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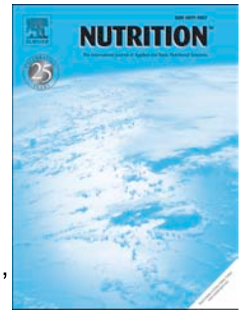

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Resistance training and protein intake synergistic effects: Practical aspects

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Abstract:

Resistance training is a potent stimulus to increase skeletal muscle mass. The muscle protein accretion process depends on a robust synergistic action between protein intake and overload. The intake of protein after resistance training increases plasma amino acids, which results in the activation of signaling molecules leading to increased muscle protein synthesis (MPS) and muscle hypertrophy. Although both essential and non-essential amino acids are necessary for hypertrophy, the intake of free L-leucine or high leucine whole proteins has been specifically shown to increase the initiation of translation that is essential for elevated MPS. The literature supports the use of protein intake following resistance training sessions to enhance MPS; however, less understood are the effects of different protein sources and timing protocols on MPS. The sum of the adaptions from each individual training session are essential to muscle hypertrophy, and thus highlight the importance of an optimal supplementation protocol. The purpose of this review is to present recent findings reported in the literature and discuss the practical application of these results. In that light, new speculations and questions will arise that may direct future investigations. The information and recommendations generated in this review will thereby benefit practicing sport and clinical nutritionists alike.

Introduction

The induction of skeletal muscle hypertrophy via resistance training as a treatment or preventative measure has received less research attention compared to the study of skeletal muscle atrophy. Muscle atrophy is considered an important public health problem due to its primary (metabolic alterations) and secondary (strength loss, decreased autonomy) consequences, and thus muscle hypertrophy should be considered not only the process of "new muscle growth" (in athletic and recreational subjects) but also muscle repair and maintenance (in atrophic patients). This places the understanding of muscle hypertrophy as an important process in both clinical and performance settings. In this context, protein supplements containing essential amino acids (EAA) and leucine may be a promising anti-atrophic/hypertrophic therapy, acting by inhibiting skeletal muscle proteolysis and/or increasing muscle protein synthesis (MPS), an effect which may be a dose-dependent process [1]. Recently, Joy et al. [2] reported a high dose of rice protein supplementation in strength trained athletes as being equally effective as whey protein to support increases in skeletal muscle mass and strength following 8 weeks of resistance training. This study questions previous studies where milk based proteins were superior to soy protein [3], and opens new possibilities for vegans or individuals with milk allergies to use vegan proteins under with resistance training to induce hypertrophy. From a different perspective, our group investigated the effects of leucine kinetics administered via bolus or pulse supplementation in hypercortisolemic rats. Surprisingly, an inverse relationship was observed, where leucine supplementation administered via multiple small doses (pulse) resulted in impaired glucose homeostasis and reduced muscle protein sparing effects [4]. Several questions arise from these novel reports: what is the optimal dose and timing of protein supplementation to promote muscle protein synthesis (MPS)? Next, what is the effect of varying sources of protein on muscle mass, and how does the amino acid and leucine compositions of these proteins affect MPS? Finally, for healthy and elderly subjects engaged in resistance training, what are the effects of pulse versus bolus supplementation schedules on MPS and glucose homeostasis?

This short review will discuss these questions with an emphasis on how protein supplementation, EAA and leucine regulates skeletal MPS. Our goal is to present data from a practical perspective demonstrating how protein supplementation synergistically interacts with resistance training and affects muscle hypertrophy in healthy and elderly populations.

Efficacy of resistance training and protein supplementation to stimulate protein synthesis

A single bout of resistance training acutely increases muscle protein degradation above MPS [5] such that net balance remains negative unless feeding occurs [6]. From a practical standpoint, as little as 20 g of protein (albumin, soy, or whey) [7,8] has been shown to increase MPS if consumed post resistance training. It is well documented that protein intake is necessary to maintain positive nitrogen balance during muscular overload in order to support muscle hypertrophy; however, the ideal amino acid composition to enhance MPS requires further examination. For example, skim milk has been shown to increase MPS to a greater degree than isonitrogenous soy milk [3] suggesting that the amino acid composition, bioavailability, and/or pattern of amino acid delivery [9] of the post exercise protein source may also effect the hypertrophic response. The intake of EAA appear to be exclusively required to stimulate MPS as the addition of non-essential amino acids does not further elevate MPS [10]. Phillips [11] suggested that the intake of 8.5 g EAA containing 1.5 g leucine maximally stimulates MPS if consumed post-work out, with protein synthesis peaking 3 h post exercise and continuing 24 h into recovery [12]. On the other hand, MPS returns to baseline 3 h following EAA and leucine intake in the resting state [13]. Thus, the interaction between resistance training and EAA ingestion is synergistic: overload likely activates the machinery required for MPS; however, increased synthesis, and therefore new muscle protein, will not begin until amino academia occurs. While an acute bout of resistance training and amino acid intake is capable of inducing MPS, the practical applications to these results are limited as it requires chronic overload over successive sessions for MPS to manifest in measurable hypertrophy. Although chronic resistance training appears to reduce the ability of overload to signal the mammalian target of rapamyacin (mTOR) [14], post-exercise intake of whey protein has been shown to prolong the mTOR response to overload [15] and mRNA expression of myoblast proliferation genes [16], indicating that chronic post exercise protein intake alters anabolic signaling and mRNA expression in a manner advantageous for muscle hypertrophy.

Chronic resistance training, protein intake, and muscle hypertrophy

The morphological and functional adaptations to resistance training have been well described and include positive neuromuscular responses (improved motor unit recruitment and rate coding), muscle architecture (angle of pennation), biochemical composition (myosin heavy chain and myosin ATPase isoform transitions), and the accumulation of myofibrillar proteins and intracellular constituents (hypertrophy). Importantly, these responses may occur according to the nature of the stimulus applied, as varying modalities of resistance training are capable of inducing a multitude of responses such as myofibrillar and mitochondrial protein synthesis [17], increased branched-chain oxoacid dehydrogenase kinase activity [18], and increased anti-oxidant activity [19]. In untrained subjects, high intensity (70 - 80% 1 RM) moderate repetition training (9 to 11 repetitions) induces the greatest improvements in muscle cross sectional area, whereas higher intensity (> 85% 1 RM) low repetition (3 to 5 repetitions) induces greater improvements in myonuclear number, and low intensity (< 55% 1 RM) high repetition (20 to 28) increases fatigue resistance and maximal oxygen uptake [20,21]. In contrast, low intensity, high repetition training with blood flow restriction has been shown increase muscle cross sectional area without significant increases in muscle force output [22]. Therefore, a variety of factors including, but not limited to mechanical tension, time under tension, muscle damage, hormones, and metabolic stress likely all play a role in regulating the hypertrophic response to resistance exercise [23]. Given that a minimal of 6 weeks of training and supplementation are required for measurable increases in muscle cross sectional area to occur [24], only training studies that included a resistance weight-lifting protocol, were at least 6 weeks in length, and contained at least two training sessions per week are included in this section of the review.

Several studies have assessed the effects of whole protein intake with chronic resistance training on muscle hypertrophy and body composition [25,26,27]. Josse et al. [25] reported 500 ml of skim milk post exercise (at 80% of 1RM) resulted in greater increases in lean mass and strength in women compared to an isoenergetic placebo drink. Differing sources of whole liquid proteins have also been evaluated. Phillips et al. [26] compared the changes in lean mass and muscle fiber cross sectional area between milk protein and soy protein in untrained, young men completing 12 weeks of resistance training consisted of whole body exercises at 80% 1RM, 5 d/wk. A trend for greater improvements in lean body mass and muscle fiber cross sectional area was found for milk protein; however, a control or placebo group was not included. The addition of a placebo group in this study may have increased the statistical power and helped to determine if the increases in lean mass were due to a training effect or the interaction between training and protein feeding. When compared to an isoenergetic placebo, Hartman et al. [27] reported that both 500 ml skim milk and an isoenergetic and isonitrogenous soy milk beverage increased type II muscle fiber cross sectional area and lean mass assessed by dual-energy X-ray absorptiometry (DEXA) following 12 weeks of resistance training (80% 1RM, 5d/wk); however, improvements in muscle cross sectional area and lean mass were greater for the skim milk group than the soy milk group. These studies indicate that post-exercise intake of proteins from milk sources likely augment resistance training induced muscle hypertrophy.

It has been suggested that eccentric contractions are more effective than concentric contractions in inducing MPS [28]; however, the synergistic effects of protein supplementation on hypertrophic adaptations to various contractions are less understood. Recently, Farup et al. [29] compared the effects of 12 weeks of progressive unilateral quadriceps eccentric and concentric only resistance training (3 d/wk) in conjunction with a post-exercise intake of either 19.4 g of whey protein or a carbohydrate placebo in recreationally active young men. Muscle hypertrophy was evaluated via computerized tomography and whey protein supplementation was found to increase muscle and tendon hypertrophy above that of carbohydrate irrespective of contraction mode. It is possible that the high volume training protocol (i.e.: 6 and 12 sets of 10-15 and 6-10 reps, respectively) induced similar levels of fatigue and overload under both conditions resulting in similar MPS stimulation. This contrasts the results of a single session where MPS was found to increase with eccentric loading only [30]. The initial increase in MPS was likely the result of enhanced activation of striated muscle activator of Rho signaling (STARS) pathway via external stress; however, chronic training results in similar accumulations of MPS, STARS mRNA expression, and hypertrophy between contraction modes [31]. This suggests that whey protein may be effective at augmenting muscle hypertrophy under a diverse set of training protocols given that successive training sessions consist of adequate volume and overload. A meta-analytic study concluded that for trained non-athletes, maximal strength gains occurs with a mean intensity of 80% 1RM, 2 d/wk and with a mean volume of 4 sets, but the effort-to-benefit ratio differ for untrained, recreationally trained, and athlete populations (reviewed by [32]).

Different Sources of Proteins

The effects of different sources of proteins on aminoacidemia, MPS and hypertrophy have been investigated via several protocols. Wilkinson et al. [3] reported that despite having similar protein digestibility corrected amino acid scores, an isonitrogenous, isoenergetic, and macronutrient-matched milk beverage resulted in a greater uptake of amino acids and rate of MPS 3 h after an acute bout of resistance training in recreationally trained men. Hartman et al. [27] later demonstrated 12 weeks of resistance training (5 d/wk, rotating upper/lower body split) and fat free milk intake resulted in greater increases in muscle CSA and fat free mass than iso-nitrogenous and energetic soy protein in novice male weight lifters. Although milk protein is composed of 80% casein (a slow digested protein) and 20% whey, and resulted in a slower appearance of aminoacidemia, the appearance of leucine in the systemic circulation was markedly increased in the milk group when compared with soy beverage [3]. The greater increase in MPS with milk despite the slower aminoacidemia was attributed to the ability of leucine to activate mTOR in the initiation of translation in protein synthesis. Studies comparing the differences in digestion and MPS induced by the intake of individual milk proteins demonstrate that the pattern of aminoacidemia and rise in leucine is greater following an isonitrogenous whey hydrolysate intake than casein [33]. Moreover, soy was found to stimulate a greater rise in MPS compared to casein, suggesting that whey, as part of whole milk protein, was responsible for the increased rate of MPS reported by Wilkinson et al. [3]. This suggests that milk protein in general, and whey in particular, may be most effective in enhancing gains in lean mass during resistance training.

On the other hand, Joy et al. [2] compared the effects of 48 g of iso-nitrogenous and iso-caloric rice protein isolate or whey protein isolate consumed post-exercise on muscle thickness, body composition, and strength following 8 weeks of non-linear resistance training program (3 d/wk, divided into hypertrophy and strength schemes, with 8-12 RM and 5 RM, respectively) in recreationally trained subjects. 48 g of rice protein and whey protein provides 3.8 g and 5.5 g of leucine, respectively, and both whey protein and rice protein resulted in similar improvements in lean mass and strength. These results lend support to the hypothesis that absolute leucine contribution from protein is more important in simulating MPS than relative content [2]; however, because the rice protein group consumed a meat based diet, caution must be taken when extrapolating these results to the application of rice protein supplementation to increase strength and hypertrophy in vegans. Additionally, although specific *p* values were not reported, there appeared to be a trend for greater increases in lean mass with whey protein (3.2 kg) compared to rice protein (2.5 kg). It is possible that more evident differences may have been observed with a longer duration or a larger subject pool. Finally, the meal plan prescriptions given 2 weeks prior to and maintained throughout the study, and the absence of a nutritionally matched control group limits the ability to detect whether increases in lean mass and strength can be attributed to supplementation or to the increase in protein and energy intakes as a result of the pre-study dietary intervention.

Protein Supplementation and Muscle Hypertrophy in the Elderly

Progressive resistance training effectively attenuates the decline in age-related functional performance by augmenting skeletal muscle mass and strength. Although resistance training stimulates MPS, muscle protein breakdown is also accelerated such that net nitrogen balance will remain negative in the fasted state. Protein and/or amino acid feeding post workout has been shown to inhibit muscle protein breakdown resulting in a positive nitrogen balance in young adults; however, these results are not always replicated in older adults. Verdijk et al. [34] administered 10 g of hydrolyzed casein supplemented pre- and post-workout during 21 weeks of progressive resistance training (60 to 80% 1RM, 3 d/wk) in healthy elderly male subjects consuming a moderate protein diet. Although strength and muscle mass as assessed by DEXA increased following 21 weeks of resistance training, there were no differences between protein and placebo. In contract, Tieland et al. [35] reported 15 g of milk protein concentrate supplemented pre- and post-workout for 24 weeks of progressive resistance training (2 d/wk) in frail elderly subjects resulted in greater improvements in lean body mass as assessed by DEXA, but not strength when compared to placebo.

The discrepancy between the two studies may be a result of the protein source. Burd et al. [36] reported a greater stimulation of myofibrillar protein synthesis with whey protein supplementation compared to casein in elderly men both at rest and following an acute bout of resistance exercise consisting of 3 sets of 10RM. Older adults appear to display a relative leucine insensitivity in the skeletal muscle, thus larger spikes in circulating leucine may be required to restore higher levels of MPS post-exercise [37-39]. Milk protein is faster digesting than casein with a higher leucine content. Therefore a higher amplitude of aminoacidemia was achieved with milk protein, whereas the threshold for a sufficiently rapid leucinemia capable to stimulate the hypertrophic response was likely not achieved with casein protein. These observations support the hypothesis that a rapid rise in circulating essential amino acids, and in particular leucine, are required to optimally stimulate MPS following resistance training in the elderly.

Leucine and amino acid signaling, a practical view

Leucine is an indispensable amino acid that constitutes 8% and 10.9% of soy and whey protein, respectively. Due to its robust isolated effects on pancreatic, hepatic and muscular cellular signaling, leucine is also considered a physiopharmacological entity. For example 0.35 g and 1.35 g leucine administration has been shown to promote the attenuation of skeletal muscle catabolism during energy restriction and the facilitation of myofiber microtrauma repair yielding improved skeletal muscle protein turnover in the elderly [40]. Moreover, although a number of molecules are required to sustain MPS, only leucine is capable of independently signaling the initiation of protein translation through the mTOR pathway [11,41]. The variance in leucine content between different protein sources may account for the distinct actions on MPS following supplementation. Norton et al [42] compared wheat gluten (6.8% of leucine), soy protein isolate (8.0% of leucine), egg white solids (8.8% of leucine) and whey protein isolate (10.9% of leucine) on muscle protein synthesis in rats. Whey protein ingestion resulted in the greatest stimulation of MPS via activation of the mTOR pathway. Moreover, when wheat gluten was enriched with 4.1% leucine (to equal the leucine content present in whey protein) no differences in MPS were observed. This suggests that leucine content is a major factor behind the variance in the ability of different protein source to stimulate muscle protein synthesis.

Given that leucine is essential to the initiation in MPS the next logical question becomes what quantity of leucine is required to maximally stimulate MPS. Wall et al. [43] demonstrated significant improvements in post-prandial muscle protein accretion in healthy elderly men when 2.5 g leucine was added to 20 g casein. Because of leucine’s ability to enhance insulin secretion, these improvements may have been partially due to the anabolic and anti-catabolic effects of insulin. Of particular importance was that the rate of the incorporation of other branched chain amino acids in muscle protein increased, as reflected through greater reductions in general plasma values of isoleucine and valine, and enhanced incorporation of isotopic radioactive phenylalanine in skeletal muscle protein. These results strengthen the evidence that leucine added to a meal or supplemental protein results in more dietary protein integrated in skeletal muscle, and suggest that leucine supplementation may reduce protein requirements in the elderly.

In contrast, Leenders et al. [44] reported 6 months of meals supplemented with leucine (2.5 g leucine per meal, 7.5 g per day) did not improve strength or lean mass in elderly diabetic subjects. Although both studies [43,44] demonstrated rises in insulin concentration with leucine supplementation in the elderly, the contradicting results may have been due to differences in the subjects used. Leenders et al. [44] employed type II diabetic subjects, which may have been resistant to the anabolic and anti-catabolic effects of enhanced insulin secretion, leading to fewer skeletal muscle adaptions. Another explanation for the discrepancy in results may have been due to the protein content and/or composition of the accompanying meals: Wall et al. [43] provided a standardized protein content whereas subjects in Leenders et al. [44] maintained their current diets. It is possible that the optimal amount of other amino acids were not present in Leenders'study.

Dardevet et al. [39] proposed that under catabolic conditions the anabolic threshold (requirements for amino acids and hormones to promote MPS) is further increased by free leucine intake. Under normal conditions an increased intake of leucine combined with amino acids will surpass the anabolic threshold and stimulate MPS; however the rise in MPS will be reduced as the anabolic threshold increases due to catabolic conditions. Moreover, even if the anabolic threshold is surpassed with leucine intake, this increase in MPS will be transient unless adequate amino acids are supplied simultaneously. Given that the anabolic threshold is increased with type II diabetes [38], the subjects in Leenders et al. [44] likely had a higher anabolic threshold and experienced a desynchronization between leucinemia and aminoacidemia by consuming free leucine in addition to a slow digesting solid meal, that may also not have supplied an adequate amount of amino acids. This may have resulted in a rise in MPS that was inadequate in duration to manifest in protein accretion thus leading to the insignificant increases in lean body mass. It is therefore likely that leucine dosages need to be adjusted and matched to protein digestion rates in order to maintain MPS duration in the elderly or under catabolic conditions; however, future research is needed to support these theories.

Investigators studying the leucine threshold to increase MPS in young resistance trained subjects have also reported conflicting results. For example, Phillips [11] reported that as little as 2.5-3 g/dose of leucine derived from 20 g whey protein following resistance training stimulates MPS with no further increase observed with dosages in excess of 3 g/dose. Other researchers have looked at the amount of leucine in vegan protein required to maximally stimulate protein synthesis. Joy et al. [2] reported a higher threshold of 3.8 g/dose was required when the leucine was derived from 48 g of rice protein. The differences in these leucine thresholds may be an extension of the ratio of amino acids and macropeptides in the mixture, not the fixed value of leucine as suggested by Joy et al. [2]. Thus, leucine intake with higher quality proteins, such as milk-based proteins, may provide a ratio of amino acids more conducive to supporting muscle growth at lower absolute protein intakes [45]. Finally, although the relationship between leucine threshold and protein synthesis exists, future research is needed to explore the variance in thresholds with different sources of proteins and varying conditions.

[FIGURE 1]

Dietary protein requirements for inducing optimum adaptations

The current recommended dietary allowance (RDA) for daily protein intake is approximately 0.8 $g.kg^{-1}.day^{-1}$ [46,47]. Individuals engaged in resistance and/or endurance exercise regimens require more protein in order to maintain a positive nitrogen balance than sedentary subjects [48,49]. Based on studies using nitrogen balance methodology, the protein intake recommendations for athletes of endurance and resistance activities is 1.2-1.7 $g.kg^{-1}.day^{-1}$ [50]. For example, Tarnopolsky et al. [49] reported that intake of a "low" protein diet (0.86 $g.kg^{-1}.day^{-1}$) by a group of strength trained athletes resulted in accommodation and impairment of protein synthesis when compared with groups consuming medium (1.4 $g.kg^{-1}.day^{-1}$) and high protein (2.4 $g.kg^{-1}.day^{-1}$) isoenergetic diets (30% of protein supplied via whey protein, the remainder comprised of "miscellaneous" plant and animal protein sources). Although there were no differences in whole body protein synthesis between medium and high protein diets, the total amino acid oxidation was elevated in the high-protein group. This observation may suggest that an increase in protein intake is necessary to optimize muscle growth and repair in strength athletes but a very high protein intake is dispensable to optimum adaptations to resistance training. On the other hand, Bray et al. [51] studied the effects of three different protein intakes on quality of weight gain during 1,000 kcal/day over feeding in healthy, sedentary subjects. Although all three groups gained the same amount of weight, the ratio of lean to fat mass gain was greatest in the high and moderate protein groups. Additionally, while the low protein group (0.7 $g.kg^{-1}.day^{-1}$) lost lean mass, both the high (1.7 $g.kg^{-1}.day^{-1}$) and very high protein group (3.0 $g.kg^{-1}.day^{-1}$) gained significantly more lean mass and trended toward a lower increase in fat mass, with the greatest changes observed in the very high protein group. These results suggest that resistance training athletes seeking to rapidly increase bodyweight may experience a higher quality of weight gain if a greater proportion of added calories are derived from protein; however, more research is needed to determine the effects of very high protein intakes in combination with caloric excess on the composition (skeletal muscle vs. splanchnic) of lean mass gains. In another study Mettler et al. [52] compared the effects of a normal (1.0 $g.kg^{-1}.day^{-1}$) vs. high (2.3 $g.kg^{-1}.day^{-1}$) protein intake on lean body mass loss and performance during 2 weeks of resistance training with a 60% caloric intake restriction. While changes in performance measures and loss of body fat were not different between groups, the high protein group lost significantly less lean mass (- 0.3 kg) compared to the normal protein group (- 1.6 kg). Based on these observations in athletes and similar observations in sedentary individuals [53], protein intakes as high as 2.3 g/kg may be required to maximize positive changes in body composition during energy restriction and weight loss.

When post resistance exercise dose response-response was evaluated, isolated egg protein fed in young men demonstrated that 20 g of egg protein maximally stimulates MPS after resistance exercise, with no statistical differences compared to the intake of 40 g [54]. In elderly men Yang et al. [55] observed a significantly greater increase in MPS with 40 g of whey protein compared to 20 g following resistance training. Given that the leucine threshold and accompanying EAA required to maximally stimulate MPS in young adults is 3 g and 10 g, respectively [11,56], it would appear that the post-exercise protein intake required to maximally stimulate MPS is around 20-25 g of high-quality protein in young adults [54] and upwards of 35-40 g in older adults [55]; however, more research is needed to evaluate differences in MPS response with the intake of different sources of proteins after resistance training (e.g. whole food sources like meat, eggs, whole milk and also novel protein supplements based on meat such as beef protein isolate).

Evidences of Nutrient Timing inducing optimum muscle adaptations

To our knowledge, Tipton et al. [57] performed the pioneer work demonstrating the presence of a window of nutrient intake required to maximally stimulate MPS. In that study, the intake of EAA and carbohydrate immediately pre exercise resulted in a significantly greater and more sustained muscle protein synthesis response compared to the same ingestion protocol immediately post exercise. In contrast, Fujita et al. [58] reported the ingestion of EAA and carbohydrate 1 h pre-exercise did not result in an increased post exercise MPS. The discrepancy in the results may be due to timing issues, in that absorption likely fully occurred prior to exercise in Fujita et al. [58] whereas absorption was still occurring post exercise in Tipton et al. [57], leading to the appearance of new EAA in the blood during the post exercise period.

Given that during exercise MPS is suppressed by the adenosine monophosphate protein kinase as ATP is conserved to maintain muscular contraction [59], debate exists in the literature whether protein intake before and/or after resistance training is optimal in promoting muscle hypertrophy. Hoffman et al. [60] examined the differences in muscle hypertrophy assessed via DEXA between two supplement schedules in resistance trained males during 10 weeks of progressive resistance training (4 d/wk). Subjects were supplemented with a total of 42 g of protein and 3.6 g leucine pre- and post-training or in the morning and evening. No differences were reported between groups for muscle hypertrophy following 10 weeks of progressive resistance training. These results refute the suggestions of Fujita et al. [58] that post exercise protein intake is most important for maximizing MPS in response to resistance training. In contrast, Cribb and Hayes [61] utilized a similar supplementation structure (morning and evening versus pre- and post-training); however the tested supplemented was comprised of a mixture of protein/creatine/glucose (1 g/kg/body weight) during 10 weeks of progressive resistance training (5 d/wk) in recreationally trained males. The pre- and post-training supplementation schedule significantly improved muscle strength (1RM) and lean body mass when compared with the morning-evening group. The discrepancy in these results highlight the need for more research to delineate the best supplementation strategy with regards to timing, protein composition, and type of resistance training performed to enhance MPS and thus recovery and hypertrophy [62].

The effects of pulse versus bolus protein intakes on MPS and changes in the rate of rise and duration of aminoacidemia have also been examined using pre- and post-training supplement protocols. Burke et al. [63] administered 25 g of whey protein and 5 g of leucine 45 min prior to resistance exercise (Bolus) or a Pulse schedule whereby the same absolute dosage was administered in 15 × 33-mL aliquots every 3 min commencing at 45 min prior to the start of training. The Pulse feeding resulted in greater MPS 1 h post exercise; however, there were no differences in MPS between Bolus and Pulse at 5 h post exercise. Bolus resulted in a spike in plasma leucine and insulin pre-exercise that dissipated post exercise, whereas Pulse resulted in elevated post exercise plasma leucine and insulin concentrations. This increase in MPS with the appearance of post-exercise aminoacidemia from pre-exercise protein intake furthers our previous explanation of the discrepancy in the results reported by Tipton et al. [57] and Fujita et al. [58]. Given a greater increase in post-exercise MPS with a pulse feeding, West et al. [64] compared the effect of a post-exercise Bolus (25 g whey protein) versus Pulse (2.5 g whey protein every 20 min for 2 h) intake on MPS. Bolus resulted in a greater post-exercise MPS leading to an increase in the translation of contractile proteins compared to Pulse supplementation. These results highlight the importance of a rapid rise in post-exercise insulin and aminoacidemia to stimulate MPS. Additional research, however, is needed to determine if a pre-exercise pulse combined with a post-exercise bolus intake of protein and BCAAs can elevate and sustain MPS over a post-exercise intake only.

An optional interpretation to the above studies is that the presence of leucine in Burke et al. [63] contributed to the enhanced result with pre-exercise pulse feeding. However, if a 1.5-3 g leucine threshold indeed exists, the whey protein dosage of 25 g used [63] theoretically should not interfere with the final result. Interestingly, our group compared a Bolus (.35 g and 1.35 g per rat) versus Pulse (0.35 g and 1.35 g consumed sporadically in drinking water) on the anti-catabolic effects of leucine intervention in an animal model [65]. When animals were treated with Dexamethasone (a potent glucocorticoid), the Pulse schedule resulted in a significantly lower muscle sparing effect. The duration of protein synthesis stimulation in response to an oral leucine dose is approximately 2 h [66], which is similar to that observed after EAA infusion [67]. This refractory effect may better explain the response of Bolus versus Pulse schedules since after the initial stimulation of MPS observed with EAA infusion, a decrease in MPS is observed with further administration despite an increase in plasma EAA levels [67]. Therefore, the magnitude of the initial spike in leucine-induced MPS may be more important for stimulating MPS than maintaining plasma concentrations of leucine with pulse intake protocols. We also observed that only the Pulse treatment interacted in a synergistic manner with Dexamethasone resulting in a robust impairment of glucose homeostasis [65]. This suggests that the rate of leucine-induced insulin release, and not the duration of elevated plasma concentrations, may be most suppressive of muscle protein breakdown during catabolic conditions, such as following exercise.

Conclusion and Future Perspectives

Inducing positive adaptations to skeletal muscle via mechanical overload and nutrient intake is a multifaceted process whereby each variable can be manipulated to increase MPS leading to muscle hypertrophy and improved physical performance. Life expectancy is increasing in most developed countries and strategies to maintain muscle mass and strength are imperative to reduce the risk of disability and loss of independence. Nutritional sciences are rapidly evolving to develop preventative and treatment protocols; however, issues such as anabolic thresholds and dose responses under clinical conditions need further examination prior to forming specific intake recommendations. Additionally, more research is needed to evaluate split protein and EAA intakes, such as before, after, and both before and after resistance training on MPS in older population.

Despite these questions, the body of evidence is substantial enough to conclude that a large synergist effect exists between resistance training, protein supplementation, and MPS. Based on the literature reviewed, we suggest that young adults consuming a moderate protein diet (1.4 $g.kg^{-1}.day^{-1}$) consume 20 - 25 g of high quality protein, providing 2.5 – 3 g of leucine post exercise. We also suggest that older adults engaged in resistance training and consuming a moderate protein diet consume 35 - 40 g of high quality, fast digesting protein following resistance training to maximize MPS, skeletal muscle recovery and adaptation.

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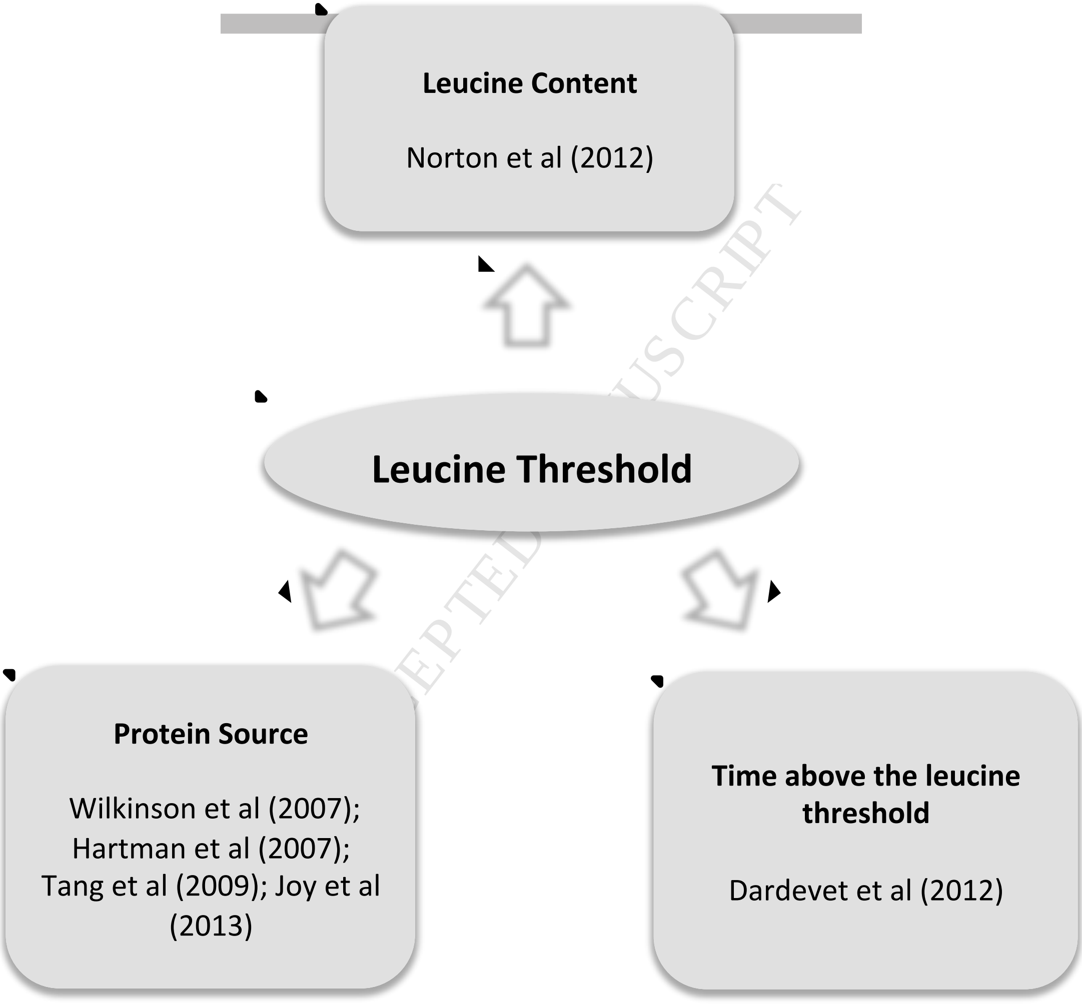
Leucine Content
Norton et al (2012)
Leucine Threshold
Protein Source
Wilkinson et al (2007); Hartman et al (2007); Tang et al (2009); Joy et al (2013)
Time above the leucine threshold
Dardevet et al (2012)