5 Dietary protein and muscle protein accretion

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Introduction

The current US and Canadian RDA and Australian RDI tells us that an adequate protein intake is somewhere between 0.75-0.80 g protein/kg/d. The American College of Sports Medicine position stand (18) on dietary practices for athletes lists as a requirement for endurance athletes and for resistance training athletes. The basis for these recommendations is nitrogen balance. From a physiological perspective to be in balance for nitrogen is a rather odd concept to grasp and it is immediately apparent that no variable of any great interest to athletes has ever been shown to be associated with being in nitrogen balance. However, a number of studies have attempted to define what protein intakes would be required to obtain a state of nitrogen balance in athletes (see (18) for review). At the same time a number of longitudinal studies have reached the conclusion that exercise training in novices actually reduces protein requirements due to reduced activation of amino acid oxidation/catabolism in endurance athletes (11) or that resistance exercise induces a more efficient use of amino acids arising from muscle protein breakdown (9, 12). What is more important perhaps that debating what nitrogen balance means for an athlete is to look at protein from a functional perspective. The function that athletes care most about would be exercise performance in their sport of choice. Often improvements in performance will involve gaining muscle mass and potentially gaining muscle mass and losing fat mass appreciating that a high lean:fat bodyweight ratio is desirable in a number of sports. With this framework in mind we can then begin to look at specific situations of how protein can act as a substrate for the synthesis of new muscle proteins leading eventually to net muscle accretion. Also, what strategies are available to aid in fat mass loss but while still maintaining lean mass.

Protein to gain muscle: quantity, quality, and timing

Gaining muscle mass requires a person to be in a state of net positive muscle protein balance. Namely, the rate of synthesis of new muscle proteins (muscle protein synthesis – MPS) must be greater than the rate of breaking down old muscle proteins (muscle protein breakdown – MPB). Such a situation occurs normally with periods of feeding throughout the day (see Figure 1A). Importantly, in this situation gains in muscle are balanced by losses and so skeletal muscle mass stays constant. Figure 1B shows what happens when protein is consumed after resistance exercise. What is immediately apparent is that feeding and resistance exercise synergistically interact to stimulate a greater rise in MPS and the change in net balance is more positive than with feeding alone (see (14) for review). While these observations are made in the acute post-exercise state over a period of hours an important point to make is that acute observations of differences in the response of MPS (22) are qualitatively predictive of longer-term changes in muscle mass.(10) The obvious questions that arise having established the aforementioned paradigm are: 1) What quantity of protein might maximize the rise in MPS to maximally stimulate muscle growth? Does the type of protein matter (i.e., animal-derived versus plant-based)? How close in time to the resistance exercise bout does protein have to be consumed to have a beneficial effect?

> ***A dose of protein that maximally stimulates MPS following resistance exercise in larger (85kg) men is about 20-25g of high quality protein, which contains ~8-10g of essential amino acids and 1.5-2g of leucine***

Two studies have examined in a dose-response fashion the requirement for either amino acids or protein to maximally stimulate MPS and they actually reached quite similar conclusions. Cuthbertson (7) found that an oral dose of 10g of essential amino acids was sufficient to maximally stimulate MPS in young people, at rest. Following a bout of resistance exercise 20g of egg protein (43% by content essential amino acids) maximally stimulated MPS (13). The dose of essential amino acids that maximally stimulated MPS either at rest or following resistance exercise appears to be between 8-10g.

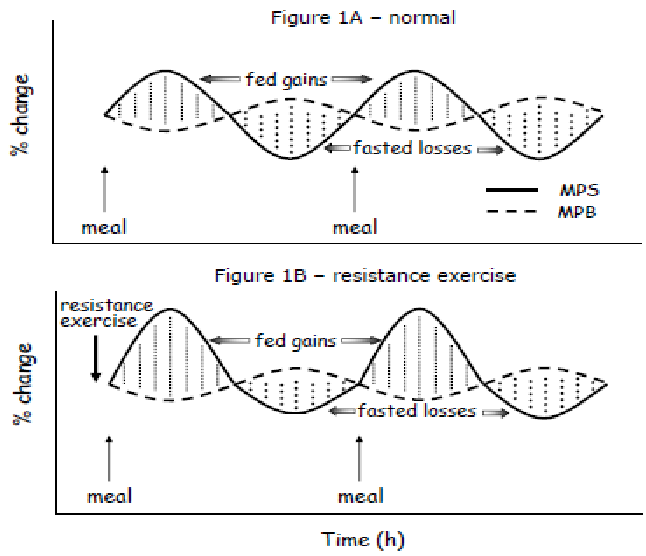

***Figure A** – normal daily changes in MPS and MPB with feeding 2 identical protein-containing meals.*
***Figure B** – the impact of performance of resistance exercise on MPS, and net balance, which eventually leads to muscle hypertrophy.*

Milk-based proteins are superior to soy-based in stimulating MPS. When broken down into constituent proteins the whey protein fraction of milk appears to be highly effective in stimulating MPS. Isolated whey proteins promote greater muscular hypertrophy than soy-based or energy-containing carbohydrate only beverages

Under the guidelines for the RDA and the RDI there is no distinction made for types of protein. That is animal and plant-based protein sources are not discriminated since nitrogen balance can be achieved with either alone or in combination. However, there are important differences when it comes to the stimulation of MPS. For example, ingestion of equivalent quantities of skimmed (non-fat) milk and a matched soy drink resulted in a greater post-exercise stimulation of MPS (22). Of note, the chronic (at least 10wk) practice of milk consumption, versus soy drinks or energy only as an isotonic sports drink, resulted in changes in whole body muscle mass and muscle fibre size that were roughly equivalent (10) to those seen acutely (22). When the constituent milk and soy proteins are isolated and consumed at rest and following resistance exercise it was noted that rates of MPS were stimulated to a greater degree by whey protein than that seen with soy or casein (19). A review of studies in which whey protein was consumed habitually during resistance training showed a benefit in terms of stimulating hypertrophy (16).

The timing of protein ingestion relative to exercise is somewhat equivocal; however, there are clearly three distinct times at which one could consume protein to promote muscle growth. These are pre-exercise, which is defined as within 1h before the start of a bout of RE, during exercise, and post-exercise (which we define as being within <2-3h after the completion of a bout of RE). Only three studies have examined pre-exercise protein consumption from a mechanistic standpoint. In the first mechanistic investigation of pre- versus post-exercise feeding an 'advantage' was ascribed to pre- versus post-exercise amino acid consumption due to the finding of pre-exercise amino acid consumption stimulated a 160% greater net uptake of phenylalanine by an exercised leg (21). However, the same group was unable to reproduce the same results when they studied the ingestion of whey protein pre- versus post-exercise (20). Fujita et al (8) also observed no benefit of pre-exercise consumption of a carbohydrate and amino acid solution on post-exercise protein accretion. Thus, pre-exercise feeding is unlikely to offer benefit for promotion of increases in MPS and long-term gains in muscle mass. A number of training studies have used pre- combined with post-exercise feeding in combination to enhance gains in muscle mass (5, 6) so it is impossible to tell whether the pre-exercise meal imparted any benefit since post-exercise meals are unequivocally beneficial (see below).

Pre-exercise protein consumption is of questionable efficacy for promotion of adaptive gains in muscle mass. Consumption of protein during exercise may promote some increases in MPS provided the rest period between exercises is long enough to allow recovery. Post-exercise protein consumption has been repeatedly shown to be beneficial in stimulating MPS.

The provision of protein during exercise would appear to be an effective strategy since the amino acid substrate may allow earlier rises to 'kick-start' MPS and/or may trigger signaling responses that promote increased MPS. During exercise muscle may, however, not be in the optimal energetic state to receive amino acids and begin incorporating them into protein since the energy charge in the muscle is low. One study in humans has shown a small but significant impact on protein feeding during exercise (1). It may be that the continual cycles of rest and recovery that humans practice in habitual performance of RE allows a degree of recovery in muscle energy charge. Thus, exercise has already started to increase signaling mechanisms during the RE bout and amino acid delivery to the muscle begins to result in a significant rise in MPS (1).

Post-exercise nutrient provision remains very convincingly positive in terms of its impact on MPS and being greater than exercise alone (3, 15). Nutrient provision either through the amino acid themselves (3) or through a rise in insulin (4) also suppresses the RE-induced rise in MPB that occurs in the absence of nutrition (2, 17). The resultant positive net protein balance has been postulated to additively sum and result in protein accrual and hypertrophy over time. In addition, a number of training studies have employed immediate post-exercise protein provision versus delayed nutrition or provision of energy alone (usually as carbohydrate) and have reported that early post-exercise protein provision is beneficial in promoting hypertrophy (6, 10). In one study it also appears as if post-exercise, versus pre-exercise, protein feeding was important even if the timing of the post-exercise protein supplement was as much as 5h after the workout (5). Thus, at this point in time there is strong and plentiful evidence to support a statement that post-exercise protein consumption supports a pronounced rise in MPS and suppresses MPB leading to increases in net muscle protein balance and protein accretion. Long-term studies that have manipulated the timing of protein provision have shown enhanced gains with earlier post-exercise protein provision in promoting hypertrophy, however, this not always the case. There are a number of factors that could affect why training studies show mixed results and those have to do with the protein dose (13), type (i.e., source) of protein (10, 19), and the age of the participants.

Leucine: a trigger for adaptation

The properties of leucine as amino acid, beyond being merely a substrate for protein synthesis, have been known for some time. We are now beginning to define what we have termed a leucine 'trigger' threshold dose to result in a rise in the blood concentration of leucine to trigger MPS to be switched on. We have evidence from multiple studies in which we have observed more rapid and greater overall rises in blood leucine which correlate quite well with the activation of MPS. The mechanism is via an intricate network of signaling proteins within the muscle that 'sense' leucine somehow and when activated turn on MPS and allow that process to take advantage of the excess of other essential amino acids to make new proteins. The leucine content of some common proteins is given in Table 1.

Table 1:
Leucine content of common isolated protein sources.

Amino acid content (mg/g)	Milk solid (non-fat)	Casein	Whey	Soy	Body protein
Leucine	77	82	108	62	75

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