

Skeletal Muscle Hypertrophy: How important is Exercise Intensity?

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Current recommendations for training protocols aimed at increasing muscle mass are commonly based on a percentage of the concentric one repetition maximum (1RM) for a particular exercise. However, research utilizing lower exercise intensities (20-30% 1RM) has been observed to result in skeletal muscle hypertrophy similar to that of higher intensity resistance training. These findings appear to question the overall importance of exercise intensity for increasing muscle mass.

Objectives: The purpose of this manuscript is to discuss the skeletal muscle hypertrophy exercise intensity recommendations and provide discussion on overall exercise volume, which is likely more important for stimulating skeletal muscle hypertrophy than exercise intensity per se.

Design and Methods: Non-systematic review

Results: It appears that a large portion of the exercise recommendations for skeletal muscle hypertrophy appear to be based on protocols that elicit short term changes in systemic 'anabolic' hormones; although little conclusive evidence exists to support that 'anabolic' hormone hypothesis. Exercise volume may be of much more importance for stimulating and maximizing the duration of the muscle protein synthesis (MPS) response than exercise intensity per se. In addition, chronic training studies confirm the acute findings that volume, not exercise intensity is the mediating factor for skeletal muscle hypertrophy.

Conclusion: The data suggests that skeletal muscle hypertrophy recommendations on the basis of exercise intensity are too simplistic and more focus should instead be placed on total exercise volume. The current recommendations for muscle hypertrophy do not reflect current science.

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Key words: exercise volume ■ systemic hormones ■ resistance training ■ growth

The maintenance and promotion of skeletal muscle mass throughout a lifetime is essential for a favorable quality of life. Like most human tissue, skeletal muscle is highly plastic and is capable of responding to a stimulus through a network of anabolic signaling which results in growth and increases in strength. Skeletal muscle functions as the largest disposal site of ingested glucose¹, plays an important role in lipid oxidation^{2,3}, and is one of the greatest modifiable contributors to the resting metabolic rate⁴, demonstrating the importance of maintaining skeletal muscle quantity and quality. In contrast, the removal of that appropriate stimulus results in the loss of favorable muscle adaptations.

Current recommendations for resistance training exercise intensities are commonly based on a percentage of the concentric one repetition maximum (1RM) for a particular exercise. By definition there is a direct relationship between the external load lifted and the exercise intensity (↑ external load= ↑ exercise intensity and vice versa). The American College of Sports Medicine (ACSM) recommends that novice lifters lift at 70-85% 1RM and advanced lifters work with intensities ranging from 70-100% 1RM⁵ in order to produce measurable changes in skeletal muscle hypertrophy.

Recommendations from the National Strength and Conditioning Association (NSCA) in their current issue of the *Essentials of Strength Training and Conditioning* textbook mirror those of the ACSM⁶.

It is acknowledged that exercise intensity is only one of many variables (e.g. contraction velocity, contraction time, rest periods, volume, etc.) that can affect the chronic adaptation from resistance training. However, we emphasize exercise intensity in this review, because both the ACSM⁵ and NSCA⁶ emphasize this as an important variable for increasing skeletal muscle mass. Therefore, the purpose of this manuscript will be to discuss the skeletal muscle hypertrophy exercise intensity recommendations and discuss what these recommendations are largely based on. This manuscript will review recent acute and chronic data which suggests that exercise intensity may be playing less of a role with skeletal muscle hypertrophy than previously thought.

Anabolic Hormone Rationale

The exercise intensity recommendations appear to be largely based off of studies investigating the acute response to

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systemic circulating hormones, which have been hypothesized to be anabolic for adult skeletal muscle tissue⁷. For example, the ACSM position stand for skeletal muscle hypertrophy supports their recommendation for high exercise intensities and short rest periods on the findings that these protocols typically result in greater acute elevations in growth hormone (GH) and testosterone.⁵ To illustrate, Kraemer et al.⁸ compared two different workouts with one condition consisting of a 5RM load and long rest period (5 sets, 3 minutes rest) and the other consisting of a 10RM load with shorter rest periods (3 sets, 1 minute rest). The study found that the testosterone response was variable with no differences between conditions when the integrated area under the curve (AUC) was compared. Serum GH was more responsive to the 10RM hypertrophy protocol than the 5RM protocol. Given that the 10RM protocol resulted in marked acute elevations in GH and that similar protocols are often used to produce skeletal muscle hypertrophy, it is intuitive to suggest the possibility that systemic hormones and muscle growth are related.

To better determine this relationship, Goto et al.⁹ investigated whether or not the acute exercise induced increase in GH would be predictive of skeletal muscle hypertrophy. In other words, would the group that saw the higher acute elevations in GH, observe greater increases in muscle hypertrophy? The study consisted of an initial acute bout of exercise to measure the systemic hormone response and two phases of chronic resistance training with the outcome measures including changes in muscle cross sectional area (CSA) and muscular strength. The study found that the group with the highest post exercise induced increase in serum GH had the greatest increase in skeletal muscle hypertrophy. The results of this study seem to corroborate at least retrospectively, that acute elevations in serum GH are predictive of skeletal muscle hypertrophy; however until recently this had not been investigated directly.

Recent studies have been completed using a within subjects design to determine whether or not the acute changes in systemic hormones are fundamentally required for skeletal muscle hypertrophy. While this design may not be optimal for testing muscular strength due to cross education, this design does appear appropriate for testing changes in muscle mass¹⁰. The initial study which looked at skeletal muscle protein synthesis (MPS) had subjects complete unilateral arm curls, which due to the small muscle mass does not elicit a large increase in systemic hormones¹¹. The other arm completed the same unilateral arm curl but followed it with a high volume leg work out to elicit a large increase in systemic hormones. The study found that despite one arm being in the presence of high levels of hormones, MPS was similar between conditions¹¹. Thus, assuming short term changes in MPS are predictive of changes in muscle mass; this study would suggest that large changes in systemic hormones are not playing a significant role with skeletal muscle hypertrophy. To test this hypothesis further, using the same protocol as the acute study, the subjects completed 15 weeks of resistance training¹². In accordance with the aforementioned MPS data, the arm in the presence of elevated systemic hormones had

neither augmented changes in muscle hypertrophy or strength. This study suggests that the acute systemic changes in hormones with resistance training are not anabolic in nature¹², and might be more reflective of energy demand.

In conclusion, it appears that although a large portion of the exercise recommendations for skeletal muscle hypertrophy appear to be based on protocols that elicit short term changes in hormones; little conclusive evidence exists to support that 'anabolic' hormone hypothesis. It appears that most evidence for the support comes from retrospective correlations⁹, and it should be mentioned that not all retrospective correlations support a link between acute changes in hormones and chronic training adaptation¹³.

Acute Anabolic Signaling and Muscle Protein Synthesis

The acute MPS response to exercise has been suggested to be predictive of long term changes in muscle mass, however it should be noted that the phosphorylated states of anabolic signaling molecules are not always related to that anabolic response^{14, 15}. With that being said, several studies have investigated the effect of resistance exercise intensity on acute anabolic signaling and MPS.

Kumar et al.¹⁶ investigated acute changes in anabolic signaling and MPS following knee extensor exercise with intensities ranging from 20-90% 1RM. The study found the MPS response was maximized at 60% 1RM and that no further increase was observed with higher exercise intensities. It is possible that the lack of difference may have been due to poor statistical power since each exercise intensity group only included 5 subjects. Nevertheless, following a pooling of the 60-90% 1RM groups data, it was observed at one hour post exercise that there was an increased phosphorylation of p70S6k on Thr389 and 4E-BP1 on Thr37/46. These effectors are located downstream of mammalian target of rapamycin (mTOR) and increased phosphorylation of these effectors are likely involved with the resistance exercise stimulation of MPS. Assuming acute changes in MPS are predictive of long term adaptation, the results of this study suggest that perhaps exercise intensities even lower than the current ACSM and NSCA recommendations may elicit long term favorable adaptations. An important consideration is that the volume of work completed by each exercise intensity group was equivalent therefore the results of this study are unable to determine if perhaps a higher volume of work completed with a lower intensity would elicit favorable changes in anabolic signaling and MPS.

To address the effect of resistance exercise intensity and volume on anabolic signaling and MPS, Burd et al.¹⁷ completed a study investigating these variables and have provided compelling evidence that when enough volume of work is completed, the acute changes in signaling and MPS are similar, independent of the exercise intensity. To illustrate, trained subjects performed unilateral knee extension at either 90% 1RM to failure, 30% 1RM work matched to 90% 1RM, and 30% 1RM to failure. The groups that went to failure

elicited a similar MPS response at 4 hours post exercise, however the group that was work matched to 90% 1RM (non-failure) did not elicit an increase in MPS. Interestingly, at 24 hours post exercise the 30% 1RM group still had significantly elevated MPS, however the 90% 1RM group had returned to baseline. The phosphorylated state of mTOR on Ser2448 was increased in all three groups at four hours; however its downstream effector p70S6k at Thr 389 was only phosphorylated in the 30% 1RM to failure group. In addition, the mitogen activated protein kinase (MAPK) signaling molecule ERK 1/2 at Thr202/Tyr204 was significantly elevated only in the 30% 1RM to failure group, which in combination with the mTOR signaling pathway may ultimately be important for maximally stimulating the MPS response¹⁸. In part, these findings support the data from Kumar et al.¹⁶ and suggest that if groups are work matched across exercise intensities, the lower exercise intensity group is unlikely to maximize the MPS response. However, if groups are allowed to complete an adequate number of sets to failure, the MPS response will be similar, regardless of the exercise intensity.

In conclusion, it appears that the exercise volume may be of much more importance for stimulating and maximizing the duration of the MPS response than exercise intensity per se. In support of this, Burd et al.¹⁹ found that subjects who completed a higher volume of work had a more sustained increase in MPS than a group performing less volume at the same exercise intensity (29 h vs. 5 h). Although research on acute changes in MPS and anabolic signaling are important from a mechanistic standpoint, chronic training studies are the only effective way to determine the actual effect of exercise intensity on skeletal muscle hypertrophy.

Chronic Training Studies on Exercise Intensity

Campos et al.²⁰ is the most commonly cited resistance training study for why exercise intensity is important for skeletal muscle hypertrophy. Subjects in that study were placed into three groups and performed lower body resistance training with either low (4 x 3-5RM), medium (3 x 9-11RM), or high (2 x 20-28RM) repetitions. The protocol found that only the low and medium repetition groups observed significant increases in Type 1, IIA, and IIB fiber cross sectional area. No significant increases were observed in the higher rep group. It should however be noted that Leger et al.²¹ was unable to replicate the findings of Campos et al.²⁰. A possible reason why includes the older age of the subjects in the Leger et al.²¹ investigation (36 vs. 22 yrs.). Although, the age discrepancy is not large, it may be large enough to capture the typical decrease in physical activity with age²². It is conceivable that 2 sets to failure was not enough volume for the younger, more active subjects; but in the older, less active subjects it provided enough volume to reach a hypothetical volume threshold for stimulating skeletal muscle growth²³.

To determine whether a higher volume (3 sets) of exercise with low exercise intensities could produce gains in muscle mass similar to higher intensity exercise, 18 subjects

completed 3 sets of unilateral knee extension exercise with their leg lifting at either three sets of 30% 1RM to failure, one set of 80% 1RM to failure, or three sets of 80% 1RM to failure (12 legs in each condition). The study found that muscle hypertrophy (MRI and fiber cross sectional area) increased in all conditions with the percent changes tending to be greatest for the 30% 1RM to failure and 3 sets of 80% 1RM to failure²⁴. This study suggests that if enough volume of exercise is completed, significant muscle hypertrophy can occur, independent of exercise intensity.

The aforementioned findings are supported by copious amounts of data collected over the past decade on low intensity exercise (20-30% 1RM) in combination with blood flow restriction (BFR), which has been observed to produce skeletal muscle hypertrophy^{25, 26}. To illustrate, Takarada et al.²⁷ investigated the chronic effects of low intensity resistance training with BFR in post-menopausal women. The women were divided into three separate groups and completed 16 weeks of elbow flexor resistance training. The groups included low intensity training (30-50% 1RM) with and without BFR, and a higher intensity training group (50-80% 1RM). Following the 16 week study, the low intensity group that exercised with BFR and the higher intensity group had similar increases in muscle size and strength; however, the low intensity group without BFR had no increase in either variable highlighting the benefit of the BFR stimulus. It is important to note that the low intensity group without BFR was submaximal in nature and was not taken to muscular failure. Although most studies investigating skeletal muscle hypertrophy with BFR have been measured using MRI or ultrasound²⁵, these changes in skeletal muscle hypertrophy have recently been observed at the fiber level following only three weeks of resistance training at 20% of the concentric 1RM²⁸.

In conclusion, recent studies suggest that volume is an important mediating factor for skeletal muscle hypertrophy. The data suggests that muscle hypertrophy recommendations on the basis of exercise intensity are too simplistic and more focus should instead be placed on total exercise volume.

Conclusions

- Skeletal muscle hypertrophy is not mediated by exercise intensity defined as the external load lifted.
- Exercise volume appears to be a more important variable with respect to skeletal muscle hypertrophy.
- Low intensity resistance exercise with a sufficient volume can increase MRI measured and individual skeletal muscle fiber cross sectional area.
- Current recommendations for skeletal muscle hypertrophy do not reflect current science.

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