Review

Dietary Protein to Support Anabolism with Resistance Exercise in Young Men

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Resistance exercise is fundamentally anabolic and as such stimulates the process of skeletal muscle protein synthesis (MPS) in an absolute sense and relative to skeletal muscle protein breakdown (MPB). However, the net effect of resistance exercise is to shift net protein balance (NPB = MPS − MPB) to a more positive value; however, in the absence of feeding NPB remains negative. Feeding stimulates MPS to an extent where NPB becomes positive, for a transient time. When combined, resistance exercise and feeding synergistically interact to result in NPB being greater than with feeding alone. This feeding- and exercise-induced stimulation of NPB is what, albeit slowly, results in muscle hypertrophy. With this rudimentary knowledge we are now at the point where we can manipulate variables within the system to see what impact these interventions have on the processes of MPS, MPB, and NPB and ultimately and perhaps most importantly, muscle hypertrophy and strength. We used established models of skeletal muscle amino acid turnover to examine how protein source (milk *versus* soy) acutely affects the processes of MPS and MPB after resistance exercise. Our findings revealed that even when balanced quantities of total protein and energy are consumed that milk proteins are more effective in stimulating amino acid uptake and net protein deposition in skeletal muscle after resistance exercise than are hydrolyzed soy proteins. Importantly, the finding of increased amino acid *uptake* would be independent of the differences in amino acid composition of the two proteins. We propose that the improved net protein deposition with milk protein consumption is also not due to differences in amino acid composition, but is due to a different pattern of amino acid delivery associated with milk *versus* hydrolyzed soy proteins. If our acute findings are accurate then we hypothesized that chronically the greater net protein deposition associated with milk protein consumption post-resistance exercise would eventually lead to greater net protein accretion (i.e., muscle fiber hypertrophy), over a longer time period. In young men completing 12 weeks of resistance training (5d/wk) we observed a tendency ($P = 0.11$) for greater gains in whole body lean mass and whole as greater muscle fiber hypertrophy with consumption of milk. While strength gains were not different between the soy and milk-supplemented groups we would argue that the true significance of a greater increase in lean mass that we observed with milk consumption may be more important in groups of persons with lower initial lean mass and strength such as the elderly.

Key teaching points:

- Resistance exercise is fundamentally anabolic; as such it stimulates MPS which pushes muscle NPB in a more positive direction.
- Muscle NPB becomes positive, only when amino acids are provided to muscle (i.e., protein or amino acids are consumed).
- After resistance exercise, the consumption of protein results in an increase in MPS that is greater than consumption of protein alone; this is due to synergistic stimulation of MPS by amino acids and exercise, which appear to be acting through different signalling pathways.
- Over time the synergistic combination of amino acid feeding and resistance exercise results in accretion of muscle proteins—muscle hypertrophy.
- Protein source acutely affects muscle amino acid uptake and NPB following resistance exercise in a manner that appears to be related not to amino acid composition but to the pattern of amino acid delivery to peripheral tissues. In this regard, milk proteins are more effective at supporting protein accretion than are soy proteins.
- The ability of milk to support muscle protein accretion may have greater relevance in populations with compromised muscle mass.

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Abbreviations: MPS = muscle protein synthesis, MPB = muscle protein breakdown, NPB = net protein balance.

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Introduction

Skeletal muscle protein mass remains essentially unchanged for lengthy periods of time in most persons who are eating regular meals and not performing exercise. The maintenance of skeletal muscle mass throughout a day is due to a fluctuation between accrual and loss of muscle proteins, defined by net protein balance (NPB). In skeletal muscle, NPB is defined as the algebraic different between muscle protein synthesis (MPS) and muscle protein breakdown (MPB). Hence NPB is positive when MPS is greater than MPB and negative when the opposite is true. The main determinant of the changes in NPB throughout the day is changes in MPS, which is responsive to amino acid provision [1–3]. However, the feeding-induced stimulation of MPS is only transient and even in the face of available amino acids returns to basal levels [2]. Hence, it is a feeding-induced stimulation of MPS that results in the undulation of muscle NPB throughout a day (Fig. 1). This effect is almost exclusively due to protein (i.e., amino acids) and while dependent on insulin does not appear to require a high concentration of the hormone for a maximal synthetic response [3–6].

High force resistance exercise is a fundamentally anabolic stimulus for muscle protein and results in a marked stimulation of MPS [7–11]. When MPB is examined at the same time as MPS after resistance exercise muscle NPB has been shown to be negative but approaches zero, due to a relatively greater stimulation of MPS than MPB [8,9,11]. When resistance exercise is performed and protein consumption follows then the effect is an interactive stimulation of MPS to promote an even more positive NPB than just exercise alone [12–15]. As Fig. 1 shows, this exercise- and feeding-induced interaction is small, but over time is the reason skeletal muscle fibers hypertrophy [16,17].

Much of our understanding of how amino acids can affect muscle NPB after resistance exercise comes from work from Wolfe's laboratory [11–15,18–20]. Rather than dissecting individual themes within this body of literature it appears that some messages are relatively clear, based on these and other studies. First, as stated previously, resistance exercise and amino acid provision (intravenous or orally fed) are synergistic in their ability to stimulate MPS and result in muscle NPB being greater than either feeding or resistance exercise alone [11,14,18]. Second, provision of amino acids before exercise may enhance muscle NPB [20]. In the post-exercise period, provision of amino acids (6g) and sucrose (35g) at either 1h or 3h post-exercise equally stimulated MPS to achieve a similar muscle NPB, indicating that a post-exercise 'window' in which the muscle is predisposed to anabolism is no different at either 1h or 3h post-exercise, at least not in young persons [14]. Third, it appears that the response of increased MPS, stimulating a positive muscle NPB, after resistance is due only to essential amino acid provision [12,13,21]. In addition, skeletal muscle appears to be fully responsive to repeated doses of amino acids when consumed only an hour apart after resistance exercise [13]. Finally, the acute responses seen post-exercise with amino acid consumption [12–14], result in a stimulation of muscle anabolism that is reflected in daily muscle protein balance [19], consistent with the scheme proposed in Fig. 1.

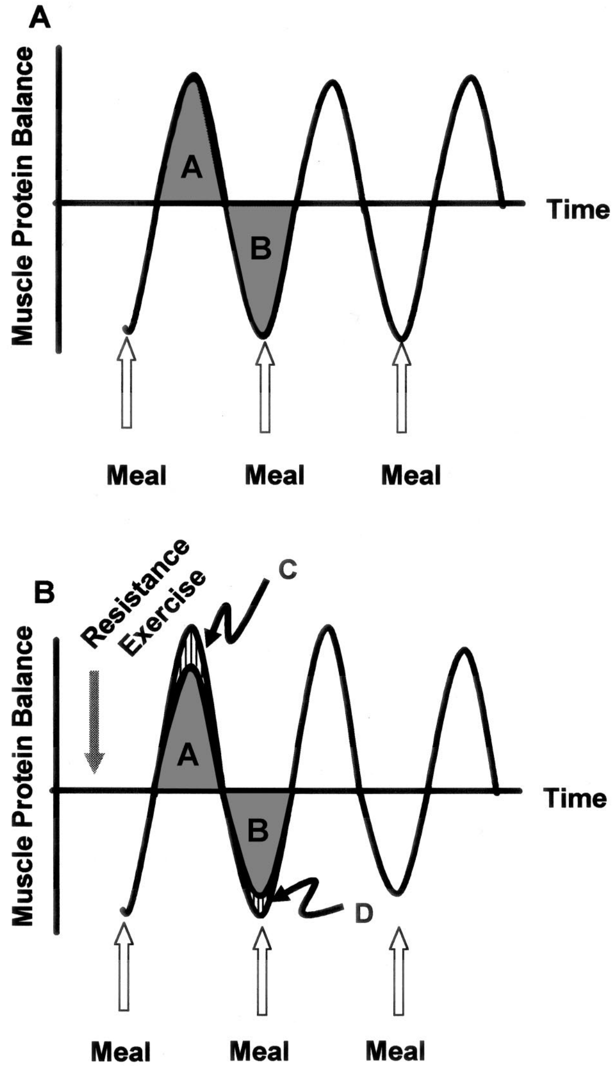

Fig. 1. Normal fed-state gains and fasted-state losses in skeletal muscle protein balance (synthesis minus breakdown). Note that the area under the curve in the fed state (I) would be equivalent to the fasted loss area under the curve (II); hence, skeletal muscle mass is maintained by feeding. B. Fed-state gains and fasted-state losses in skeletal muscle protein balance with performance of resistance exercise. In this scenario, fasted state gains are enhanced by an amount equivalent to the stimulation of protein synthesis brought about by exercise (III). Additionally, fasted-state losses appear to be less (IV), due to persistent stimulation of protein synthesis in the fasted state. Reproduced from reference [16] with permission.

Protein Source and Digestibility

Different proteins yield different patterns of amino acid appearance into the systemic circulation [22–25]. Most notably, casein protein is what has been termed a 'slow' protein in that it results in a relatively slow delivery of amino acids to the systemic circulation [23–25]. By contrast whey protein, and most other protein sources for that matter, result in a relatively rapid delivery of amino acids to peripheral tissues. It has also been reported that milk consumption (containing ~1:4 ratio of whey to casein protein) also results in a slower rate of amino acid appearance in the peripheral circulation as *versus* soy proteins [26–28]. Interestingly, the impact of a faster rate of appearance of amino acids from protein in the form of whey *versus* casein is that whey stimulates whole-body amino acid oxidation to a greater extent than casein [23,25,29]. In addition, while whey proteins promote a greater rise in whole-body protein synthesis than do casein proteins, the casein proteins attenuate whole-body proteolysis; the result is a greater retention of protein with casein than with whey [23,25,29].

When whey and casein are consumed in the form of milk and compared to an isonitrogenous quantity of soy proteins the results show that milk supports greater protein anabolism in the peripheral (i.e., non-splanchnic) tissues [26–28,30]. These results appear to be due almost solely to a differing pattern of amino acid delivery to the peripheral circulation; as such soy protein derived amino acids were digested more rapidly and were directed toward both deamination pathways and liver protein synthesis more than milk-derived amino acids [27]. These authors did not, however, rule out differences in amino acid composition as playing a role in the differing net retention of nitrogen [27]. Notably, when subjects consumed a higher protein intake (2g protein/kg/d) *versus* a lower protein intake (1 g protein/kg/d) it was found that the efficiency of utilization of milk proteins, which is normally high [30], was reduced but that the efficiency of soy protein utilization was reduced to a far greater degree [26]. These findings are interesting in light of the habitually high dietary protein intake consumed by many resistance training athletes [16]. Clearly, much work remains to be done in this area in terms of delineating the functional consequences of the improved protein utilization with milk as opposed to soy proteins.

Skeletal Muscle Anabolism and Protein Source: Acute Effects

Given that soy proteins appear to be preferentially directed toward the splanchnic region and milk proteins toward peripheral tissues, a framework for how different protein sources might affect peripheral tissue protein accretion can be postulated [27,28,31]. Given the interest of our group in determining how protein can support anabolism, mainly the feeding- and exercise-induced rise in MPS, with resistance exercise we pursued this issue with the a priori knowledge that milk proteins may actually be a better source of protein to support peripheral tissue protein synthesis, such as that in skeletal muscle.

Our first study was an acute examination of how milk *versus* soy proteins would support protein accretion following resistance exercise. Subjects performed an intense workout on only one of their legs to isolate the effect of exercise to a single muscle mass and have maximal perfusion of leg after exercise so as to maximize amino acid delivery to the tissue. Immediately following exercise, subjects consumed an isonitrogenous (18.2 g protein) and isoenergetic (750kJ) beverage of either low fat milk or a beverage that contained hydrolyzed soy proteins as a protein source in a 500ml bolus. We utilized arterial-venous differences combined with muscle biopsies to estimate protein kinetics using a 3-pool model [32]. We observed that the soy protein beverage promoted a more rapid and transient hyperaminoacidemia than did the milk. Insulin and glucose concentrations were no different between the two beverages, which was fortuitous given that the carbohydrate sources were actually different between the two drinks (i.e., lactose in milk and maltodextrin in the soy drink). Over the ensuing 3h following resistance exercise we observed a markedly greater uptake of amino nitrogen following milk consumption. This occurred in the absence of differences in blood flow and bulk delivery of amino acids. While many would immediately assume that differences in the amino acid contents may be playing a role in these findings, and we cannot rule this out entirely, our analysis of the amino acid content of the two proteins indicated relatively minor differences in individual amino acids (Fig. 2), at least none that we considered quantitatively important enough to explain our findings.

These results have important implications since the greater uptake of amino acids in the milk condition reflected a greater essential amino acid uptake. In addition, we also infused a tracer amino acid of phenylalanine ([$^2H_5$]phenylalanine), which confirmed that the net chemical balance of amino acid uptake was indeed due to increased disappearance from the arterial inflow. Hence, our young male subjects would have reaped a greater benefit of drinking milk post-exercise, in terms a greater anabolic response following resistance exercise. However, a more clinically poignant consequence of this research may be that populations in whom muscle mass is compromised, such as the elderly, that the consumption of milk proteins as *versus* soy proteins post-exercise would be more beneficial in terms of

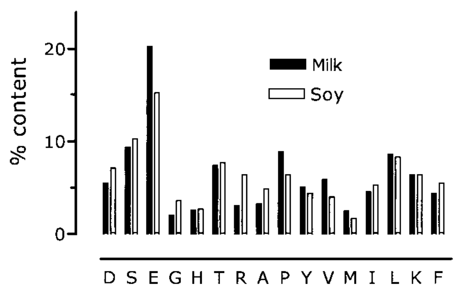

Fig. 2. Comparison of amino acid content of milk protein with hydrolyzed soy protein beverage. Values are percent content by mass of total protein. Glutamine is not available since it converted to glutamate during acid hydrolysis. Neither tryptophan nor cysteine were analyzed.

supporting hypertrophic gains as a result of resistance exercise. The findings of Esmarck *et al.* [33] indicate the importance of timing of protein delivery post-exercise in elderly men in terms of maximizing hypertrophy. While the exact protein source of the supplement used in this study was not given it was listed a mixture of protein from skimmed milk and soybean. Interestingly, Dangin *et al.* [29] observed that so-called fast dietary proteins (i.e., whey) appeared to be more beneficial in terms of supporting whole-body leucine balance than were 'slow' proteins for both young and old men, but the effect was far greater for the elderly subjects. Clearly further research is needed to elucidate in which tissue(s) the improvements in whole-body balance seen with whey protein [29] is occurring in the elderly and whether there is an interaction with resistance exercise and muscle protein accretion.

Skeletal Muscle Anabolism and Protein Source: Chronic Effects

If the scheme in Fig. 1 is correct, then an acute increase in anabolism should be predictive of a long-term response leading to greater hypertrophy, or at least hypertrophy that would be present earlier in a training program. Hence, we wished to test our finding of a greater post-exercise anabolic response acutely following resistance exercise in a chronic resistance training setting. Chronically, we could not control protein intake for the entire time the subjects were participating in the study; however, given the apparent importance of the post-exercise period in terms of supporting lean mass accretion, at least in elderly men [33], we controlled what subjects consumed for the 2h immediately pre- and post-exercise. Subjects always exercise at least 2h post-prandial and in the post-exercise period consumed a drink immediately post-exercise and a second drink 1h later, before they were allowed to consume food or drink *ad libitum*. Two drinks were consumed with the knowledge that MPS responds readily, and with a full anabolic response, to a second protein meal 1h following an initial meal [13]. Subjects were randomly assigned to either the milk group who consumed low fat milk (500ml, 18.2g protein, 750kJ), an isonitrogenous and isoenergetic protein energy control group who received a hydrolyzed soy protein-containing drink, or an energy control group who consumed energy equivalent to the previous two groups in the form of maltodextrin. Our main outcome variables were whole-body fat and bone-free mass (i.e., lean mass) by DEXA, muscle fiber cross-sectional area, and strength in various resistive exercises. We also collected food records to ascertain that our post-exercise drinks were in fact a 'supplement' that is they provided protein and/or energy over and above the persons normal dietary intake.

What we observed was a greater whole-body lean mass gain in the milk *versus* the energy control group, but with no difference between the soy consuming group and either the milk or energy control group. Therefore, by comparison to simply consuming more energy as carbohydrate, milk proteins were more effective at supporting resistance exercise-induced lean mass gains. Similarly, the increase in muscle fiber (vastus lateralis) cross sectional area, while not statistically different, was greater in the milk consuming group than the other two groups ($P = 0.08$). Thus, our short-term findings were borne out when a long-term comparison was made. Since the long-term study was only 12 weeks long it can be argued that what we observed was an early hypertrophic response and that the milk supplemented group simply gained their new muscle sooner. While this may be true for healthy young men, the potential clinical significance of our findings is high particularly when one considers that resistance exercise in combination with milk protein consumption would potentially support greater and more rapid lean mass gain. Given that exercise alone, both resistance and aerobic, can favourably modify cardiovascular disease risk [34], we argue that faster and more rapid gains in skeletal muscle might promote a wider range of further health benefits related to training sustainability in the young and reduced risk for falls in the elderly.

Conclusion

Underscoring our belief that our findings have widespread clinical relevance is what we view as a substantial underappreciation of the role of declining skeletal muscle mass, due either to disease, aging, or disuse, plays in overall health. Skeletal muscle has a large working range of ATP turnover rates as such it has tremendous potential to consume energy, and hence is important in weight maintenance or loss. Due to its mass, skeletal muscle is a highly important thermogenic tissue and the prime determinant of basal metabolic rate, which for most of us is the largest single contributor to daily energy expenditure [35]; again, this fact highlights the importance of maintaining muscle mass. Because of its oxidative capacity (i.e., mitochondrial content) skeletal muscle is also a large site of lipid oxidation, potentially playing a role in maintaining balance in lipoprotein and triglyceride homeostasis [36,37]. Skeletal muscle is also, mostly by virtue of its mass, the primary site of glucose disposal in the post-prandial state [38]; and is highly responsive to exercise as a stimulus to increase glucose uptake. Hence, maintaining a metabolically active (i.e., elevated mitochondrial potential) skeletal muscle mass would also play a role in reducing risk for development of type II diabetes. Finally, the decline in maximal aerobic capacity with age, and with other muscular wasting conditions, has also been found to be due, in large part, to a decline in skeletal muscle mass [39]. For the above reasons we propose that interventions that are designed to maintain or increase lean mass, such as resistance exercise, represent a very powerful and economically feasible form of treatment for a variety of diseases. Relevant to the topic discussed here, however, we offer the suggestion that optimal nutritional support for promotion of lean mass gains with resistance exercise will enhance lean mass gains and that milk proteins appear particularly efficacious in this regard. We believe that populations such as the elderly, who appear to have a diminished capacity for hypertrophy without nutritional support [33], would therefore be best served by post-exercise consumption of milk proteins (particularly whey protein [29]). Both whey and casein protein have recently been demonstrated to be effective in supporting a positive leucine and phenylalanine balance following resistance exercise, with no apparent difference between the two proteins [22]. What impact these two proteins acutely have on the synthetic rate of muscle proteins following resistance exercise has yet to be determined. More importantly, whether long-term supplementation of whey or casein is more effective in supporting lean mass gain. Future research is undoubtedly required to clarify the potential benefit of milk and its individual protein components in support of anabolism with resistance exercise.

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References

1. Bohé J, Low A, Wolfe RR, Rennie MJ: Human muscle protein synthesis is modulated by extracellular, not intramuscular amino acid availability: a dose-response study. J Physiol 552:315–324, 2003.
2. Bohé J, Low JF, Wolfe RR, Rennie MJ: Latency and duration of stimulation of human muscle protein synthesis during continuous infusion of amino acids. J Physiol 532:575–579, 2001.
3. Cuthbertson D, Smith K, Babraj J, Leese G, Waddell T, Atherton P, Wackerhage H, Taylor PM, Rennie MJ: Anabolic signaling deficits underlie amino acid resistance of wasting, aging muscle. FASEB J [Published online December 13, 2004].
4. Svanberg E: Amino acids may be intrinsic regulators of protein synthesis in response to feeding. Clin Nutr 17:77–79, 1998.
5. Svanberg E, Jefferson LS, Lundholm K, Kimball SR: Postprandial stimulation of muscle protein synthesis is independent of changes in insulin. Am J Physiol 272:E841–E847, 1997.
6. Svanberg E, Moller-Loswick AC, Matthews DE, Korner U, Andersson M, Lundholm K: The role of glucose, long-chain triglycerides and amino acids for promotion of amino acid balance across peripheral tissues in man. Clin Physiol 19:311–320, 1999.
7. Chesley A, MacDougall JD, Tarnopolsky MA, Atkinson SA, Smith K: Changes in human muscle protein synthesis after resistance exercise. J Appl Physiol 73:1383–1388, 1992.
8. Phillips SM, Tipton KD, Aarsland A, Wolf SE, Wolfe RR: Mixed muscle protein synthesis and breakdown following resistance exercise in humans. Am J Physiol 273:E99–E107, 1997.
9. Phillips SM, Tipton KD, Ferrando AA, Wolfe RR: Resistance training reduces the acute exercise-induced increase in muscle protein turnover. Am J Physiol 276:E118–E124, 1999.
10. Yarasheski KE, Zachwieja JF, Bier DM: Acute effects of resistance exercise on muscle protein synthesis rate in young and elderly men and women. Am J Physiol 265:E210–E214, 1993.
11. Biolo G, Maggi SP, Williams BD, Tipton KD, Wolfe RR: Increased rates of muscle protein turnover and amino acid transport after resistance exercise in humans. Am J Physiol 268:E514–E520, 1995.
12. Borsheim E, Tipton KD, Wolf SE, Wolfe RR: Essential amino acids and muscle protein recovery from resistance exercise. Am J Physiol Endocrinol Metab 283:E648–E657, 2002.
13. Miller SL, Tipton KD, Chinkes DL, Wolf SE, Wolfe RR: Independent and combined effects of amino acids and glucose after resistance exercise. Med Sci Sports Exerc 35:449–455, 2003.
14. Rasmussen BB, Tipton KD, Miller SL, Wolf SE, Wolfe RR: An oral essential amino acid-carbohydrate supplement enhances muscle protein anabolism after resistance exercise. J Appl Physiol 88:386–392, 2000.
15. Tipton KD, Ferrando AA, Phillips SM, Doyle DJ, Wolfe RR: Postexercise net protein synthesis in human muscle from orally administered amino acids. Am J Physiol 276:E628–E634, 1999.
16. Phillips SM: Protein requirements and supplementation in strength sports. Nutrition 20:689–695, 2004.
17. Rennie MJ, Wackerhage H, Spangenburg EE, Booth FW: Control of the size of the human muscle mass. Annu Rev Physiol 66:799–828, 2004.
18. Biolo G, Tipton KD, Klein S, Wolfe RR: An abundant supply of amino acids enhances the metabolic effect of exercise on muscle protein. Am J Physiol 273:E122–E129, 1997.
19. Tipton KD, Borsheim E, Wolf SE, Sanford AP, Wolfe RR: Acute response of net muscle protein balance reflects 24-h balance after exercise and amino acid ingestion. Am J Physiol Endocrinol Metab 284:E76–E89, 2003.
20. Tipton KD, Rasmussen BB, Miller SL, Wolf SE, Owens-Stovall SK, Petrini BE, Wolfe RR: Timing of amino acid-carbohydrate ingestion alters anabolic response of muscle to resistance exercise. Am J Physiol Endocrinol Metab 281:E197–E206, 2001.
21. Tipton KD, Gurkin BE, Matin S, Wolfe RR: Nonessential amino acids are not necessary to stimulate net muscle protein synthesis in healthy volunteers. J Nutr Biochem 10:89–95, 1999.
22. Tipton KD, Elliott TA, Cree MG, Wolf SE, Sanford AP, Wolfe RR: Ingestion of casein and whey proteins result in muscle anabolism after resistance exercise. Med Sci Sports Exerc 36:2073–2081, 2004.
23. Boirie Y, Dangin M, Gachon P, Vasson MP, Maubois JL, Beaufrere B: Slow and fast dietary proteins differently modulate postprandial protein accretion. Proc Natl Acad Sci USA 94:14930–14935, 1997.
24. Dangin M, Boirie Y, Guillet C, Beaufrere B: Influence of the protein digestion rate on protein turnover in young and elderly subjects. J Nutr 132:3228S–3233S, 2002.
25. Dangin M, Boirie Y, Garcia-Rodenas C, Gachon P, Fauquant J, Callier P, Ballevre O, Beaufrere B: The digestion rate of protein is an independent regulating factor of postprandial protein retention. Am J Physiol Endocrinol Metab 280:E340–E348, 2001.
26. Morens C, Bos C, Pueyo ME, Benamouzig R, Gausseres N, Luengo C, Tome D, Gaudichon C: Increasing habitual protein intake accentuates differences in postprandial dietary nitrogen utilization between protein sources in humans. J Nutr 133:2733–2740, 2003.

27. Bos C, Metges CC, Gaudichon C, Petzke KJ, Pueyo ME, Morens C, Everwand J, Benamouzig R, Tome D: Postprandial kinetics of dietary amino acids are the main determinant of their metabolism after soy or milk protein ingestion in humans. J Nutr 133:1308–1315, 2003.
28. Fouillet H, Gaudichon C, Bos C, Mariotti F, Tome D: Contribution of plasma proteins to splanchnic and total anabolic utilization of dietary nitrogen in humans. Am J Physiol Endocrinol Metab 285: E88–E97, 2003.
29. Dangin M, Guillet C, Garcia-Rodenas C, Gachon P, Bouteloup-Demange C, Reiffers-Magnani K, Fauquant J, Ballevre O, Beaufrere B: The rate of protein digestion affects protein gain differently during aging in humans. J Physiol 549:635–644, 2003.
30. Bos C, Mahe S, Gaudichon C, Benamouzig R, Gausseres N, Luengo C, Ferriere F, Rautureau J, Tome D: Assessment of net postprandial protein utilization of 15N-labelled milk nitrogen in human subjects. Br J Nutr 81:221–226, 1999.
31. Fouillet H, Mariotti F, Gaudichon C, Bos C, Tome D: Peripheral and splanchnic metabolism of dietary nitrogen are differently affected by the protein source in humans as assessed by compartmental modeling. J Nutr 132:125–133, 2002.
32. Biolo G, Chinkes D, Zhang XJ, Wolfe RR: Harry M. Vars Research Award. A new model to determine in vivo the relationship between amino acid transmembrane transport and protein kinetics in muscle. JPEN J Parenter Enteral Nutr 16:305–315, 1992.
33. Esmarck B, Andersen JL, Olsen S, Richter EA, Mizuno M, Kjaer M: Timing of postexercise protein intake is important for muscle hypertrophy with resistance training in elderly humans. J Physiol 535:301–311, 2001.
34. Banz WJ, Maher MA, Thompson WG, Bassett DR, Moore W, Ashraf M, Keefer DJ, Zemel MB: Effects of resistance versus aerobic training on coronary artery disease risk factors. Exp Biol Med (Maywood) 228:434–440, 2003.
35. Elia M, Stratton R, Stubbs J: Techniques for the study of energy balance in man. Proc Nutr Soc 62:529–537, 2003.
36. Heilbronn L, Smith SR, Ravussin E: Failure of fat cell proliferation, mitochondrial function and fat oxidation results in ectopic fat storage, insulin resistance and type II diabetes mellitus. Int J Obes Relat Metab Disord 28 Suppl 4:S12–S21, 2004.
37. Thyfault JP, Kraus RM, Hickner RC, Howell AW, Wolfe RR, Dohm GL: Impaired plasma fatty acid oxidation in extremely obese women. Am J Physiol Endocrinol Metab 287:E1076–E1081, 2004.
38. Perez-Martin A, Raynaud E, Mercier J: Insulin resistance and associated metabolic abnormalities in muscle: effects of exercise. Obes Rev 2:47–59, 2001.
39. Neder JA, Nery LE, Silva AC, Andreoni S, Whipp BJ: Maximal aerobic power and leg muscle mass and strength related to age in non-athletic males and females. Eur J Appl Physiol Occup Physiol 79:522–530, 1999.

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