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Nutrition Noteworthy

Title

Protein and Amino Acid Supplementation for Resistance Training: Are We Being Sold Products That We Don't Need?

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Journal

Nutrition Noteworthy, 7(1)

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Publication Date

2005

Peer reviewed

Introduction

Dietary supplementation for athletes has become a big industry. Companies like GNC and Met-Rx bombard the print and broadcast media with advertisements for the latest products that will help us lose fat and build muscle. Prominent among these products are protein and amino acid supplements aimed at athletes undergoing resistance training. These advertisements claim that protein supplements such as whey or casein and amino acid products such as essential amino acid mixes, glutamine, and β -hydroxy- β -methylbutyrate (HMB), a leucine metabolite, speed the gains achieved through resistance training. But is there any merit to these claims, or are we simply being sold products that we don't need?

The state of muscle protein balance involves the actions of two antagonistic processes, muscle protein breakdown, or catabolism, and muscle protein synthesis, or anabolism. If anabolism is greater than catabolism, then net muscle protein balance is positive, resulting in increases in muscle strength and total body fat free mass. Supplements that could tip the catabolism/anabolism balance in favor of net muscle protein synthesis would have therapeutic uses not only for resistance training athletes, but also for patients recovering from injuries, for the prevention of age-associated muscle loss, and also for those with physiologic wasting conditions such as severe burns, surgery, and cancer. Thus, evaluation of the effectiveness of these "pro-anabolic" supplements has potentially far-reaching clinical applications. This work reviews the primary literature regarding the effectiveness of amino acid supplements including glutamine and HMB and whole protein mixes on the catabolic/anabolic state of muscle following resistance exercise, and also the proper timing of such supplementation for maximal effects.

Mixed Amino Acid Supplements

It has long been known that resistance exercise acutely causes a net catabolism of muscle proteins due to an increase in protein degradation without a corresponding increase in protein synthesis. It was first shown in 1997, however, that creating a state of amino acid excess by direct intravenous infusion of a complete mixture of amino acids causes an increase in protein synthesis as well as a decrease in protein degradation in the period following resistance training, resulting in a net anabolic effect on muscle (1). It had also previously been shown that resistance training acutely causes an increase in the rate of production of nonessential amino acids such that plasma levels remain relatively unchanged following resistance training (2). In contrast, resistance exercise causes an acute decrease in the plasma levels of nonessential amino acids. It was hypothesized that this decrease reflects an increase in muscle amino acid uptake in response to the anabolic stimulus that occurs following weight training. According to this theory, the relatively stable plasma level of nonessential amino acids is a result of a balance between increased muscle uptake and increased amino acid synthesis. Since essential amino acids cannot be synthesized by the body, it has been hypothesized that their relative lack of abundance following resistance training is what limits the anabolic response of muscle to the exercise stimulus.

Tipton *et al.* were the first to show that a mixture of essential amino acids delivered orally post-exercise was sufficient to increase net muscle protein balance above that of placebo (3). In this study, net muscle protein balance was calculated by subtracting the amino acid concentration in the venous blood draining from an exercised muscle from the concentration in the arterial blood supplying the muscle, and then multiplying this value by the rate of blood flow to the muscle (3). Thus, an increased net muscle protein balance indicates a greater difference in amino acid concentration in the arterial than venous blood, suggesting that the muscle has increased its uptake of amino acids from the blood to supply an increased rate of protein synthesis. This study is important for a number of reasons. Foremost, it extended the findings of the earlier study showing that IV infusion of amino acids following exercise increased muscle protein synthesis, by showing that amino acids could also be administered orally and have the same effect. In this study, net muscle protein balance was negative after exercise and no supplementation, reflecting net muscle protein breakdown, but was significantly positive after exercise and supplementation with a complete mix of essential and nonessential amino acids (3). Interestingly, the net muscle protein balance was even more positive following exercise and supplementation with essential amino acids only, suggesting that as hypothesized, the availability of essential amino acids is the limiting factor in the protein anabolic response following resistance exercise (3).

These findings have since been replicated (4, 5), confirming that an abundant supply of essential amino acids following resistance training is sufficient to tip the balance between catabolism and anabolism in favor of net muscle protein synthesis. The question remains, however, of how to time the intake of essential amino acids with the resistance training session to achieve the largest increases in muscle protein synthesis. This issue was addressed in a study in which subjects received an oral bolus of essential amino acids either immediately before, or immediately after a one hour workout. As expected, receiving the supplement before the workout resulted in increased amino acid delivery to the exercising muscle (calculated as amino acid concentration in arterial blood supplying the muscle multiplied by the rate of blood flow to the muscle) during the exercise session (6). What was not expected, however, was that the amino acid delivery and net muscle protein balance remained more positive after the workout for the group receiving the supplement before the workout than for the group receiving it after (6). This difference resulted in an amino acid uptake over the entire time period sampled that was 2.5-fold higher for the pre-workout group than for the post-workout group (6). It has been hypothesized that the increased blood flow to exercising muscles during the workout is the major factor resulting in increased amino acid delivery and uptake in the pre-workout supplementation group (6). These results indicate that the most effective way to supply amino acids to exercised muscles and stimulate protein anabolism after a workout is to use an oral essential amino acid supplement immediately before beginning the workout.

Whole Protein Supplements

Because whole protein sources are more widely available than essential amino acid mixtures, it is important to determine whether whole proteins can be an effective source of essential amino acids in stimulating muscle anabolism following resistance training. Since it has been shown that oral administration of essential amino acids following

resistance training is able to switch net muscle protein balance from negative to positive and thus stimulate a net muscle anabolic state, any whole protein source that supplies essential amino acids should have the same effect. A number of studies have demonstrated that supplementation with whey protein (7, 8) or milk (9) immediately following exercise results in greater gains in strength measures and fat free mass than post-exercise consumption of an isocaloric carbohydrate-only drink over the course of a 10-12 week resistance training program. These studies demonstrate that whole protein sources, like essential amino acid supplements, can stimulate muscle protein anabolism better than can resistance training with no protein/amino acid supplementation.

The question remains, however, as to what the most effective whole protein source is and when it should be consumed to achieve maximal results. Tipton *et al.* recently compared supplementation with one of two popular whole protein supplements, whey and casein, with isocaloric carbohydrate supplementation following resistance training. They found that both whey and casein significantly increased net muscle protein balance over supplementation with carbohydrates alone, confirming the earlier findings that whole proteins effectively provide the essential amino acids required to stimulate muscle protein anabolism after a workout (10). They also found that supplementation with whey protein results in a significantly more positive net protein balance for the 1.5 hours following drink ingestion than supplementation with casein, but that casein resulted in a more prolonged increase in net muscle protein balance compared with placebo than did whey (10). These findings reflect the differing kinetics of the two protein sources in the GI tract, where whey is emptied from the stomach and thus absorbed more quickly. It remains unclear, however, if these differences in the kinetics of amino acid delivery have any impact on gains in muscle strength and fat free mass in subjects taking whey or casein over the course of a resistance training program. Another study found that in elderly men, supplementation with whey protein five minutes after completing a resistance training workout resulted in greater gains in strength and fat free mass than supplementation with whey two hours after completing exercise (11). Thus, while the most effective whole protein source has yet to be identified, it is believed that whole protein supplements should be consumed as near to the time of the workout as possible.

Single Amino Acid Supplements

In addition to amino acid mixture and whole protein supplements, a number of single amino acid supplements are touted as being pro-anabolic and deserve mention. β -hydroxy- β -methylbutyrate (HMB) is a leucine metabolite that is believed to be anti-catabolic, and thus to stimulate a net muscle anabolic state following resistance exercise. HMB has been found to cause significant gains in fat free mass and strength, and to decrease markers of protein catabolism such as plasma creatine phosphokinase and urinary 3-methylhistidine in a dose-response relationship with the amount of HMB ingested per day (12, 13). Glutamine is considered a “conditionally essential” amino acid because it is the most abundant amino acid in muscle and the body’s rate of glutamine synthesis can easily fall below the level required to maintain homeostasis in states of physiologic stress (14). It has also been proposed that glutamine can increase intramuscular glycogen levels by serving as a substrate for hepatic gluconeogenesis (14), thus, glutamine is commonly used as a resistance training supplement. Glutamine has

been shown, however, to have no significant benefits versus placebo in terms of increasing fat free mass or strength, or decreasing muscle catabolism over the course of a resistance training program (14). Finally, a number of amino acids including arginine, lysine, and ornithine are touted for their ability to increase plasma levels of growth hormone. Because resistance training itself is a potent stimulus for growth hormone release, however, supplementation with these amino acids has not been conclusively shown to raise growth hormone levels over physiologic exercise response levels (reviewed in 15).

Conclusions and Directions for Future Research

Using supplements to maximize gains from resistance training is important not only for athletes and for those wishing to increase fat free mass for aesthetic reasons, but also for patients recovering from injuries, for the prevention of aging-associated muscle loss, and for those with wasting states such as burns, surgery, and cancer. Current research suggests that the most important factor promoting muscle anabolism following resistance training is an abundant supply of essential amino acids, which can be supplied by amino acid mixtures or by whole proteins, and that such supplementation should occur as close to the time of the workout as possible. In addition, the anti-catabolic leucine metabolite HMB is a useful adjunct to protein/amino acid supplementation for achieving maximal gains from a resistance training program. Future research should compare supplementation with essential amino acid mixes versus whole proteins to determine which is more effective in stimulating muscle anabolism. It should also compare whole protein sources such as whey and casein over the course of a prolonged resistance training program to determine if any single protein source results in more efficient gains in fat free mass and strength. Finally, future research should address the question of whether whole protein supplementation is more effective before or immediately after a workout session as essential amino acid supplementation appears to be.

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