

Bigger weights may not beget bigger muscles: evidence from acute muscle protein synthetic responses after resistance exercise

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Abstract: It is often recommended that heavier training intensities (~70%–80% of maximal strength) be lifted to maximize muscle growth. However, we have reported that intensities as low as 30% of maximum strength, when lifted to volitional fatigue, are equally effective at stimulating muscle protein synthesis rates during resistance exercise recovery. This paper discusses the idea that high-intensity contractions are not the exclusive driver of resistance exercise-induced changes in muscle protein synthesis rates.

Key words: anabolic signaling, resistance exercise, adaptation, skeletal muscle growth, myofibrillar, mitochondrial, skeletal muscle protein turnover.

Résumé : Pour maximiser la croissance musculaire, on recommande souvent de s'entraîner à plus forte intensité (~70–80 % de la force maximale). Toutefois, nous avons déjà rapporté que soulever jusqu'à épuisement volontaire des charges équivalant à aussi peu que 30 % de la force musculaire stimule la synthèse des protéines dans les muscles durant la phase de récupération consécutive aux exercices contre résistance. Cet article analyse l'idée selon laquelle des contractions de forte intensité ne seraient pas le seul moyen pour modifier le taux de synthèse des protéines musculaires causée par les exercices contre résistance.

Mots-clés : signalisation anabolique, exercice contre résistance, adaptation, croissance du muscle squelettique, renouvellement des protéines musculaires squelettiques, mitochondriales et myofibrillaires.

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Introduction

Acute studies examining protein phosphorylation or muscle protein synthetic responses after resistance exercise and protein ingestion are often used to predict longer-term training outcomes. Is there concrete evidence suggesting these acute studies provide meaningful information? Indeed, definitive evidence is lacking and it is clear that this is a research gap that needs to be filled. The relevance of using static “snapshots” of protein phosphorylation that represent a single stage of the translational process to represent dynamic measurements of the phenotypic response, such as muscle protein synthesis rates (MPS), is dwindling, at least in humans (Burd et al. 2009). This disconnect between the measurements are likely due to the single point measurement or a minimum threshold where greater protein phosphorylation

would have little additive effect on the dynamic rate measurement of MPS. Moreover, the existence of multiple redundant pathways to activate MPS also makes interpretation difficult. Conversely, for a muscle fibre to hypertrophy there must be a period of net muscle protein accretion at some point over the course of a day. Resistance exercise is an effective stimulus to improve muscle protein balance, primarily by the stimulation of MPS (Phillips et al. 1997), and when accompanied by protein ingestion the stimulation of MPS is greater than either stimulus alone (Biolo et al. 1997; Tipton et al. 1999; Moore et al. 2009). The ultimate outcome, therefore, is an acute positive muscle protein balance that will lead to eventual hypertrophy after chronic resistance training (RT). To our knowledge, there is no other physiological mechanism that a muscle fibre can hypertrophy to a substantial extent

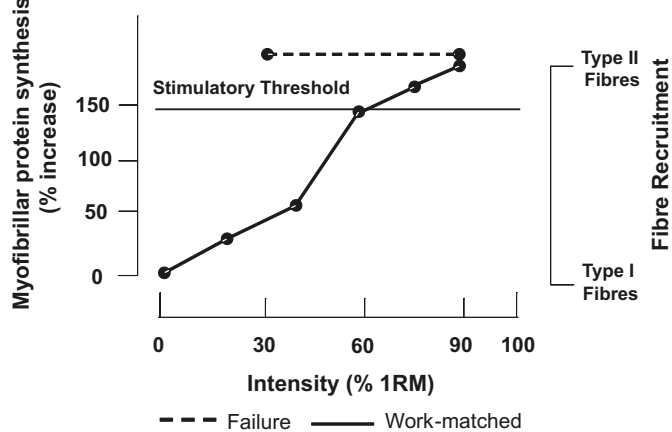
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Fig. 1. An illustration representing the relationship between resistance exercise intensity (*x* axis) and myofibrillar protein synthesis (left *y* axis). The bold line represents the reported dose-dependent relationship between resistance exercise intensity and myofibrillar protein synthesis rates that rises to a plateau at 60%–90% of 1 repetition maximum (1RM) after external work-equated exercise (Kumar et al. 2009). During lower intensity work-matched conditions, less muscle fibre activation (right *y* axis) is required to maintain muscle tension and thus results in less stimulation of a myofibrillar protein synthesis. However, based on the orderly recruitment of muscle fibres (Henneman et al. 1965) performance of resistance exercise, even at lower intensities, until volitional fatigue (i.e., failure) will necessitate maximal fibre recruitment and culminate in a similar fibre recruitment resulting in the stimulatory threshold being surpassed. The end result is the maximal stimulation of myofibrillar protein synthesis rates (dashed line).



after RT without some type of muscle proteins being synthesized and incorporated into new muscle proteins. Thus, acute measurements of MPS must have some indication of training-mediated hypertrophy. Furthermore, indirect evidence suggests that acute measurements of MPS after anabolic (Fujita et al. 2007; Wilkinson et al. 2007; West et al. 2009; Holm et al. 2010) or catabolic (Glover et al. 2008) stimuli can translate into muscle growth (Takarada et al. 2000; Hartman et al. 2007; Holm et al. 2008; West et al. 2010) or loss (Yasuda et al. 2005). Given all this, there is scientific evidence to support the idea that acute measurements of MPS are linked to long-term outcomes.

Our laboratory conducted a series of acute experiments that manipulated various resistance exercise variables (e.g., intensity, volume, and muscle time under tension) that has led to the thesis that maximal fibre activation represents the primary stimulus to maximize MPS during resistance exercise recovery. Our findings uncovered a concept that is commonly not recognized. Specifically, high-intensity contractions (lifting heavy loads) are not the only driver of exercise-induced rates of MPS. The aim of this article, therefore, is to discuss the idea that full muscle fibre recruitment, and not merely high-intensity contractions, is the fundamental variable underpinning resistance exercise-induced MPS rates.

The contraction stimulus driving MPS

There are a myriad of resistance exercise variables, beyond intensity, which can be manipulated to produce diverse training-

mediated hypertrophy; these variables can include volume, muscle action, muscle time under tension, lifting cadence, contraction mode, and inter-set rest interval (American College of Sports Medicine 2009). Indeed, for each of these variables to have independent effects on muscle protein turnover, and thus hypertrophic adaptation, the skeletal muscle must be able to “gauge” these variables as distinct mechanical stimuli, such as interacting with the metabolic and hormonal milieu, that can subsequently be transformed into intramuscular signals that leads to the stimulation of MPS. Theoretically, each variable would elicit a specific muscle phenotypic response. However, such evidence is, at least in our view, lacking. From a systems perspective, the input into a skeletal motor unit–muscle fibre to lift a weight would come from the neural signals it received, and these signals would determine whether to fire or not fire and at what frequency. The surrounding nutrient milieu would then dictate (to a variable degree) the response of the fibre in terms of MPS (Biolo et al. 1997), which would ultimately sum to yield hypertrophy over time. When viewed from this perspective, there is an underlying commonality between many RT variables such that application of any variable in such a way to induce muscle activation ultimately serves to activate the same intramuscular signaling pathways necessary to stimulate MPS and potentially training-induced hypertrophy. Indeed, many will argue that the phenotype of ultimate importance with any program of RT is both strength and hypertrophy and we do not disagree with this. However, a common link between these variables is hypertrophy, and thus we focus on gains in muscle protein mass in this review. Strength gains are, however, a product of neuromuscular and muscular adaptations as reviewed elsewhere (Sale 1988).

Resistance exercise intensities of ~70%–80% of 1 repetition maximum (1RM) for 8–12 repetitions are the classically prescribed protocols to use to maximize training-induced muscle hypertrophy (American College of Sports Medicine 2009). What is so intrinsically unique about high-intensity resistance exercise in terms of promoting exercise-induced MPS? It may be related to the existence of a positive relationship between greater force development and increased muscle electromyographic activity (Alkner et al. 2000). Accordingly, a greater recruitment of muscle fibres at high exercise intensities may occur to stimulate a robust MPS response. Kumar and colleagues (2009) provide support for the concept of a dose–response relationship between external work-equated exercise intensities and MPS. From this work it appears the relationship reaches a plateau between intensities of ~60–90% of 1RM (Kumar et al. 2009). This outcome, we propose, is likely a product of maximal, or at least near maximal, muscle fibre recruitment at contraction intensities beyond 60% of 1RM. Thus, there would be little reason to expect a large difference in MPS unless the muscle fibre had an intricately sensitive mechanism to detect a difference between 60% and 90% of 1RM, a concept that appears, at least according to all available data, highly unlikely. It is generally accepted that motor units are recruited in accordance with the size principle during voluntary muscle contraction (Henneman et al. 1965). Against this background, it would seem reasonable to assume that lower intensities performed to volitional fatigue (i.e., task failure) could achieve a similar degree

of muscle fibre activation to that of high-intensity resistance exercise regimes performed to task failure, and presumably a similar stimulation of MPS during recovery (Fig. 1). Certainly, such a thesis would be dependent on the notion that maximal fibre activation occurs at the moment of fatigue, which is an idea that has support (Wernbom et al. 2009).

Our laboratory has recently tested the thesis that eliciting failure during high- or low-intensity resistance exercise leads to maximal muscle fibre activation, and thus a similar stimulation of MPS. It was demonstrated, in resistance-trained young men, that lower intensity (30% of 1RM) and higher volume (24 ± 3 repetitions, means \pm SD) resistance exercise performed until failure was equally effective in stimulating myofibrillar protein synthesis rates during 0–4 h recovery as heavy intensity (90% of 1RM) and lower volume (5 ± 1 repetitions) resistance exercise (Burd et al. 2010*b*). Interestingly, exercise performed at 30% of 1RM induced a longer-lasting effect on MPS at 21–24 h of exercise recovery (Burd et al. 2010*b*). The observation of a sustained elevation in myofibrillar protein synthesis rates after the low-intensity–higher volume regime corroborates recent data demonstrating that exercise volume is an integral factor for sustaining the myofibrillar protein synthetic response during exercise recovery (Burd et al. 2010*a*). Thus, an additional benefit of low-intensity resistance exercise is that it allows for higher total number of repetitions to be performed, which is an important variable to sustain the response, and still eventually results in full motor unit recruitment.

For clarity, the performance of dynamic knee extension exercise at 30% of 1RM to failure, as we did previously (Burd et al. 2010*b*), induces fatigue in the contracting leg within 24 repetitions. This number of repetitions effectively minimizes the time that loaded muscle is under tension and likely prevents a shift toward the synthesis of non-contractile proteins (Burd et al. 2012). Also, leg extension exercise, even at low intensities, is effective at inducing temporary occlusion of blood flow (Wernbom et al. 2009). Thus, other types of resistance exercises (e.g., leg press) would require more repetitions to induce fatigue with an intensity at 30% of 1RM (Hoeger et al. 1990). An argument that is commonly put forward is the sustained elevation in postabsorptive MPS observed after the low-intensity–higher volume condition, such as in our previous study (Burd et al. 2010*b*), simply represents a state of increased muscle protein turnover as compared with the high-intensity condition. We cannot completely dismiss such an argument as invalid. It is clear the substrates to support MPS, in the fasting state, are the amino acids released from muscle protein breakdown (Phillips et al. 1997). However, examining the 24-h responses after feeding 15 g of high-quality protein, and thus decreasing muscle protein breakdown (Biolo et al. 1997), demonstrates that myofibrillar protein accretion is occurring in similar magnitude to the high-intensity condition (Burd et al. 2011). Thus, we speculate that low-intensity training would result in a similar amount of training-induced muscle mass as high-intensity resistance training.

Perspective

A central tenet of this review is that achieving maximal muscle fibre activation during acute resistance exercise is fundamental in eliciting robust increase in MPS (Fig. 1).

Also, the authors wish to be clear that the prescription of an “optimal” resistance training program will never be possible as substantial variation exists in the ability of individuals to respond to a training stimulus. Moreover, differential training goals among cohorts of individuals will also need to be considered when developing training programs. However, the perspective provided within this review highlights that other resistance exercise protocols, beyond the often discussed high-intensity training (American College of Sports Medicine 2009), can be effective in stimulating an acute anabolic response (Burd et al. 2010*b*) that may translate into training-mediated increases in hypertrophy (Léger et al. 2006). A larger metabolically active muscle mass, and discussing other avenues beyond high-intensity contractions to achieve this, will have important implications from a public health standpoint. For example, skeletal muscle mass is a large contributor to daily energy expenditure and will assist in weight management. Additionally, skeletal muscle, because of its overall size, is the primary site of blood glucose disposal and thus will likely play a role in reducing the risk for the development of type II diabetes (Wolfe 2006). However, if the goal is to achieve maximal strength development, since neural factors are a significant contributor to this outcome (Sale 1988), then high-intensity training regimes are superior in this regard. Training with high-intensity contractions allows the trainee to get “practice” in activating muscle mass during a single maximal lift. However, greater strength would not require continual training at higher intensity resistance exercise, merely the periodic practice of higher intensity lifts during a low-intensity training program.

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