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Defining the anabolic window of opportunity

Is protein intake immediately post resistance exercise critically important for muscle growth?

KEYWORDS: Protein timing, anabolic window of opportunity, daytime pattern of protein ingestion, resistance exercise training, muscle anabolism, muscle protein synthesis

Abstract The anabolic response of muscle to resistance exercise and protein feeding is influenced by multiple factors, including the timing of protein feeding. A common perception is that a 45-60 min post-exercise ‘anabolic window of opportunity’ time frame exists, within which dietary protein must be consumed to achieve muscle anabolism (and ultimately muscle growth). In this review, we argue the importance of feeding protein immediately following exercise is not as critical as has been espoused. Indeed, muscle remains responsive to protein ingestion for at least 24 h post-exercise. On the other hand, given that feeding protein immediately post-exercise is unlikely to impair the muscle anabolic response, and could improve it, from a practical standpoint, we recommend athletes and exercisers consume some protein, as a meal or supplement, in the immediate period following resistance exercise.

INTRODUCTION

Recent nutrition interest has focussed on nutrient timing for recovery from resistance-type exercise, in particular for maximising skeletal muscle hypertrophy. The focus of interest has been primarily on the timing of dietary protein intake. Seemingly, the most prevalent opinion is that a source of dietary protein should be consumed immediately, or as close as possible, post exercise (1-4). The belief is that the anabolic response of skeletal muscle will be impaired – or even alleviated - if a source of dietary protein is not ingested within as little as 45-60 min following resistance exercise (1-4). This time period has been coined the “anabolic window of opportunity” (1-4). In this review, we critically examine the importance of post-exercise protein ingestion in the context of this so-called 45-60 min “anabolic window of opportunity.” We evaluate scientific evidence generated from chronic training studies and from acute metabolic studies that support the “anabolic window of opportunity”, as well as evidence that does not support this concept. Given the limited data currently available, unfortunately it is not possible to directly ascertain the optimal timing of protein intake post resistance exercise for maximal muscle hypertrophy. However, we propose a theoretical framework that attempts to depict the influence of protein timing on the muscle anabolic response. Essentially, we make the argument that, whereas the timing of protein intake clearly impacts the muscle anabolic response to exercise, the precise timing of protein ingestion in relation to resistance exercise for optimal anabolic adaptations may not be as firmly established as is often advocated. This review has implications for many populations, including athletes and exercisers that strive to increase skeletal muscle mass and strength, and populations such as the elderly, who wish to counteract or reduce the loss of muscle mass.

METHODOLOGICAL APPROACHES FOR INVESTIGATING PROTEIN TIMING AND MUSCLE HYPERTROPHY

Two basic study designs are typically utilized to investigate the critical importance of dietary protein timing for muscle hypertrophy. These study designs can be classified as acute, metabolic studies and longitudinal, endpoint studies. Recently published (5-8) and unpublished (9) data have examined the impact of protein timing in relation to exercise on acute changes in muscle protein metabolism may be used to qualitatively predict long-term phenotypic changes. Primary endpoint measurements for acute metabolic studies are typically either net muscle protein balance (NBAL) or muscle protein synthesis (MPS). The metabolic basis for a change in muscle protein levels resulting in muscle hypertrophy is NBAL, i.e. the difference between MPS and muscle protein breakdown (MPB), over a predetermined period of time (10). Hence, to accrue muscle proteins, the rate of MPS must exceed MPB, resulting in a positive NBAL over a given period of time. Studies have shown that provision of an amino acid source combined with exercise is required to switch NBAL from negative to positive (6, 11). This switch is largely due to increases in MPS rather than changes in MPB (10). Thus, skeletal muscle hypertrophy depends on the interaction between exercise and nutrition. This interactive effect seems to be influenced by a number of factors, including the timing of protein ingestion relative to the exercise bout (10). This narrative reviews the results of these acute studies to help establish the influence of protein timing on the accretion of muscle protein with training.

Whereas acute, metabolic studies have predictive value, longitudinal, endpoint studies also are effective for studying the importance of nutrient timing for muscle hypertrophy. Indeed, the utility of longitudinal, endpoint study designs is intuitively obvious for the study of adaptations to training. Longitudinal studies are used to measure specific adaptations that are important, e.g. increased muscle mass or strength in response to resistance-type exercise training. The length of the training period for any given study may be weeks, months or, in theory, even years. Thus, both longitudinal and acute studies may provide valuable information concerning the timing of protein intake for maximising the muscle anabolic response to resistance-type exercise. On the other hand, training studies often reach equivocal, or even conflicting, conclusions regarding a nutritional intervention, such as timing of intake. Inherent difficulties controlling numerous extraneous variables, such as dietary intake, emotional issues, sleep patterns, etc., have undoubtedly contributed to variable results, thus hindering a clear interpretation of longitudinal endpoint studies which attempt to address the importance of timing of protein intake (10). However, ultimately the importance of nutrient timing for individuals involved in resistance training is determined by the resulting adaptations rather than a metabolic response per se and more quantitative conclusions are possible if the studies are performed properly. Therefore, the determination of long-term changes in muscle size, strength and function in studies controlled as tightly as possible are important.

THE "ANABOLIC WINDOW OF OPPORTUNITY": FACT OR FICTION?

A common recommendation for maximizing the muscle anabolic response to resistance exercise and protein intake is to consume dietary protein within close temporal proximity to the exercise session (2, 3). Advocates of the importance of the "anabolic window of opportunity" often cite longitudinal studies by Esmarck *et al.* (2001) and Cribb and Hayes (2006) to support this notion (12, 13). Esmarck *et al.* compared changes in muscle size and strength in older adult men following 12 weeks of resistance exercise training (13). Participants were divided into two groups. One group ingested a protein-containing supplement immediately after exercise and the other waited two hours to ingest the same supplement. Results were interesting, albeit somewhat puzzling. Strength increases were greater in the immediate ingestion group and were very limited in the group ingesting the supplement two hours after exercise. Moreover, muscle hypertrophy was observed only in the immediate ingestion group. Interestingly, the hypertrophy measured with immediate ingestion of the protein supplement was similar to that reported in other resistance training studies with older adult volunteers that included no particular feeding intervention (14, 15). Hence, on closer inspection, the results of this study (13) suggest that immediate ingestion of protein does not confer any advantage over unsupervised nutrition with training – at least in older adults. Thus, it could be argued that these findings actually failed to demonstrate any superior muscle anabolic response with immediate ingestion of protein during resistance training (13). Moreover, it should be noted that waiting two hours to ingest the protein actually inhibited the 'normal' anabolic response to resistance exercise training (13). In fact, that group lost lean body mass (a very unusual situation with resistance exercise training), making these results quite puzzling and difficult to interpret. It should be emphasized that these results were noted in elderly, albeit healthy, volunteers and may not apply to younger weight lifters.

Other longitudinal training studies may be used to provide support for the notion that optimal muscle and strength gains stem from ingestion of protein within close proximity to resistance exercise. Cribb and Hayes (2006) reported that during 10 weeks of resistance training, protein supplementation immediately before and after each workout resulted in significantly greater improvements in maximal strength and hypertrophy compared with a matched group of young individuals who consumed an identical supplement following a time-divided regimen, i.e. isocaloric and isonitrogenous but consumed at times not associated with the exercise, strategy (12). Whereas these data support the notion that protein ingestion in close temporal proximity to exercise may provide optimal anabolic results, the argument also can be made that these data do not, necessarily, demonstrate that dietary protein must be ingested immediately following resistance exercise. Given the design of this study (12), there is no way to rule out the possibility that pre-exercise protein ingestion played an important role in stimulating the muscle anabolic response. Indeed, given our data from acute metabolic studies, it may be argued that post-exercise feeding does not seem necessary to optimize the interactive metabolic response to resistance exercise and an amino acid source. In young males that did not report a background in resistance training, both essential amino acids (7) and whey protein (8) ingestion prior to exercise resulted in a superior or similar, respectively, anabolic response compared to immediately following exercise. Moreover, previous studies have shown the exercise-induced stimulation of MPS were similar when a protein-containing meal was ingested ~2 h prior to exercise (16), as when an amino acid source is provided following exercise (17, 18) (Figure 1). Thus, taken together, these results infer that skeletal muscle may be as responsive to the ingestion of a protein source during time periods outside the limits usually ascribed to the anabolic window (2), compared with a situation whereby protein is consumed within this window.

Other, more recent, longitudinal studies fail to support the necessity for protein ingestion in close temporal proximity to resistance exercise for maximal muscle hypertrophy. Hoffman and colleagues (19) used a study design very similar to Cribb and Hayes (2006) (12) and reported conflicting results. Furthermore, a recent investigation found a greater increase in lean body mass when protein was not consumed in close proximity to resistance exercise than when consumed in close proximity over eight weeks of training (20). However, in neither group was there immediate post-exercise feeding in that study (20). Nevertheless, these studies provide evidence that ingestion of dietary protein immediately post-exercise is unnecessary for achieving gains in muscle mass and strength in some circumstances.

Clearly, there is a great deal of equivocation in the results from studies investigating the importance of immediate post-exercise ingestion of protein for gains in muscle. The reasons for this lack of certainty likely are multi-factorial and may have to do with the differences in study design between these studies. In the studies described above, the subjects varied from completely untrained (20) to recreationally trained (12) to very well-trained (19). The impact of the training state of the subjects on the interactive response of muscle hypertrophy to resistance exercise and nutrition is unknown. Furthermore, these studies used variable amounts of protein and other nutrients in the context of variable total protein and energy consumption, such that direct comparisons may not be possible. The dearth of studies directly assessing this question makes it all but impossible to make solid conclusions about the optimal timing. Moreover, it appears that the optimal timing of protein and/or amino acid ingestion may differ depending on the type of amino acid source, as well as concurrent ingestion of other nutrients (10). Therefore, definitive conclusions cannot be made at this juncture.

The criticality of protein feeding immediately post-exercise for optimizing the anabolic response of muscle also has been cast into doubt by data generated from a series of acute metabolic studies. When untrained young males ingested essential amino acids one, two or three hours following resistance exercise, the response of MPS and NBAL is similar (6,16). Hence, it may be argued that the anabolic window may extend longer than merely the first hour or less following exercise. The stimulation of MPS and NBAL extends to at least 36 up to 48 h following resistance exercise performed in the fasted state (21, 22). Thus, it seems somewhat nonsensical that the interactive effect of exercise and protein ingestion also does not extend to these time points. This contention is supported by a study that showed protein ingestion 24 h following resistance exercise resulted in a greater response of MPS than protein ingested with no exercise (23). Admittedly, a direct comparison of the response of MPS or NBAL to ingestion of protein immediately and 24 h following exercise has yet to be made and thus the anabolic response could, in fact, be slightly greater immediately following exercise than 24 h after. However, it is clear that skeletal muscle is still responsive for at least 24 h following exercise. Thus, the importance of immediate post-exercise ingestion of protein does not seem as critical as has been espoused (2, 3). Clearly, the timing of amino acid and/or protein ingestion undoubtedly alters the metabolic response (24), however much more work is necessary before definitive conclusions may be made about the optimal time of ingestion.

We propose that the pattern of accumulation of skeletal muscle proteins in response to resistance exercise (performed in the fasted state) may follow a scenario as depicted in Figure 2. Essentially, that total muscle protein accumulation will reach similar levels after a certain period of time. Whereas there may be an initial rate of MPS with immediate ingestion of protein that is greater than if no protein is ingested, subsequent protein ingestion stimulates MPS as well (6,9). After so many hours – provided all other nutrient intake (particularly protein) and activity patterns are the same – theoretically the accumulation of muscle protein will be the same for both immediate and delayed timing situations. In Figure 2, we have rather arbitrarily chosen the time at which protein accumulation is equivalent as ~48h. Obviously, given that this is a theoretical scenario, no one knows exactly how this pattern would develop. In addition, how this pattern would develop if resistance exercise was performed in the fed state – as is often the case for many people who engage in resistance-based exercise training – is interesting to consider.

PRACTICAL IMPLICATIONS

Despite the lack of clear evidence for the unambiguous efficacy of immediate post-exercise protein ingestion, we maintain that it is probably a wise recommendation for most individuals that desire increased muscle mass and strength with resistance training. The operative question is, "what risks are associated with ingesting protein immediately following exercise?" For the vast majority of individuals, there are no appreciable risks to that approach. Thus, it is unlikely to impair the anabolic response and could improve it, so why not consume protein in the first hour or two following resistance exercise. Most athletes and exercisers are quite likely to consume some protein, whether as part of a meal or as a post-exercise supplement, in the natural scheme of things in any case.

CONCLUSION

The timing of dietary protein ingestion markedly influences the acute anabolic response of skeletal muscle to resistance exercise(10). Unfortunately, the optimal time to ingest a single dose of protein is complex and remains to be fully elucidated. Determinants of the optimal timing are almost certainly multifactorial and likely depend on an intricate combination of protein type, dose of protein available and content of the essential amino acids (in particular leucine content), and other nutrients ingested concurrently (10). We argue that the 'anabolic window of opportunity' is not as critical as reported. That is, skeletal muscle remains responsive to protein ingestion for much longer than the once purported one hour

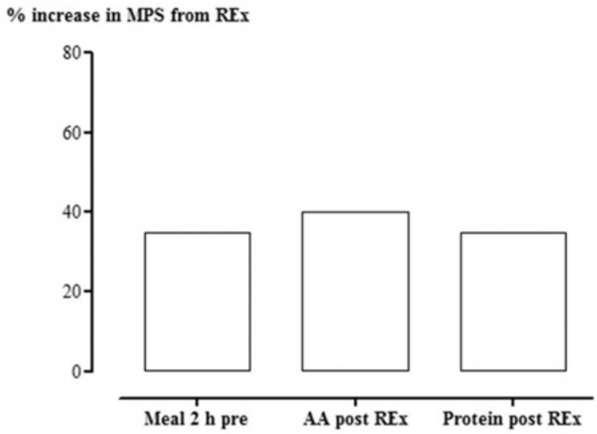

Figure 1. Additive effect of exercise on muscle protein synthesis when a source of protein is ingested prior to exercise compared with following exercise (16-18).

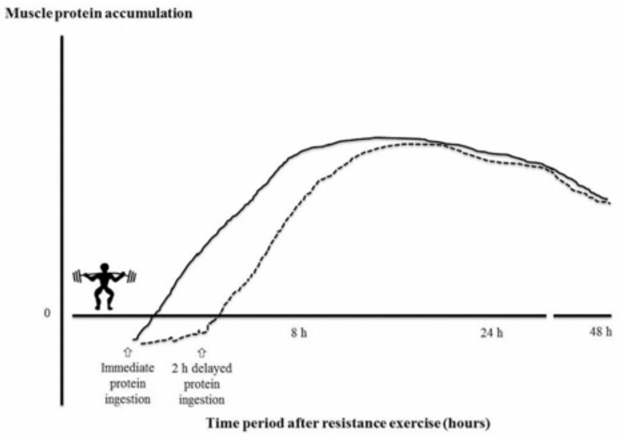

Figure 2. Proposed depiction of the accumulation of muscle proteins when protein is ingested immediately after- (broken line) or postponed for a period of time, e.g. ~2h, after (solid line) completion of a resistance exercise session performed in the fasted state. We theorize that the initial accumulation of protein rises steeply when protein is ingested immediately following exercise, but plateaus as muscle protein synthesis and net muscle protein balance return to post absorptive values. Since net muscle protein balance remains negative following exercise, when protein ingestion is delayed, a small amount of muscle protein is lost until amino acids from protein consumption become available to provide the interactive effect of exercise and amino acids on muscle protein synthesis. However, the response of muscle protein synthesis and net muscle protein balance is similar to immediate protein ingestion, thus accumulation of protein follows a similar pattern, albeit delayed by 2h. Assuming equivalent activity patterns and nutrient (particularly protein) ingestion during recovery, there would be little difference, at least of any physiological significance, in muscle protein accumulation between immediate and delayed protein ingestion regimens. Instead, temporal diversities in muscle protein accumulation may be achieved by varied timing approaches.

following resistance exercise. This said, from a purely practical standpoint, protein ingestion within one hour post exercise is likely to be a convenient time to ingest protein. There certainly is no evidence that protein ingested immediately post exercise will impede the muscle anabolic response.

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