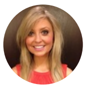
Role of protein and amino acids in promoting lean mass accretion with resistance exercise and attenuating lean mass…

Article *in* Amino Acids · May 2013

DOI: 10.1007/s00726-013-1506-0 · Source: PubMed

4 authors:

Tyler A Churchward-Venne
Maastricht University



Caoileann Murphy
McMaster University

Thomas M Longland
St. Joseph's Healthcare Hamilton

Stuart M Phillips
McMaster University

Amino Acids
DOI 10.1007/s00726-013-1506-0

INVITED REVIEW

Role of protein and amino acids in promoting lean mass accretion with resistance exercise and attenuating lean mass loss during energy deficit in humans

Tyler A. Churchward-Venne · Caoileann H. Murphy · Thomas M. Longland · Stuart M. Phillips

Received: 12 December 2012 / Accepted: 25 April 2013

Abstract Amino acids are major nutrient regulators of muscle protein turnover. After protein ingestion, hyperaminoacidemia stimulates increased rates of skeletal muscle protein synthesis, suppresses muscle protein breakdown, and promotes net muscle protein accretion for several hours. These acute observations form the basis for strategized protein intake to promote lean mass accretion, or prevent lean mass loss over the long term. However, factors such as protein dose, protein source, and timing of intake are important in mediating the anabolic effects of amino acids on skeletal muscle and must be considered within the context of evaluating the reported efficacy of long-term studies investigating protein supplementation as part of a dietary strategy to promote lean mass accretion and/or prevent lean mass loss. Current research suggests that dietary protein supplementation can augment resistance exercise-mediated gains in skeletal muscle mass and strength and can preserve skeletal muscle mass during periods of diet-induced energy restriction. Perhaps less appreciated, protein supplementation can augment resistance training-mediated gains in skeletal muscle mass even in individuals habitually consuming 'adequate' (i.e., >0.8 g kg^{-1} day^{-1}) protein. Additionally, overfeeding energy with moderate to high-protein intake (15–25 % protein or 1.8–3.0 g kg^{-1} day^{-1}) is associated with lean, but not fat mass accretion, when compared to overfeeding energy with low protein intake (5 % protein or $\sim$0.68 g kg^{-1} day^{-1}). Amino acids represent primary nutrient regulators of skeletal muscle anabolism, capable of enhancing lean mass accretion with resistance exercise and attenuating the loss of lean mass during periods of energy deficit, although factors such as protein dose, protein source, and timing of intake are likely important in mediating these effects.

Keywords Amino acids · Protein · Lean body mass · Energy deficit · Resistance exercise

Introduction

It is well established that amino acid ingestion stimulates increased rates of muscle protein synthesis (MPS) and decreases muscle protein breakdown after resistance exercise, thereby promoting net muscle protein accretion (Biolo et al. 1995; Tipton et al. 1999). Because of its profound effects on muscle protein metabolism, protein/amino acid supplementation is often promoted as a dietary strategy to enhance resistance exercise-mediated increases in skeletal muscle mass. Further, higher protein intake during periods of energy restriction has been shown to help offset the lean tissue loss typically associated with higher carbohydrate energy-restricted diets (Krieger et al. 2006; Wycherley et al. 2012). Additionally, higher protein intake coupled with resistance exercise acts synergistically to maintain (Layman et al. 2005; Mettler et al. 2010), and in some cases increase (Josse et al. 2011), lean body mass during diet-induced weight loss. The effectiveness of protein supplementation as part of a dietary strategy to augment muscle mass with resistance exercise and/or preserve lean mass during periods of diet-induced weight loss may in part be influenced by factors such as the protein dose, protein source, timing or 'spread' of ingestion over the day and relative to exercise, and age of the participants.

T. A. Churchward-Venne · C. H. Murphy ·
T. M. Longland · S. M. Phillips (✉)
Exercise Metabolism Research Group, Department
of Kinesiology, McMaster University, Hamilton, ON, Canada
e-mail: phillis@mcmaster.ca

Inter-individual variability in the size of the musculoskeletal mass is determined by differences in both the number and/or size of the individual skeletal muscle fibers. Skeletal muscle fiber number in particular is dependent upon genetic factors, as fiber numbers in the vastus lateralis have been reported to range from 3 to 9 × 10^5 (Lexell et al. 1988) and do not appear to increase in human muscle in response to prolonged resistance exercise training (Abernethy et al. 1994). However, skeletal muscle fiber size and consequently, lean tissue mass can be increased following resistance exercise training (Hartman et al. 2007; Josse et al. 2010), although the magnitude of training-induced gains among individuals is highly variable (Hubal et al. 2005). Additionally, consuming energy above that required for weight maintenance, even in the absence of resistance exercise training, can substantially increase lean body mass (Bray et al. 2012; Forbes et al. 1986), with the amount of lean mass gained related to the amount of excess energy provided from dietary protein (Bray et al. 2012). The ability of resistance exercise and dietary amino acids, to act as stimuli capable of increasing lean tissue mass, resides in the profound effects that these stimuli have on muscle protein turnover.

The rationale for protein/amino acid intake within the context of resistance exercise training to enhance lean mass

In skeletal muscle, protein accretion or loss is determined by net protein balance, which is the algebraic difference between MPS and protein breakdown (Phillips et al. 2005). The effects of amino acids on MPS are driven by their uptake from circulation after a protein containing meal and subsequent incorporation into skeletal muscle proteins. Additionally, amino acids are important in inhibiting the process of muscle protein breakdown (Biolo et al. 1997). In healthy active individuals, skeletal muscle protein synthesis and breakdown, collectively termed protein turnover occurs at a rate of ~1.5–2 %/day and exists in a state of dynamic equilibrium. In the fasted state, the rate of skeletal muscle protein breakdown exceeds skeletal muscle protein synthesis resulting in a net negative protein balance and a net loss of protein (Biolo et al. 1997). This situation is reversed following amino acid provision as amino acids stimulate increased rates of MPS (Churchward-Venne et al. 2012a; Tipton et al. 1999; Moore et al. 2009b), which ultimately results in a positive net protein balance and protein accretion (Biolo et al. 1997). Additionally, amino acid provision immediately after resistance exercise results in greater rates of MPS and greater net protein balance than amino acid provision at rest (Biolo et al. 1997). Therefore, it is the synergistic effect of amino acid intake and resistance exercise on MPS that forms the rationale for the recommendation to consume protein in close temporal proximity to the performance of resistance exercise. However, factors such as protein/amino acid dose, protein source, and timing relative to exercise have all been shown to be important in regulating the response of skeletal muscle protein synthesis to protein intake (for a recent review see Churchward-Venne et al. 2012b).

Role of dietary protein supplementation in enhancing the anabolic effects of resistance exercise training

A recent meta-analysis examining the efficacy of protein supplementation to increase lean body mass and strength during prolonged resistance exercise training concluded that protein supplementation resulted in a significant increase in fat-free mass (~0.7 kg) and strength (13.5 kg for single repetition maximum in the leg press) in both young and elderly subjects (Cermak et al. 2012). However, the ability of protein intake to enhance the adaptive response of skeletal muscle to prolonged resistance exercise may be modulated by factors such as the timing of intake relative to the training stimulus (Esmarck et al. 2001; Burk et al. 2009; Cribb and Hayes 2006; Hartman et al. 2007), the source of dietary protein ingested (Hartman et al. 2007; Cribb et al. 2006; Candow et al. 2006a), and/or to the dose of protein consumed (Verdijk et al. 2009). For example, our research group reported that post-exercise ingestion of bovine milk resulted in more favorable changes in body composition (i.e., greater lean mass accretion and greater fat mass loss) than consumption of an isonitrogenous, isoenergetic soy protein beverage or an energy matched carbohydrate beverage following 12 weeks of resistance training in young men (Hartman et al. 2007). In addition, Cribb et al. (2006) reported significantly greater gains in muscle mass in subjects ingesting supplemental whey protein vs. supplemental casein protein (5.0 kg with whey vs. 0.8 kg with casein) following 10 weeks of resistance training in recreational bodybuilders. Other studies have, however, been unable to detect protein source-dependent differences in lean mass gain following prolonged resistance training. For example, Candow et al. (2006a) reported that while supplemental protein enhanced lean mass accrual following 6 weeks of resistance training when compared to supplemental carbohydrate, gains in lean mass with training were similar following supplemental whey (2.5 kg) and soy (1.7 kg). Discrepancies between the studies of Hartman et al. (2007) and Candow et al. (2006a) in the ability to detect differences between dairy- and soy-based proteins may relate to differences in the duration of the resistance exercise training program (12 vs. 6 weeks) and/or to differences in sample size ($n = 56$ vs. 27).

The temporal pattern of protein/amino acid intake relative to exercise may also impact the amount of lean mass accrual following more long-term resistance exercise training. Some (Esmarck et al. 2001; Cribb and Hayes 2006; Burk et al. 2009) but not all studies (Hoffman et al. 2009) have reported greater lean mass accrual when supplement timing occurs in close temporal proximity to resistance exercise (i.e., immediately before and/or after exercise) as compared to the same supplement provided at times temporally dissociated from the exercise stimulus (i.e., in the morning several hours before exercise). For example, delaying protein intake by 2 h after resistance exercise in a group of elderly men ablated lean mass gains and greatly diminished strength gains when compared to a group of elderly men who ingested protein within ∼5 min after resistance exercise (Esmarck et al. 2001). It is, however, hard to envision that delaying protein intake by such a short period of time would have such a marked impact on muscle protein accretion since we know that exercise in and of itself will stimulate increased rates of MPS for up to 48 h in young subjects (Phillips et al. 1997). Differences between studies may relate to factors such as the age of the participants, training status, or protein source administered during the study. The temporal meal-to-meal pattern of protein/amino acid ingestion may also be an important consideration during the implementation of nutrition-based strategies to promote skeletal muscle anabolism. Areta et al. (2013) demonstrated greater rates of MPS over 12 h following resistance exercise after ingestion of 4 × 20 g protein feedings spaced every 3 h as compared to both 2 × 40 g protein feedings every 6 h and 8 × 10 g protein feedings every 1.5 h in young men. Research is warranted to investigate the impact of the temporal meal-to-meal pattern of protein intake in both young and elderly when practiced over several weeks on lean body mass accretion within the context of resistance exercise training. Indeed, an important consideration in our view when examining the potential efficacy of supplemental protein/amino acids within the context of enhancing lean body mass accretion with resistance exercise training is the dose of protein administered, particularly in studies involving elderly participants. Recent studies have shown that ∼35 of protein during a single feeding stimulates a greater incorporation of dietary protein-derived amino acids into muscle in elderly subjects than 20 g of protein at rest (Pennings et al. 2012), while 40 g protein following resistance exercise stimulates greater rates of MPS than 20 g (Yang et al. 2012a, b). This is in contrast to young subjects in whom 20 g protein is sufficient to maximally stimulate rates of MPS after resistance exercise (Moore et al. 2009a); see Fig. 1. This may explain why some studies in the elderly that have utilized less than 35–40 g protein in a per meal serving have been unable to detect a benefit from supplemental protein/amino acids (Candow et al. 2006b; Verdijk et al. 2009).

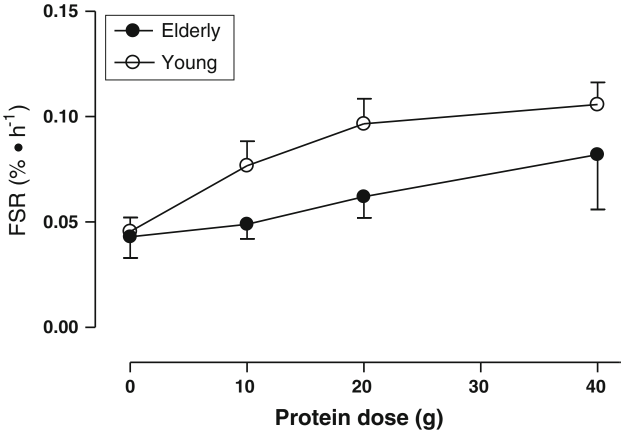


Fig. 1 Comparison of the protein dose response of myofibrillar protein synthesis per protein dose in young and elderly subjects from Moore et al. (2009a) and Yang et al. (2012a) is shown. Note that the proteins used were egg for young and whey for elderly which may favor increased amplitude of response per gram of protein (due to leucine content) in the elderly. Also, values from Moore et al. (2009a) have been corrected from mixed to myofibrillar protein based on comparisons of standard differences observed in our laboratory

Amino acids can increase lean body mass even in the absence of resistance exercise training

Although the notion of increasing lean body mass from 'over-consumption' of dietary protein has been questioned due to the transient nature of feeding-induced increases in MPS (Atherton and Smith 2012), recent evidence demonstrates that in conditions of excess energy intake, dietary protein can result in significant lean mass accrual even in the absence of a resistance exercise training program (Bray et al. 2012). In an elegant study, Bray et al. (2012) confined healthy participants to an in-house environment where they were overfed ∼1,000 kcal daily (corresponding to a ∼40 % increase in energy above that required for weight maintenance) for 8 weeks with diets composed of either low (5 % or ∼0.68 g kg^{-1} day^{-1}), medium (15 % or ∼1.79 g kg^{-1} day^{-1}), or high (25 % or ∼ 3.0 g kg^{-1} day^{-1}) protein. The excess energy from overfeeding resulted in significantly less overall weight gain in the low protein group (3.16 kg) compared with the normal (6.05 kg) or high-protein groups (6.51 kg). However, total body fat increased similarly in all three groups (5 % protein 3.66 kg, 15 % protein 3.45 kg, 25 % protein 3.44 kg). In addition, while the low protein group lost ∼0.7 kg of lean mass, the medium and high-protein groups gained 2.87 and 3.18 kg of lean mass, respectively, and this was

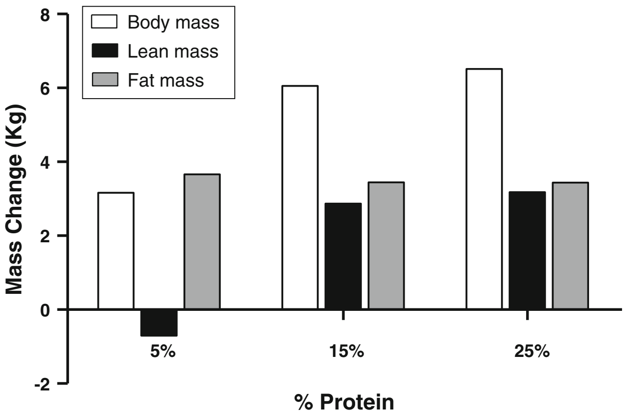


Fig. 2 The effects of over-consuming ($\sim$1,000 kcal day^{-1}) diets composed of low (5 %), normal (15 %), or high (25 %) amounts of energy from protein are shown. Over-consuming diets composed of 15–25 % energy from protein resulted in significant lean mass accretion compared to over-consuming a diet composed of 5 % energy from protein. Note there are no differences between groups in fat mass gain over the overfeeding intervention; the additional weight gain (body mass) in the 15–25 % groups is accounted for by lean body mass accretion. Redrawn from Bray et al. (2012)

associated with an increase in resting energy expenditure (Fig. 2). However, what is not entirely clear is the exact composition of the lean mass accretion (i.e., muscle vs. splanchnic protein accretion) and future work is warranted to address this question. The conclusion from this work was that during a highly positive energy balance, a moderate to high proportion of dietary protein (15–25 %) increases lean mass gain and resting energy expenditure without additional fat mass gain as compared to excess energy intake from carbohydrate and fat (Bray et al. 2012). From the viewpoint of the athlete, future work is warranted to examine the effects of a moderate to higher proportion (i.e., up to 35 % of total energy intake) of dietary protein during a period of controlled excess energy intake on lean body mass gain, fat mass loss, and changes in muscle function when combined with a program of resistance exercise.

Role of protein and amino acids in the alleviation of lean body mass loss during energy restriction

Weight loss represents a significant health goal for a variety of population groups. The prevalence of overweight and obesity has produced an extraordinary challenge to healthcare systems (Finucane et al. 2011). Weight loss in obese and overweight individuals is associated with a host of well-established health benefits including a decreased risk of type 2 diabetes, cardiovascular disease and cancer (Katzmarzyk 2006). The fundamental variable determining weight loss is the relative energy deficit created by dietary energy restriction, increased energy expenditure, or their combination. While it is undisputed that energy restriction is an effective weight loss strategy, it is often associated with a reduction in both fat and muscle mass. In fact, approximately 75 % of weight loss achieved through energy restriction (with protein intakes comprising $\sim$15 % by energy content) is composed of fat tissue, while the remaining 25 % is composed of lean tissue (Weinheimer et al. 2010).

The loss of muscle mass that can occur during weight loss can have a number of deleterious short- and long-term consequences, which may in the long run lessen or negate some of the benefits of weight loss. Beyond its role in locomotion, skeletal muscle plays a number of important roles in blood glucose regulation (Samuel et al. 2010) and lipidemia (Lewis et al. 2002), indicating that the loss of muscle may ultimately have detrimental effects for metabolic health (Wolfe 2006). Furthermore, skeletal muscle is a major contributor to basal metabolic rate (BMR), which represents for many the largest component of daily energy expenditure (Johnstone et al. 2005). Therefore, it has been proposed that a reduction in skeletal muscle mass, and the subsequent decrease in BMR, may hinder further weight loss, long-term weight stability, and contribute to risk for weight regain (Stiegler and Cunliffe 2006; Strychar et al. 2009). In addition, aging per se is characterized by a progressive loss of muscle mass and strength, termed sarcopenia, which is a contributor, along with the loss of strength (dynapenia) to age-associated disability and loss of independence (Baumgartner 2000). In many aging populations, the coexistence of diminished muscle mass and increased fat mass, referred to as 'sarcopenic obesity', is emerging as an important public health problem (Li and Heber 2012). Sarcopenic obesity presents a complex challenge as the appropriate treatment must reduce the health risks associated with excess fat mass, while preserving muscle mass to reduce the risk of loss of strength and increased risk of disability in addition to the metabolic issues incumbent with low muscle mass (Weinheimer et al. 2010). This highlights the need for weight loss interventions that are aimed at achieving high 'quality' weight loss, which can be defined as the loss of body weight with the greatest ratio of fat to lean mass (Josse et al. 2011). The last decade has seen an increased interest in the role of protein intake during periods of energy restriction, with manipulations of the content, type and distribution of protein within the diet emerging as potential strategies to minimize skeletal muscle mass loss (Frimel et al. 2008; Villareal et al. 2011).

High protein during an energy deficit alleviates diet-induced lean mass loss

A substantial body of evidence shows that protein intakes exceeding the current recommended daily allowance (RDA) of 0.8 g kg^{-1} day^{-1} can enhance the preservation of muscle mass during periods of energy restriction (Layman et al. 2005; Leidy et al. 2007; Mojtahedi et al. 2011; Josse et al. 2011), although this is not a universal finding (Campbell and Leidy 2007). One meta-analysis concluded that diets which are higher in protein, substituted for carbohydrates, increased the loss of fat mass and the retention of lean mass (Krieger et al. 2006; Wycherley et al. 2012). Krieger and colleagues reported that protein intakes of ≥1.05 g kg^{-1} day^{-1} were associated with 0.60 kg additional fat-free mass retention in short-term studies compared with lower protein diets. Furthermore, in studies which extended beyond 12 weeks, this difference increased to 1.21 kg (Krieger et al. 2006).

In addition to dietary protein, resistance exercise provides a marked anabolic stimulus for muscle and, when performed during periods of energy restriction, can diminish diet-induced decrements in lean mass (Campbell et al. 2009; Villareal et al. 2011). Moreover, it appears that a synergism exists between resistance exercise training and high-protein intakes during weight loss, resulting in an even greater ratio of fat to lean mass loss when the two strategies are combined (Layman et al. 2005; Mettler et al. 2010; Weinheimer et al. 2010; Josse et al. 2011). A recent study from our laboratory compared the effect of diets varying in total protein and dairy content (15, 7.5, <2.0 % of total energy) on body composition changes during 16 weeks of energy restriction and exercise training (resistance and aerobic) in overweight and obese premenopausal women (Josse et al. 2011). Despite similar total weight loss between diets, there was significantly greater fat mass loss and lean mass preservation in women consuming higher protein/dairy (15 % total energy from dairy and ~1.3 g kg^{-1} day^{-1} total protein), with almost 50 % of total protein intake coming from dairy sources, compared to those counseled to consume protein at a level similar to the RDA (0.8 g kg^{-1} day^{-1}). A notable observation was that the higher protein/dairy group in this study was able to gain lean body mass during the weight loss intervention, meaning that the weight lost was exclusively accounted for by fat. This challenges the notion that skeletal muscle mass gain and fat mass reduction cannot occur simultaneously and corroborates the findings of a handful of studies that have combined higher protein intakes (1.2–2.3 g kg^{-1} day^{-1}) with resistance training during energy restriction in athletic populations (Garthe et al. 2011; Mettler et al. 2010). Importantly, Josse et al. (2011) demonstrated that the increase in lean body mass in the high-dairy protein group (1.3 g kg^{-1} day^{-1}) also translated into greater strength gains compared to the groups consuming less protein and dairy, despite identical exercise training between groups. In a recent study by Mojtahedi et al. (2011), some provisional evidence was provided that the combination of exercise and higher protein intake may offset skeletal muscle loss and also improve physical function during weight loss in aging individuals. In this study, overweight and obese older women performed light exercise training during 6 months of energy restriction. While women consuming higher protein intakes (1.2 g kg^{-1} day^{-1}) experienced larger reductions in absolute, whole-body lean mass compared to those in the normal-protein group (0.87 g kg^{-1} day^{-1}), this was likely accounted for by the fact that they lost more total body-mass than those in the normal-protein group (Mojtahedi et al. 2011). Furthermore, using MRI the same researchers demonstrated improved maintenance of muscle relative to weight loss in the higher protein group, which in turn was associated with enhanced physical function (Mojtahedi et al. 2011). Of note, the exercise intervention in this study, which consisted of moderate intensity walking and flexibility exercises, may not have provided a sufficient anabolic stimulus to retain muscle protein. Thus, it is plausible that an even greater attenuation of muscle loss may have occurred in the higher protein group if resistance exercise had been incorporated into the training regimen, although this thesis requires confirmation by future studies.

High-dairy protein consumption promotes lean mass retention during diet-induced weight loss

Acute studies performed in conditions of energy balance have shown that the amplitude and duration of increases in MPS after feeding can be affected by the protein source, both at rest and after resistance exercise (Burd et al. 2012; Tang et al. 2009; Yang et al. 2012b). For example, we have previously reported that fat-free fluid milk consumption results in a greater nitrogen balance and MPS response following a bout of resistance exercise as compared to an isonitrogenous and isoenergetic soy beverage in young men (Wilkinson et al. 2007). Similarly, the chronic consumption of fat-free milk after resistance exercise was found to promote greater gains in lean body mass than soy protein over 12 weeks of training in young men (Hartman et al. 2007). Hartman et al. (2007) also observed a greater reduction in body fat mass associated with post-exercise milk consumption, despite participants being in positive energy balance, suggesting that dairy foods may be advantageous for fat loss and lean mass retention. The role of dairy foods within the context of weight loss has been reviewed in a recent meta-analysis of randomized controlled trials and reported that consumption of high-dairy hypoenergetic diets result in a significantly greater weight loss, fat mass reduction and lean mass gain compared with conventional calorie-restricted diets (Abargouei et al. 2012). While a number of bioactive components in dairy foods could contribute to their anti-obesity effects, the amino acid leucine, a potent stimulus for stimulating MPS (Churchward-Venne et al. 2012a; Smith et al. 1992), may be critically important for the muscle-sparing effect.

To date few studies have directly compared the effect that isonitrogenous hypoenergetic diets composed of different protein sources (i.e., dairy, vegetable, meat, and soy) have on body composition. In one study, Yamashita et al. (1998) reported similar weight loss between groups consuming a meat-based diet and a soy-based diet; however, both diets were mixed-protein and contained similar amounts of vegetable and dairy proteins (36 and 18 % of total protein, respectively), making differentiation between the effects of animal and plant proteins difficult. Furthermore, body composition was not assessed in this study. Indeed, the preservation of muscle mass would result in less weight loss overall and potentially mask the importance of protein source if lean body mass is not measured. Recently, Abete et al. (2009) found that a hypoenergetic, high-legume (18 % energy from protein) and high-protein (30 % energy from protein) diet composed mainly of animal proteins resulted in similar reductions in total body weight and lean body mass assessed by bioelectrical impedance after 8 weeks. Regrettably, important differences in the macronutrient and fiber content between the diets preclude a direct comparison between the two protein sources and further work is needed to establish whether animal or plant sources of protein may differ in their ability to spare muscle mass during weight loss (Campbell et al. 1999; Haub et al. 2002).

The rationale for considering protein distribution throughout the day

As mentioned previously, reports of a dose–response relationship between protein intake and MPS have shown that ~20 g of high-quality protein [8–10 g essential amino acids (EAA)] is sufficient to induce a maximal stimulation of MPS in the young after resistance exercise (Moore et al. 2009a). On the other hand, doses in the range of 35–40 g whey protein appear more effective at stimulating increased rates of MPS in the elderly both at rest and following resistance exercise (Yang et al. 2012a; Pennings et al. 2012), with protein doses below this threshold resulting in a reduced MPS response in older individuals (Katsanos et al. 2005; Yang et al. 2012a). Taken together, these data suggest that, on a meal-to-meal basis, ingestion of 20–25 g (or ~0.25 g kg^{-1} meal^{-1} for individuals of normal bodyweight) of high-quality protein to provide ~10 g EAA at each meal would repeatedly stimulate optimal rates of MPS in young participants. Given what we know about the responses of MPS in younger versus older persons, it seems these estimates may be even higher in older persons. However, dietary intake data indicate that the majority of adults do not follow a balanced pattern of protein intake, but rather a 'skewed' pattern, ingesting relatively small amounts of dietary protein with breakfast (8–12 g) and consuming ~50 % of daily protein intake during a large protein rich evening meal (Almoosawi et al. 2012; Tieland et al. 2012).

In light of the detrimental effect of prolonged energy deficit on skeletal muscle mass, it has been hypothesized that a balanced dietary protein distribution may play a particularly important role during conditions of weight loss (Layman 2009). To date, only one study has investigated the effect of protein distribution under conditions of energy deficit. Adechian et al. (2012) compared the effect of an 'unbalanced' and a 'balanced' protein feeding pattern on lean body mass and protein turnover during 6 weeks of energy restriction in obese men and women. In this study, total daily protein intake was matched between groups (~1 g kg^{-1} day^{-1}) and was distributed in four meals per day in the proportion 8/80/4/8 % in 'unbalanced' and 25/25/25/25 % in 'balanced' groups. The authors reported significant lean mass loss in both groups, with no effect of protein distribution pattern. However, considering the accumulating evidence that higher protein intakes (i.e., 1.2–2.3 g kg^{-1} day^{-1}) may be necessary to attenuate muscle mass loss during energy restriction, it remains possible that the total protein intake was simply too low in the aforementioned study and thus may have a limited potential muscle-sparing effect. Moreover, this study was performed in the absence of any exercise training. Whether an anabolic stimulus-like resistance exercise may have amplified any benefit from protein distribution pattern requires further examination in future studies (Fig. 3).

Rapid changes in body composition through exercise and diet

Within the Acceptable Macronutrient Distribution Ranges (AMDR) outlined by the US/Canadian dietary guidelines committee, there is tremendous flexibility with the stated recognition that health can be achieved with intakes of carbohydrates varying from 40 to 65 %, fat from 20 to 35 %, and protein from 10 to 35 % of total energy intake. What macronutrient range is optimal during weight loss can vary widely; however, the main aim of weight loss should be to promote fat mass loss while sparing lean mass.

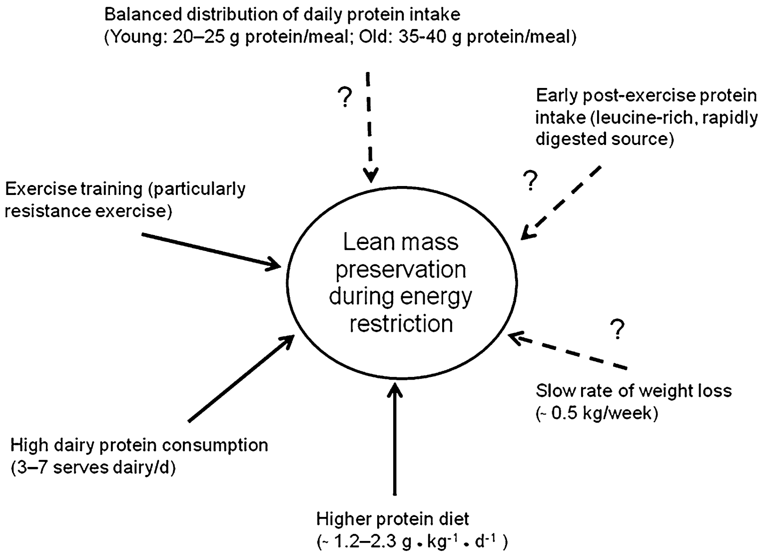


Fig. 3 The factors that promote (*solid arrows*) lean mass preservation during a period of energy restriction, and factors that may be important (*dashed arrows*) but for which more research is needed are shown

Aggressive weight loss strategies to maximize fat mass loss while sparing lean mass would likely involve a relatively large energy deficit and exercise training; such a program may be sought by competitive athletes attempting to gain weight for a weight-class restricted sport, improve their power-to-weight ratio, or improve leanness for esthetic-focused sports. However, avoiding decrements in performance is essential to athletes who are involved in dietary/exercise interventions aimed at promoting rapid changes in body composition. Even though carbohydrate represents the primary energy substrate to support sports performance, increasing protein intake and reducing carbohydrate during energy restriction appear to be an effective strategy to promote lean mass retention and fat mass loss, without negatively affecting performance (Mettler et al. 2010; Paoli et al. 2012). For example, Mettler et al. (2010) compared the influence of a high-protein energy-restricted diet vs. a normal-protein energy-restricted diet on lean body mass loss and performance in healthy, resistance-trained athletes. For both groups, energy intake was reduced to 60 % of their baseline habitual energy intake, while protein intake was ~1.0 g kg^{-1} day^{-1} for the control group and ~2.3 g kg^{-1} day^{-1} for the high-protein group. Participants maintained their habitual training throughout the study and changes in body composition and performance were assessed. Although there were no differences between groups in either fat loss (both groups lost ~1.2 kg) or performance measures, the normal-protein group experienced a significant loss of lean mass (−1.6 kg), while the high-protein group preserved lean mass (−0.3 kg). In another study, Paoli et al. (2012) subjected elite gymnasts to a 30-day ketogenic diet (~22.0 g carbohydrate per day) during which they performed their normal training. After the diet, subjects experienced a −1.9-kg loss of fat mass, no loss of lean body mass, and no decrements in performance (Paoli et al. 2012). Although resistance training is clearly the most effective exercise modality to promote muscle anabolism, accumulating evidence suggests that high-intensity interval training (HIIT) can promote lean mass accretion (Heydari et al. 2012; Trapp et al. 2008), and prevent lean mass loss during diet-induced energy restriction (Sartor et al. 2010). Sartor et al. (2010) subjected participants to 14 days of a low carbohydrate (to ~35 from 54 % of the energy provided) energy-restricted diet, while half of the participants additionally performed HIIT at 90 $\%VO_{2\text{peak}}$ 3 times per week, to assess the combined effects of HIIT training and the carbohydrate reduced diet. Although both groups lost the same amount of fat, HIIT training resulted in a 1-kg gain in lean mass, whereas the diet only group experienced ~1 kg loss in lean mass (Sartor et al. 2010). Therefore, resistance and HIIT-based exercise interventions appear advantageous as exercise modalities to promote lean mass retention during an energy deficit, with an increased benefit from a relatively high-protein diet. It is important to note that aggressive strategies to promote rapid changes in body composition are unlikely to be sustained during more prolonged time periods; however, reducing carbohydrate drastically, increasing protein intake, and integrating HIIT and resistance training may be useful to certain populations (i.e., athletes, military) as part of a short-term ‘aggressive’ strategy to promote rapid, quality changes in body composition.

Conclusions

Amino acids/protein represent the primary nutrient effectors of skeletal muscle protein metabolism through their ability to stimulate increased rates of MPS, suppress protein breakdown, and promote a positive net protein balance, (Biolo et al. 1997; Tipton et al. 1999; Phillips et al. 1997). Perhaps underappreciated, overfeeding energy in the form of protein ($\sim$1.8 g kg^{-1} day^{-1}) can lead to significant lean mass accretion in the complete absence of any resistance exercise program (Bray et al. 2012); however, the effects of amino acids/protein on skeletal muscle anabolism are greatly increased in the acute period by prior resistance exercise (Biolo et al. 1997; Tipton et al. 1999), and data support the use of protein supplementation as an effective strategy to increase resistance exercise-mediated gains in skeletal muscle mass and strength in both young and old participants. Similarly, higher protein intake ($\sim$1.2 g kg^{-1} day^{-1}) during an energy deficit facilitates a sparing of lean body mass, particularly when coupled with a program of resistance exercise training (Weinheimer et al. 2010). However, several factors appear to be important in mediating the anabolic response of skeletal muscle to amino acid/protein provision, including protein source, protein dose, timing relative to exercise, age of the participants, and potentially the meal-to-meal pattern of protein intake over the day. We propose that consumption of high-quality animal-based proteins such as dairy proteins, consumed at a dose of 20–25 g in the young, and perhaps 35–40 g in the elderly equally spread into repeated feeding of four, or at most five, times over the course of the day may be useful to promote skeletal muscle anabolism, particularly when coupled with a program of resistance exercise.

Acknowledgments We thank Dr. Daniel R Moore for his feedback on the manuscript. TAC-V is supported by a Natural Sciences and Engineering Research Council of Canada (NSERC) PGS Doctoral Award and acknowledges their support.

Conflict of interest The authors declare that they have no conflict of interest.

References

Abargouei AS, Janghorbani M, Salehi-Marzijarani M, Esmaillzadeh A (2012) Effect of dairy consumption on weight and body composition in adults: a systematic review and meta-analysis of randomized controlled clinical trials. Int J Obes (Lond). doi:10.1038/ijo.2011.269

Abernethy PJ, Jurimae J, Logan PA, Taylor AW, Thayer RE (1994) Acute and chronic response of skeletal muscle to resistance exercise. Sports Med 17(1):22–38

Abete I, Parra D, Martinez JA (2009) Legume-, fish-, or high-protein-based hypocaloric diets: effects on weight loss and mitochondrial oxidation in obese men. J Med Food 12(1):100–108. doi:10.1089/jmf.2007.0700

Adechian S, Balage M, Remond D, Migne C, Quignard-Boulange A, Marset-Baglieri A, Rousset S, Boirie Y, Gaudichon C, Dardevet D, Mosoni L (2012) Protein feeding pattern, casein feeding, or milk-soluble protein feeding did not change the evolution of body composition during a short-term weight loss program. Am J Physiol Endocrinol Metab 303(8):E973–E982. doi:10.1152/ajpendo.00285.2012

Almoosawi S, Winter J, Prynne CJ, Hardy R, Stephen AM (2012) Daily profiles of energy and nutrient intakes: are eating profiles changing over time? Eur J Clin Nutr 66(6):678–686. doi:10.1038/ejcn.2011.210

Areta JL, Burke LM, Ross ML, Camera DM, West DW, Broad EM, Jeacocke NA, Moore DR, Stellingwerff T, Phillips SM, Hawley J, Coffey VG (2013) Timing and distribution of protein ingestion during prolonged recovery from resistance exercise alters myofibrillar protein synthesis. J Physiol. doi:10.1113/jphysiol.2012.244897

Atherton PJ, Smith K (2012) Muscle protein synthesis in response to nutrition and exercise. J Physiol 590(Pt 5):1049–1057. doi:10.1113/jphysiol.2011.225003

Baumgartner RN (2000) Body composition in healthy aging. Ann N Y Acad Sci 904:437–448

Biolo G, Maggi SP, Williams BD, Tipton KD, Wolfe RR (1995) Increased rates of muscle protein turnover and amino acid transport after resistance exercise in humans. Am J Physiol 268(3 Pt 1):E514–E520

Biolo G, Tipton KD, Klein S, Wolfe RR (1997) An abundant supply of amino acids enhances the metabolic effect of exercise on muscle protein. Am J Physiol 273(1 Pt 1):E122–E129

Bray GA, Smith SR, de Jonge L, Xie H, Rood J, Martin CK, Most M, Brock C, Mancuso S, Redman LM (2012) Effect of dietary protein content on weight gain, energy expenditure, and body composition during overeating: a randomized controlled trial. JAMA 307(1):47–55. doi:10.1001/jama.2011.1918

Burd NA, Yang Y, Moore DR, Tang JE, Tarnopolsky MA, Phillips SM (2012) Greater stimulation of myofibrillar protein synthesis with ingestion of whey protein isolate v. micellar casein at rest and after resistance exercise in elderly men. Br J Nutr 108(6):958–962. doi:10.1017/S0007114511006271

Burk A, Timpmann S, Medijainen L, Vahi M, Oopik V (2009) Time-divided ingestion pattern of casein-based protein supplement stimulates an increase in fat-free body mass during resistance training in young untrained men. Nutr Res 29(6):405–413. doi:10.1016/j.nutres.2009.03.008

Campbell WW, Leidy HJ (2007) Dietary protein and resistance training effects on muscle and body composition in older persons. J Am Coll Nutr 26(6):696S–703S

Campbell WW, Barton ML Jr, Cyr-Campbell D, Davey SL, Beard JL, Parise G, Evans WJ (1999) Effects of an omnivorous diet compared with a lactoovovegetarian diet on resistance-training-induced changes in body composition and skeletal muscle in older men. Am J Clin Nutr 70(6):1032–1039

Campbell WW, Haub MD, Wolfe RR, Ferrando AA, Sullivan DH, Apolzan JW, Iglay HB (2009) Resistance training preserves fat-free mass without impacting changes in protein metabolism after weight loss in older women. Obesity (Silver Spring) 17(7):1332–1339. doi:10.1038/oby.2009.2

Candow DG, Burke NC, Smith-Palmer T, Burke DG (2006a) Effect of whey and soy protein supplementation combined with resistance training in young adults. Int J Sport Nutr Exerc Metab 16(3):233–244

Candow DG, Chilibeck PD, Facci M, Abeysekara S, Zello GA (2006b) Protein supplementation before and after resistance training in older men. Eur J Appl Physiol 97(5):548–556. doi:10.1007/s00421-006-0223-8

Cermak NM, Res PT, de Groot LC, Saris WH, van Loon LJ (2012) Protein supplementation augments the adaptive response of skeletal muscle to resistance-type exercise training: a meta-analysis. Am J Clin Nutr. doi:10.3945/ajcn.112.037556

Churchward-Venne TA, Burd NA, Mitchell CJ, West DW, Philp A, Marcotte GR, Baker SK, Baar K, Phillips SM (2012a)

Supplementation of a suboptimal protein dose with leucine or essential amino acids: effects on myofibrillar protein synthesis at rest and following resistance exercise in men. J Physiol. doi: 10.1113/jphysiol.2012.228833

Churchward-Venne TA, Burd NA, Phillips SM, Research Group EM (2012b) Nutritional regulation of muscle protein synthesis with resistance exercise: strategies to enhance anabolism. Nutr Metab (Lond) 9(1):40. doi:10.1186/1743-7075-9-40

Cribb PJ, Hayes A (2006) Effects of supplement timing and resistance exercise on skeletal muscle hypertrophy. Med Sci Sports Exerc 38(11):1918–1925. doi:10.1249/01.mss.0000233790.08788.3e

Cribb PJ, Williams AD, Carey MF, Hayes A (2006) The effect of whey isolate and resistance training on strength, body composition, and plasma glutamine. Int J Sport Nutr Exerc Metab 16(5):494–509

Esmarck B, Andersen JL, Olsen S, Richter EA, Mizuno M, Kjaer M (2001) Timing of postexercise protein intake is important for muscle hypertrophy with resistance training in elderly humans. J Physiol 535(Pt 1):301–311

Finucane MM, Stevens GA, Cowan MJ, Danaei G, Lin JK, Paciorek CJ, Singh GM, Gutierrez HR, Lu Y, Bahalim AN, Farzadfar F, Riley LM, Ezzati M, Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group (2011) National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. Lancet 377(9765):557–567. doi:10.1016/S0140-6736(10)62037-5

Forbes GB, Brown MR, Welle SL, Lipinski BA (1986) Deliberate overfeeding in women and men: energy cost and composition of the weight gain. Br J Nutr 56(1):1–9

Frimel TN, Sinacore DR, Villareal DT (2008) Exercise attenuates the weight-loss-induced reduction in muscle mass in frail obese older adults. Med Sci Sports Exerc 40(7):1213–1219. doi: 10.1249/MSS.0b013e31816a85ce

Garthe I, Raastad T, Refsnes PE, Koivisto A, Sundgot-Borgen J (2011) Effect of two different weight-loss rates on body composition and strength and power-related performance in elite athletes. Int J Sport Nutr Exerc Metab 21(2):97–104

Hartman JW, Tang JE, Wilkinson SB, Tarnopolsky MA, Lawrence RL, Fullerton AV, Phillips SM (2007) Consumption of fat-free fluid milk after resistance exercise promotes greater lean mass accretion than does consumption of soy or carbohydrate in young, novice, male weightlifters. Am J Clin Nutr 86(2): 373–381

Haub MD, Wells AM, Tarnopolsky MA, Campbell WW (2002) Effect of protein source on resistive-training-induced changes in body composition and muscle size in older men. Am J Clin Nutr 76(3):511–517

Heydari M, Freund J, Boutcher SH (2012) The effect of high-intensity intermittent exercise on body composition of overweight young males. J Obes 2012:480467. doi:10.1155/2012/480467

Hoffman JR, Ratamess NA, Tranchina CP, Rashti SL, Kang J, Faigenbaum AD (2009) Effect of protein-supplement timing on strength, power, and body-composition changes in resistance-trained men. Int J Sport Nutr Exerc Metab 19(2):172–185

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 (2005) Variability in muscle size and strength gain after unilateral resistance training. Med Sci Sports Exerc 37(6):964–972

Johnstone AM, Murison SD, Duncan JS, Rance KA, Speakman JR (2005) Factors influencing variation in basal metabolic rate include fat-free mass, fat mass, age, and circulating thyroxine but not sex, circulating leptin, or triiodothyronine. Am J Clin Nutr 82(5):941–948

Josse AR, Tang JE, Tarnopolsky MA, Phillips SM (2010) Body composition and strength changes in women with milk and resistance exercise. Med Sci Sports Exerc 42(6):1122–1130. doi: 10.1249/MSS.0b013e3181c854f6

Josse AR, Atkinson SA, Tarnopolsky MA, Phillips SM (2011) Increased consumption of dairy foods and protein during diet- and exercise-induced weight loss promotes fat mass loss and lean mass gain in overweight and obese premenopausal women. J Nutr 141(9):1626–1634. doi:10.3945/jn.111.141028

Katsanos CS, Kobayashi H, Sheffield-Moore M, Aarsland A, Wolfe RR (2005) Aging is associated with diminished accretion of muscle proteins after the ingestion of a small bolus of essential amino acids. Am J Clin Nutr 82(5):1065–1073

Katzmarzyk PT (2006) A summary of the symposium "Current strategies in the prevention and treatment of obesity". Appl Physiol Nutr Metab 31(6):767–768. doi:10.1139/h06-049

Krieger JW, Sitren HS, Daniels MJ, Langkamp-Henken B (2006) Effects of variation in protein and carbohydrate intake on body mass and composition during energy restriction: a meta-regression 1. Am J Clin Nutr 83(2):260–274

Layman DK (2009) Dietary Guidelines should reflect new understandings about adult protein needs. Nutr Metab (Lond) 6:12. doi:10.1186/1743-7075-6-12

Layman DK, Evans E, Baum JI, Seyler J, Erickson DJ, Boileau RA (2005) Dietary protein and exercise have additive effects on body composition during weight loss in adult women. J Nutr 135(8):1903–1910

Leidy HJ, Carnell NS, Mattes RD, Campbell WW (2007) Higher protein intake preserves lean mass and satiety with weight loss in pre-obese and obese women. Obesity (Silver Spring) 15(2): 421–429. doi:10.1038/oby.2007.531

Lewis GF, Carpentier A, Adeli K, Giacca A (2002) Disordered fat storage and mobilization in the pathogenesis of insulin resistance and type 2 diabetes. Endocr Rev 23(2):201–229

Lexell J, Taylor CC, Sjostrom M (1988) What is the cause of the ageing atrophy? Total number, size and proportion of different fiber types studied in whole vastus lateralis muscle from 15- to 83-year-old men. J Neurol Sci 84(2–3):275–294

Li Z, Heber D (2012) Sarcopenic obesity in the elderly and strategies for weight management. Nutr Rev 70(1):57–64. doi:10.1111/j.1753-4887.2011.00453.x

Mettler S, Mitchell N, Tipton KD (2010) Increased protein intake reduces lean body mass loss during weight loss in athletes. Med Sci Sports Exerc 42(2):326–337. doi:10.1249/MSS.0b013e3181b2ef8e

Mojtahedi MC, Thorpe MP, Karampinos DC, Johnson CL, Layman DK, Georgiadis JG, Evans EM (2011) The effects of a higher protein intake during energy restriction on changes in body composition and physical function in older women. J Gerontol A Biol Sci Med Sci 66(11):1218–1225. doi:10.1093/gerona/glr120

Moore DR, Robinson MJ, Fry JL, Tang JE, Glover EI, Wilkinson SB, Prior T, Tarnopolsky MA, Phillips SM (2009a) Ingested protein dose response of muscle and albumin protein synthesis after resistance exercise in young men. Am J Clin Nutr 89(1): 161–168. doi:10.3945/ajcn.2008.26401

Moore DR, Tang JE, Burd NA, Rerecich T, Tarnopolsky MA, Phillips SM (2009b) Differential stimulation of myofibrillar and sarcoplasmic protein synthesis with protein ingestion at rest and after resistance exercise. J Physiol 587(Pt 4):897–904. doi: 10.1113/jphysiol.2008.164087

Paoli A, Grimaldi K, D'Agostino D, Cenci L, Moro T, Bianco A, Palma A (2012) Ketogenic diet does not affect strength performance in elite artistic gymnasts. J Int Soc Sports Nutr 9(1):34. doi:10.1186/1550-2783-9-34

Pennings B, Groen BB, de Lange A, Gijsen AP, Zorenc AH, Senden JM, van Loon LJ (2012) Amino acid absorption and subsequent muscle protein accretion following graded intakes of whey protein in elderly men. Am J Physiol Endocrinol Metab. doi:10.1152/ajpendo.00517.2011

Phillips SM, Tipton KD, Aarsland A, Wolf SE, Wolfe RR (1997) Mixed muscle protein synthesis and breakdown after resistance exercise in humans. Am J Physiol 273(1 Pt 1):E99–E107

Phillips SM, Hartman JW, Wilkinson SB (2005) Dietary protein to support anabolism with resistance exercise in young men. J Am Coll Nutr 24(2):134S–139S

Samuel VT, Petersen KF, Shulman GI (2010) Lipid-induced insulin resistance: unravelling the mechanism. Lancet 375(9733):2267–2277. doi:10.1016/S0140-6736(10)60408-4

Sartor F, de Morree HM, Matschke V, Marcora SM, Milousis A, Thom JM, Kubis HP (2010) High-intensity exercise and carbohydrate-reduced energy-restricted diet in obese individuals. Eur J Appl Physiol 110(5):893–903. doi:10.1007/s00421-010-1571-y

Smith K, Barua JM, Watt PW, Scrimgeour CM, Rennie MJ (1992) Flooding with L-[1-13C]leucine stimulates human muscle protein incorporation of continuously infused L-[1-13C]valine. Am J Physiol 262(3 Pt 1):E372–E376

Stiegler P, Cunliffe A (2006) The role of diet and exercise for the maintenance of fat-free mass and resting metabolic rate during weight loss. Sports Med 36(3):239–262

Strychar I, Lavoie ME, Messier L, Karelis AD, Doucet E, Prud'homme D, Fontaine J, Rabasa-Lhoret R (2009) Anthropometric, metabolic, psychosocial, and dietary characteristics of overweight/obese postmenopausal women with a history of weight cycling: a MONET (Montreal Ottawa New Emerging Team) study. J Am Diet Assoc 109(4):718–724. doi:10.1016/j.jada.2008.12.026

Tang JE, Moore DR, Kujbida GW, Tarnopolsky MA, Phillips SM (2009) Ingestion of whey hydrolysate, casein, or soy protein isolate: effects on mixed muscle protein synthesis at rest and following resistance exercise in young men. J Appl Physiol 107(3):987–992. doi:10.1152/japplphysiol.00076.2009

Tieland M, Dirks ML, van der Zwaluw N, Verdijk LB, van de Rest O, de Groot LC, van Loon LJ (2012) Protein supplementation increases muscle mass gain during prolonged resistance-type exercise training in frail elderly people: a randomized, double-blind, placebo-controlled trial. J Am Med Dir Assoc. doi:10.1016/j.jamda.2012.05.020

Tipton KD, Ferrando AA, Phillips SM, Doyle D Jr, Wolfe RR (1999) Postexercise net protein synthesis in human muscle from orally administered amino acids. Am J Physiol 276(4 Pt 1):E628–E634

Trapp EG, Chisholm DJ, Freund J, Boutcher SH (2008) The effects of high-intensity intermittent exercise training on fat loss and fasting insulin levels of young women. Int J Obes (Lond) 32(4):684–691. doi:10.1038/sj.ijo.0803781

Verdijk LB, Jonkers RA, Gleeson BG, Beelen M, Meijer K, Savelberg HH, Wodzig WK, Dendale P, van Loon LJ (2009) Protein supplementation before and after exercise does not further augment skeletal muscle hypertrophy after resistance training in elderly men. Am J Clin Nutr 89(2):608–616. doi:10.3945/ajcn.2008.26626

Villareal DT, Chode S, Parimi N, Sinacore DR, Hilton T, Armamento-Villareal R, Napoli N, Qualls C, Shah K (2011) Weight loss, exercise, or both and physical function in obese older adults. N Engl J Med 364(13):1218–1229. doi:10.1056/NEJMoa1008234

Weinheimer EM, Sands LP, Campbell WW (2010) A systematic review of the separate and combined effects of energy restriction and exercise on fat-free mass in middle-aged and older adults: implications for sarcopenic obesity. Nutr Rev 68(7):375–388. doi:10.1111/j.1753-4887.2010.00298.x

Wilkinson SB, Tarnopolsky MA, Macdonald MJ, Macdonald JR, Armstrong D, Phillips SM (2007) Consumption of fluid skim milk promotes greater muscle protein accretion after resistance exercise than does consumption of an isonitrogenous and isoenergetic soy-protein beverage. Am J Clin Nutr 85(4):1031–1040

Wolfe RR (2006) The underappreciated role of muscle in health and disease. Am J Clin Nutr 84(3):475–482

Wycherley TP, Moran LJ, Clifton PM, Noakes M, Brinkworth GD (2012) Effects of energy-restricted high-protein, low-fat compared with standard-protein, low-fat diets: a meta-analysis of randomized controlled trials. Am J Clin Nutr 96(6):1281–1298. doi:10.3945/ajcn.112.044321

Yamashita T, Sasahara T, Pomeroy SE, Collier G, Nestel PJ (1998) Arterial compliance, blood pressure, plasma leptin, and plasma lipids in women are improved with weight reduction equally with a meat-based diet and a plant-based diet. Metabolism 47(11):1308–1314

Yang Y, Breen L, Burd NA, Hector AJ, Churchward-Venne TA, Josse AR, Tarnopolsky MA, Phillips SM (2012a) Resistance exercise enhances myofibrillar protein synthesis with graded intakes of whey protein in older men. Br J Nutr 108(10):1780–1788. doi:10.1017/S0007114511007422

Yang Y, Churchward-Venne TA, Burd NA, Breen L, Tarnopolsky MA, Phillips SM (2012b) Myofibrillar protein synthesis following ingestion of soy protein isolate at rest and after resistance exercise in elderly men. Nutr Metab (Lond) 9(1):57. doi:10.1186/1743-7075-9-57