Published in final edited form as:

Eur J Appl Physiol. 2011 June ; 111(6): 1063–1071. doi:10.1007/s00421-010-1735-9.

Progression of volume load and muscular adaptation during resistance exercise

Mark D. Peterson,

Department of Physical Medicine and Rehabilitation, Laboratory for Physical Activity and Exercise Intervention Research, University of Michigan, Ann Arbor, MI, USA

Emidio Pistilli,

Muscle Institute, University of Pennsylvania, Philadelphia, PA, USA

G. Gregory Haff,

Department of Human Performance, West Virginia University, Morgantown, VA, USA

Eric P. Hoffman, and

Research Center for Genetics, Children's National Medical Center, Washington, USA

Paul M. Gordon

Department of Physical Medicine and Rehabilitation, Laboratory for Physical Activity and Exercise Intervention Research, University of Michigan, Ann Arbor, MI, USA; Department of Physical Medicine and Rehabilitation, University of Michigan, 325 E. Eisenhower, Suite 300, Ann Arbor, MI 48108, USA

Paul M. Gordon: gordonp@med.umich.edu

Abstract

Volume load (VL) is suggested to influence the adaptation of muscle to resistance exercise (RE). We sought to examine the independent association between total VL and hypertrophy and strength following a progressive RE protocol of equated sets and intensity. Total VL was calculated in 83 subjects ($n = 43$ males, $n = 40$ females; age = 25.12 ± 5.5 years) who participated in unilateral arm RE for 12 weeks. Subjects were tested for biceps muscle volume (MRI of the upper arm), isometric maximal voluntary contraction (MVC), and dynamic biceps strength (1RM), at baseline and following RE. Linear regression analysis revealed that sex was a significant predictor of hypertrophy ($\beta = 0.06$; $p = 0.01$) and strength ($\beta = 0.14$; $p = 0.04$), and that males had greater increases. Total VL was independently associated with hypertrophy only among females ($\beta = 0.12$; $p < 0.01$). For males, only baseline strength was (inversely) related to hypertrophy ($\beta = -0.12$; $p = 0.04$). VL was strongly associated with changes in 1RM strength improvement for both males ($\beta = 0.66$; $p < 0.01$) and females ($\beta = 0.26$; $p = 0.02$), but only related to MVC among females ($\beta = 0.20$; $p = 0.02$). Findings reveal that VL was independently associated with hypertrophy only among females. For males baseline strength was independently and inversely

Correspondence to: Paul M. Gordon, gordonp@med.umich.edu.

Electronic supplementary material The online version of this article (doi:10.1007/s00421-010-1735-9) contains supplementary material, which is available to authorized users.

related to changes in muscle mass. Conversely, VL was found to be strongly associated with changes in 1RM for both males and females, controlling for age, body mass, and baseline strength.

Keywords

Strength training; Volume load; FAMuSS; Muscle mass; Periodization

Introduction

Manipulating the volume of resistance exercise over several weeks of training has been suggested to influence metabolic and hormonal responses (Kraemer et al. 1991; Kraemer and Ratamess 2005), morphological/architectural changes (Aagaard et al. 2001; McCall et al. 1996), and neural adaptations (Aagaard et al. 2002), which may in turn reflect the respective alteration capacity of muscular hypertrophy and strength (Aagaard et al. 2001; Kraemer et al. 2004). There has been substantial debate concerning the appropriate operational definition of training volume within the resistance exercise literature making this a difficult parameter to evaluate and replicate in research, and/or provide practical guidelines for exercise prescription. One of the most widely accepted definitions for this variable is volume load (VL), which takes into account the total number of performed repetitions and weight (kg) lifted (i.e., [repetitions (no.) $\times$ external load (kg)]). Volume load has been used to compare dosages in experimental conditions (Kok et al. 2009; Tran et al. 2006), as well as for use in monitoring athlete development (Haff et al. 2008). Since it represents the aggregate of several modifiable variables in resistance exercise design, VL consideration is specifically advantageous for periodizing and manipulating training, as well as for comparing similar protocols with equated frequencies and relative intensities.

Alternatively, total number of training sets, total work (TW), maximum dynamic strength volume load and time under tension have also been used to quantify training volume. Of these, TW was recently demonstrated to provide the most valid data across acute bouts of “strength”, “hypertrophy”, and “power” training, particularly when assessing exercises with no external load (i.e., body weight exercises), due to the ability to simultaneously evaluate actual muscle force production and center of mass displacement (McBride et al. 2009). However, the direct measurement of muscular force production is not a practical condition when quantifying the total volume of external stimuli during controlled resistance exercise outside the laboratory. Rather, through the use of VL assignment, it is possible to manipulate respective dosage by altering (1) the number of sets performed per exercise, (2) the total number of exercises performed, (3) the loading parameters of exercise (i.e., the absolute intensity or load lifted), and/or (4) through variation in repetitions, making this a simplistic and adaptable, yet valid designation of total training volume (ACSM 2009).

Previous investigations have suggested that volume is a critical predictor of the adaptive response to resistance exercise (Marx et al. 2001; Ronnestad et al. 2007). Much of this research has been performed with small samples, or incorporated less sensitive outcome measures to evaluate specific phenotype adaptations. Further, there is a great deal of variability in the dose–response relationship reported in the literature concerning models of

increased volume loading for different populations. These incongruent findings are particularly evident when examining differential volume assignments to determine sex-specific adaptation, as well as among individuals with dissimilar baseline physiological characteristics (i.e., baseline strength and muscle size). Evidence exists to suggest that both males and females make significant increases in hypertrophy (Hubal et al. 2005), but very little is known with regard to these sex comparisons as they also relate to variation in VL during training. Furthermore, it has been suggested that among untrained populations, increasing training volume may yield a distinct diminishing return of affect. This contention is based in part on the prospect that initial strength improvement is predominantly a result of neuromuscular adaptation (Moritani and de Vries 1979). However, much of the evidence to support this notion has been drawn from studies that did not incorporate highly sensitive methods of examining muscle tissue (Young et al. 1983). On the contrary, recent evidence has revealed that changes in muscle architecture and increases in muscle cross-sectional area may actually occur much earlier than previously reported (Seynnes et al. 2007).

With regard to general volume dosage comparisons, several investigations have demonstrated similar adaptation between low volume and moderate volume resistance exercise among untrained subjects (McBride et al. 2003; Starkey et al. 1996), whereas others have demonstrated the superiority of moderate-to-high volumes (Kraemer et al. 2000; Marx et al. 2001; Ronnestad et al. 2007). Despite these inconsistencies, a recent recommendation for novice individuals has been sanctioned, which suggests that specific training for muscular hypertrophy is optimized using moderate-to-high loading (i.e., 70–85% of 1RM), 2–3 days per week, for 8–12 repetitions per set, and for one to three sets per muscle group (ACSM 2009).

Although this evidence and respective recommendation provides a basic systematic framework through which RE prescription may occur, more research is needed to clarify the specific dose–response relationship between volume load variation and muscular phenotype alterations. To date, there has been no research conducted to strictly examine the independent association between volume load variation, as exhibited through individual progression, and subsequent hypertrophy and strength within a fixed protocol of equated sets and relative intensity. Such an investigation is necessary to isolate the discrete contribution of volume load as a predictive variable for muscular adaptation. Therefore, the purpose of this study was to examine the association between total VL and muscle hypertrophy and strength adaptation after 12 weeks of unilateral elbow flexion RE in a large sample of young, healthy untrained males and females. A subsequent objective was to evaluate the hierarchical contribution of secondary moderators of adaptation. Based on previous findings and recommendations (ACSM 2009; Marx et al. 2001), we hypothesized that total training VL would be significantly associated with changes in muscular hypertrophy and strength, and that we would observe a sex-specific adaptation such that males would improve to a greater extent in both hypertrophy and strength than females.

Methods

Subjects and experimental design

This study was a subset of the Functional Polymorphisms Associated with Human Muscle Size and Strength (FAMuSS) investigation. Briefly, the FAMuSS study was a large, NIH-funded multi-center effort to examine the genetic factors associated with baseline muscle, bone and fat tissue, as well as the subsequent adaptive response potential to 12 weeks of progressive RE of the elbow flexors. The experimental design of FAMuSS has been previously described (Hubal et al. 2005; Thompson et al. 2004). Subjects were excluded if they had performed strength training or employment requiring repetitive use of the arms within the prior 12 months. For the current investigation, workout training logs were analyzed for a subset of subjects with complete data, who participated in the FAMuSS study at WVU. All subjects were asked to maintain normal dietary practices and refrain from additional (i.e., non-habitual) exercise or weight loss practices. Each subject was tested prior to and following the training intervention on precise measures of muscular mass and strength. A total of 82 subjects ($n = 43$ males, $n = 40$ females; age = 25.12 ± 5.5 year) were included in these analyses. Each subject signed an informed consent document and all procedures were approved by an institutional review board for research with human subjects.

Materials and methods

Baseline and follow-up anthropometric measures included body mass (kg), height (cm) and body mass index (BMI) (kg m^{-2}). Upper arm volumetric measurements were assessed through standard magnetic resonance imaging (MRI) technique to specifically evaluate whole muscle volume. Isometric and dynamic strength capacity were also assessed prior to and following the RE intervention.

Volumetric measurements

Magnetic resonance imaging (MRI) was performed before and after the 12-week training intervention to assess subjects' baseline and post-intervention whole muscle volume (biceps brachii and brachialis) and subcutaneous fat volume as previously described (Hubal et al. 2005). Subjects were scanned in the supine position with arms at their sides and palms facing up on the scanner bed surface. The hand was supinated and taped in place on the scanner bed surface, and the point of measurement centered to the alignment light of the MRI. Baseline MRI was performed 24–48 h before the first strength measurement. To avoid any latent effects that strength testing/training might have on the outcomes (e.g., cellular fluid retention), MRI scans for post-assessment took place 48–96 h after the last session. MRI was performed at the maximum circumference of the upper arm (i.e., belly of the muscle). The maximum circumference of the upper arm was identified with the biceps maximally contracted, the shoulder abducted to 90° and elbow flexed at 90° . After determining the circumference using an elastic measuring tape, the corresponding location was marked on the subject's skin (point of measurement, POM) using a radiographic bead (Beekley Spots, Beekley Corp., Bristol, CT, USA). This POM was subsequently used for the alignment light of the MRI. Using an MRI scout image, six to nine slices were obtained to locate the long axis of the humerus. Subsequently, using the POM as the central point, 15

serial fast-spoiled gradient images of each arm were obtained (TE = 1.9 s, TR = 200 ms, flow artifact suppression, 30° flip angle). These image slices began at the top of the upper arm and proceeded distal toward the elbow. This arrangement provided an image of the muscle belly that corresponded to slices 8 and 9. Each slice was 16-mm thick, with a 0-mm interslice gap, 256 × 192 matrix resolution, 22 × 22 cm field of view and number of acquisitions (NEX) = 6. This method allowed for 24-cm length images to be collected of each upper arm, which were subsequently analyzed volumetrically using a computer-based, 3-D interactive system called Rapidia (3D Med Co. Ltd., Seoul, Republic of Korea), and a custom-designed interactive processing and visualization program using Matlab (The Math Works, Inc., Natick, MA, USA). To ensure accurate and reliable measurements, six slices from each image were analyzed using the metaphyseal-diaphyseal junction landmark, making sure the same regions were measured from pre- and post-images. Muscle and fat were each isolated using image signal intensity differences between tissues, and once the region of interest was segmented, total volume was taken from the six evaluated slices. Repeatability and reliability of Rapidia volume measurements were verified using a phantom of known volume.

Strength assessment

Baseline and post-intervention strength was evaluated through isometric and dynamic tests. Peak torque was taken as the isometric maximal voluntary contraction (MVC) of the elbow flexors and tested using a strain gauge attached to a strength evaluation system (Model 32628CTL, Lafayette Instrument Company, Lafayette, IN, USA). The distance between the handheld strain gauge and the axis of the elbow joint (moment arm) was individually determined on the basis of forearm length. Pre-intervention MVC was determined following three separate trials, and results were recorded as the average of the second and third trials. During all MVC tests, the arm was positioned on a preacher curl bench with the elbow fixed at 90° of flexion. The upper arm support was stationary and intended to produce an angle between the trunk and upper arm of approximately 45°. Three MVC tests lasting 3 s were performed on each arm and were separated by 1-min rest periods. Peak force values were averaged for each testing day.

Dynamic strength testing consisted of a modified one repetition maximum (1RM) protocol for dumbbell curl (Powerblocks; Intellbell, Inc., Owatonna, MN, USA), on a standard preacher curl bench (45°). Prior to testing, an incremental warm-up took place and subjects were instructed to perform a full range of motion repetition (i.e., from 180° to full elbow flexion) with a load that was estimated to be 100% of maximal ability. If this initial attempt was successful, it was followed by a small load increase (approximately 0.563–1.125 kg) and a 3-min rest period. Each failed attempt was succeeded by a small load decrease and also a 3-min rest. This process was repeated until a true 1RM was determined, which was identified if a subject failed to complete an additional incremental load increase after a given successful attempt. All 1RMs were determined within three to five attempts, and the maximal load was recorded in kilograms.

Exercise training program

All RE took place with the non-dominant arm, with the dominant arm serving as a non-training control. Throughout the 12-week intervention, subjects met twice per week (i.e., 24 total training sessions) for approximately 45-60 min/session. Compliance to training was monitored by the research group and fitness staff responsible for training implementation. Exclusion criterion for analyses was set at anything in excess of two missed workouts during the entire training intervention. The specific details of the resistance training program have been documented previously (Thompson et al. 2004). Briefly, each session of RE was preceded by a specific warm-up of two sets of 12 repetitions with moderate resistance for an arm flexion and extension exercise. Subsequent training incorporated dumbbell exercises (Power Blocks; Intellbell Inc., Owatonna, MN, USA) for biceps preacher curl, biceps concentration curl and standing biceps curl (each of which included a supinated forearm position), as well as overhead triceps extension, and triceps kickbacks. The tempo was controlled for every contraction and included a 2-s concentric and 2-s eccentric repetition cadence. The specific progression of weekly training included: weeks 1–4: three sets of 12 repetitions, with a 12-repetition maximum weight ($3 \times 12\text{RMs}$); weeks 5–9: three sets of 8 repetitions, with an 8-repetition maximum weight ($3 \times 8\text{RMs}$); weeks 10–12: three sets of 6 repetitions, with a 6-repetition maximum weight ($3 \times 6\text{RMs}$). In accordance with the principle of progressive overload, individual variations in load and repetitions (i.e., VL) occurred as subjects progressed in strength capacity. Specific load increases occurred on an incremental basis (i.e., 0.5–2 kg) if an individual was able to complete two or more repetitions over his/her assigned repetition goal for any exercise, in the last set, for two consecutive workouts [i.e., the “2-for-2 rule”(Baechle et al. 2008)].

Volume load calculation

The total volume load was calculated from training logs for each participant using the following formula: total VL = weight (kg) lifted (i.e., [repetitions (no.) $\times$ external load (kg)]). Total VL was determined for each training session and summed to compile an overall VL aggregate for the entire 12 weeks of RE. Complete repetitions were counted only if a participant was able to achieve full range of motion. Incomplete repetitions were recorded as $\frac{1}{2}$ of an attempt.

Dietary control

All participants were instructed to maintain habitual dietary practices during the course of the intervention. Individuals who were currently taking supplemental dietary protein and/or other supplements reported to build muscle or to cause weight gain (i.e., dietary supplements containing protein, creatine or androgenic precursors) were not eligible for recruitment in the study. Moreover, data from individuals who had lost significant body mass during the course of the 12 weeks were not analyzed.

Statistical analysis

Differences between males and females for baseline demographic, anthropometric and morphological measures were evaluated through independent *t* tests. Pearson product–moment correlations were used to examine selected bivariate correlations between various

baseline subject characteristics (i.e., age, body mass, body mass index, baseline strength capacity, baseline subcutaneous fat volume), total VL and the dependent variables. A minimum criterion alpha level of $p = 0.05$ was used to determine statistical significance. Data are reported as means and standard deviations (SDs).

Initially, linear regression was used to examine for sex-specific differences in the adaptive response to RE. Previous data have demonstrated specific adaptation profiles to RE (Hubal et al. 2005), which we confirmed through an initial model testing of the association of sex with hypertrophy ($\beta = 0.06$; $p = 0.01$) and strength change ($\beta = 0.14$; $p = 0.04$). Further, because sex was identified to be a significant moderator of several baseline characteristics, all analyses were conducted separately for males and females.

Analysis of covariance was conducted to assess the adaptive responses for outcomes after resistance exercise. Specifically, multiple linear regressions took place for each of the following outcomes: (1) whole muscle volume, (2) MVC and (3) 1RM strength capacity. In each of these models, post-intervention values were entered as dependent variables (i.e., post-intervention whole muscle volume, MVC and 1RM strength). To examine the independent association of VL on hypertrophy, total VL was entered as the independent predictor, baseline muscle mass and strength were entered as covariates, and age (a significant correlate) was entered as a potential moderator. Likewise, to examine both strength adaptation outcomes, total VL was again entered as the independent predictor, baseline strength was entered as the covariate, and body mass and age were entered as potential moderators. This method was completed to reduce the risk of regression to the mean, which may lead to an over- or underestimation of the intervention effect, and is a potential issue when assessing pre- to post-intervention change scores (i.e., absolute mean differences) (Twisk and Proper 2004). Further, since total VL is largely contingent upon baseline strength and muscle mass, it was necessary to control for these in the regression model (i.e., as covariates). Collinearity was examined using the variance inflation factor (VIF), and tests revealed no issues of collinearity for any model. For each model, standard regression coefficients (β) were determined, and paired t tests were used to evaluate the respective 0 difference. Further, percent variance attributable to the main outcome within each model was tested using an ANOVA to determine the significance of each model.

Results

Sex-specific pre-training demographic and muscle phenotype comparisons

No significant differences between males and females were found for baseline body mass index (BMI) or whole muscle volume ($p > 0.05$). Baseline body mass, MVC and 1RM strength were greater among males ($p < 0.05$).

Main outcomes

Pre- and post-intervention data and respective changes in whole muscle volume, MVC and 1RM strength are presented in Table 1. Males experienced greater improvement in muscle hypertrophy ($\beta = 0.06$; $p = 0.01$) and 1RM strength capacity ($\beta = 0.14$; $p = 0.04$) following

12 weeks of RE. No differences were demonstrated between males and females for pre- to post-intervention changes in MVC ($p > 0.05$).

VL and the adaptive response to RE

With regard to the influence of VL on adaptive response to RE, regression revealed an independent association between VL and hypertrophy ($\beta = 0.12$; $p < 0.01$) among females, controlling for baseline muscle mass, strength and age. Further, age was identified as a negative predictor of hypertrophy ($\beta = -0.07$; $p = 0.03$). For males, the only association with hypertrophic response was baseline strength capacity, which was determined to be a negative predictor ($\beta = -0.12$; $p = 0.04$) (Table 2).

VL was strongly associated with changes in 1RM strength improvement for both males ($\beta = 0.66$; $p < 0.01$) and females ($\beta = 0.26$; $p = 0.02$). For males, age was determined to be a significant moderator of 1RM strength change ($\beta = 0.20$; $p = 0.04$) (Table 2). VL was only associated with MVC among females ($\beta = 0.15$; $p = 0.02$).

Discussion

This is one of the first investigations to isolate and examine the *discrete* influence of total volume load (VL) as a predictor of muscular hypertrophy and strength capacity across a large cohort of males and females. Further unique to this investigation was the use of precise imaging techniques to evaluate muscular volumetric data prior to and following a periodized unilateral RE protocol. Primary findings demonstrate a sex-specific response to RE as well as a differential contribution of VL to muscular adaptation. In particular, among females VL was positively associated with changes in whole muscle volume, and thus higher VLs appear to be predictive of hypertrophic adaptation. Conversely, among male participants total VL was not independently associated with hypertrophy.

Sex-specific changes for strength capacity also revealed equivocal results. Total VL was robustly and independently associated with 1RM strength adaptation for both males and females; however, it was found to be only associated with MVC among female subjects. It is conceivable that the discrepancy in findings between MVC and 1RM is due, in part, to the fact that dynamic strength testing (i.e., 1RM testing) was more biomechanically “specific” to the dynamic RE training protocol. However, this rationale does not explain the sex-specific differences in the relation between VL and MVC changes. These discrepancies, notwithstanding, current findings demonstrate the utility of VL as a predictor of dynamic strength improvement, independent of baseline 1RM, age or body mass.

Previous research examining the differential effects of VL on muscular phenotypes and/or muscle function has not isolated VL dosages as a predictor of subsequent adaptive response. Rather, most existing interventions have compared single versus multiple set training (Kraemer et al. 2000; Marx et al. 2001; Marzolini et al. 2008; Ronnestad et al. 2007; Starkey et al. 1996), low versus high loading parameters (Campos et al. 2002; Holm et al. 2008), periodized versus non-periodized protocols (Kok et al. 2009; Kraemer et al. 2000; Marx et al. 2001) or some combination of these treatments. Data appear generally conclusive with respect to the superiority of high versus lower volume loads for muscle mass (Holm et al.

2008; Kraemer et al. 2000; Ronnestad et al. 2007), lean body mass (Kraemer et al. 2000; Marx et al. 2001) and strength capacity (Holm et al. 2008; Kraemer et al. 2000; Marx et al. 2001; Ronnestad et al. 2007) in both trained and untrained subjects. Findings from these studies have prompted the universal acceptance of VL as a critical prescription component, such that progression in VL is deemed necessary to elicit chronic adaptation (ACSM 2009). However, since VL is an aggregate of multiple potential RE prescription entities (i.e., sets, repetitions and load), it is conceivable that interpretation of these previous investigations has misconstrued the fundamental association between individual progression in VL and subsequent hypertrophic adaptive responses. Specifically, as it pertains to progressive overload during a *fixed* resistance training protocol of equated sets and relative intensity, the current findings suggest that total VL is only a moderate predictor of muscle hypertrophy among females.

By examining total VL across the 12-week RE intervention, it was possible to directly analyze the influence of this parameter on adaptation. Despite a significant increase in biceps muscle volume from baseline, regression failed to identify an association between total VL and hypertrophy among males. In fact, only baseline strength capacity was a significant predictor of subsequent change following the 12 weeks of training and was determined to be reciprocally associated with hypertrophy. Moreover, using the median of baseline strength to stratify male subjects, we observed significantly greater percent changes in hypertrophy among males with low strength as compared to high baseline strength capacity ($p < 0.05$) (Supplementary File 1: Fig. 1). Stronger males were also found to have nearly 23% greater baseline muscle mass ($p < 0.05$) than weaker males. Not surprisingly, over the course of 12 weeks of training, stronger males performed greater ($p < 0.05$) total VLs ($78,309.2 \pm 14,271.1$ vs. $61,276.3 \pm 11,823.2$ kg for weaker males), which represented nearly a 30% discrepancy in mean total volume of work throughout the RE program. Previous research suggests that RE intensity and volumes mediate physiological stress and respective cardiometabolic demand (Kang et al. 2005; Luebbers et al. 2008; Mazzetti et al. 2007). Within the context of the current investigation, since stronger males performed significantly greater total VLs throughout RE, these individuals experienced a disproportionate degree of absolute stress and less hypertrophic adaptation, as compared to weaker males.

Although training frequency (2 days/week) was identical for all subjects, relative rest per a given volume of work was not commensurate. Due to significantly higher absolute VLs being performed, stronger males may have needed more rest between bouts of training. Nevertheless, we cannot disregard that within the confines of a fixed RE protocol of equated sets and relative intensity, total VL was not found to be associated with muscle hypertrophy, which may be reflective of a “glass-ceiling” effect among stronger males. Certainly, future research is needed to characterize the trajectory of progression among individuals with discrepant baseline muscular phenotypes and strength capacities.

The current RE protocol incorporated a commonly used set- and repetition scheme; however, individual progression was restricted to progressive resistance in which absolute load was increased if, and only if, target repetitions were met or exceeded. Notwithstanding the potential efficacy of an alternative dosing assignment, the training prescribed in this

study was consistent with current recommendations for inducing muscular hypertrophy and strength (ACSM 2009), and is a generalizable and commonly implemented protocol within the professional setting. However, based on current results, it appears that VL is not a sufficient, *independent* predictor of adaptation among males. Nevertheless, all subjects engaged in the same nine sets of biceps training, and across the board, experienced significant hypertrophic adaptation. It is possible that if RE prescription had included a manipulation of total sets of training, a longer total intervention (i.e., 6 months or 24 total sessions) and/or a similar VL-to-recovery ratio for all subjects, the respective association between total VL and hypertrophic adaptive response may have been more robustly characterized, as has been previously documented (Holm et al. 2008; Kraemer et al. 2000; Marx et al. 2001; Ronnestad et al. 2007). Moreover, we recognize that although the use of a unilateral RE protocol is advantageous for controlling various potential confounding variables, this model may also reduce external validity as compared to full-body RE protocols.

In addition to the influence of total VL, among females age was identified as an independent, reciprocal moderator of hypertrophy. Accordingly, it appears that females who perform higher VL resistance exercise can expect greater hypertrophic adaptation, and that younger women are also potentially capable of superior training-induced responses. Indeed, research consistently demonstrates that muscle-protein synthesis rates gradually diminish with age (Yarasheski 2003); however, the vast majority of previous studies characterize differences between young and older adults. RE intervention research indicates that stimulation of increased muscle-protein synthesis is possible through higher volume resistance training, independent of age (Yarasheski et al. 1993). Current data are reflective of this phenomenon, and yet additional investigations are warranted to examine the sex- and age interaction for resistance exercise as it applies to respective hypertrophic adaptations, lean body mass and changes in protein synthesis. Indeed, emerging data from our laboratory indicate that there are sex-specific gene transcriptional patterns that may influence muscle hypertrophy in response to RE (unpublished observations).

Conclusions

Our findings demonstrate a sex-specific adaptation to resistance exercise such that during a fixed protocol of equated sets and relative intensity, total VL is at best a modest predictor of hypertrophy among females. Data further suggest that VL is a robust predictor of 1RM strength improvement for both males and females; however it is only related to changes in MVC among females. For males, baseline strength capacity appears to be negatively associated with hypertrophy, and thus stronger males may be less likely to experience the same degree of hypertrophic adaptation over 12 weeks as compared to weaker males. Although all females in this study were young adults, our data indicate that age was a negative predictor of hypertrophy, such that younger females may expect greater improvements in muscle mass following RE. These data implicate that muscle adaptation to RE may follow a gender-specific trajectory with aging.

Certainly, a great deal of research has been devoted to ascertaining the utility of resistance exercise, as well as the respective optimal prescription of training variables for different

populations. This study is unique in that we were able to isolate and examine the discrete influence of total VL as a predictor of site-specific hypertrophy and localized strength across a large data set. The current findings are important, as they provide insight pertaining to the contribution of total volume load for hypertrophy and strength capacity, as manifested through individual progression. Also, unique to this study is the identification of sex-specific characteristics, which seem to modulate adaptive response potential of males and females during resistance exercise. Subsequent investigations are warranted to thoroughly examine these characteristics and to identify the mechanistic rationale for such findings.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We acknowledge Ms. Pheobe Stapleton and Mr. Mathew Kampert for their assistance with this investigation. This research was supported by the NIH, NICHD, NCMRR Grant #5-T32-HD007422. No financial disclosures were reported by the authors of this paper. The results of the present study do not constitute endorsement by ACSM.

References

- Aagaard P, Andersen JL, Dyhre-Poulsen P, Leffers AM, Wagner A, Magnusson SP, Halkjaer-Kristensen J, Simonsen EB. A mechanism for increased contractile strength of human pennate muscle in response to strength training: changes in muscle architecture. *J Physiol.* 2001; 534:613–623. [PubMed: 11454977]
- Aagaard P, Simonsen EB, Andersen JL, Magnusson P, Dyhre-Poulsen P. Increased rate of force development and neural drive of human skeletal muscle following resistance training. *J Appl Physiol.* 2002; 93:1318–1326. [PubMed: 12235031]
- ACSM. American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. *Med Sci Sports Exerc.* 2009; 41:687–708. [PubMed: 19204579]
- Baechle, T.; Earle, R.; Wathen, D. Resistance Training. In: Baechle, T.; Earle, R., editors. *Essentials of strength training and conditioning.* Human Kinetics; Champaign: 2008. p. 381–412.
- Campos GE, Luecke TJ, Wendeln HK, Toma K, Hagerman FC, Murray TF, Ragg KE, Ratamess NA, Kraemer WJ, Staron RS. Muscular adaptations in response to three different resistance-training regimens: specificity of repetition maximum training zones. *Eur J Appl Physiol.* 2002; 88:50–60. [PubMed: 12436270]
- Haff GG, Jackson JR, Kawamori N, Carlock JM, Hartman MJ, Kilgore JL, Morris RT, Ramsey MW, Sands WA, Stone MH. Force–time curve characteristics and hormonal alterations during an eleven-week training period in elite women weight-lifters. *J Strength Cond Res.* 2008; 22:433–446. [PubMed: 18550958]
- Holm L, Reitelseder S, Pedersen TG, Doessing S, Petersen SG, Flyvbjerg A, Andersen JL, Aagaard P, Kjaer M. Changes in muscle size and MHC composition in response to resistance exercise with heavy and light loading intensity. *J Appl Physiol.* 2008; 105:1454–1461. [PubMed: 18787090]
- Hubal MJ, Gordish-Dressman H, Thompson PD, Price TB, Hoffman EP, Angelopoulos TJ, Gordon PM, Moyna NM, Pescatello LS, Visich PS, Zoeller RF, Seip RL, Clarkson PM. Variability in muscle size and strength gain after unilateral resistance training. *Med Sci Sports Exerc.* 2005; 37:964–972. [PubMed: 15947721]
- Kang J, Hoffman JR, Im J, Spiering BA, Ratamess NA, Rundell KW, Nioka S, Cooper J, Chance B. Evaluation of physiological responses during recovery following three resistance exercise programs. *J Strength Cond Res.* 2005; 19:305–309. [PubMed: 15903367]
- Kok LY, Hamer PW, Bishop DJ. Enhancing muscular qualities in untrained women: linear versus undulating periodization. *Med Sci Sports Exerc.* 2009; 41:1797–1807. [PubMed: 19657289]

- Kraemer WJ, Ratamess NA. Hormonal responses and adaptations to resistance exercise and training. *Sports Med.* 2005; 35:339–361. [PubMed: 15831061]
- Kraemer WJ, Gordon SE, Fleck SJ, Marchitelli LJ, Mello R, Dziados JE, Friedl K, Harman E, Maresh C, Fry AC. Endogenous anabolic hormonal and growth factor responses to heavy resistance exercise in males and females. *Int J Sports Med.* 1991; 12:228–235. [PubMed: 1860749]
- Kraemer WJ, Ratamess N, Fry AC, Triplett-McBride T, Koziris LP, Bauer JA, Lynch JM, Fleck SJ. Influence of resistance training volume and periodization on physiological and performance adaptations in collegiate women tennis players. *Am J Sports Med.* 2000; 28:626–633. [PubMed: 11032216]
- Kraemer WJ, Nindl BC, Ratamess NA, Gotshalk LA, Volek JS, Fleck SJ, Newton RU, Hakkinen K. Changes in muscle hypertrophy in women with periodized resistance training. *Med Sci Sports Exerc.* 2004; 36:697–708. [PubMed: 15064598]
- Luebbbers PE, Potteiger JA, Warren BJ, Clore JN, Jennings C, Bond DS. Glucose uptake after resistance training of different intensities but of equal work volume. *J Strength Cond Res.* 2008; 22:1094–1100. [PubMed: 18545202]
- Marx JO, Ratamess NA, Nindl BC, Gotshalk LA, Volek JS, Dohi K, Bush JA, Gomez AL, Mazzetti SA, Fleck SJ, Hakkinen K, Newton RU, Kraemer WJ. Low-volume circuit versus high-volume periodized resistance training in women. *Med Sci Sports Exerc.* 2001; 33:635–643. [PubMed: 11283441]
- Marzolini S, Oh PI, Thomas SG, Goodman JM. Aerobic and resistance training in coronary disease: single versus multiple sets. *Med Sci Sports Exerc.* 2008; 40:1557–1564. [PubMed: 18685538]
- Mazzetti S, Douglass M, Yocum A, Harber M. Effect of explosive versus slow contractions and exercise intensity on energy expenditure. *Med Sci Sports Exerc.* 2007; 39:1291–1301. [PubMed: 17762362]
- McBride JM, Blaak JB, Triplett-McBride T. Effect of resistance exercise volume and complexity on EMG, strength, and regional body composition. *Eur J Appl Physiol.* 2003; 90:626–632. [PubMed: 12923645]
- McBride JM, McCaulley GO, Cormie P, Nuzzo JL, Cavill MJ, Triplett NT. Comparison of methods to quantify volume during resistance exercise. *J Strength Cond Res.* 2009; 23:106–110. [PubMed: 19130641]
- McCall GE, Byrnes WC, Dickinson A, Pattany PM, Fleck SJ. Muscle fiber hypertrophy, hyperplasia, and capillary density in college men after resistance training. *J Appl Physiol.* 1996; 81:2004–2012. [PubMed: 8941522]
- Moritani T, de Vries HA. Neural factors versus hypertrophy in the time course of muscle strength gain. *Am J Phys Med.* 1979; 58:115–130. [PubMed: 453338]
- Rønnestad BR, Egeland W, Kvamme NH, Refsnes PE, Kadi F, Raastad T. Dissimilar effects of one- and three-set strength training on strength and muscle mass gains in upper and lower body in untrained subjects. *J Strength Cond Res.* 2007; 21:157–163. [PubMed: 17313291]
- Seynnes OR, de Boer M, Narici MV. Early skeletal muscle hypertrophy and architectural changes in response to high-intensity resistance training. *J Appl Physiol.* 2007; 102:368–373. [PubMed: 17053104]
- Starkey DB, Pollock ML, Ishida Y, Welsch MA, Brechue WF, Graves JE, Feigenbaum MS. Effect of resistance training volume on strength and muscle thickness. *Med Sci Sports Exerc.* 1996; 28:1311–1320. [PubMed: 8897390]
- Thompson PD, Moyna N, Seip R, Price T, Clarkson P, Angelopoulos T, Gordon P, Pescatello L, Visich P, Zoeller R, Devaney JM, Gordish H, Bilbie S, Hoffman EP. Functional polymorphisms associated with human muscle size and strength. *Med Sci Sports Exerc.* 2004; 36:1132–1139. [PubMed: 15235316]
- Tran QT, Docherty D, Behm D. The effects of varying time under tension and volume load on acute neuromuscular responses. *Eur J Appl Physiol.* 2006; 98:402–410. [PubMed: 16969639]
- Twisk J, Proper K. Evaluation of the results of a randomized controlled trial: how to define changes between baseline and follow-up. *J Clin Epidemiol.* 2004; 57:223–228. [PubMed: 15066681]
- Yarasheski KE. Exercise, aging, and muscle protein metabolism. *J Gerontol A Biol Sci Med Sci.* 2003; 58:M918–M922. [PubMed: 14570859]

- Yarasheski KE, Zachwieja JJ, Bier DM. Acute effects of resistance exercise on muscle protein synthesis rate in young and elderly men and women. *Am J Physiol.* 1993; 265:E210–E214. [PubMed: 8368290]
- Young A, Stokes M, Round JM, Edwards RH. The effect of high-resistance training on the strength and cross-sectional area of the human quadriceps. *Eur J Clin Invest.* 1983; 13:411–417. [PubMed: 6416856]

Table 1
Pre- and post-intervention subject characteristics and change scores for males and females

Group	Body mass (kg)	BMI (kg m ²)	Whole muscle volume (mL)	Isometric MVC (Nm)	IRM strength (kg)
Males (N = 43)					
Pre-training	78.5 ± 18.1 *	24.6 ± 5.0	563.9 ± 150.0	178.6 ± 46.4 *	10.5 ± 2.5 *
Post-training	78.7 ± 18.2	24.6 ± 5.1	649.7 ± 162.5	210.3 ± 54.2	15.6 ± 2.9
Pre-/post-change	0.2 ± 1.8	-0.01 ± 0.7	85.7 ± 36.5 ‡‡	31.8 ± 17.0 ‡	5.1 ± 1.8 ‡
Females (N = 40)					
Pre-training	62.3 ± 13.8	23.9 ± 4.6	508.7 ± 160.0	72.1 ± 27.3	6.1 ± 1.7
Post-training	62.2 ± 14.3	23.8 ± 4.8	570.5 ± 168.3	90.0 ± 31.8	10.2 ± 2.2
Pre-/post-change	-0.1 ± 1.7	-0.01 ± 0.77	62.4 ± 33.3 ‡	17.8 ± 12.3 ‡‡	4.1 ± 1.1 ‡‡

All values are reported as means and standard deviations

kg Kilograms; BMI body mass index; mL milliliters; MVC maximal voluntary contraction; Nm Newton meters; IRM1 repetition maximum

* A significant gender difference at baseline ($p < 0.05$)

‡ A significant effect by time ($p < 0.05$)

‡‡ A significantly greater sex × time interaction ($p < 0.05$)

Table 2
Multiple regression models for hypertrophic (i.e., whole muscle volume) and strength (i.e., 1RM) adaptive responses to resistance exercise for both males and females

Model: predictor(s)		β	t	p	F	Adjusted R^2	VIF
Post-intervention muscle volume							
Males	Baseline muscle volume	1.00	20.70	<0.01	189.40	0.95	1.8
	Total VL	0.06	0.83	0.41			3.4
	Baseline strength (1RM)	-0.12	-2.10	0.04			2.4
	Age	0.01	0.18	0.86			1.6
Females	Baseline muscle volume	0.96	23.50	<0.01	317.80	0.97	2.1
	Total VL	0.12	2.90	<0.01			2.1
	Baseline strength (1RM)	0.00	-0.02	0.99			3.0
	Age	-0.07	-2.30	0.03			1.4
Post-intervention muscular strength (1RM)							
Males	Baseline strength (1RM)	0.34	2.70	0.01	36.30	0.77	2.3
	Total VL	0.72	4.60	<0.01			2.5
	Age	0.22	2.10	0.05			1.3
	Baseline body mass	-0.12	-0.82	0.42			1.8
Females	Baseline strength (1RM)	0.74	5.20	<0.01	38.30	0.80	2.5
	Total VL	0.23	2.00	0.05			2.1
	Age	-0.14	-1.41	0.17			1.3
	Baseline body mass	-0.07	-0.45	0.65			1.7