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Editorial

Proteins for protein synthesis: Quantity and timing

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Introduction

The credibility attributed to the calculation of nitrogen balance (1) has consolidated over time the notion that there is a "limit" of 30g of protein per meal, suggesting that doses above this amount would not be absorbed. Excess protein leads to oxidation and urea production, with the relationship between these parameters serving as an indicator of overconsumption. Since the 1990s, these measures have been considered valid (2) for sedentary adults. However, this data has always been studied in sedentary individuals. It wasn't until the early 2000s that the first studies specifically targeting exercise and using advanced analytical systems were conducted (3, 4). These studies raised doubts about the previously recommended daily allowance, suggesting a doubling of protein intake over 24 hours, from 0.9 g/kg to 1.7-2 g/kg. The procedure that allowed for the adjustment of earlier guidelines dates back to the early 1990s with Wolfe's studies (5), which introduced the analysis of fractional synthesis rate (FSR), measuring the rate at which a metabolite is incorporated into muscle per unit of mass. These studies unequivocally demonstrated the daily protein needs of physically active individuals. Around the same time, researchers began investigating the relationship between muscle protein synthesis (MPS) and muscle protein breakdown (MPB) (6), leading to the concept of the "anabolic window." This concept was supported by studies such as Esmarck's (7), which showed that older individuals experienced greater hypertrophy and strength gains when consuming a protein-carbohydrate supplement immediately post-exercise compared to waiting two hours. However, subsequent experiments indicated that delayed intake (3 hours) produced the same response as immediate intake (1 hour) (8). More precise experimental studies with modern tools have disproven the "anabolic window" or have shown that its duration is much longer than previously believed, making it less time-sensitive and not strictly dependent on immediate post-exercise protein intake (9). Nevertheless, MPS remains an extremely important parameter and the most credible to date.

Protein timing and synthesis

Immediately following strength training, the AKT-MAPK-mTOR-4EBP1-p70S6K1 pathway activates myofibrillar regeneration (10-12), i.e., MPS. This increase in synthesis rate and responsiveness to protein intake lasts up to 48 hours post-exercise (13), contrary to earlier assumptions. During this phase, nutrient absorption changes significantly, invalidating evaluations made for sedentary individuals and justifying protein intakes well above previously suggested limits for sedentary people. One key factor in this phenomenon is insulin and the increased sensitivity of various tissues to it, not just muscle (13). Once it is understood that exercise activates this metabolic pathway, the next step is determining the optimal amount of protein and whether there is a "dose-response" relationship, both for total daily intake and a potential post-exercise bolus.

Daily protein intake

Some studies have recommended very high daily protein intakes (3 g/kg) (14), finding a negative nitrogen balance and considering 2 g/kg a reasonable limit. Rigorous meta-analyses conducted in recent years confirm that exercise requires significantly higher protein intakes than those suggested for sedentary individuals, typically 2-2.2 g/kg. However, the benefits of further increasing protein intake remain unclear (16). A recent review of 69 articles created a dose-response curve "protein intake vs. strength gains," demonstrating increased strength with higher protein intake, up to 1.5 g/kg per day, with no additional benefits observed beyond that threshold (17).

Concerns about high protein intake primarily relate to kidney and bone health. However, many studies now confirm the safety of high protein doses for athletes, with amounts up to 2.8 g/kg (18) and even 3.3 g/kg (19) showing no adverse effects on kidney function. A recent review of nearly 15,000 subjects found a significantly lower risk of chronic kidney disease associated with higher total, plant, or animal protein intake (20). Similarly, the potential negative effects of high protein intake on bone health have been disproven. Doses exceeding 2.2 g/kg (21) and even 3.2 g/kg (22) have been deemed safe, showing no adverse effects on bone density. A recent review (23) also confirms that a high-protein diet is not harmful to bone health or associated with other negative effects.

Timing of protein intake

Given the clear need for athletes to consume approximately double the protein intake of sedentary individuals, researchers have questioned whether the timing of this protein intake could present risks. Experimental data suggests that post-exercise protein doses of 40g are effective for performance without any indication of harm or inefficiency (24). Additional studies have explored timing, confirming the benefits of a protein-rich meal post-exercise. Areta et al. demonstrated that dividing 80g of protein into four 20g doses over 12 hours post-exercise maximized MPS compared to eight 10g doses or two 40g doses (25). Recently, Moore's review identified 0.31 g/kg of body weight as the optimal amount of high-quality protein for maximizing MPS following resistance training (26).

Mallison's research found that post-exercise intake of 30 or 60 g of protein in young women enhanced MPS more effectively than 15 g, with no significant difference between the 30 and 60 g doses (27). In 2023, a study demonstrated the acute effect of consuming 100 g of protein immediately post-exercise (28). This groundbreaking research has reopened the discussion on protein timing and intake, raising both curiosity and skepticism.

Distribution of protein intake

Earlier studies (29) suggest that evenly distributing protein across meals (e.g., breakfast: 0.33 g/kg, lunch: 0.46 g/kg, dinner: 0.48 g/kg) leads to greater lean mass gains after 12 weeks of resistance training compared to an unbalanced distribution (e.g., breakfast: 0.12 g/kg, lunch: 0.45 g/kg, dinner: 0.83 g/kg). This raises the possibility that Trommelen's 100 g post-exercise dose (28) might yield greater total MPS if distributed into smaller doses of approximately 0.3 g/kg.

As Witard (26) highlights in a comprehensive review, any conclusions at this stage remain premature, as Trommelen's study (27) was not designed to assess the impact of protein meal distribution on muscle's anabolic response to ingested protein.

Future directions

The findings from Trommelen's study emphasize how limited our understanding still is and underscore the need for further research to fully grasp these mechanisms. Exercise induces metabolic changes that render sedentary knowledge inapplicable. While there are no definitive conclusions on optimal protein doses, shared hypotheses exist.

The timing of protein intake remains an open debate. Recent studies highlight the benefits of consuming protein both immediately post-exercise and before sleep (31). As with many scientific articles, this one concludes with a call for further research to verify and confirm these findings.

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