. The values averaged from both analyzed images (in a specific region) were used for statistical analysis. Prior to the investigation, intraclass correlation coefficients ($ICC_{3,K}$), standard error of the measurement (SEM), and minimal difference (MD) values for the RF (MT: $ICC_{3,K} = 0.93$, $SEM_{3,K} = 0.17$, MD = 0.45cm; CSA: $ICC_{3,K} = 0.88$, $SEM_{3,K} = 1.78$, MD = $4.60 cm^2$), VL (MT: $ICC_{3,K} = 0.88$, $SEM_{3,K} = 0.16$, MD = 0.42cm; CSA: $ICC_{3,K} = 0.99$, $SEM_{3,K} = 1.11$, MD = $3.05 cm^2$), PM ($ICC_{3,K} = 0.98$, $SEM_{3,K} = 2.86$, MD = $7.84 cm^2$), and TB ($ICC_{3,K} = 0.97$, $SEM_{3,K} = 1.28$, MD = $3.50 cm^2$) were determined as previously recommended (Weir,

2005) on ten active, resistance-trained men (25.3 ± 2.0y; 90.8 ± 6.8kg; 180.3 ± 7.1cm) using the methodology described above.



Note. A. Rectus Femoris; B. Vastus Lateralis; C. Triceps Brachii; D. Pectoralis Major

Figure 3. Cross-sectional image analysis using ultrasonography



Note. A. Rectus Femoris; B. Vastus Lateralis

Figure 4. Longitudinal image analysis using ultrasonography

Maximal strength testing

Maximal strength assessment in the bench press and squat exercises occurred on the last day of PRE and POST (Figure 1). During both occasions, participants were scheduled for testing at a time similar to their normal training schedule. Prior to testing, each participant completed a general warm-up consisting of riding a cycle ergometer for 5 minutes at a self-selected resistance. The general warm-up was followed by a specific warm up consisting of 10 body weight squats, 10 alternating lunges, 10 walking knee hugs and 10 walking butt kicks.

To assess maximal upper- and lower-body strength, standardized procedures were used for the one-repetition maximum (1RM) barbell bench press and barbell back squat, respectively (Hoffman, 2006). For each exercise, a warm-up set of 5 – 10 repetitions was performed using 40 – 60% of the participant's perceived maximum 1RM. After a 1-minute rest period, a set of 2 – 3 repetitions was performed at 60 – 80% of the participant's perceived maximum 1RM. Subsequently, 3 – 5 maximal trials (1-repetition sets) were performed to determine the 1RM. For the bench press, proper technique was enforced by requiring all participants to maintain contact between their feet and the floor; their buttocks, shoulders, and head with the bench; and use a standard grip (slightly wider than shoulder-length) on the bar. Furthermore, upon lowering the bar to their chest, participants were required to pause briefly and wait for an "UP!" signal before initiating concentric movement. The purpose for this pause was to eliminate the influence of bouncing and distinguish eccentric from concentric muscle activation during electromyography analysis. Any trials that involved "cheating," such as excessive arching of the back or bouncing of the weight were discarded. For the back squat, a successful attempt required the participant to descend to the "parallel" position, where the greater trochanter of the femur was aligned with the knee. At this point, an investigator located lateral to the participant, provided an "UP!" signal, indicating that proper range of motion had been achieved; no pause was required for the squat exercise. Rest periods between attempts were 2 – 3 minutes in length. Upon determining their 1RM for each exercises, each participant was allotted a five minute rest period before completing three additional one-repetition sets with 40%, 60%, and 80% of their 1RM; one minute rest

periods were provided between these sets. All testing was completed under the supervision of a CSCS.

Electromyography measurements

To assess changes in muscle activation efficiency, electromyography (EMG) data were collected using previously described configurations for bipolar (4.6 cm center-to-center) surface electrode (Quinton Quick-Prep silver-silver chloride) placement (Hermens et al., 1999). Briefly, for the back squat, the electrodes were placed over the VL (60% of distance between the head of the greater trochanter and lateral aspect of the patella) and RF (50% of distance between the inguinal crease and superior border of the patella) muscles, with the reference electrode being placed over the lateral epicondyle of femur. For all participants, electrodes were placed on the participant's dominant side, 2cm apart, and parallel to the active fibers. The same investigator was used to identify landmarks and place electrodes at PRE and POST. Additionally, the inter-electrode impedance was kept below 5,000 ohms by shaving and cleaning (with alcohol) the placement site prior to testing. EMG signals were obtained using a differential amplifier (MP150 BIOPAC Systems, Inc., Santa Barbara, CA) sampled at 1,000 Hz and then transferred as a file to a personal computer for analysis. EMG signals were band-pass filtered from 10 Hz to 500 Hz, rectified (full-wave), and expressed as integrated EMG (iEMG) values (±0.01 Volts · sec) by software (AcqKnowledge v4.2, BIOPAC Systems, Inc., Santa Barbara, CA). Improvements in muscular efficiency were determined by comparing the changes in the activation regression slope following increases in load (40, 60, 80, and 100%1RM) during the squat assessment (deVries, 1968).

Resistance training intervention

Participants reported to the HPL four times per week to complete their assigned training program (Table 1). Briefly, the INT training program required the participants to perform 4 sets at 3 – 5 RM, with 3 minute rest periods between sets, while the VOL group performed 4 sets at 10 – 12 RM, with only a 1 minute rest period between sets. Both groups performed the same exercises. Training intensity was determined from 1RM testing, and each participant's performance during the preparatory training phase. In both training programs, progressive overload was achieved by increasing the load when all prescribed repetitions (for a particular exercise) were achieved on two consecutive workouts. Weekly training volume load was calculated as the average of the number of repetitions x load in the squat and bench press exercises. Following each training session, participants were provided 8oz of chocolate milk (170 calories; 2.5g Fat; 29g Carbohydrate; 9g protein), or 8oz of chocolate Lactaid® (150 calories; 2.5g Fat; 24g Carbohydrate; 8g protein) for lactose-intolerant participants. All training sessions occurred in the presence of a CSCS.

Blood measurements

Blood samples were collected on Day 1 of week 3 (WK3) and week 10 (WK10). During each blood collection trial, blood samples were obtained at four time points: baseline (BL), immediately post-exercise (IP), 30 minutes post-exercise (30P), and 60 minutes post-exercise (60P). Participants reported to the HPL 3 hours post-prandial, at a time of day consistent with their normal training schedule. All blood samples at POST were taken at the same time of day as PRE to avoid diurnal variations. All blood samples

were obtained using a Teflon cannula placed in a superficial forearm vein using a three-way stopcock with a male luer lock adapter and plastic syringe. The cannula was maintained patent using an isotonic saline solution (Becton Dickinson, Franklin Lakes, NJ, USA). Blood samples at BL were obtained following a 15-minute equilibration period. Following the BL blood sample, participants were provided ~235 mL of chocolate milk (170 calories; 2.5g Fat; 29g Carbohydrate; 9g protein) or Lactaid® (150 calories; 2.5g Fat; 24g Carbohydrate; 8g protein). Following the resistance exercise protocol, participants remained in the HPL for all subsequent blood draws. IP blood samples were taken within one minute of exercise cessation. Following IP blood samples, participants were provided their normal ~235 mL of chocolate milk. Participants were instructed to lie in a supine position for 15 minutes prior to 30P and 60P blood draws.

All blood samples were collected into two Vacutainer® tubes, one containing no anti-clotting agent (6 ml) and the second containing K_2EDTA (6 ml). A small aliquot of whole blood was removed and used for determination of hematocrit and hemoglobin concentrations. The blood in the first tube was allowed to clot at room temperature for 30 minutes and subsequently centrifuged at 3,000×g for 15 minutes along with the remaining whole blood from the second tube. The resulting plasma and serum were placed into separate micro-centrifuge tubes and frozen at −80°C for later analysis.

Biochemical analysis

Hematocrit concentrations were analyzed from whole blood via microcentrifugation (CritSpin, Westwood, MA, USA) and microcapillary technique. Hemoglobin concentrations were analyzed from whole blood using an automated analyzer (HemoCue, Cypress, CA, USA). Blood lactate concentrations were analyzed from plasma using an automated analyzer (Analox GM7 enzymatic metabolite analyzer, Analox instruments USA, Lunenburg, MA, USA). Coefficient of variation for each assay was 1.53% for hematocrit, 0.55% for hemoglobin, and 0.98% for blood lactate. Plasma volume shifts were calculated using the formula established by Dill & Costill (1974). To eliminate inter-assay variance, all samples were analyzed in duplicate by a single technician.

Circulating concentrations of testosterone (TEST), cortisol (CORT), insulin-like growth factor (IGF-1), growth hormone (GH), and insulin (INSL) were assessed via enzyme-linked immunosorbent assays (ELISA) and a spectrophotometer (BioTek Eon, Winooski, VT, USA) using commercially available kits. To eliminate inter-assay variance, all samples for each assay were thawed once and analyzed in duplicate in the same assay run by a single technician. Samples were analyzed in duplicate, with an average coefficient of variation of 3.74% for TEST, 4.03% for CORT, 6.77% IGF-1, 3.50% for GH, and 6.54% for INSL. The area under the curve (AUC), expressed in arbitrary units (au) via the trapezoidal method was calculated and used to analyze the total training response.

Nutrient intake and dietary analysis

Participants were asked to maintain their normal caloric intake habits throughout the course of the investigation. Nevertheless, caloric and macronutrient intake was monitored via weekly food diaries, given the effect any changes would have on muscular adaptation. Consequently, all participants were required to record all food and beverage intake over the course of 3 days (two weekdays and one weekend day) during the week of PRE (Week 2) and POST (Week 10). The FoodWorks Dietary Analysis software version 13 (The Nutrition Company, Long Valley, NJ) was used to analyze dietary recalls. For statistical analysis, total caloric, macronutrient (protein, carbohydrate, and fat), and branched-chain amino acid (leucine, isoleucine, and valine) intake were analyzed relative to body mass.

Statistical analysis

To identify differences between training protocols on changes in muscular size, strength, and activation, an analysis of covariance (ANCOVA) was performed on all measures collected at POST. Associated values collected at PRE were used as the covariate to eliminate the possible influence of initial group differences (significant and non-significant) on training outcomes. Following any significant F-ratio, a paired-samples t-test was used to determine if significant difference existed between measures collected prior to and immediately following eight weeks of training.

To examine group differences in the acute endocrine response to exercise during WK3 and WK10, a repeated measures ANCOVA was performed, where hormone concentrations at baseline were used as the covariate. In the event of a significant main

effect, a repeated measures analysis of variance (ANOVA) was performed on each group individually at WK3 and WK10. A significant F ratio was followed by a least squared distance (LSD) post-hoc analysis to determine significant differences between each time point (i.e. IP, 30P, and 60P) and baseline hormone concentrations. The effect of training on the acute endocrine response was also analyzed by a repeated measures ANOVA, using AUC values. In the event of a significant F ratio, an independent *t*-test was used to assess group differences at WK3 and WK10.

All between group differences were further analyzed using effect sizes (η^2p: Partial eta squared). Interpretations of effect size were evaluated in accordance with (Cohen, 1988) at the following levels: small effect (0.01 – 0.058), medium effect (0.059 – 0.137) and large effect (> 0.138). A criterion alpha level of $p \leq 0.05$ was used to determine statistical significance. All data are reported as mean ± standard deviation. Statistical Software (V. 21.0, SPSS Inc., Chicago, IL) was used for all analyses.

CHAPTER 4: RESULTS

Resistance training program comparisons

The average training volume was significantly higher ($p < 0.001$) for VOL (squat: 8753 ± 1033kg; bench press: 4412 ± 729kg) compared to INT (squat: 4528 ± 889kg; bench press: 2757 ± 696kg). Additionally, the average time to completion for each training session for VOL (68.2 ± 5.6 min) was significantly ($p < 0.001$) faster than INT (95.0 ± 8.7 min).

Anthropometric and morphological changes

Following 8 wks of resistance training, lean arm mass was significantly ($F = 4.816$, $p = 0.037$; $\eta^2_p = 0.156$) greater in INT (5.2 ± 2.9%; $p < 0.001$) compared to VOL (2.2 ± 5.6%; $p = 0.314$). Further, 93.3% of participants in INT experienced a change in lean arm mass that was greater than the minimal difference for the measure. In contrast only 64.3% of participants in VOL experienced such a change. Although no other significant group differences were observed, INT experienced more real changes in response to training when considering LBM (INT: 60.0%; VOL: 35.7%), lean leg mass (INT: 46.7%; VOL: 21.4%), and VL CSA (INT: 50%; VOL: 21.4%). Less than 10% of all participants experienced real changes in MT (RF & VL) and CSA (RF, PM, and TB), while ~31% of participants experienced real changes in %FAT (INT: 33.3%; VOL: 28.6%). Changes in muscle size and total body anthropometrics following the training intervention are presented in Table 2.

Table 2. Anthropometric changes and muscle hypertrophy following 8wks of training

	VOLUME			INTENSITY		
Dual-energy X-ray Absorptiometry	PRE	POST	%Change	PRE	POST	%Change
Body Mass (kg)	90.1 ± 11.7	90.7 ± 13.2	0.6 ± 2.5	90.0 ± 15.3	91.2 ± 15.2	1.7 ± 2.5
Body Fat (%)	21.6 ± 6.2	21.4 ± 6.0	0.6 ± 7.0	19.8 ± 8.8	19.7 ± 8.2	1.8 ± 8.6
Lean Body Mass (kg)	67.6 ± 7.9	68.6 ± 7.9	1.4 ± 3.4	68.6 ± 7.7	69.9 ± 7.5	2.1 ± 2.6
Lean Mass - Arms (kg)	9.5 ± 1.4	9.7 ± 1.1	2.2 ± 5.6	9.8 ± 1.7	10.3 ± 1.7	5.2 ± 2.9#
Lean Mass - Legs (kg)	23.0 ± 2.6	23.4 ± 3.0	1.4 ± 3.3	23.4 ± 3.1	23.8 ± 2.9	2.3 ± 3.5
Ultrasound Measures	PRE	POST	%Change	PRE	POST	%Change
Rectus Femoris						
Muscle Thickness (cm)	2.8 ± 0.4	2.8 ± 0.3	-0.5 ± 7.1	2.7 ± 0.4	2.6 ± 0.4	-0.6 ± 7.0
Cross-Sectional Area (cm^2)	16.7 ± 2.9	16.8 ± 2.9	0.7 ± 6.5	15.3 ± 4.7	15.8 ± 4.9	3.1 ± 8.3
Vastus Lateralis						
Muscle Thickness (cm)	1.9 ± 0.3	1.9 ± 0.3	3.2 ± 7.7	1.7 ± 0.3	1.9 ± 0.2	10.7 ± 15.9
Cross-Sectional Area (cm^2)	38.8 ± 7.4	40.1 ± 7.1	3.6 ± 7.0	37.6 ± 5.9	41.3 ± 9.6	9.6 ± 12.9
Pectoralis Major						
Cross-Sectional Area (cm^2)	75.5 ± 16.8	77.1 ± 16.6	2.4 ± 4.1	82.1 ± 11.2	86.5 ± 13.7	5.2 ± 4.9
Triceps Brachii (Long)						
Cross-Sectional Area (cm^2)	9.9 ± 4.9	11.7 ± 5.6	21.3 ± 19.0	10.3 ± 5.2	11.3 ± 5.6	10.8 ± 16.6

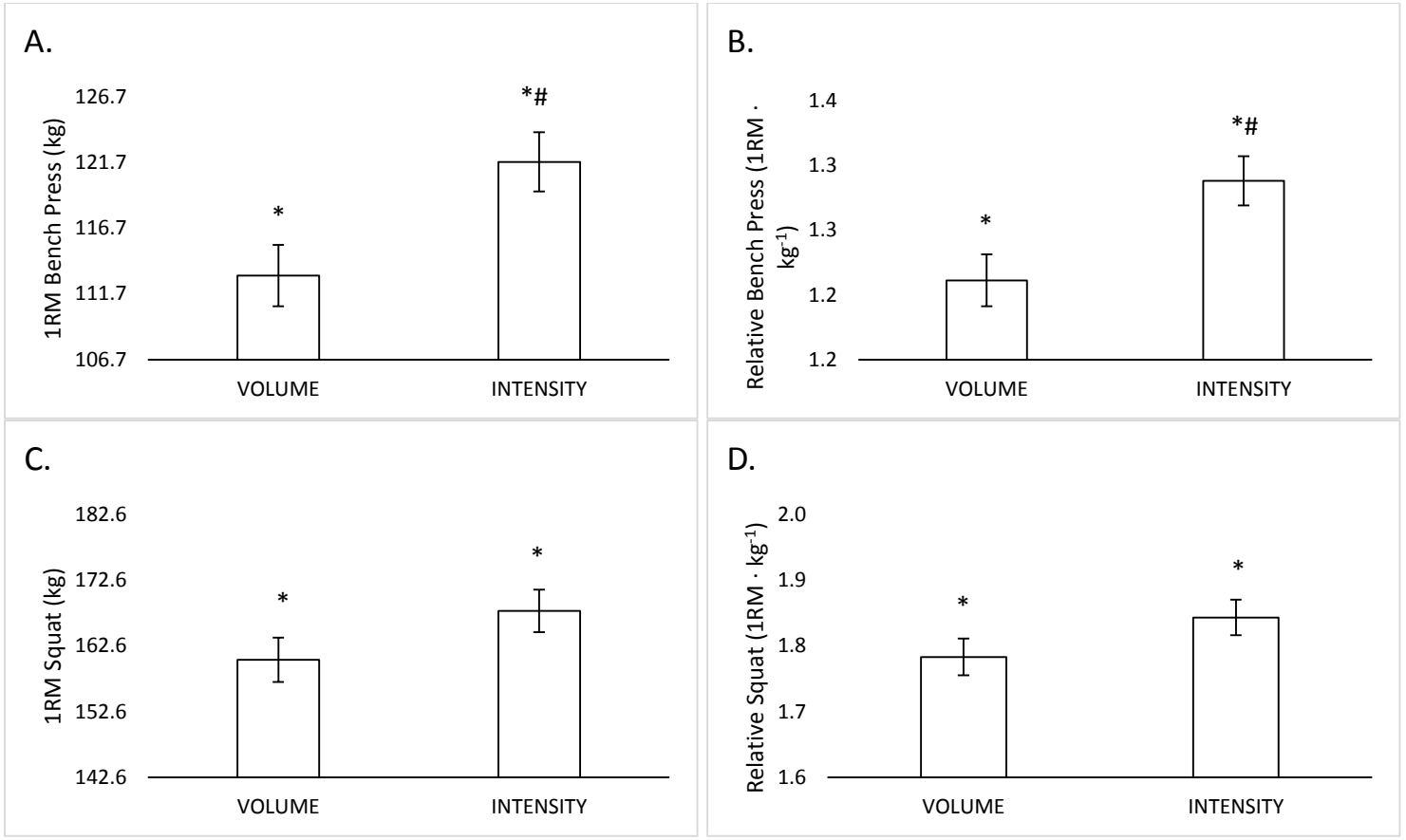
Note. #Significant ($p < 0.05$) difference between INT and VOL

Maximal strength improvement

Changes in bench press and squat strength can be observed in Figure 5. Significant improvements in 1RM bench press were observed in both VOL (PRE: 104.5 ± 19.2kg; POST: 110.9 ± 17.5kg; $p = 0.018$) and INT (PRE: 108.8 ± 31.8kg; POST: 123.8 ± 34.1kg; $p < 0.001$) groups, however the change in upper body strength was significantly ($F = 7.098$; $p = 0.013$; $\eta^2p = 0.214$) greater for INT than VOL (see Figure 5A). These findings were consistent even when examined relative to body mass ($F = 7.558$; $p = 0.011$; $\eta^2p = 0.225$) (see Figure 5B). No group differences were observed in absolute or relative 1RM squat (see Figures 5C and 5D).

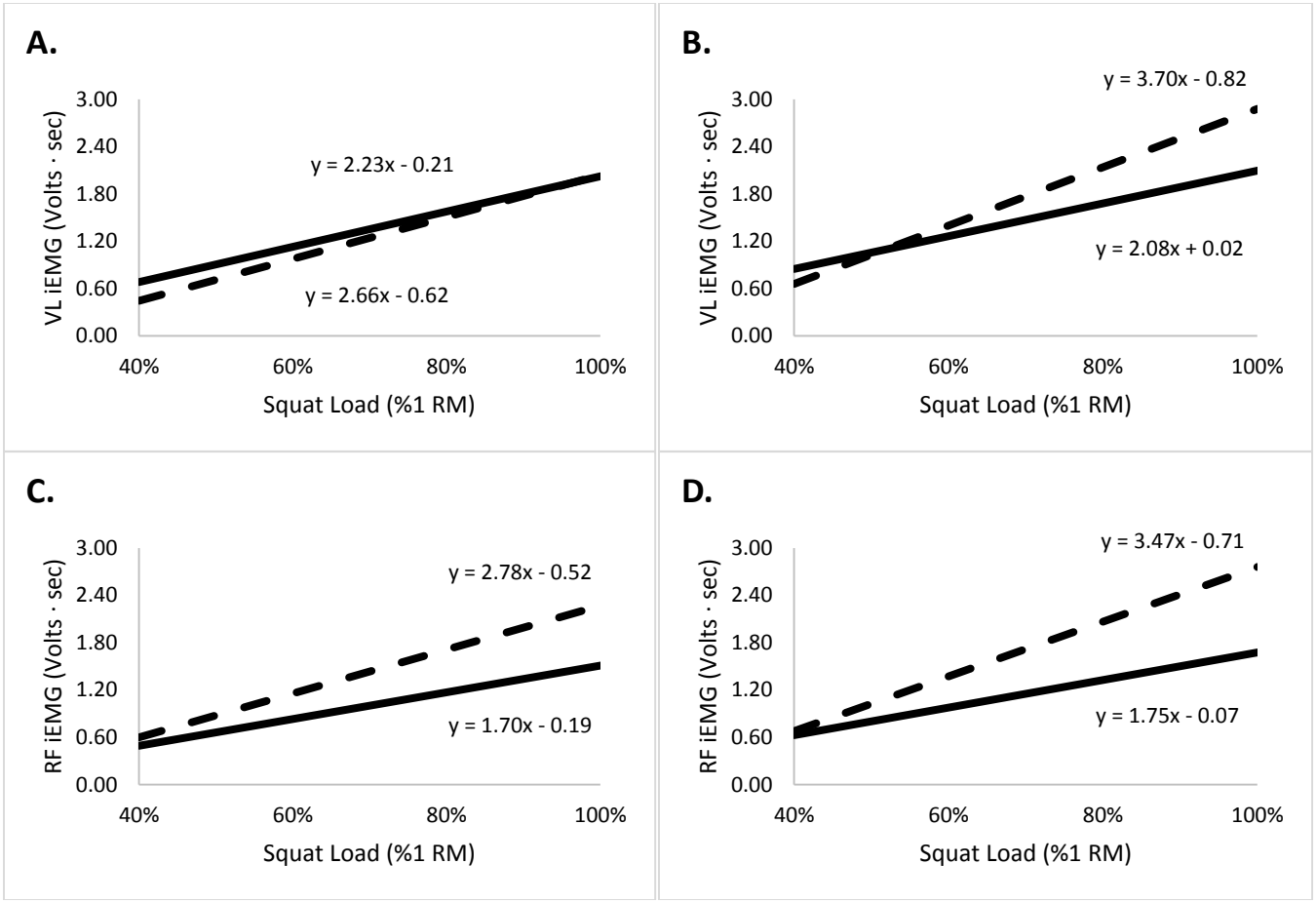
Electromyography

Changes in the regression slope for muscle activation with increases in intensity are illustrated in Figure 6. No group differences were observed for VL (VOL: 2.66 ± 1.18 Volts · sec; INT: 3.70 ± 1.50 Volts · sec; $p = 0.053$) or RF (VOL: 2.78 ± 1.93 Volts · sec; INT: 3.47 ± 1.73; $p = 0.333$) activation at PRE, as determined from the slope of the regression. Following the training intervention, the VL activation slope decreased for VOL (–0.43 ± 1.47 Volts · sec) and INT (–1.62 ± 1.80 Volts · sec), while RF activation also decreased for VOL (–1.09 ± 1.28 Volts · sec) and INT (–1.72 ± 1.47 Volts · sec). However, no group differences were observed (see Table 3).



Note. Mean values (±SD) for posttest scores adjusted for initial differences in pretest: A. Bench Press (covariate; adjusted pretest mean = 106.7); B. Relative Bench Press (covariate; adjusted pretest mean = 1.2); C. Squat (covariate; adjusted pretest mean = 142.6); D. Relative Squat (covariate; adjusted pretest mean = 1.6). *Significant ($p < 0.05$) difference between PRE and POST. #Significant ($p < 0.05$) difference between VOL and HVY.

Figure 5. One repetition maximum (1RM) and relative bench press and squat strength



Note: A. Vastus Lateralis – Volume; B. Vastus Lateralis – Intensity; C. Rectus Femoris – Volume; D. Rectus Femoris – Heavy. Pre-training (PRE; Dashed Line) and post-training (POST; Solid Line) line of best fit.

Figure 6. Changes in muscular activation efficiency during squat assessments

Table 3. Group differences in changes in muscle activation efficiency during submaximal and maximal squat assessment following 8wks of training

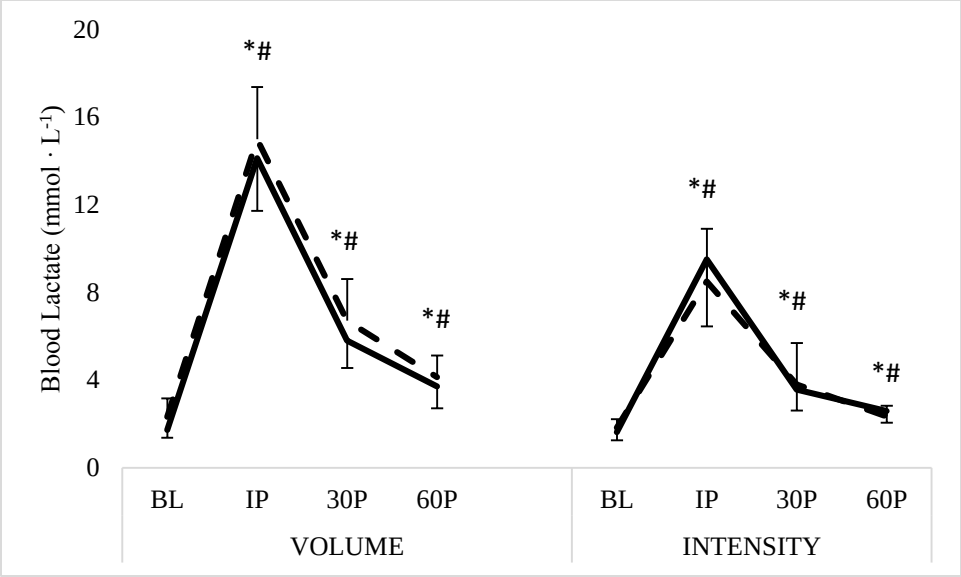
	Covariate	POST	F	p-value	η^2p
Vastus Lateralis (β1)					
VOLUME	3.18	2.23 ± 1.78	0.664	0.423	0.026
INTENSITY		2.08 ± 0.84			
Rectus Femoris (β1)					
VOLUME	3.12	1.70 ± 1.17	0.468	0.500	0.018
INTENSITY		1.75 ± 0.83			

Note. Muscle activation efficiency was calculated as the percent change (β1) in muscle activation as resistance increased from 40% to 100% 1RM at PRE.

Biochemical and Hormonal Responses

Lactate

While controlling for baseline values, significant group x time interactions were observed in the lactate response to exercise at WK3 ($F = 16.223$; $p < 0.001$; $\eta^2p = 0.585$) and WK10 ($F = 12.679$; $p < 0.001$; $\eta^2p = 0.524$). Significant main effects ($p < 0.001$) were observed for both groups at WK3 and WK10. At WK3 blood lactate concentrations were significantly ($p < 0.001$) higher at IP compared to BL for both VOL (12.66 ± 2.31 $mmol \cdot L^{-1}$) and INT (6.66 ± 2.44 $mmol \cdot L^{-}1$) and remained significantly ($p < 0.001$) elevated from BL at 30P and 60P for both groups (see Figure 7). Blood lactate concentrations were significantly ($p < 0.001$) higher for VOL than INT at each time point.



Note. Note: Pre-training (PRE; Dashed) and post-training (POST; Solid) values are presented as Mean ± SD. *Significant ($p < 0.05$) difference from baseline at Week 3. #Significant ($p < 0.05$) difference from baseline at Week 10.

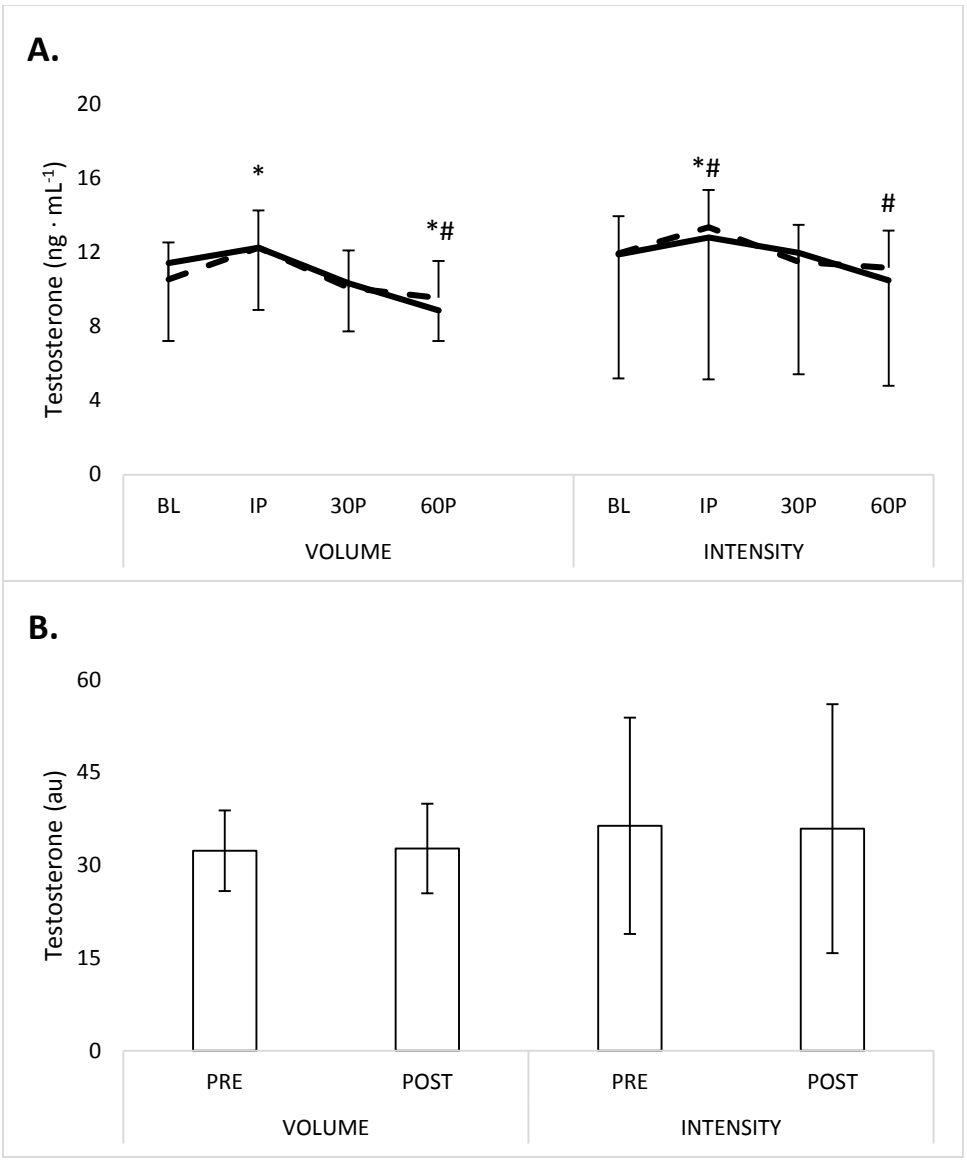
Figure 7. Changes in the blood lactate response to exercise following eight weeks of training

Changes in blood lactate concentrations at WK10 for each group were similar to WK3. Blood lactate concentrations at IP during both VOL and INT (12.39 ± 2.22 mmol · L^{-1} and 7.88 ± 3.17 mmol · L^{-1}, respectively) were significantly ($p < 0.001$) higher than seen at BL. Blood lactates remained significantly ($p < 0.001$) elevated at 30P and 60P, for both groups, but VOL experienced significantly ($p < 0.002$) greater elevations in blood lactate than INT at each time point.

Testosterone

The TEST response to exercise for VOL and INT can be observed in Figure 8A. There were no group x time interactions observed at WK3 ($p = 0.585$) or WK10 ($p =$

0.286), when controlling for baseline values. However, significant main effects ($p < 0.001$) were observed in the acute TEST responses for both VOL and INT. TEST was significantly elevated from BL for VOL ($p = 0.002$) and INT ($p = 0.009$) at IP, but returned to resting levels by 30P for both groups. At 60P, TEST was significantly ($p = 0.004$) lower than BL for VOL only. During WK10, a significant main effect was observed for VOL ($p = 0.008$) and INT ($p = 0.002$). The TEST response was significantly elevated at IP for INT ($p = 0.018$), but not for VOL ($p = 0.468$). At 60P, TEST concentrations were significantly reduced from BL for both VOL ($p = 0.035$) and INT ($p = 0.012$). AUC analysis (Figure 8B) did not reveal a significant group x time interaction ($p = 0.701$) or main effect ($p = 0.996$) from training in the TEST response to exercise.



Note. (A. Testosterone Response Time Course; B. Area under the curve). Pre-training (PRE; Dashed) and post-training (POST; Solid) values are presented as Mean ± SD. *Significant ($p < 0.05$) difference from baseline at Week 3. #Significant ($p < 0.05$) difference from baseline at Week 10.

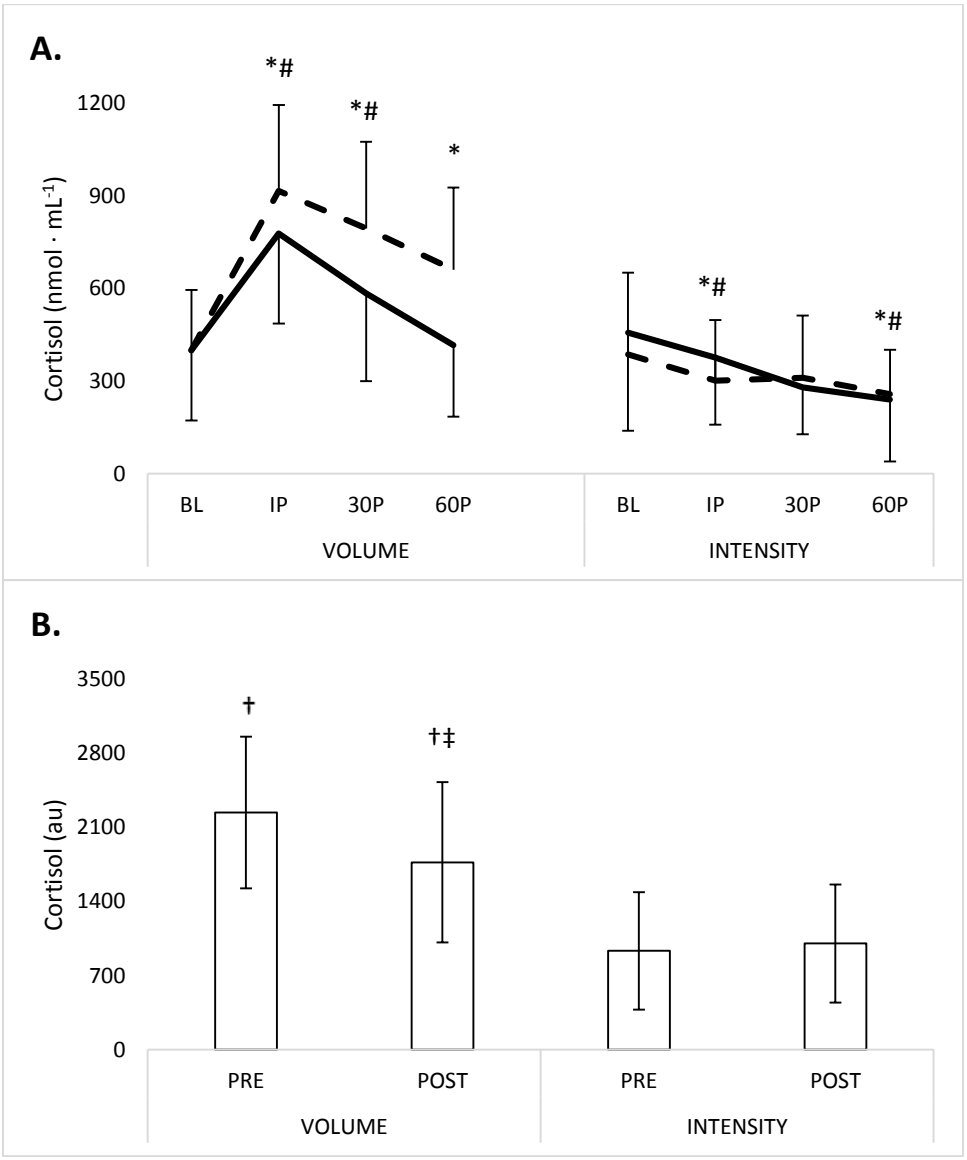
Figure 8. Changes in the testosterone response to exercise following eight weeks of training

Cortisol

Comparisons between VOL and INT in the CORT response to exercise can be observed in Figure 9A. While controlling for baseline values, a significant group x time interaction was observed at WK3 ($F = 8.687$; $p = 0.002$; $\eta^2p = 0.441$) and WK10 ($F = 5.922$; $p = 0.009$; $\eta^2p = 0.350$). Significant main effects were observed in CORT concentrations in response to exercise at WK3 for VOL ($p < 0.001$) and INT ($p = 0.025$). CORT concentrations were significantly elevated (p values < 0.001) from BL at IP, 30P and 60P for VOL. In contrast, CORT concentrations during INT were significantly reduced at IP ($p = 0.026$), but returned to BL at 30P ($p = 0.089$), and then further declined at 60P ($p = 0.032$). At WK10, exercise had a significant main effect on CORT concentrations for VOL ($p < 0.001$) and INT ($p = 0.010$). For VOL, CORT concentrations were significantly elevated from BL at IP ($p < 0.001$) and at 30P ($p = 0.020$), but returned to BL by 60P ($p = 0.768$). CORT concentrations for INT remained at BL levels at IP ($p = 0.278$), but were significantly reduced at 30P ($p = 0.023$) and 60P ($p = 0.001$). No significant interactions were seen between WK3 and WK10 comparisons between the groups.

AUC analysis (Figure 9B) for the CORT response to exercise revealed a significant group x time interaction ($F = 7.604$; $p = 0.011$; $\eta^2p = 0.241$). At WK3, the acute CORT response for VOL (2240 ± 716 nmol $\cdot$ mL^{-1}) was 2.4 times greater ($p < 0.001$) than INT (934 ± 556 nmol $\cdot$ mL^{-1}). In comparison to WK3, VOL experienced a significantly ($-13.1 \pm 17.8\%$, $p = 0.019$) diminished response during WK10, while the response for INT remained the same ($p = 0.452$). However, the CORT response for VOL

(1770 ± 757 nmol · mL^{-1}) was still greater (p = 0.007) than INT (1004 ± 558 nmol · mL^{-1}) at WK10.



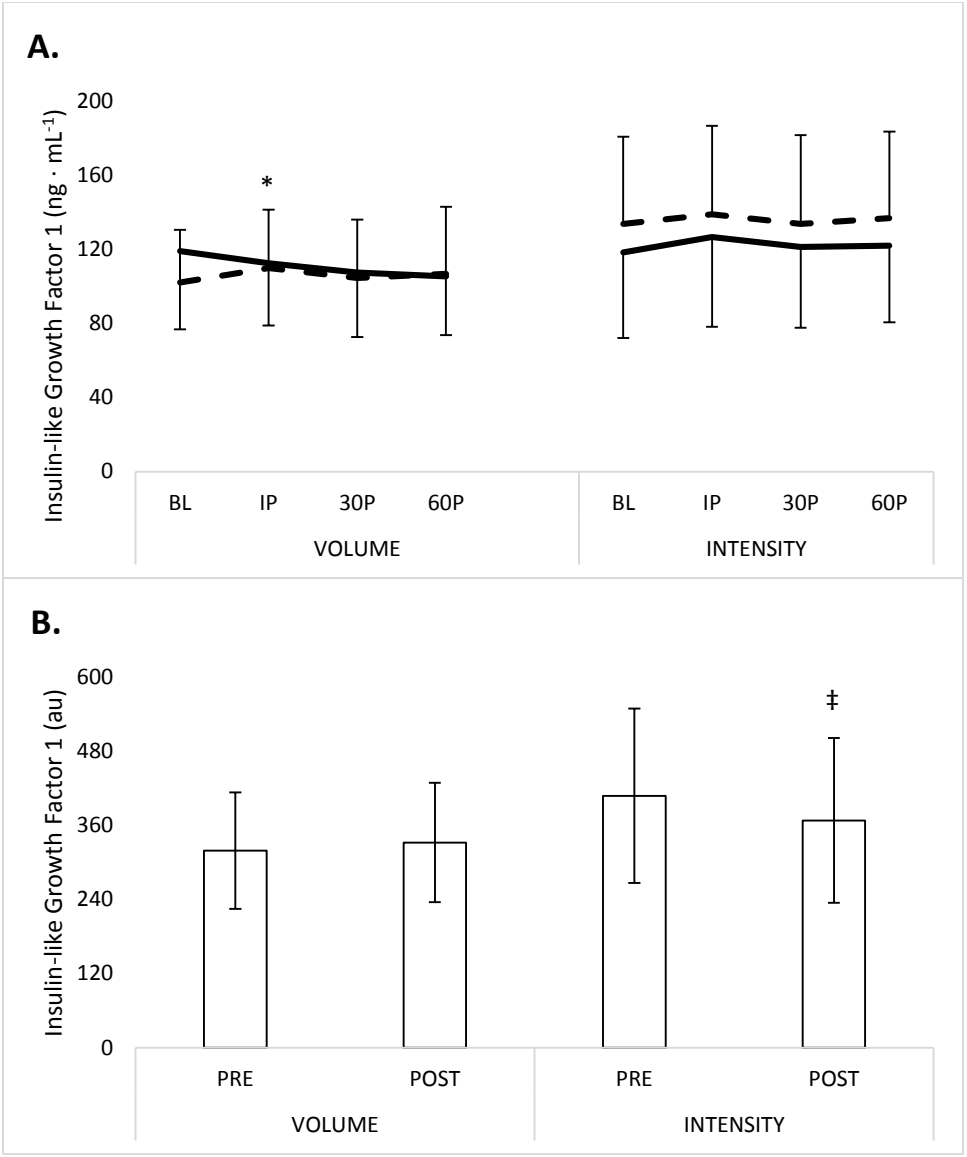
Note. (A. Cortisol Response Time Course; B. Area under the curve). Pre-training (PRE; Dashed) and post-training (POST; Solid) values are presented as Mean ± SD. *Significant (p < 0.05) difference from baseline at Week 3. #Significant (p < 0.05) difference from baseline at Week 10. ‡Significant (p < 0.05) difference from Week 3. †Significant (p < 0.05) difference between VOL and INT.

Figure 9. Changes in the cortisol response to exercise following eight weeks of training

Insulin-like Growth Factor I

The IGF-1 response to exercise for VOL and INT are depicted in Figure 10A. There were no group x time interactions observed at WK3 ($p = 0.966$) or WK 10 ($p = 0.899$), when controlling for baseline values. However, a significant main effect on IGF-1 concentrations was observed for VOL ($p = 0.027$) but not for INT ($p = 0.341$) at WK3. For VOL, IGF-1 was significantly elevated from BL at IP ($p = 0.005$), but returned to BL by 30P. During WK10, no main effects were observed in the IGF-1 response to exercise for either group.

AUC analysis (Figure 10B) for the acute IGF-1 response to exercise revealed a significant group x time interaction ($F = 6.020$; $p = 0.021$; $\eta^2p = 0.194$). Although no differences ($p = 0.068$) were observed between VOL (318.7 ± 94.3 ng $\cdot$ mL^{-1}) and INT (407.6 ± 141 3 ng $\cdot$ mL^{-1}) at WK3, INT experienced a significantly lower ($-9.4 \pm 12.6\%$, $p = 0.019$) response following training while no changes occurred for VOL ($p = 0.416$) in comparison to WK3. Consequently, no differences ($p = 0.436$) were observed between VOL (332 ± 96.6 ng $\cdot$ mL^{-1}) and INT (367.7 ± 133.4 ng $\cdot$ mL^{-1}) at WK10.



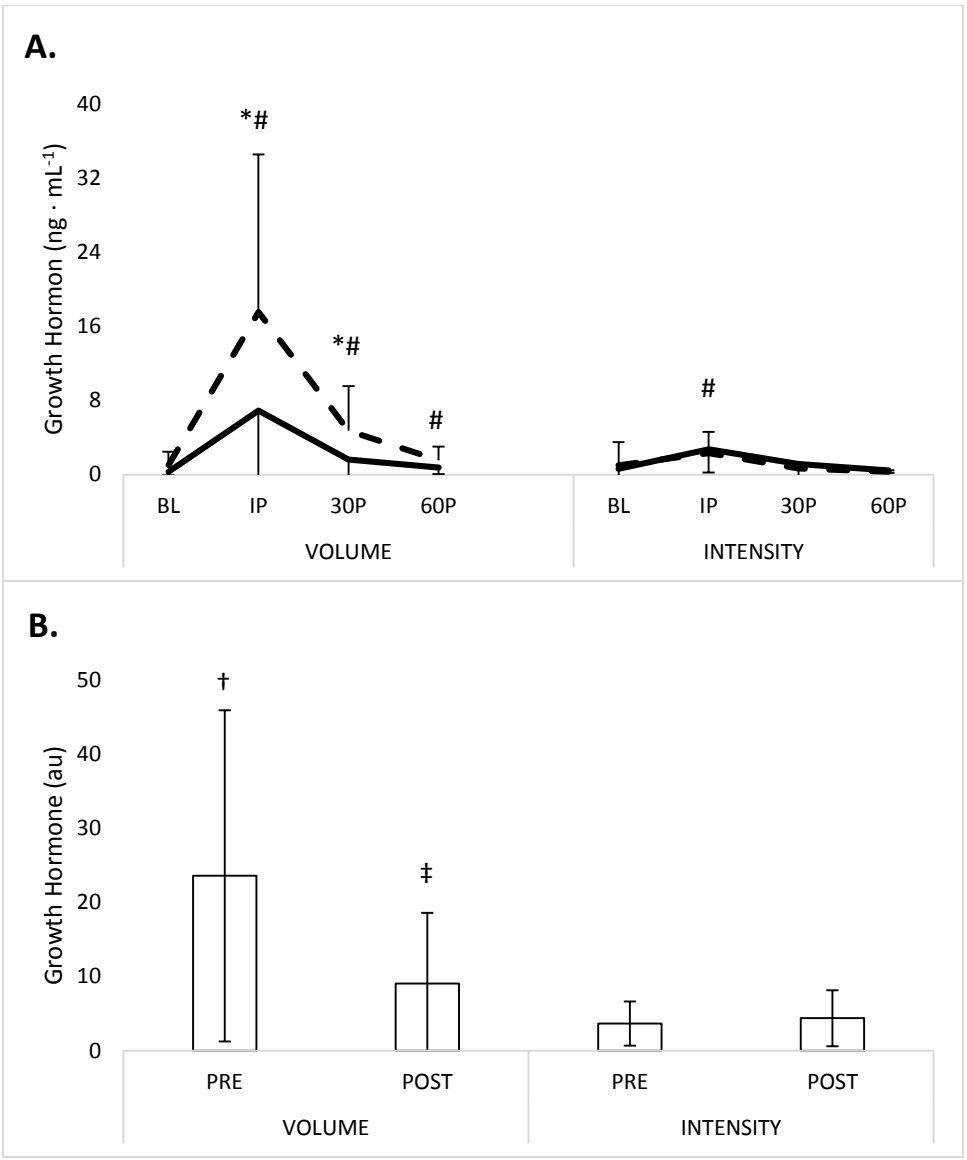
Note. (A. Insulin-like Growth Factor 1 Time Course; B. Area under the curve. Pre-training (PRE; Dashed) and post-training (POST; Solid) values are presented as Mean ± SD. *Significant ($p < 0.05$) difference from baseline at Week 3. #Significant ($p < 0.05$) difference from baseline at Week 10. ‡Significant ($p < 0.05$) difference from Week 3.

Figure 10. Changes in the insulin-like growth factor 1 response to exercise following eight weeks of training

Growth Hormone

The GH response to exercise for VOL and INT can be seen in Figure 11A. While controlling for baseline values, a significant group x time interaction ($F = 5.411$; $p = 0.012$; $\eta^2p = 0.320$) at WK3. Main effects analysis revealed a significant GH response for VOL ($p = 0.003$) but not for INT ($p = 0.054$) at WK3. For VOL, the GH concentrations were significantly elevated from BL at IP ($p = 0.003$) and 30P ($p = 0.013$), then returned to BL by 60P ($p = 0.245$). At WK10, the group x time interaction was not significant ($F = 3.262$; $p = 0.057$; $\eta^2p = 0.221$), though significant main effects were observed for both groups ($p = 0.006$). The GH response experienced by VOL indicated significant elevations from BL at IP ($p = 0.006$), 30P ($p = 0.014$), and 60P ($p = 0.024$). During INT the GH response was significantly elevated from BL at IP ($p = 0.020$), but returned to BL levels by 30P.

AUC analysis (Figure 11B) for the GH response to exercise revealed a significant group x time interaction ($F = 5.964$; $p = 0.022$; $\eta^2p = 0.193$). At WK3, the GH response for VOL (23.6 ± 22.3 ng $\cdot$ mL^{-1}) was 6.5 times greater ($p = 0.007$) than INT (3.6 ± 3.0 ng $\cdot$ mL^{-1}). In comparison to WK3, VOL experienced a significantly ($-55.7 \pm 29.7\%$, $p = 0.041$) diminished response during WK10, while the response for INT remained the same ($p = 0.562$). Consequently, the GH responses for VOL (9.1 ± 9.5 ng $\cdot$ mL^{-1}) and INT (4.4 ± 3.8 ng $\cdot$ mL^{-1}) were no longer statistically ($p = 0.119$) different at WK10.



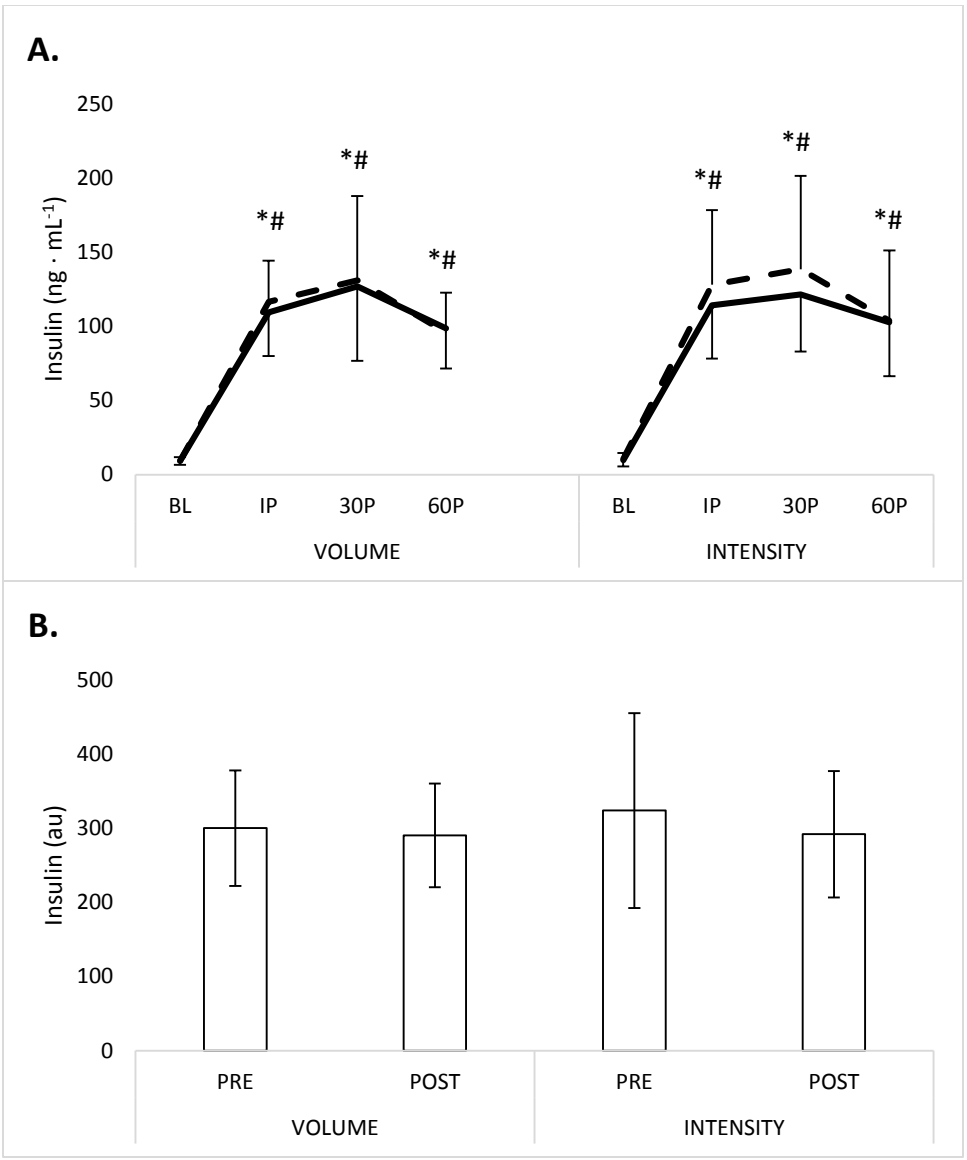
Note. (A. Growth Hormone Response Time Course; B. Area under the curve). Pre-training (PRE; Dashed) and post-training (POST; Solid) values are presented as Mean ± SD. *Significant ($p < 0.05$) difference from baseline at Week 3. #Significant ($p < 0.05$) difference from baseline at Week 10. ‡Significant ($p < 0.05$) difference from Week 3. †Significant ($p < 0.05$) difference between VOL and INT.

Figure 11. Changes in the growth hormone response to exercise following eight weeks of training

Insulin

The INSL response to exercise for both VOL and INT can be seen in Figure 12A. There were no significant group x time interactions observed at WK3 ($p = 0.960$) or WK10 ($p = 0.823$), when controlling for baseline measures. However, significant main effects ($p < 0.001$) were observed during the acute responses at WK3 and WK10 for both groups. The INSL response for both VOL and INT was significantly ($p < 0.001$) elevated from BL at every time point during both WK3 and WK10 assessments. No significant interactions were noted between VOL and INT in WK3 and WK10 comparisons. AUC analysis (Figure 12B) did not reveal a significant group x time interaction ($p = 0.544$) or main effect ($p = 0.257$) from training on the INSL response to exercise.

Plasma volumes at WK3 decreased -8.78 ± 8.62% for all participants at IP, and then increased 5.17 ± 7.68% and 4.66 ± 6.35% at 30P and 60P, respectively. At WK10, plasma volumes decreased -11.87 ± 5.26% at IP, then increased 3.24 ± 3.98%) and 5.82 ± 10.42% at 30P and 60P, respectively. No differences were found between groups at either time point. Blood variables were not corrected for plasma volume shifts due to the importance of molar exposure at the tissue receptor level.



Note. (A. Insulin Response Time Course; B. Area under the curve). Pre-training (PRE; Dashed) and post-training (POST; Solid) values are presented as Mean ± SD. *Significant ($p < 0.05$) difference from baseline at Week 3. #Significant ($p < 0.05$) difference from baseline at Week 10.

Figure 12. Changes in the insulin response to exercise following eight weeks of training

Nutritional intake and dietary analysis

Relative caloric and macronutrient intake did not change significantly over the course of the investigation in either group. In addition, no differences were observed between groups. The nutritional habits of the participants are presented in Table 4.

Table 4. Caloric and macronutrient intake during the 8wk training investigation

	VOLUME			INTENSITY		
	PRE	POST	Change	PRE	POST	Change
Calories (kCal · kg^{-1})	31.7 ± 7.0	29.2 ± 8.1	-2.4 ± 7.3	38.3 ± 11.1	31.1 ± 5.3	-7.21 ± 10.96
Protein (g · kg^{-1})	1.8 ± 0.4	1.7 ± 0.7	-0.1 ± 0.5	2.0 ± 0.7	1.7 ± 0.4	-0.31 ± 0.58
Leucine (g · kg^{-1})	0.11 ± 0.03	0.10 ± 0.07	-0.01 ± 0.07	0.10 ± 0.06	0.09 ± 0.04	-0.01 ± 0.05
Isoleucine (g · kg^{-1})	0.06 ± 0.02	0.06 ± 0.05	0.00 ± 0.04	0.06 ± 0.04	0.05 ± 0.03	-0.01 ± 0.03
Valine (g · kg^{-1})	0.07 ± 0.02	0.07 ± 0.05	0.00 ± 0.05	0.07 ± 0.04	0.06 ± 0.03	-0.01 ± 0.03
Carbohydrate (g · kg^{-1})	3.1 ± 1.0	2.9 ± 1.0	-0.2 ± 0.5	4.3 ± 1.5	3.7 ± 1.2	-0.55 ± 1.74
Fat (g · kg^{-1})	1.3 ± 0.3	1.1 ± 0.4	-0.2 ± 0.4	1.3 ± 0.6	0.9 ± 0.4	-0.40 ± 0.58

CHAPTER 5: DISCUSSION

The major findings of this study indicated that 8 weeks of high intensity, long rest resistance training stimulated significantly greater strength and muscle hypertrophy gains compared to high volume, short rest resistance training in experienced resistance-trained men. These results are consistent with previous studies reporting that high intensity, long rest training programs are more conducive for greater strength improvements, along with similar outcomes in muscle growth, in comparison to high volume, short rest training schemes in experienced resistance trained individuals (Brandenburg & Docherty, 2002; Schoenfeld et al., 2014). However, the greater gains in muscle growth observed in the high intensity training group is in contrast with the general understanding associated with high volume resistance training programs. It is generally thought that high volume, short rest resistance training will stimulate a greater anabolic hormone response to exercise (W. J. Kraemer & Ratamess, 2004, 2005; Ratamess et al., 2009). However, our results are not consistent with that hypothesis. At WK3 only the GH response was observed to be greater for VOL compared to INT, while no differences were noted in the testosterone, IGF-1 and insulin responses between the different exercise protocols. In addition, the cortisol response was significantly higher in VOL compared to INT. Following 8 weeks of training (WK10), both the growth hormone and cortisol response in VOL were attenuated. As a result, out of all the endocrine measures only the cortisol response to exercise remained different between groups. Therefore, differences in strength and muscle morphology changes may have been more of a function in the difference of

mechanical stress invoked by each program, rather from differences in their respective endocrine response.

Changes in strength are generally thought to be the result of a combination of neurological activation and skeletal muscle adaptation (Moritani, 1993; Moritani & deVries, 1979; Phillips, 2000; Ploutz et al., 1994; Staron et al., 1994). Initial strength gains in the previously untrained individual have been associated with neurological adaptations that primarily involve a greater or more efficient activation pattern of the associated musculature (Moritani & deVries, 1979). However, in a resistance-trained population, improvements in the magnitude and efficiency of muscle activation during exercise appears to be limited (deVries, 1968; Moritani, 1993; Moritani & deVries, 1979; Ploutz et al., 1994). Consequently, any change in muscle activation is likely the result of a change in muscular size. A previous study in experienced, resistance trained athletes reported significant gains in strength within the first few weeks of training (Hoffman, Ratamess, Klatt, et al., 2009). This was attributed to rapid neurological adaptations that were likely seen following several weeks of detraining. In lieu of this, the present study utilized a 2-week "pre-training" period to minimize any "relearning effect" from participants that may have been in a potentially reduced or no training period prior to the onset of the study. As such, any change in muscle activation is likely the result of the specific training program and not related to a relearning effect. Results of this study noted similar changes in muscular activation efficiency for both groups, which also coincided with similar changes in muscular strength and size of the lower extremity. These findings are in agreement with previously published improvements in muscular

efficiency following 12 weeks of isometric training (Komi, Viitasalo, Rauramaa, & Vihko, 1978). Although no differences were observed between groups, it is possible that 8 weeks was not sufficient to reveal differences in the lower extremity of resistance-trained adults (Abe et al., 2000; T. C. Chen, Lin, Chen, Lin, & Nosaka, 2011; Hoffman, Ratamess, Tranchina, et al., 2009). Unlike the upper extremity, where group differences in strength gains and hypertrophy were observed, the musculature of the lower limb has been observed to be more resistant to exercise-induced muscle damage (T. C. Chen et al., 2011) and slower to respond to training (Abe et al., 2000). Thus a longer training period may be necessary to determine whether high intensity or high volume training is more advantageous for inducing lower extremity strength and size improvements in an experienced population.

The mechanical and metabolic stresses imposed by resistance training are believed to influence changes in muscle size (deVries, 1968; Evans, 2002; Jones & Rutherford, 1987; Moritani, 1993; Moritani & deVries, 1979; Thomsen & Luco, 1944; Vandenburgh, 1987). In the present study, the greater mechanical stress imposed by INT also resulted in greater muscle growth. In previous investigations, however, the influence of mechanical and metabolic stresses on muscle growth appeared to be similar (Brandenburg & Docherty, 2002; Schoenfeld et al., 2014). These differences may be explained by the limited number of multi-joint, structural exercises used per training session in those studies. Brandenburg and Docherty (2002) had participants complete only two single-joint, open-chain exercises (i.e. preacher curl and supine elbow extension) per session, while Schoenfeld and colleagues (2014) required three exercises

per session (i.e. 1 x upper-body push, 1 x upper-body pull, and 1 x lower-body) out of a pool of nine exercises that included both single- and multi-joint movements. This strategy can be a disadvantage because less muscle is activated during single-joint open-chain movements in comparison to multi-joint, closed-chain exercises (Augustsson et al., 1998; Gentil et al., 2013; Stensdotter et al., 2003). As a result, Brandenburg and Docherty (2002) did not observe any change in muscle size, whereas Schoenfeld and colleagues (2014) observed similar changes between high intensity and high volume groups. However, mechanical stress may have been limited on days when only single-joint exercises were used during training. In contrast, several studies have imposed significant metabolic stress when using a limited number (< 3) of multi-joint exercises (Hulmi et al., 2012; McCaulley et al., 2009; Nicholson et al., 2014; Schwab et al., 1993) or only single-joint movements (Gentil, Oliveira, & Bottaro, 2006; Macdougall et al., 1999; Sjogaard, Adams, & Saltin, 1985; Takarada, Nakamura, et al., 2000). Thus in the present study, it is possible that the greater morphological changes observed in INT were the consequence of greater muscle activation generated from the inclusion of several multi-joint exercises per workout. The higher intensity protocol likely activated more muscle fibers during exercise (Abbott et al., 1952; Henneman et al., 1965; Katz, 1939), stimulating greater adaptation across a larger percentage of muscle (Barash et al., 2004; Brentano & Martins, 2011; Clarkson et al., 1992; Ratamess et al., 2009).

The acute endocrine responses observed in our study were consistent with previous investigations (Gregory et al., 2013; Hakkinen & Pakarinen, 1993; Hakkinen et al., 2000; Hameed et al., 2004; W. J. Kraemer et al., 1990; McCaulley et al., 2009;

McKay et al., 2008; Schwab et al., 1993; Smilios et al., 2003; West et al., 2010; West et al., 2009). The high volume resistance training protocol resulted in significantly greater elevations in GH and cortisol concentrations, compared to the high intensity training protocols. However, similar increases were observed between VOL and INT in testosterone, IGF-1, and insulin responses to exercise. Increases in the anabolic hormones testosterone, GH, and IGF-1 are thought to be advantageous for muscle growth and possible strength gain (Evans, 2002; Jones & Rutherford, 1987; W. J. Kraemer & Ratamess, 2004, 2005; Ratamess et al., 2009), however the results of this study do not provide support for this hypothesis. More specifically, they do not support a greater GH response to exercise as being associated with greater muscle growth or strength gain. Rather, it is possible that the greater elevations in GH and cortisol observed in VOL were simply a response to the metabolic demands of the programming, as reflected by the significantly higher lactate measures seen in VOL compared to INT (Goldberg et al., 1980; Gravholt et al., 1999; Moller et al., 1995; Schakman et al., 2013). The effect of 8 weeks of training for VOL appeared to lower both the GH and cortisol response to exercise. This was contrary to previous reports (Ahtiainen, Pakarinen, Alen, et al., 2003; Buresh et al., 2009; Hakkinen et al., 2000; W. J. Kraemer, Staron, et al., 1998; McCall et al., 1999; Mitchell et al., 2013), but may reflect metabolic adaptations to the exercise stimulus (Burgomaster et al., 2003; Hagerman et al., 2000; W. J. Kraemer & Ratamess, 2005). In contrast, the elevated GH observed at IP (WK10) for INT may reflect the increase in load being used, making this program metabolically more stressful; though it was not sufficient to alter the cortisol response.

The similar responses of testosterone, IGF-1, and insulin observed between INT and VOL, at both WK3 and WK10, suggest that differences in acute program variables (i.e., intensity, volume and rest) may not stimulate significant differences in these anabolic hormones during an 8-week training cycle. In regards to an acute response, previous investigations have reported a similar testosterone response following both heavy (3 – 6 RM) and moderate (9 – 10 RM) loading schemes (W. J. Kraemer et al., 1990; McCaulley et al., 2009; Schwab et al., 1993), while a consistent response pattern has not been observed for IGF-1 in response to a variety of high volume resistance training protocols (Gregory et al., 2013; McKay et al., 2008; Nindl et al., 2001; Spiering et al., 2008; West et al., 2010; West et al., 2012; West et al., 2009; Wilkinson et al., 2006). Variability in the testosterone response is likely related to the degree of mechanical stress present (i.e. loading). For instance, Kraemer and colleagues (1990) demonstrated elevated testosterone concentrations only when heavy (i.e. 5 RM with 1 or 3 minutes rest) or moderate (i.e. 10 RM with 1 minute rest) loadings were used to induce fatigue. When moderate loads and long rest (i.e. 10 RM with 3 minutes rest) are used, this stimulus does not appear to be sufficient to cause consistent elevations in testosterone concentrations. Similarly, IGF-1 concentrations did not change from baseline following high volume resistance exercise when programming included only two unilateral exercises and long rest periods (6 – 10 RM; 3 minutes rest) (Wilkinson et al., 2006), or when training included both high (5RM) and moderate (10RM) intensity with longer rest periods (2 – 3 minutes) (Nindl et al., 2001; Spiering et al., 2008). The variability seen in the acute testosterone and IGF-1 response to a bout of resistance exercise suggests that

different combinations of both metabolic and mechanical stimuli are required to foster such changes.

Increases in IGF-1 concentrations are thought to be stimulated by a high mechanical stimulus (Bamman et al., 2001; Devol et al., 1990; Gregory et al., 2013; Hameed et al., 2004), however elevations in GH have also been reported to stimulate IGF-1 release (Clemmons et al., 1981; Gregory et al., 2013; Hameed et al., 2004; Iida et al., 2004). In this present study, GH and IGF-1 were both elevated in VOL at WK3, but by WK10 the magnitude of the GH response to the exercise program was attenuated with no change noted in the IGF-1 response to exercise. The response seen for INT was slightly different. During WK3, no changes from baseline were observed in the GH or IGF-1 responses to exercise. By WK10 however, a significant elevation at IP was observed in the GH response, with no concomitant change in the IGF-1 response. It is possible the increase in GH at IP was related to the ~34% increase in the lactate response observed at the same time point at WK10 for INT. Although this did not change the total GH (AUC) response to exercise, an attenuation in the IGF-1 (AUC) response was noted. These results do appear to be consistent with other investigations that have reported no elevation in IGF-1 despite an increase in GH concentrations following resistance exercise (Hasani-Ranjbar et al., 2012; Spiering et al., 2008; Wilkinson et al., 2006). Hameed and colleagues (2004) reported that elevations in GH combined with a resistance exercise stimulus can result in significant elevations in both circulating and intramuscular IGF-1. However, they used exogenously administered GH to accompany the resistance exercise protocol. The combination of both GH administration and resistance exercise, resulted in

a greater IGF-1 response than any of the stimuli alone. Interestingly, 12 weeks of GH administration was reported to increase intramuscular IGF-1 concentrations, but attenuate circulating IGF-1 concentrations. Although intramuscular IGF-1 was not examined in this study, the attenuation in the IGF-1 response to INT at WK10 does appear to support these results.

Unlike the GH and IGF-1 responses to exercise, which appear to be influenced by changes in metabolic stress (Hakkinen & Pakarinen, 1993; Vanhelder et al., 1984) and GH (Clemmons et al., 1981; Gregory et al., 2013; Hameed et al., 2004; Iida et al., 2004), respectively, the mechanisms underlying the changes in the testosterone response to exercise are less clear. Previous research has reported no changes in the testosterone response to exercise (Alen et al., 1988; Bell et al., 2000; Hakkinen et al., 2000; Hansen et al., 2001; McCall et al., 1999; Reaburn et al., 1997; Wilkinson et al., 2006) or an attenuated response (Buresh et al., 2009; Mitchell et al., 2013; West et al., 2010) following prolonged training (2 – 6 months). In the present study, neither protocol induced any changes in the testosterone response to exercise. These results are consistent with previous research using high volume (Bell et al., 2000; Hansen et al., 2001; McCall et al., 1999; Reaburn et al., 1997; Wilkinson et al., 2006) and high intensity (Bell et al., 2000) resistance training protocols 8 – 12 weeks in duration. While it may be possible that the 8-week training period used in this study was too short to stimulate any adaptation, the testosterone response to an acute bout of resistance exercise has also been reported to remain similar for up to 6 months of training (Hakkinen et al., 2000). Others have reported a reduced response following 10 – 15 weeks of high volume training

(Buresh et al., 2009; West et al., 2010), as well as from 16 weeks of periodized training (2 – 4 sets; 6 – 12 RM; 1 – 2 min rest) (Mitchell et al., 2013). Consequently, there does not appear to be a clear pattern or mechanism of change in the testosterone response to resistance training.

Insulin concentrations in both groups were shown to be significantly elevated from BL at IP through 60P during both WK3 and WK10. While this response is in contrast to many studies showing insulin concentrations decreasing from baseline during exercise (Raastad et al., 2000; Spiering et al., 2008; Thyfault et al., 2004; Volek et al., 2004), these differences may be related to the feedings provided during the study. All participants were provided ~235 ml of chocolate milk (or Lactaid ®) following baseline blood sample collection (before exercise), and immediately following the IP blood draw. Previous research has demonstrated that ingestion of a protein/carbohydrate beverage surrounding the workout will result in an elevation in insulin concentrations (Bird et al., 2006; Børsheim et al., 2004; Rasmussen et al., 2000; Thyfault et al., 2004; Tipton et al., 2001). It is possible that any differences in the insulin response to the different training protocols may have been masked by the pre- and post-exercise feedings.

In conclusion, the results of this study indicate that high intensity (3 – 5 RM), longer rest (3 min) resistance training programs are more advantageous than a high volume (10 – 12 RM), short rest (1 min) protocols for stimulating upper body strength gains and muscle hypertrophy in experienced, resistance-trained men during an 8-week study. Furthermore, the strength and morphological improvements demonstrated during the 8-week study responded better to a submaximal endocrine response. These

observations question the utility of high volume training programs that are designed to maximize the acute hormonal response as being ideal for stimulating muscle growth, at least during a relatively short duration of training. Thus, emphasizing training intensity over volume may be a better strategy for accelerating muscle growth and strength gains.

APPENDIX A: IRB APPROVAL LETTER

NEW ENGLAND INSTITUTIONAL REVIEW BOARD

May 29, 2014

Gerald T. Mangine
Institute of Exercise Physiology & Wellness at the University of Central Florida
4000 Central Florida Boulevard, Education Complex
Orlando, FL 32828

Re: (IRB# 14-195): SBE-14-10276: "Magnitude of Hypertrophy in Response to Training Volume Versus Intensity in Resistance-Trained Men"

This is to inform you that New England Institutional Review Board (NEIRB)'s Tuesday Board has approved the above-referenced research protocol and the participation of the above-referenced investigative site in the research. The approval period is **5/29/2014 to 5/12/2015. Your study number is 14-195. Please be sure to reference either this number or the name of the principal investigator in any correspondence with NEIRB.**

Continued approval is conditional upon your compliance with the following requirements:

- A copy of the **Informed Consent Document, NEIRB version 1.0**, approved as of 5/29/2014 is enclosed. Only NEIRB-approved informed consent documents should be used. It must be signed by each subject prior to initiation of any protocol procedures. In addition, each subject must be given a copy of the signed consent form.
- The following must be promptly reported to NEIRB: changes to the study site, and all unanticipated problems that may involve risks or affect the safety or welfare of subjects or others, or that may affect the integrity of the research.
- Approval is valid for enrollment of the number of subjects indicated on your submission form. If you anticipate enrolling more than this number of subjects, NEIRB approval must be obtained prior to exceeding the approved enrollment number.
- All protocol amendments and changes to approved research must be submitted to the IRB and not be implemented until approved by the IRB except where necessary to eliminate apparent immediate hazards to the study subjects.
- Compliance with all federal and state laws pertaining to this research, and with NEIRB's SOPs.
- The enclosed recruitment advertisement has been approved (Recruitment Script). Advertisements, letters, internet postings and any other media for subject recruitment must be submitted to NEIRB and approved prior to use. Please refer to *NEIRB Guidelines for Recruitment and Advertising*, available at www.neirb.com.
- All deaths, life-threatening problems or serious or unexpected adverse events, *whether related to the study article or not*, must be reported to the IRB. The Serious Adverse Event Form is available at www.neirb.com.
- Any and all necessary FDA approvals must be received prior to your initiation of the trial. If this study is being conducted under an IDE, a copy of the FDA IDE approval letter must be submitted to NEIRB.
- The study cannot continue after 5/12/2015 until re-approved by NEIRB. A Study Renewal Report must be completed and returned to NEIRB prior to the expiration of the approval period.
- When the study is completed, terminated, or if it is not being renewed - complete and submit a Study Completion Report to NEIRB. The Study Completion Report can be accessed via the NEIRB website at www.neirb.com.

Sharon Wang, CIP
Lead Administrator

Copy: NEIRB Chair
University of Central Florida IRB
Enclosures

APPENDIX B: EXTERNAL IRB RELIANCE LETTER

University of Central Florida Institutional Review Board
Office of Research & Commercialization
12201 Research Parkway, Suite 501
Orlando, Florida 32826-3246
Telephone: 407-823-2901, 407-882-2901 or 407-882-2276
www.research.ucf.edu/compliance/irb.html

Notice that UCF will Rely Upon Other IRB for Review and Approval

From : **UCF Institutional Review Board**
FWA00000351, IRB00001138

To : **Gerald T. Mangine**

Date : **June 12, 2014**

IRB Number: SBE-14-10276

Study Title: **MAGNITUDE OF HYPERTROPHY IN RESPONSE TO TRAINING VOLUME VERSUS INTENSITY IN RESISTANCE-TRAINED MEN**

Dear Researcher:

The research protocol noted above was reviewed by the University of Central Florida designated Reviewer on **June 12, 2014**. The UCF IRB accepts the New England Institutional Review Board's review and approval of this study for the protection of human subjects in research. **The expiration date will be the date assigned by the New England Institutional Review Board and the consent process will be the process approved by that IRB.**

This project may move forward as described in the protocol. It is understood that the New England IRB is the IRB of Record for this study, but local issues involving the UCF population should be brought to the attention of the UCF IRB as well for local oversight, if needed.

All data must be retained for a minimum of five years (six if HIPAA applies) past the completion of this research. Additional requirements may be imposed by your funding agency, your department, or other entities. Access to data is limited to authorized individuals listed as key study personnel.

Failure to provide a continuing review report for renewal of the study to the New England IRB could lead to study suspension, a loss of funding and/or publication possibilities, or a report of noncompliance to sponsors or funding agencies. If this study is funded by any branch of the Department of Health and Human Services (DHHS), an Office for Human Research Protections (OHRP) IRB Authorization form must be signed by the signatory officials of both institutions and a copy of the form must be kept on file at the IRB office of both institutions.

On behalf of Sophia Dziegielewski, Ph.D., L.C.S.W., UCF IRB Chair, this letter is signed by:

Signature applied by Patria Davis on 06/12/2014 11:25:49 AM EDT

IRB Coordinator

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