RESISTANCE EXERCISE REPETITION LOAD ON HYPERTROPHY AND STRENGTH

THE EFFECT OF RESISTANCE TRAINING REPETITION LOAD ON MUSCULAR HYPERTROPHY AND STRENGTH IN YOUNG RESISTANCE TRAINED MEN

By  
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**Lay Abstract**

Resistance training (RT) results in an increase in muscle growth and an increase in strength. Previously, we have shown in young untrained males, that when exercise is performed until failure, or until the weight can no longer be lifted, that gains in muscle and strength were similar with the use of either light or heavy weights. The purpose of the study was to determine the effects of 12 weeks of RT on muscle growth and strength in young men who were already regularly participating in resistance exercise when performing either lower load high repetition RT (HR) or higher load low repetition RT (LR). Maximum strength and changes in muscle mass were assessed prior to and upon completion of the training protocol. Following 12 weeks of RT both groups increased muscle mass and strength to a similar extent with the exception of bench press which increased more in the LR group.

**Abstract**

Resistance training (RT)-induced skeletal muscle hypertrophy is partly responsible for the RT-induced increase in strength. Previously, we reported that exercise repetition load played a minimal role in the promotion of RT-induced gains in hypertrophy and strength gains in RT-naïve participants performing RE to volitional failure. Thus, the main aim of this study were to determine the effects of 12 weeks of RT on muscle strength and hypertrophy in a trained population.49 resistance-trained men (mean ± SEM, 23 ± 1 years, 85.9 ± 2.2 kg, 181 ± 1 cm) were randomly allocated into a lower load-high-repetition group (HR, n=24) or a higher load-low-repetition group (LR, n=25). Repetition load was set so that volitional lifting failure was achieved within the repetition ranges of 20-25 (~35-50% of 1RM) for HR or 8-12 for LR (~70-85% of 1RM). Strength as one repetition maximum (1RM) was assessed pre and post. Changes in lean body mass (LBM), appendicular lean mass (ALM) and leg lean mass (LLM) were assessed using dual-energy x-ray absorptiometry (DXA). There were significant increases in strength in all exercises with no differences between groups (p> 0.05) with the exception of bench press where LR showed a greater increase in 1RM than HR (*p* = 0.012). Similarly, LBM, ALM, and LLM increased significantly following training in the HR group (1.0 ± 0.9kg, p < .001; 0.8 ± 1.1 kg, p< 0.05; 0.7 ± 0.9 kg, p < 0.01 respectively) and the LR group (1.6 ± 1.4 kg, p< .001; 1.0 ± 1.2 kg, p< 0.05; 0.7 ± 1.0 kg, p< 0.01 respectively) with no significant differences between groups (all p> 0.05). These data show that RE performed to volitional failure using either HR or LR induces similar adaptations strength and lean mass accrual in young resistance-trained men.

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**LIST OF ABBREVIATIONS**

1RM one repetition maximum

ALM appendicular lean mass

BFR blood flow restriction

CSA cross-sectional area

DXA dual-energy X-ray absorptiometry

LBM lean body mass

LLM leg lean mass

iEMG integrated electromyographical

MRI magnetic resonance imaging

MPB muscle protein breakdown

MPS muscle protein synthesis

mTORC-1 mechanistic target of rapamycin complex 1

MU motor unit

MVC maximum voluntary contraction

PDCAAS protein digestibility-corrected amino acid score

RE resistance exercise

RT resistance training

**DECLARATION OF ACADEMIC ACHIEVEMENT**

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**CHAPTER I**

SKELETAL MUSCLE HYPERTROPHY AND STRENGTH WITH RESISTANCE EXERCISE

# I Resistance Exercise

The human body is comprised of ~45% skeletal muscle by mass [1]. Skeletal muscle is a critical organ that plays a key role in the generation of contractile force, post-prandial glucose disposal [2], and maintenance of this tissue is positively associated with metabolic health [3]. Skeletal muscle is also a unique and highly plastic tissue capable of changing its phenotype in response to alterations in the load, frequency, and duration of contractile activity. The nature of these adaptions is, however, specific to the type of stimulus. For example, performing endurance exercise results in improved fatigue resistance due in part to an increase in mitochondrial density and oxidative capacity [4]. In contrast, repeated bouts of high intensity, loaded contractions (i.e., resistance exercise), induces the rapid recruitment of type 2 fibers and an increase in muscle fiber cross-sectional area and a lesser stimulation of oxidative capacity [5,6]. Resistance exercise training also induces favorable strength adaptations [7]. Thus, it is unsurprising that exercise, particularly resistance exercise, has long been utilized as an effective strategy to improve human health and athletic performance [8].

Resistance exercise (RE) is the only non-pharmacological method for inducing gains in skeletal muscle mass, termed hypertrophy. These gains are often highly variable between individuals but have been cited as occurring at a rate of ~0.1% per day up to a certain point [9]. The definition of RE is the purposeful, repeated movement of a resistance (load) to muscular contraction that is greater than what would be observed in activities of daily living [10]. The goals of chronic resistance exercise, resistance training (RT), often involve the manipulations of: (i) load per repetition (often called intensity), which is most often prescribed as a percentage of single best lift or one repetition maximal strength (1RM); (ii) number of sets performed; (iii) recovery between sets; (iv) muscle action (concentric vs. eccentric); and (v) total exercise volume (i.e., load × repetitions). The effects of differing regimes of RT on strength and muscular hypertrophy were first documented in 1945 by Thomas Delorme who examined the impact of RT to restore strength and power in atrophied muscles following injuries in soldiers [11]. These guidelines were then investigated in *poliomyelitic* patients to determine the response of the *quadriceps femoris* to chronic RE [8]. Interestingly, it was shown that following approximately four months of progressive RT, there was a significant increase in muscular strength and thigh circumference [8]. These initial investigations preceded an array of studies attempting to elucidate the mechanisms by which RT increases human muscle size and strength. Despite this large body of work, a definitive RE program that is ‘optimal’ in inducing skeletal muscle hypertrophy has yet to be determined. Moreover, we remain largely ignorant as to the biology underpinning skeletal muscle hypertrophy in response to RE, especially in experienced RT athletes. As such, it is the aim of this chapter to synthesize an understanding of the literature relating to RT-induced skeletal muscle hypertrophy. For the purposes of concision and relevance to the human model, an in depth discussion of the molecular regulation of muscle mass will not be undertaken, nor will there be a focus on animal model-derived data; however, in the absence of experimental human data, animal research studies are cited to substantiate discussion points.

# II Neural Adaptions to RE training

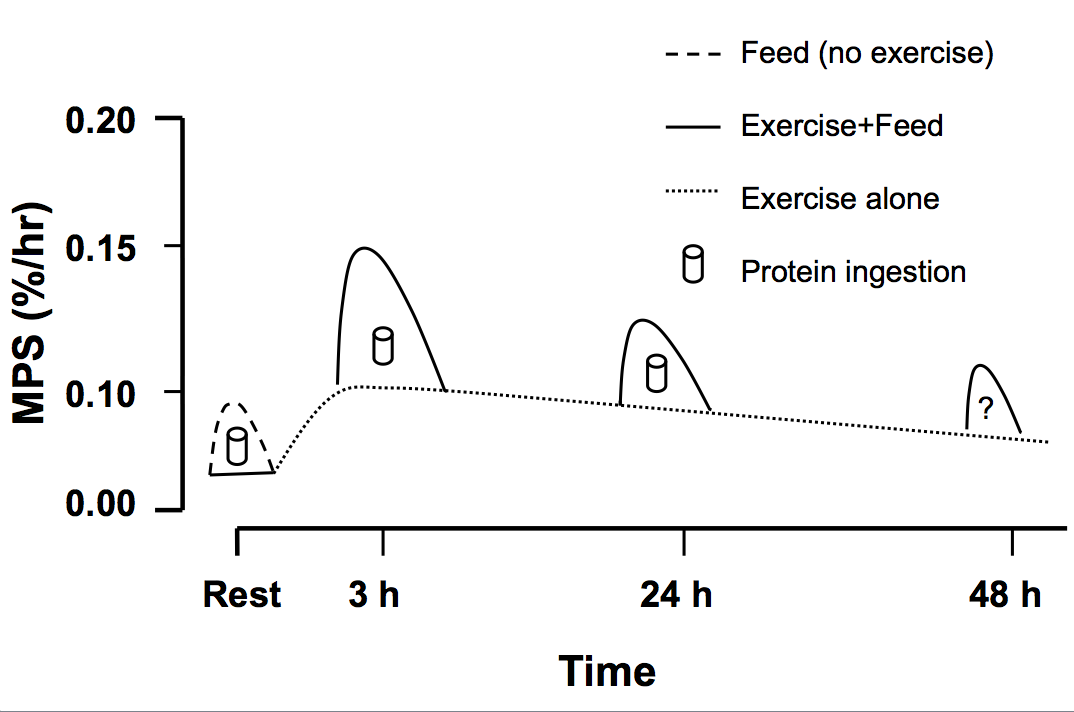
Neural adaptations to RT generally involve changes in muscle fibre/motor unit coordination, and central ‘learning’ that occur to facilitate increased motor unit recruitment, improved coordinated activation of motor units, and/or reduced antagonist muscle activation [10]. An increase in force production as a result of chronic loading is a hallmark phenotypic adaptation of skeletal muscle to chronic RE. Despite the correlation between muscle cross sectional area (CSA) and strength [12], it is clear that increases in muscle strength precede measurable changes in indices of skeletal muscle hypertrophy by ~3-4 weeks in naïve RT participants [13,14]. Following 3 weeks of training, however, it appears to be predominantly hypertrophy of the skeletal muscle fibers and an increase in cross-sectional area of the muscle that contribute to maximal developments in strength [14]. The ability to increase strength despite ‘maximal’ neural adaptation is of substantial importance for several populations but especially those who chronically perform RE. For example, Judge and colleagues examined sport-specific knee strengthening exercises in elite athletes to determine if maximal voluntary contraction (MVC) of the quadriceps could be increased with chronic RE [15]. They found that individuals who performed the RT intervention had a 10% increase in MVC despite no change in central (voluntary) activation of the quadriceps muscle [15]. The absence of an increase in neural activation with RT in a previously trained population is in agreement with the findings of Häkkinen et al. [16]. In studying elite weight lifters, these authors noted an increase in maximal Olympic-style lifting of ~7.5 kg following training over a 2 year span with no measurable change in muscle fiber cross-sectional area [16]. These studies provide evidence that despite training status or the achievement of ‘full’ neural recruitment, the potential still exists for further increases in strength above what is thought to be maximal.

Past examinations of alterations in motor unit recruitment have yielded variable findings. The integrated electromyographical (iEMG) signal (muscle fibre activation) has been widely accepted as the common measurement to assess neural activity within skeletal muscle. As the bulk electrical signal that represents the sum of electrical contributions made by active motor units, iEMG is usually measured by electrodes placed on the skin above the activated muscle and is often used to determine if a muscle activation is increased following a training stimulus [17]. Using iEMG, Narici and colleagues observed the effects of strength training using an isokinetic movement on a dynamometer on quadriceps muscle activation over 60 days in untrained males [18]. Participants performed six sets of ten isokinetic knee extensions 4 times per week on one leg only. Training resulted in a significant increase (~42%) in the iEMG signal in the trained leg and, despite remaining untrained, they also observed a non-significant increase in iEMG of 25% in the untrained leg [18]. These findings suggest that studies implementing a unilateral RT design as a within-subject control would have to be aware of cross-adaptation to the untrained limb [18]. There are inherent issues in using surface EMG analysis across time in a longitudinal manner, however, such as electrode placement and replacement, changes in impedance (thickness) of the skin/fat, and changes in muscle morphology that could cause variability in the repeatability and reliability of these measurements with chronic RE [19–22]. Furthermore, contradictory evidence exists as to whether maximum activation of the motor units innervating fibres of a given muscle are increased as a result of RT [23,24]. In summary, changes in neural activation of skeletal muscle fibres are seen early with RT and have an impact on strength gains seen in the initial weeks of beginning RE and are a greater contributor to strength gains in untrained persons; however, increases in muscle mass/muscle fibre CSA drive the increases in strength in the latter phases of most RT programs.

# III Protein Synthesis and Hypertrophy

## III.i Protein Synthesis and Resistance Exercise

Changes in skeletal muscle size are underpinned, in part, by the feeding-driven changes in muscle protein synthesis (MPS) and muscle protein breakdown (MPB). Increases in muscle fibre cross-sectional area due to RT occur when aggregate rates of MPS exceed those of MPB [25]. In the post-absorptive state, MPB exceeds MPS resulting in a state of net catabolism. With provision of amino acids (protein ingestion), MPS is stimulated and MPB is reduced such that MPS is greater than MPB resulting in net protein accretion [26,27]. Young healthy men and women who consume adequate daily protein fluctuate between periods of negative and positive protein balance which remain roughly equal throughout a day resulting in the maintenance of muscle mass [28]. Changes in the rates of MPS in response to a bout of acute fasted-state RE have been examined with several variations in training stimulus. Phillips and colleagues aimed to determine the changes in MPS associated with an acute RE routine in untrained participants. They found that RE resulted in a significant increase in mixed muscle protein fractional synthetic rate (FSR, the tracer-derived measurement of MPS) above rest in the quadriceps muscle at times 3 hours (112%), 24 hours (65%) and 48 hours (34%) [29]. These data are in agreement with Kim et al. who compared the acute MPS response in a within subject design, where one limb performed chronic RE for 8-weeks while the other did not. In response to an acute bout of RE it was determined that rates of myofibrillar protein MPS were elevated in both the trained (+44%) and untrained limbs (+42%) [30]. Taken together what these data show is that RE is a potent stimulus for inducing changes in MPS, however, we know that in order to maximize the MPS response that protein consumption is necessary. When a sufficient, high quality dose of protein is consumed following RE there is a synergistic interaction between the post-meal hyperaminoacidemia and the contractile stimulus to further augment MPS [28,31]. Thus, RE serves to ‘sensitize’ skeletal muscle to the anabolic impact of protein feeding. As such, repeated bouts of RE and protein ingestion often lead to expansion of the muscle protein pool and thus skeletal muscle hypertrophy. Although it is known that protein ingestion enhances RE-induced rates of MPS, the timing of protein ingestion has been shown to have an important mediating effect on MPS. Immediate post exercise consumption of high quality protein serves as an effective strategy to enhance MPS greater than RE alone [32–34]. Timing of protein consumption is of critical importance as exercise induced stimulation of MPS is the greatest following exercise [35]. This concept has been termed the “anabolic window wherein a dose of protein, and subsequent hyperaminoacidemia, will have the greatest stimulatory effect when consumed in close temporal proximity following the performance of exercise. The duration of this anabolic window is, however, still debated. Dreyer and colleagues demonstrated that following an intense bout of RE in young males, that rates of MPS of the quadriceps were increased by 145% from baseline an hour following the immediate consumption of an essential-amino acid and carbohydrate beverage compared to a 41% increase following the consumption of a control beverage [36]. West and et al, examined the MPS response 3-5 hours following a bout of RE in combination with the consumption of amino acids where they saw significant continued elevations in FSR [37]. Burd and colleagues then carried out similar investigation over a 24-hour period following RE to determine if this window would remain sensitive to protein feeding a full day after intense exercise. Groups performed one of three exercise sets; a high load (90% of the subjects maximal strength – 1RM) until volitional failure, a work matched set with a low load (30% 1RM, matched) or at a low load until volitional failure (30% 1RM, failure). Interestingly, it was only when exercise was performed to failure, that sensitization of the quadriceps muscle remained elevated 24-hours following the protocol alluding to the concept that perhaps it is a high recruitment of the muscle, particularly type II fibers, that are required for maximum sensitization to aminoacidemia [38]. Taken together, what these data highlight is that RE serves to sensitize skeletal muscle to the anabolic impact of amino acid ingestion; however, this an effect that can persist for up to 48 h following the cessation of a maximal exercise bout (Figure i).



Evidently, protein ingestion has the ability to maximize the acute MPS response following RE though it is ultimately the sum of frequent episodic bouts of heightened anabolism resulting from chronic RT that are fundamental for the augmentation of lean mass. Willoughby and colleagues [39] examined whether supplementation with protein before and after RE would result in greater gains in fat free mass than a placebo control over a 10-week training period. Nineteen untrained young men participated in RT 4 times peer week and consumed either a total of 40 grams of protein before and after training or a placebo control composed of dextrose. Following the training period, individuals consuming the protein supplement had a greater increase in body mass (2.65 kg), fat free mass (2.93 kg), and thigh mass (0.32 kg) compared to the placebo control [39]. Similarly, Kerksick et al. [40] examined the effects of protein consumption and exercise on body composition over 10 weeks. Participants were randomized to consume either 42 grams of protein or a placebo control immediately following exercise. Ingestion of protein resulted in an increase in lean mass of 1.9 kg while ingestion of the placebo beverage resulted in no change in total lean body mass [40].

**Figure i.** Resistance exercise stimulates a prolonged elevation in MPS that can remain elevatd for up to 48 hours; used, with permission, from Churchward-Venne et al., 2012 [27].

It is also important to consider the timing of protein ingestion and its effects over a training period. Cribb and colleagues [41] examined the effects of protein supplementation timing in recreational male body builders. Participants were randomized to consume 40 grams of protein either PRE-POST (prior to and immediately following RE) or MOR-EVE (prior to breakfast and prior to sleep) on each training day, 4 times per week for 10 weeks. Individuals consuming protein in the PRE-POST pattern were able to significantly increase lean body mass by 2.8 kg compared to 1.5 kg in those consuming protein in the MOR-EVE pattern. Similarly, the PRE-POST supplementation group demonstrated an increase in the CSA of type IIa and type IIx fibers by 25% and 25.3% respectively following the 10-week protocol compared to a 17% and 17.8% increase in the MOR-EVE group. Taken together, protein consumption in close temporal proximity to a RE bout results in significant lean mass increases when performed chronically. Therefore several factors should be taken into account when aiming to maximize RE-induced lean mass gains with protein consumption.

## III.ii Role of Protein Dose and Quality

Protein quality and dose are also critical when targeting maximal increases in lean mass accrual. Protein quality was previously defined with the use of the protein digestibility-corrected amino acid score (PDCAAS), which defines proteins according to their essential amino acid content and digestibility relative to the reference (egg) protein [42]. This amino acid score is used to predict protein quality to determine the potential capacity of the protein in food sources to provide amino acid needs. The importance of amino acid digestibility is crucial as undigested dietary proteins may be unabsorbed and excreted rather than being absorbed in the small intestine or contributions to lean mass [43]. Proteins with the highest digestibility and quality scores are given a maximum value of 1.0 and include casein protein, soy protein, whey protein and egg protein [44]. More recently, the Food and Agriculture Organization (FAO) has endorsed the digestible indispensible amino acid score (DIAAS) to assess protein quality which improves upon the PDCAAS as it is able to distinguish between proteins that were previously classed at an equivalent value [45]. The DIAAS score also samples protein digestibility from the ileum rather than from fecal matter as was measured for the determination of the PDCAAS. Using the DIAAS, proteins with the highest digestibility and quality scores are the two main milk proteins casein and whey, which have scores of 1.18 and 1.09, respectively. These DIAAS scores for casein and whey are in comparison to soy protein which was given a value of 0.91 but was previously scored as equivalent to milk proteins under the PDCAAS at 1.0 [45]. The impact of the difference in proteins, reflective of the DIAAS scores, was shown by Wilkinson et al. [46] who investigated the acute effects of either fluid skimmed milk (containing both whey and casein protein in a ratio of 1:4) or an isonitrogenous soy protein beverage on MPS three hours following acute maximal RE. Milk ingestion (500mL) resulted in an FSR of 0.1%/h which was significantly greater than that stimulated by soy protein of 0.07%/h [46]. When translated into chronic consumption, during a 12-week resistance training protocol, Hartman and colleagues [47] demonstrated a significantly greater increase in lean body mass and Type II muscle fiber cross-sectional area only in participants consuming milk as a post-exercise supplement versus a soy beverage or an isoenergetic control [47]. The results of Wilkinson et al. [46] and Hartman et al. [47] are potentially a reflection of the higher DIAAS of whey and casein protein as compared to soy protein. Importantly, casein and whey have higher leucine contents than soy, let alone a number of other essential amino acids. This is particularly important as data from our own laboratory has demonstrated that increasing the leucine concentration of a low protein mixed macronutrient beverage rescues rates of postprandial MPS to those seen with higher protein contents [48]. Moreover, leucine is a key trigger of the mechanistic target of rapamycin complex 1 (mTORC1), a 280 kDa serine/threonine kinase known to activate key translation initiation factors involved in MPS [49].

Given that supplementing with higher quality protein is crucial to maximizing lean mass accretion with RT, dosing of protein should also be considered. In healthy young men, ~20 grams of protein is optimal to maximally stimulate MPS following a RE bout. This dosage was determined to be sufficient by Moore and colleagues where they examined the dose-response relationship of MPS and protein consumption [33]. Healthy male participants ingested 0, 5, 10, 20 or 40 grams of high quality protein on five separate occasions throughout the study period. Rates of MPS increased in a dose-dependent manner until the dose exceeded 20 grams, after which no significant increase in MPS was detected [33]. This graded response of MPS to lower doses of protein is also in agreement with the findings of Tipton and colleagues who observed a similar increase in post RE net amino acid balance following the ingestion of 21 grams and 40 grams of high quality protein [50].Thus, it is evident that protein quality, supplement dose, and supplement timing should be considered when aiming to capitalize on the anabolic response of RE to feeding.

# IV Measurement of Skeletal Muscle Hypertrophy

Skeletal muscle hypertrophy, due to RT is postulated to occur as the result of summed periods of repeated acute exercise-induced increases in MPS followed by protein consumption. Though increases in strength are attainable without changes in muscle CSA, increases in muscle hypertrophy are crucial to sustain and/or perpetuate changes in muscle strength as RT progresses. Previously, reliable measurements for assessing changes in muscle hypertrophy were not widely available and thus strength was often used as a proxy measure [8,14]. For example, in a series of studies by Berger et al. the aim was to determine the optimum prescription for RE with strength remaining the primary outcome measure [51]. For example, in 1962 Berger conducted a 12-week randomized trial in an attempt to determine the optimal number of sets, repetitions, and frequency of RE to increase muscular strength. He determined that 3 sets of 6 repetitions per set, 3 times per week was the most effective way to maximize bench press strength by comparing 6 different exercise regimens [51]. Although the sample size was not what one would consider valid (one participant per exercise group), the results are nonetheless similar to those that are prescribed to this day when individuals are aiming for strength gains. It has only been more recently that changes in body composition as a result of RE have become a major area of study. In 1980, MacDougall [52] and colleagues investigated the effects of chronic RE followed by immobilization or vice versa to examine strength and lean mass changed in healthy young males. Not surprisingly, fast and slow twitch fiber CSA increased with RE and decreased with immobilization as was determined by the measurement of muscle fibers. Similarly, strength, which was measured by maximum voluntary isometric contraction, varied as a function of CSA change [52]. Therefore it is clear that muscle CSA mediates changes in muscle strength in young adults and as such if a goal of a RT program is to increase strength by a substantial amount, focusing on strategies to enhance muscular hypertrophy are of the utmost importance.

Various techniques have been adopted to evaluate changes in muscle hypertrophy. Each has differing sensitivities to detect change and also to discriminate between tissue types. Previous rudimentary assessments such as measurement of muscle girth [8] have been replaced by advanced imaging techniques which can be used to evaluate single muscle, muscle fibre, or whole body changes. Currently, Dual-Energy X-ray Absorptiometry (DXA) is the most widely used method to determine changes in whole body lean mass. The DXA method uses two low energy x-rays and their relative attenuation by body tissues to quantify body tissues into a 3 compartment model (see Figure II below), but is primarily aimed at measuring bone mineral content and density (the main purpose of the DXA machine), fat content, and fat- and bone-free (i.e., lean) content. Fat- and bone-free mass is a proxy for lean mass and when this DXA-derived body compartment increases with RT it is assumed to represent growth of muscle. The major disadvantage of the DXA for use as a body composition measure is its lack of sensitivity to determine smaller changes in lean mass and also that it cannot examine the compartments of a single muscle; however, it can be used to analyze muscle by groups in the body [53]. Muscle fibre CSA measured using histochemical approaches is another way in which hypertrophy can be assessed. As opposed to a whole body estimate, muscle fibre CSA change is indicative only of the muscle fibre. In this method, a muscle biopsy sample is fixed, sectioned, mounted on a slide and histologically stained, usually for fiber type, to derive area. The slides are then digitally photographed and quantified, and the change in CSA of varying fiber types can be compared following an intervention involving hypertrophy or atrophy of the muscle fibers [54]. The disadvantage to this approach is that the mounted image is a sample of only a small portion of the muscle biopsied and thus may not be representative of changes occurring elsewhere in the body. A risk also exists when assessing muscle fibre CSA in that fibres that are not completely perpendicular to the cutting plain of the cryotome resulting in obliquely oriented fibres that are larger than they would normally be. Nonetheless, problems with fibre orientation can be corrected by remounting and re-sectioning the tissue to obtain a more accurate fibre CSA. The gold standard for measuring whole muscle hypertrophy is with magnetic resonance imaging (MRI). Using MRI involves capturing high-resolution cross-sectional images of the desired muscle group and the compartments of muscle, fat, and bone can be determined using grey-scale algorithms using image-processing software. Knowing the image width, sequential cross-sectional images can then be used to calculate muscle volume resulting in indications of changes in size in 3 dimensions [6]. The only major disadvantage of the use of MRI as a body composition tool is that in many instances in which multiple assessments are required, it is financially untenable. As a result, many scientists employ other approaches to measure, or infer, changes in skeletal muscle size. For example, ultrasound has also more recently been employed for use of evaluating muscle thickness, as a proxy measure of muscle hypertrophy, as it is non-invasive and low cost [55]. However, the benefits of ultrasound-measured muscle thickness are balanced by a method that has lower reproducibility, as it is highly dependent on the skill of the operator, sensitive to the position of the limb or segment, and the pressure applied to the probe. Muscle thickness also yields a one-dimensional image of the muscle and therefore it is not sensitive to three-dimensional changes in muscle morphology [56,57]. It is clear that all of the aforementioned methods have various advantages and disadvantages depending on the muscle or body composition variable being studied though over all, DXA is the most widely used to determine whole body composition (Figure ii).

# Macintosh HD:Users:SaraOikawa:Documents:MSc.:MSc. Thesis:Thesis Documents:3 compartment Model:Slide1.jpgV Resistance Training Recommendations

**Figure ii.** Compartments represented in the 2 and 3 compartment models of body composition. FFM; Fat free mass, FBFM; Fat bone-free mass.

The first recommendations for inducing skeletal muscle hypertrophy with the goal of increasing strength and performance were documented in a seminal paper by Delorme in 1945 [11]. Delorme studied the effects of varying protocols of RT to affect the quadriceps function in soldiers who were rehabilitating after World War 2. From his findings he concluded that low repetition, higher resistance exercises should be used to produce ‘favourable’ changes in muscle strength while high repetition, low resistance exercises should be used to produce muscular endurance. Furthermore, the author concluded that “*each of these two types of exercise is incapable of producing results obtained by the other*” [11]. Although 70 years have passed since the work of Delorme, the accepted protocols for promoting changes in muscle phenotype remain remarkably unchanged. The most recent position stand from the American College of Sports Medicine likely represents one of the most widely accepted and implemented guidelines used in the development of resistance training programs, aiming to increase muscle mass [58]. The 2002 ACSM position stand entitled *Progression models in resistance training for healthy adults* states that the *optimum* [59] RT program for the increase in muscular hypertrophy involves repetition ranges of 8-12 repetitions per set at a load between 70-85% of maximal strength, which is most often guided by measurement of single-lift maximal strength or 1RM. Additionally, the same position stand suggests a repetition range of 10-25 reps per set at a lighter resistive load as being more favourable for adaptations to promote muscular endurance not unlike what was suggested by Delorme [58]. It is proposed that a careful reading of the ACSM position stand also implies, as did Delorme, that the goal of muscular strength and muscular endurance are mutually exclusive.

The purpose of the most current ACSM position stand (2009) [58] was to include a more robust selection of literature which had been recently developed following the publication of the position stand created in 2002. Upon close examination it is clear that references within the 2009 document detailing the guidelines for optimize hypertrophy contain only a single study supporting the notion that heavier loads are associated with greater hypertrophy [5]. The cited study [5] by Campos et al., detailed the examination of the effects of an 8-week resistance training program on hypertrophy and strength in young, untrained men performing either low repetition (3-5 repetitions/set), intermediate repetition (9-11 repetitions/set) or high repetition (20-28 repetitions/set) whole body exercise. Exercise was performed twice per week for the first 4 weeks and then three times per week for the final 4 weeks of the program. The authors reported that the lower repetition group had the greatest increases in muscular CSA and strength measured by 1RM. While the higher repetition group demonstrated improvements, overall these improvements were not maximally beneficial. It is interesting to note that the groups performing “intermediate” repetitions and “high” repetitions as dictated by study design, are reflective of the suggestions made by the ACSM position stand and when these groups are compared there was no significant difference in the increase in leg extension or squat 1RM. However, strength gains were greater in the low repetition group. Nonetheless, strength gains were attainable based on the recommendations by the ACSM. It is also likely that the groups in this study were too small and thus, the study was underpowered, to show differences between groups [5]. Sample sizes ranged from 7-11 participants per group and it is well documented that the hypertrophic response to RE is highly variable [60]. It should be noted that this particular publication [5] was extremely influential in shaping the 2009 guidelines and that many of the authors of this study [5] were also those who authored the ACSM position stand [58]. Unfortunately, in the position stand, the authors failed to include data from a study performed by Léger and colleagues [61] that implemented the identical RT protocol as that used by Campos et al [5], however, in which significant differences between higher- and lower-repetition groups were not observed. In addition, 1RM strength in the squat, leg press or leg extension exercises were significantly increased from baseline; however, there were no differences between groups and similarly that increases in quadriceps volume following training were approximately 10% with no differences between groups [61]. Clearly, the current ACSM position stand lacks clarity and bona fide experimental evidence in regards to their suggested prescriptions for inducing hypertrophy and strength and thus one of the overarching purposes of the current study was to better elucidate the phenotypic changes that occur with RT in subjects engaging in protocols utilizing differing repetition ranges, performed to fatigue.

Recommendations for the use of heavy loads during RT to induce muscle hypertrophy have been prescribed despite what I view as there being a sparse supply of evidence that confirms the superiority of this prescription over the use of lighter RE loads. It is important to acknowledge that strength training with heavy loads is effective at increasing muscle CSA when RE is performed over a significant period of time [13,18,62]. Whether heavy loads are superior to lighter loads is still, I would propose, equivocal as the results of a recent meta-analysis would suggest [63].

When comparing the effects of RE load on CSA, it is important to consider the volume of exercise that is performed. Holm et al. used a unilateral model to evaluate the adaptive changes in muscle size with RE loads of either 16% of 1RM for 36 repetitions or 70% of 1RM for 8 repetitions on each leg. Following 12 weeks of training, limbs training with both heavy and light loads demonstrated a significant increase in quadriceps CSA; however, the limbs performing heavier loading showed a 5% greater increase (7.6% increase in the lower rep group and 2.6% in the higher rep) [64]. Thus upon initial investigation it would appear that heavier RE loads do result in greater hypertrophy if repetition ranges are set to ensure similar workloads and that lighter RE loads are inefficient in attaining similar muscular hypertrophy.

Contrary to the ACSM guidelines [58], it has recently been suggested that repetition-load (exercise load) plays a lesser role in the hypertrophy response so long as volitional fatigue is achieved when lifting with a lighter load [63]. Another example of how lighter loads can result in hypertrophy comes from studies in which blood flow restriction (BFR) has been employed. Using BFR with flow occlusion cuffs, a process that induces the rapid fatiguing of smaller MUs and thus, type I muscle fibres at a low loads resulting in early onset recruitment and fatigue of larger MUs and type II fibres. Results from with the use of this technique have reported similar increases to traditional RE-induced MPS. Fujita and colleagues [65] examined the effects of low-load RE with and without vascular occlusion of the quadriceps. Subjects acted as both intervention and control with a wash out period of three weeks in-between. RE was performed at 20% of 1RM for 30 repetitions and the MPS response was measured 3 hours following exercise. The authors reported that vascular occlusion induced an increase in MPS of 46% while the non-occluded condition yielded no change in MPS [65]. This increase in MPS was most likely due to the more rapid MU recruitment and resulting increased muscle fiber recruitment associated with earlier fatigue induced by vascular occlusion despite the use of a lower load. Henneman’s size principal [66] dictates that MUs within a muscle are recruited in an orderly fashion from smallest to largest based on neuronal diameter to generate a required force. MUs that innervate type I fibres tend to have smaller diameters while MU innervating type IIa and IIx muscle fibres have larger neuronal diameters [67]. For a ‘low demand’ force that is less strenuous, it would be primarily type I MUs would be recruited. In contrast, for a more strenuous demand such as lifting a heavy load, or when vascular occlusion is used to cause premature fatigue, the recruitment of larger MUs innnervating type IIa or type IIx fibres would be more rapid to match the required force output [68–70]. Taken together, it can be argued that inducing significant fatigue, through BFR, will result in increased MU recruitment and fibre activation resulting in similar hypertrophic adaptations. However, this is not restricted to BFR, since RE with high or low loads, so long as fatigue were achieved, would hypothetically result in hypertrophy of the muscle fibers caused by increased activation [24]. Thus, with lower loads it is the repetitive full recruitment of MUs that helps to drive increases in skeletal muscle hypertrophy and strength. Table I lists several studies that have been conducted involving the use of high and low repetition ranges where outcomes measures were hypertrophy and strength.

**Table I**. Overview of studies examining chronic high and low repetition RE protocols on hypertrophy and strength.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Study | Participants | Design | Volume Equated | Failure | Hypertrophy measure | Findings |
| Alegre et al. (2015)[71] | 15 UT young women | Unilateral design with one limb performing increasing intensity (50-80% RM) 3 sets, 6 reps and the other at 50% RM for 3 sets. 3 days per week, 10 weeks | Yes | No | B-mode ultrasound and DXA for muscle mass | Significant increases in strength and hypertrophy. No significant difference between groups |
| Bemben et al. (2000)[72] | 25 UT postmenopausal women | RA to 3 sets of 80%RM for 8 reps or 40% RM for 16 reps. 3 days per week, 6 months | Yes | No | B-mode ultrasound, DXA | Significant increases in strength and hypertrophy. No significant difference between groups except in upper body strength in which low rep was significantly greater |
| Campos et al. (2002)[5] | 32 UT young men | RA to either 3-5 RM, 9-11 RM, 20-28 RM. 2-4 sets, 3 days a week, 8 weeks | Yes | No | Muscle biopsy (fibre CSA) | Significant increases in CSA for low rep group. Significantly greater increases in strength for low repetition |
| Holm et al. (2008)[64] | 12 UT young men | Unilateral exercise with one limb performing 70% RM for 8 reps and the other limb performing 15.5% RM for 36 reps. 3 days per week, 12 weeks | Yes | No | MRI, muscle biopsy | Significant increases in CSA and strength in both groups. Greater increases in low repetition |
| Léger et al. (2004)[61] | 25 UT young men | RA to either 3-5 RM, 9-11 RM, 20-28 RM. 2-4 sets, 3 days a week, 8 weeks | Yes | No | CT | Significant increases in strength and CSA. No significant difference between groups |
| Mitchell et al. (2012)[6] | 18 UT young men | RA to perform 2 of 3 unilateral leg extension protocols: 3 sets of 30% RM, 3 sets of 80% RM or 1 set of 80% RM. 3 days per week, 10 weeks. | No | Yes | DXA scan | No differences in CSA between low and high repetition. Significantly greater strength gains in low repetition |
| |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | Taffe et al. (1996)[73] | 36 UT postmenopausal women | RA 3 sets of either 40% RM for 14 reps or 80% RM for 7 reps. 3 days per week 12 weeks | Yes | No | Muscle biopsy | Significant increases in strength and CSA. No significant difference between groups | | 36 UT postmenopausal women | RA 3 sets of either 40% RM for 14 reps or 80% RM for 7 reps. 3 days per week 12 weeks | Yes | No | Muscle biopsy | Significant increases in strength and CSA. No significant difference between groups |
| Van Roie et al. (2013)[74] | 56 UT elderly adults | RA to either 2 sets of 10-15 reps at 80% RM, 1 set of 80-100 reps at 20% RM or 1 set of 60 reps at 20% RM followed by 10-20 reps at 40% RM. 3 days per week, 12 weeks | No | Yes | CT | No differences in muscle volume between groups. Greater increases in strength for groups performing 80% RM and the greater volume of exercise (20% + 40% RM) |
| RM, repetition maximum; CSA, cross-sectional area; CT, computerized tomography; MRI, magnetic resonance imaging; UT, untrained; T, trained; RA, randomly assigned | | | | | | |

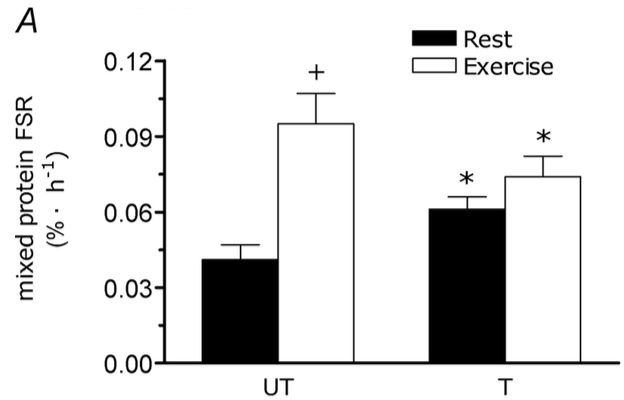
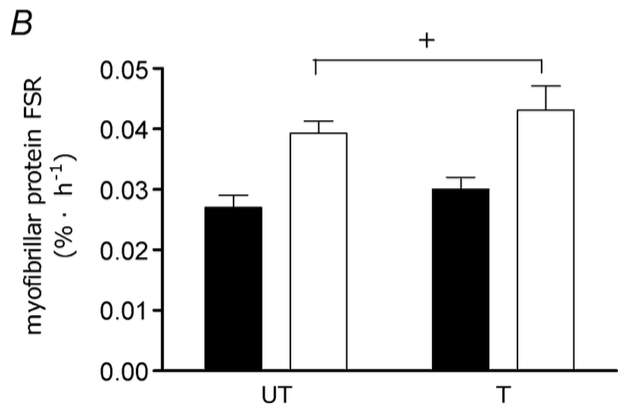
Despite controversies in RT program development, a result of RT-induced hypertrophy is an increase in strength. As the studies detailed in Table I show, as well as the results of a recent meta-analysis [63], evidence is emerging that supports a lack of a divergent hypertrophic response after performing higher or lower repetition RT. As was mentioned previously, Campos et al. [5] reported a significant difference in hypertrophy and strength with high and low repetition RT in *untrained men*; however, this result was not mirrored when the same program was replicated by Léger et al [61] In addition, previous work from our group demonstrated similar increases in quadriceps volume when participants performed RT either at 30% or 80% of their 1RM, with both conditions taken to failure [6]. Using MRI to quantify quadriceps volume, it was found that there were no significant differences in the increase in quadriceps hypertrophy between the 80-3 and 30-3 groups as can be seen in Figure iii. These data substantiate the notion that lower loads can induce muscle accretion that is comparable to that induced by higher loads. These results were contrasted by a significantly greater increase in 1RM following training in that both 80-3 group demonstrating that heavy loads were superior in inducing strength gains if not muscular hypertrophy [6]. These significant differences in strength are in contrast to studies in which whole body, high and low load RE programs were compared and found no significant differences between groups in strength or in changes in lean mass as determined by DXA scan following training [71–73]. Clearly the optimal program for augmenting muscle strength and hypertrophy has yet to be elucidated for a healthy population, let alone for specific sub sets.

It should be noted that a common criticism of many of the studies included in Table I is that the participants involved were not experienced resistance trained persons and thus the responses are simply a response to any form of RT to induce hypertrophy in RT-naïve subjects. Thus, the applicability of these RT protocols may be redundant to a trained population. Indeed, support for the contention that training status matters can be seen in a study by Ahtiainen and colleagues [75] who compared a traditional RT protocol of 6-12 reps per set in untrained participants and strength athletes. They identified a significant increase in CSA of the quadriceps in the untrained participants of approximately 5 cm2 but no significant change in the quadriceps of the experienced weight lifters. The authors attributed a lack of increase in CSA in the trained population to the lack of specificity and potency of the RE stimulus to initiate a hypertrophic response [75]. However, it is more than likely that the trained participants had simply reached a ceiling in their hypertrophic response. It is important to note that the training program in this study [75] was not supervised and thus it is possible that participants did not fully adhere to the experimental instruction prescribed. The marginal hypertrophic response in a previously resistance trained population is not unanticipated since studies in which the acute MPS response to RE in the trained and untrained condition have shown a dampened MPS response in the trained state. For example, Tang et al., investigated the acute MPS response to a high intensity bout of RE following an 8-week intervention where only one limb of each subject performed RE [76]. In this model, MPS was measured in both a trained and untrained state from the same person. They found that RE resulted in a significantly elevated MPS in both the trained and untrained leg 4 hours following exercise however, it was only in the untrained leg that MPS remained significantly elevated following 28 hours [76]. This is in slight contrast to the results of Kim and colleagues [30] who saw no increase in FSR following RT in the trained leg but a significant increase in the untrained leg by 132% from baseline. It should be specified that the measurement of MPS in both the previous examples were of mixed muscle protein synthesis meaning that they incorporate the sarcoplasmic, mitochondrial, and myofibrillar fractions. When Kim and colleagues examined the myofibrillar fraction alone, they demonstrated a very similar, significant increase in both the trained (44%) and untrained (42%) legs as shown in Figure iv below.

**Figure iii.** Percentage change in quadiceps muscle volume following 10 weeks of RE at high load (80% 1RM) and low load (30% 1RM). There was a significant main effect for time (increase in quadicrps volume pre- to post- training, *p < 0.0001*). N=12 per condition. Drawn using data from Mitchell et al., 2012 [6].



Kim et al. [30] speculated that in the untrained state, RE is a novel stimulus and thus creates a disturbance in homeostatic balance causing an increase in the synthesis of all proteins. This is compared to the trained state where RE is no longer a novel stimulus and thus the rise in MPS is less pronounced in response to the exercise. The result is that in a trained state, the stimulus of RE is preferentially directed towards the synthesis of myofibrillar proteins that are essential for hypertrophy [30]. Taken together, it appears that the capacity does exist for a resistance-trained population to benefit from additional RE however, how load affects these adaptations remains unknown.



**Figure iv**. **A -** *mixed muscle protein FSR (% h*-1) in the UT and T legs at rest and following an acute bout of RE. \* Significantly different (p < 0.01) from the same value in the UT state; +Significantly different from rest in the same leg (p < 0.05**). B -** myofibrillar protein FSR (% h-1) in the UT and T legs at rest and following an acute bout of RE. +Significantly different from rest (main effect for exercise; p < 0.05). Note differences in axes scales between panels A and B. Values are means ± S.E.M. (n = 8). Data taken with permission from Kim et al, 2005 [30].

# VI Statement of Research Question and Hypothesis

It is clear from the review of published data that there exists a number of studies that suggest RE load is not a variable that markedly affects RT-induced training hypertrophy so long as loads are lifted to fatigue [6,61]. There are however, several studies that suggest that resistance exercise load is crucial in determining gains in measures of strength [5,64,74]. It is my contention that the discrepancies in strength gains may be a result of lack of full fibre recruitment in groups performing sets at a lower load as well as using equated volume between the groups. In an attempt to reconcile existing evidence debating the variation in strength gains with low load RE we aimed to assess the effects of 12 weeks of RT with ~30-50% of 1RM (20-25 repetitions) as compared with ~70-80% of 1RM (8-12 repetitions) both to volitional failure on skeletal muscle hypertrophy and strength. Specifically, it was hypothesized that significant increases in strength and skeletal muscle accrual would be observed *with no differences between repetition range groups*. These results are expected, since those performing 20-25 repetitions per set will perform a greater volume (repetitions x load) of work compared to those performing 8-12 repetitions per set and also result in greater fatigue at the end of each set (HR, 50-70% fatigued and LR, 20-30% fatigued). I also propose that the use of trained participants for this investigation will help to eliminate strength increases between the groups due to neural factors as these participants should have already attained strength via neural adaptations previously.

**CHAPTER II**

RESISTANCE EXERCISE LOAD DOES NOT MEDIATE SKELETAL MUSCLE HYPERTROPHY AND STRENGTH INCREASES IN TRAINED YOUNG MEN

# 1. Methods

## 1.1 Participants and Ethics

Forty-nine healthy, active males, (mean ± SD, 23 ± 1 years, 85.9 ± 2.2 kg, 181 ± 1 cm) that were resistance training for at least the past 2 years (4.4 ± 2.3 years, training > 2 sessions per week, for the past 2 years including at least 1 lower body session) volunteered to participate in this study. The rationale for choosing trained participants was to allow for comparison between trained versus untrained persons from a similar study, but in an untrained population [6]. Participants did not have any existing musculoskeletal conditions and were free of consuming anabolic steroids or other agents known to increase muscle mass. All participants were informed of the purpose of the study, experimental procedures and associated risks prior to participation and exercise testing. All participants gave verbal and written consent to the protocol approved by the Hamilton Integrated Research Ethics Board, conforming to the standards for the use of human subjects in research as outlined in the most recent Tri-Council policy statement on the use

of human participants in research (http://www.pre.ethics.gc.ca/pdf/eng/tcps2-2014/TCPS\_2\_FINAL\_Web.pdf). Participants’ characteristics can be seen in Table 1.

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | HR(n=24) | LR (n=25) | *p* |
|  |  |  |  |
| Age, *y* | 23 ± 2 | 23 ± 3 | 0.73 |
| Total body mass, *kg* | 84.6 ± 11.7 | 87.1 ± 18.2 | 0.57 |
| Height, *m* | 1.81 ± 1.0 | 1.80 ± 1.0 | 0.81 |
| BMI, *kg/m2* | 26.9 ± 4.6 | 26.0 ± 2.9 | 0.41 |
| Lean mass, *kg* | 65.7 ± 7.6 | 65.7 ± 7.4 | 0.99 |
| Total fat mass, % | 22.3 ± 7.0 | 20.2 ± 5.7 | 0.26 |
| Leg press 1RM, *kg* a | 357 ± 62 | 353 ± 82 | 0.87 |
| Bench press 1RM, *kg* a | 98 ± 19 | 97 ± 17 | 0.88 |
| Leg extension 1RM, *kg* a | 76 ± 15 | 76 ± 15 | 0.92 |
| Shoulder press 1RM, *kg* a | 91 ± 18 | 92 ± 22 | 0.87 |

**Table 1.** Participants' characteristics at baseline

Values are means ± SD, HR, high repetition group (20-25 repetitions per set), LR, low repetition group (8-12 repetitions per set). a Maximal isotonic strength measured as single best weight lifted (see METHODS for details).

## 

## 1.2. Experimental Design

Participants completed 12-weeks of whole-body resistance exercise training in a between-group design. Subjects were allocated to one of two possible conditions: performing three sets of 20-25 repetitions per set (~35-50% of 1RM), which we refer to as high repetition (HR) or performing three sets of 8-12 repetitions per set at approximately (~70-85% of 1RM), which we refer to as low repetition (LR).

## 1.3 Familiarization and Muscle Strength

Two weeks prior to the start of the training protocol, participants reported to the Exercise and Metabolism Research Laboratory and completed a familiarization session with all related exercise equipment to determine appropriate 10RM loads. Following 48-hours of rest from any exercise, participants returned to the laboratory to complete 1RM testing for the leg press (Maxam Fitness, Hamilton, ON, CAN), bench press, leg extension (Atlantis Inc., Laval, PQ, CAN), and shoulder press (Life Fitness, Rosemont, IL, USA). 1RM tests were completed at the start of each week during training following the completion of every 3-weeks of training and then again following the final training session. All strength testing was performed in strict and rigorous fashion by the same investigator and in accordance with published guidelines for assessment of strength. In brief, participants performed a warm-up prior to testing that consisted of light cardiorespiratory exercise on a cycle ergometer for ~5 minutes. A specific warm up of the given exercise was then performed at approximately 50% of the participant’s estimated 1RM based on 10RM testing [77]. Following the warm up, weight was increased by 10-20% for one repetition. Three to five minutes was of rest were given between each attempt. A successful attempt of 1RM was determined by full range of motion which was considered to be complete by the following: leg press 1RM, knee flexion of 90 degrees followed by full extension of the knees; bench press 1RM, contact of the bar against the chest in five-point body contact position followed by full extension of the elbows; for leg extension 1RM, full extension of the knee; for shoulder press 1RM, full extension of the elbows from a starting position of 90 degrees.

## 1.4 Body Composition

Body composition was assessed at the same time of day and in the same condition for each participant throughout the protocol. Following an overnight fast (~12h), when the participants were euhydrated and had not exercised for at least 24-hour prior. Dual-energy X-ray absorptiometry (DXA) measurements were conducted using a GE Lunar iDXA total body scanner (GE Medical Systems Lunar, Madison, WI, USA) and analyzed with software (Lunar enCORE version 14.1, GE Medical Systems Lunar, Madison WI, USA) in the medium scan mode. The machine was calibrated daily by using a 3-compartment Universal Whole Body DXA Phantom (Oscar, Jr; Orthometrix, Naples, FL). Participants were measured while wearing a pair of compression shorts (same for all scans). Each scan lasted ~10 minutes. The analysis regions used were standard regions where the head, torso, arms, and legs were subdivided by the software, but were subsequently checked manually, and in a blinded-manner, by an investigator.

## 1.5 Resistance Training Protocol

The RE-protocol consisted of 3 sets of 5 exercises per session that targeted all major muscle groups. Training sessions were circuit style and included 2 supersets and 1 single exercise. Supersets (exercises done in succession with no rest between exercises) consisted of 2 exercises (5 exercises per day) and were repeated for 3 sets with one minute of rest between sets. Exercises performed were:

incline leg press bench press

seated row cable hamstring curl

seated shoulder press bicep curls

skull crushers wide grip pull down

machine leg extension plank

Participants were asked to refrain from additional resistance exercise as well as aerobic exercise training. Exercise training was performed 4 d/wk (Monday, Tuesday, Thursday, and Friday). Circuit 1 consisted of the leg press, seated row, bench press, hamstring curl and planks and was repeated on Monday and Thursday. Circuit 2 consisted of shoulder press, standing bicep curls, prone skull crushers, lat pull down and leg extensions and was repeated on Tuesday and Friday of each week. Sets were performed in a drop-set fashion- i.e. until volitional failure at the set weight. To maintain repetitions within the designated repetition range, the exercise load was adjusted between sets. Reductions in exercise load between sets varied depending on the exercise performed but was approximately a 5% drop for the LR group and 10% for the HR group. All exercise sessions were individually supervised by personal trainers who instructed participants on correct form and technique. Both HR and LR groups performed 1RM testing at baseline and at weeks 3, 6, 9 and 12. 1RM tests were completed on the first day (Monday) every 3 weeks during training. Weeks that included 1RM testing (4, 7 and 10) involved only 3 prescribed RE days with 1RM testing to serve as the 4th exercise day. Participants consumed 30 grams of whey protein (BioPRO, Davisco Foods International, Le Sueur, MN) twice per day, following RE on training days to potentiate increases in MPS following training and immediately before bed to maximize increases in MPS while at rest [50]. On non-exercise days, participants consumed the first 30 grams in the morning and the second dose immediately before bed, similar to training days.

## 1.6 Statistical Analysis

All analyses were performed using SPSS (version 22.0, Chicago, IL, USA). The Shapiro- Wilk test was used to check data for normality. Baseline characteristics (body mass, height, strength and percent fat and lean mass) were compared between groups using an unpaired T-test. Strength and body composition measures were analyzed using a two-factor (group x time) mixed-model analysis of variance (ANOVA) with repetition load (between) and time (within) as the experimental variables. Significant interaction effects were further analyzed using a Tukey’s posthoc test whenever a significant interaction was found to isolate specific differences. Statistical significance was accepted when p ≤ .05. Results are presented as means ± SEM in text and graphs and as means ± SD in tables.

# 2. Results

## 2.1 Participant Characteristics and Anthropometrics

Participants were matched at baseline for age, height, total body mass, lean body mass (determined by DXA) and 1RM strength for leg press, bench press, leg extension and shoulder press with no differences between groups (*p* > 0.05; Table 2). Twelve weeks of RT resulted in a significant increase in LBM, appendicular lean mass (ALM), and leg lean mass (LLM) in the HR group (1.01 ± 0.87kg, *p* < .001; 0.81 ± 1.14 kg, *p* < 0.05; 0.66 ± 0.92 kg, *p* < 0.01 respectively) and the LR group (1.62 ± 1.4 kg, *p* < .001; 1.01 ± 1.18 kg, *p* < 0.001; 0.66 ± 0.99 kg, *p* < 0.01 respectively) with no significant interaction between groups (*p* < 0.05). Figure 1a represents the individual changes in LBM in the HR group and Figure 1b represents the individual changes in LBM in the LR group.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Variable | HR(n=24) | | |  | LR (n=25) | | |
| Pre | Post\* |  | Pre | | Post\* | |
| Total LBM, *kg* | 64.6 ± 8.2 | 65.4 ± 8.2 | |  | 64.6 ± 7.0 | | 66.2 ± 6.9 |
| ALM, *kg* | 32.8 ± 4.5 | 33.6 ± 4.3 | |  | 33.2 ± 3.5 | | 34.4 ± 3.8 |
| LLM, *kg* | 24.7 ± 4.0 | 25.2 ± 3.7 | |  | 24.2 ± 2.7 | | 24.8 ± 2.9 |
| Total fat mass, *kg* | 19.6 ± 10.1 | 18.6 ± 9.9 | |  | 16.8 ± 6.7 | | 16.7 ± 6.4 |

**Table 2.** Participant body composition following 12 weeks of resistance exercise training

Values are means ± SD, HR, high repetition group (20-25 repetitions per set), LR, low repetition group (8-12 repetitions per set). LBM, lean body mass; ALM, appendicular lean mass; LLM, leg lean mass. \*Significantly different from pre (p < 0.05).

Figure 1

**Figure 1.** Individual changes in LBM in the HR(a) and LR (b) groups following 12 weeks of resistance exercise training



## 2.2 Strength Changes

Maximum isotonic strength for leg press, leg extension and shoulder press increased significantly in the HR group (leg press Δ = 116 ± 47 kg, *p* < 0.001, leg extension Δ = 29 ± 13 kg, *p* < 0.01, 22 ± 17 kg, *p* < 0.01 respectively) and the LR group (134 ± 53 kg, *p* < .001; 33 ± 12 kg, *p* < 0.01, 18 ± 34 kg, *p* < 0.01 respectively) following RT with no significant differences between groups (*p* < 0.05). Bench press 1RM increased significantly following RT in both the

HR (9 ± 7 kg, *p* < 0.01) and in the LR (14 ± 7 kg, *p* < 0.01) groups; however bench press isotonic strength increased in the LR group to a greater extent than the HR group (*p* = 0.012). Figure 2 represents strength changes for HR and LR leg press (2a), bench press (2b), leg extension (2c) and leg press (2d). Data are summarized in Table 3.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | HR(n=24) | |  | LR (n=25) | | *p*-value |
| Pre | Post\* |  | Pre | Post\* |
| Leg press 1RM, *kg* a | 357 ± 62 | 469 ± 83 |  | 357 ± 62 | 490 ± 65 | >0.05 |
| Bench press 1RM, *kg* a | 97 ± 17 | 106 ± 19 |  | 97 ± 19 | 112 ± 17 | 0.012\*‡ |
| Leg extension 1RM, *kg* a | 76 ± 16 | 105 ± 16 |  | 76 ± 15 | 109 ± 15 | >0.05 |
| Shoulder press 1RM, *kg* a | 92 ± 22 | 114 ± 24 |  | 91 ± 18 | 114 ± 16 | >0.05 |

****

**Figure 2**. Strength changes in the HR and LR groups following 12 weeks of resistance training for the leg press (a), bench press (b), leg extension (c), and shoulder press (d) exercises. Values are median ± min/max, + indicates mean. HR, high repetition group (20-25 repetitions per set), LR, low repetition group (8-12 repetitions per set). \*Significantly different from baseline, ‡ significantly different between HR and LR.

**Table 3**. Participant strength following 12 weeks of resistance exercise training

Values are means ± SD, HR, high repetition group (20-25 repetitions per set), LR, low repetition group (8-12 repetitions per set). a Maximal isotonic strength measured as single best weight lifted (see METHODS for details). *P* value indicates differences between groups. \* Significant difference from baseline (*p* < 0.05). ‡ Significantly different between HR and LR (*p* < 0.05).

## 2.3 Volume of Exercise

Total volume (repetition x sets x load) was significantly different between groups (*p* < 0.05) where average volume completed per exercise session was 52893 ± 10335 kg for the HR group and 31732 ± 4317 kg for the LR group. Volume per session was calculated by taking the total volume and dividing by 45 (4 sessions x 12 weeks – 3 1RM sessions). The volume of exercise performed by the LR repetition group was on average 66% of the total load lifted by the HR group per session. Figure 3 represents the average volume of exercise performed per session.



**Figure 3**. Average volume of exercise performed per training session

Values are median ± min/max, + indicates mean. HR, high repetition group (20-25 repetitions per set), LR, low repetition group (8-12 repetitions per set). \*Significantly different between HR and LR

## 2.4 Discussion

Previously, it has been shown that repetition load is not a primary determinant of RT-induced skeletal muscle hypertrophy in untrained males as long as volitional failure is achieved [6,63]. The data from this study have been criticized on these points as being unique to the situation (using untrained participants) and the model (unilateral RT) [6]. The purpose of this investigation was to expand upon these findings by using a robust sample size, a between group comparison, and in experienced resistance-trained young men to determine the effects of high and low repetition range (low and high load respectively) during RT on hypertrophy and strength. We provide novel data showing that 12 weeks of supervised, high and low repetition range RT performed to volitional failure are similarly effective at inducing skeletal muscle hypertrophy in trained participants. Additionally, increases in muscular strength also were no different between groups with the exception of 1RM bench press strength that increased to a greater extent in the low repetition group (6.2%; Figure 2a). These findings confirm that high and low repetition (low and high load) training paradigms can elicit a comparable stimuli for the accretion of skeletal muscle mass and when taken together with previous reports [6,61,71] suggests that these effects are not contingent upon training status.

## 2.4.1 High vs. Low Repetition RT and Hypertrophy

Few studies have addressed the effect of repetition load with the main outcome as hypertrophy and strength when the exercise sessions are not volume-matched (repetition x load) [6,61]. Total volume performed per exercise session, defined here as the number of repetitions performed per exercise multiplied by the sets performed, by the exercise load [78]. It is evident that when exercise sessions are volume matched, volitional failure is not reached and as such, low repetition exercise is often delineated as providing the greatest beneficial response [5,64]. Following 12 weeks of progressive RT we found that both the HR and LR groups showed significant gains in whole body lean mass gains of (Table 2) with no differences between groups. Total volume performed in the LR group was approximately 66% of the total exercise performed by the HR group and therefore, we hypothesize that the increased work performed by the HR group was likely part of what contributed to the similar adaptations seen in the LR group.

Previous studies have focused on the use of specific repetition ranges that progress similarly between groups with the aim of matching total volume lifted [5,64]. More often these same studies had participants lifting weights in the lower repetition (higher load) range to fatigue and then matching the volume lifted in that condition to the higher repetition (lower load) [64,73]. Work from our group examining the MPS response in such a matching condition clearly indicates that higher repetition-lower load volume-matched to a lower repetition-higher load group produces a substantially inferior MPS response [38]. In contrast, we showed that lower loads, when lifted to fatigue (i.e., a greater volume than the higher load condition) results in a superior stimulation of MPS [38] and equivalent hypertrophy [6]. Thus, in the current protocol our participants performed their exercise regardless of group assignment to reach volitional fatigue and thus it was not a volume-matched protocol. As mentioned previously, the performance of RE to volitional muscular fatigue is essential, based on our data [6,79], as it is necessary for maximal motor unit recruitment and thus hypertrophy of muscle fibres innervated by both large and small MUs [6,66]. Based on previous results [5,64,72], when high and low load protocols are not performed until volitional fatigue (i.e. not volume equated), it is evident that equivalent hypertrophy is unlikely to occur. For example, Holm and colleagues examined 12 untrained young men who performed volume-matched unilateral RT where one leg performed low repetition RT (70% of 1RM for 8 reps) while the other leg performed high repetition RT (16% of 1RM for 36 reps) [64]. They found that low repetition (high load) resistance exercise resulted in a significantly greater increase in muscle CSA (7.6%) compared to the high repetition group (2.6%). These findings are similar to those of Campos and colleagues who compared young, untrained men performing either 9-11 repetitions per set or 20-28 repetitions per set that were volume equated. They found that following 8 weeks of progressive RT that the group performing the low repetitions (9-11 repetitions per set) had a significant increase in type I, type IIA and type IIB fibre CSA of 12%, 19%, and 26% respectively. In contrast, muscle fibre CSA did not increase in the high repetition group [5]. The non-significant increase in fibre CSA reported by Campos et al [5] is in contrast to work from our group where total exercise volume was not matched between groups performing RE lifting at 30% of 1RM or 80% of 1RM to volitional muscular failure for 10 wk [6]. In this model it was identified that groups performing 30% of 1RM for 3 sets to failure, and 80% for 3 sets to failure, achieved similar increases in fibre CSA in type I and type II fibres (17 ± 4% and 16 ± 5%; 30 ± 12% and 18 ± 8%, respectively) with no significant differences between groups. These changes in fibre CSA translated to similar training-induced increases in quadriceps muscle volume of approximately 7% in both groups [6]. Together these findings suggest that the capacity for hypertrophic response is not dictated by the exercise load being lifted, but rather by ensuring complete motor unit recruitment and fatigue, which can be achieved by lifting a load, be it heavy or light, to the point of momentary muscle fatigue.

Muscle hypertrophy occurs as a result of short periods where the rates of MPS are greater than that of MPB that summed over time lead to hypertrophy [26]. Resistance exercise is a potent stimulator of MPS, especially when protein is consumed in the peri-workout period [39]. Differences in the acute response of MPS to varying RE loads have only been investigated once, to our knowledge. Burd and colleagues, had participants perform either 90% of their one repetition maximum (1RM) to failure, 30% of their 1RM which was work matched to the 90% of 1RM, or finally 30% of 1RM to failure. Measurements were taken up to 24 hours following the bout of RE and demonstrated that although all exercise loads were able to increase MPS above rested levels, the limbs performing exercise to failure were able to increase MPS above the work matched condition regardless of load. Furthermore, it was only the limbs performing 30% to failure that showed a persistent (24h after the RE bout) stimulation of myofibrillar MPS [79]. Given this knowledge it is therefore not surprising that our results reflect similar increases in muscle hypertrophy between intervention groups.

## 2.4.2 High vs. Low Repetition Resistance Exercise and Strength

In addition to similar increases in muscle size, high and low repetition progressive RT resulted in similar increases in muscular strength between groups following the 12-week intervention. Specifically, both HR and LR increased leg press (31% vs 37%), leg extension (38% vs 43%) and shoulder press (23% vs 25%) 1 RM with no differences between groups. However, while both groups increased chest press 1 RM, the increase was greater in the LR as compared with the HR group (15% vs 9%). Current literature supports the use of both low loads (high reps) [61,71,73] and high loads (low reps) [5,6,74] to induce increases in maximal strength. Indeed the majority of our strength results support the concept that maximal strength increases can be achieved with the use of either low or high repetitions, so long as there is periodic practice of lifting heavier loads (i.e., more frequent 1RM testing), whereas the disparity in maximum bench press strength changes remain in agreement with literature supporting the use of low repetitions with a high load. Tanimoto and colleagues observed similar increases in knee extensor 1RM strength following 12 weeks of progressive RT in untrained, healthy young men [80], finding a 27% increase in strength in the high repetition group (performing ~50% of 1RM) and a 33% increase in strength in the low repetition group (~80% of 1RM) with no difference between groups [80]. In contrast, Mitchell et al. [6], evaluated knee extensor strength changes in a similar population of healthy, untrained young men performing either 30% (high repetition) or 80% (low repetition) of their 1RM to failure and found that following 10 weeks of RT 3-times per week, that both groups significantly increased knee extensor 1RM, however, the low repetition group had a greater increase in strength (33%) compared to the high repetition group (20%) [6]. The observation that the group performing high repetitions in this study experienced similar increases in strength in the majority of the selected strength tests adds to the idea that high repetition exercise is as effective as low repetition RT at inducing significant strength adaptations when exercise is performed to volitional fatigue.

We chose to test our participants’ maximal (1RM) strength every three weeks during the 12wk training study. We did so to minimize the possibility that the measured strength gains would not be affected by training specificity [5,78]. Specially, in the LR group, who were lifting weights at between 70-80% of their 1RM this load is only 20-30% less than their 1RM while in contrast the HR group lifting weight at ~40-50% of 1RM would be 60-50% less than their 1RM. Thus, the principle of specificity would dictate that the LR group would be much more ‘practiced’ at lifting closer to a 1RM load than the HR group as the LR group would have a greater positive transfer of learning by the motor system resulting in an increase in neural coordination [81]. Thus, simply measuring 1RM pre- and post-intervention would bias the results toward a result for greater strength gains that would favour the LR group due to learning/practice. In fact we observed equivalent gains in strength in all of 1RM results between groups with the exception of bench press. We speculate that the disparity in the increase in maximal bench press strength between our intervention groups could be caused by a lesser capacity for neural adaptation as compared to the other exercises given that bench press was included in all of our subjects’ habitual training regimes and thus is more familiar to those who perform RT regularly and may have already reached a plateau [82]. This is in comparison to the other strength measures examined in the current study such as leg press, leg extension, and shoulder press which were less frequently reported as being included in the RT program of these previously trained individuals (less than 5% of participants regularly used machine based leg exercises and less than 8% used a machine based shoulder exercise). These exercises were chosen both for comparison to existing literature, as well as to reduce the risk of injuries resulting from the use of free weights which have a higher degree of instability, especially with higher repetitions and with volitional fatigue. Therefore it is possible that despite training status, if the capacity exists for significant neural adaptation, high and low repetition resistance exercise are likely equivalent in their ability to stimulate muscle hypertrophy and strength gains. However when the exercise is well-practiced, high-load, low-repetition programs are more beneficial at inducing increases in maximum strength.

## 2.4.3 Limitations

To our knowledge, this study is only the second to examine the effects of high and low repetition RT in previously resistance trained young men. Unique to this study, is the inclusion of a large sample size (n=49 total: 24 vs. 25 participants) to ensure validity of the comparisons which is in contrast to the smaller sample size (n=16: 8 vs. 8) used previously [83]. Nonetheless, there are still inherent limitations within our study design. The use of DXA (in our laboratory an iDXA) was used in place of MRI, which is the gold standard technique for determination of muscle hypertrophy. The iDXA gives an excellent measure of whole body fat- and bone-free (i.e., lean) mass; however the error of iDXA has been shown to be approximately 1.5% and this variability is greater when estimating body segments [84]. One of the major limitations of iDXA is the variability in lean mass estimation as changes in soft tissue hydration status can result in inconsistent measures. Despite the limitations, the iDXA is still much improved from previous models of dual-energy x-ray absorptiometry [85]. I propose that our day-to-day calibration of the iDXA using the whole-body 3-compartment phantom allowed us to have greater internal validity than previous work.

## 2.4.4 Conclusions

In conclusion, these data show that a low-load, high-repetition resistance training regime can induce significant increases in muscle hypertrophy and strength that are comparable to those found with a high-load, low-repetition training regime as long as the load is lifted until volitional fatigue. It was found that increases in LBM occurred in both LR and HR groups with no differences between groups. We also found a significant increase in 1RM strength for the leg press, leg extension and shoulder press exercises again with no differences between groups. While 1RM bench press increased in both groups, it increased to a greater extent in the LR group. We speculate that the increases in muscle strength and hypertrophy seen in our previously resistance trained participants in the HR group was due to them performing a greater volume of exercise and lifting to volitional failure.

## 2.4.5 Future Directions

The present study aimed to compare the effectiveness of a high and low repetition chronic resistance exercise training protocol on strength and muscle hypertrophy in previously trained men. It would be of practical interest to examine changes in hypertrophy and strength as well as perceived exertion and pain in populations where heavy loaded resistance exercise may not be feasible, safe, or enjoyable to participants such as with elderly populations or in individuals with inflammatory conditions, such as osteoarthritis. Finally, the molecular mechanisms that govern skeletal muscle plasticity in response to resistance exercise remain largely unknown. Future work using a range of biochemical and molecular techniques are now needed in order to elucidate how the mechanical signal from RE is transmitted and leads to the biochemical events that lead to an upregulation of the translational machinery and, ultimately, hypertrophy in humans.

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