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A Critical Review of the Anabolic Window Hypothesis: Protein Timing and Myofibrillar Protein Synthesis after Resistance Training

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Abstract. The proposed "1-2 h post-exercise anabolic window" remains widely discussed in resistance-training nutrition, although the effects of protein timing on muscle adaptation remain unclear. To address this debate, this critical narrative review synthesizes evidence from stable-isotope tracer studies, randomized controlled trials (RCTs), a position stand, a systematic review and meta-analysis, and research on the mechanistic target of rapamycin (mTOR) signaling pathway. In particular, it explores whether protein ingestion within 1-2 h after resistance exercise independently affects acute myofibrillar protein synthesis (MyoPS) or longer-term muscle hypertrophy when total daily protein intake is controlled. Existing evidence indicates that adequate daily protein intake and sufficient per-meal doses matter more than adherence to a narrowly defined post-exercise ingestion period. Although protein timing may influence acute anabolic responses under certain conditions, there is insufficient evidence to show that protein must be consumed within 1-2 h to maximize muscle growth. In practice, meeting daily protein needs and getting enough protein at each meal should come first, while consuming protein around training is a useful strategy rather than a strict requirement.

Keywords: Anabolic Window, Protein Timing, Myofibrillar Protein Synthesis, Resistance Training, mTOR Signaling Pathway

1. Introduction

In the field of sports nutrition, the recommendation to consume protein within 1-2 h after resistance training is widely adopted. This practice is partly rooted in isotope-tracer evidence showing that resistance exercise elevates mixed-muscle protein synthesis for up to 48 h, while concurrent protein breakdown can maintain a negative net protein balance without nutrient intake [1, 2]. These findings informed the "anabolic window" hypothesis but did not establish that protein ingestion within 1-2 h yields superior outcomes compared with equivalent intake at other times. However, acute fractional synthesis rate (FSR) responses may not reliably predict long-term muscle hypertrophy [3]. Besides, a randomized controlled trial matching total daily protein intake found no significant differences in body composition or strength between immediate and delayed protein intake [4]. Although these findings cast doubt on the need for a strict post-exercise deadline, protein timing may still influence

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outcomes in certain conditions or populations. Thus, this review examines whether protein timing independently affects myofibrillar protein synthesis (MyoPS) and muscle hypertrophy when total daily protein intake is controlled. In particular, it draws on ten sources addressing exercise-induced protein metabolism, stable-isotope studies, nutrient timing, a position stand, and a randomized trial [1-5]. Besides, it covers editorial analysis, mTOR signaling, a systematic review and meta-analysis, and studies of protein quality and leucine supplementation [6-10]. The review asks whether protein timing has effects beyond total intake, how long post-exercise anabolic sensitivity lasts in different populations, and how protein amount, intake patterns, protein sources, and leucine levels influence muscle protein synthesis (MPS). Accordingly, the study compared various aspects such as research design, protein intake, feeding conditions, training status, and outcomes like acute protein synthesis and long-term muscle hypertrophy.

2. The classical anabolic window hypothesis and early evidence

2.1. Early evidence for the anabolic window

The anabolic window hypothesis was based on isotope-tracer studies showing prolonged changes in muscle protein turnover after resistance exercise. Notably, Phillips et al. found that mixed-muscle protein synthesis stayed high for up to 48 h, but protein breakdown also increased, and net protein balance remained negative during fasting, as shown in Table 1 [2]. Furthermore, Tipton and Wolfe emphasized that muscle protein accretion requires synthesis to exceed breakdown and described exercise-induced changes in protein metabolism lasting approximately 24–48 h [1]. However, these studies did not directly establish a strict 1-2 h post-exercise protein ingestion window.

Table 1. Muscle protein turnover after resistance exercise

Time post-exercise	FSR vs. rest	FBR vs. rest	Net protein balance
3 h	+112% ($P < 0.01$)	+31%	Negative
24 h	+65% ($P < 0.01$)	+18%	Negative
48 h	+34% ($P < 0.01$)	≈ rest (NS)	Negative

Note: Data from Phillips et al. [2]. Participants were 8 untrained adults (4 men, 4 women) who performed 8 sets × 8 repetitions of unilateral leg extension at 80% 1RM. Measurements were obtained in the fasted state.

2.2. Physiological basis of the anabolic window

Resistance training makes muscles more responsive to insulin and amino acids, which may support recovery after exercise [1]. Moreover, exercise may affect amino acid transport, thus allowing more amino acids to enter muscle cells. Meanwhile, protein intake provides essential amino acids needed for muscle protein synthesis (MPS), while insulin helps to reduce muscle protein breakdown [1, 3]. These effects can support muscle protein turnover and repair after exercise.

Furthermore, resistance exercise combined with protein intake may enhance MPS. Specifically, exercise stimulates muscle remodeling, while amino acids supply the building blocks required for new muscle protein formation. Besides, insulin may further support this process by reducing protein breakdown. These effects helped explain the anabolic window hypothesis, suggesting that protein intake around exercise may support muscle recovery and growth.

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2.3. Reassessment of the classic hypothesis

Aragon and Schoenfeld re-examined the classical anabolic window theory and identified several weaknesses [3]. Acute fractional synthetic rate (FSR) measurements reflect short-term changes in muscle protein synthesis but cannot independently predict long-term muscle hypertrophy. This is because muscle growth depends on the balance between protein synthesis and breakdown over time, as well as training status and recovery duration.

Early studies often examined exercise under fasted conditions, which may have increased the perceived need for immediate post-exercise protein intake. Protein intake before exercise helps maintain amino acid availability during recovery, reducing the need for immediate supplementation. In addition, differences in total daily protein intake may influence the apparent effects of protein timing. Thus, timing should be assessed alongside total protein intake and pre-exercise nutrition rather than as a fixed post-exercise deadline. Whether protein timing independently affects muscle adaptation when total daily protein intake is matched remains to be established through controlled intervention studies.

3. Evidence evaluation and theoretical revision of the anabolic window hypothesis

3.1. Evidence from meta-analyses and randomized trials

Evidence from controlled trials helps establish whether protein timing independently affects muscle adaptation. In this context, Lak et al. assigned 40 resistance-trained males (24 ± 4 years) to an 8-week resistance-training intervention with matched protein intake of 2 $g \cdot kg^{-1} \cdot d^{-1}$ [4]. Participants consumed protein either immediately before and after exercise or 3 h before and after exercise, with 31 completing the study. Both groups significantly increased skeletal muscle mass and strength ($P < 0.05$), without significant between-group differences ($P > 0.05$). These findings indicate that the two timing schedules produced no statistically significant differences in the measured outcomes over 8 weeks when total protein intake was matched; they do not establish physiological equivalence.

Regarding acute responses, Ji et al. examined acute responses in 21 randomized controlled trials, 15 of which were included in the meta-analysis [8]. The meta-analysis showed that whey protein supplementation combined with exercise increased myofibrillar FSR (Hedges' $g = 1.24$; 95% CI: 0.71–1.77; $P < 0.001$). Individual studies reported 1.3–1.6-fold FSR increases following immediate post-exercise supplementation and up to a 2.5-fold increase when whey protein was consumed 45 min before exercise. However, differences in experimental protocols prevent these findings from establishing an independent timing advantage. Therefore, although acute evidence supports protein supplementation around exercise, the available protein-matched trial provides no clear evidence that immediate ingestion produces superior long-term adaptations.

3.2. Relative importance of protein intake and timing

Existing evidence suggests that nutritional factors should be prioritized in a specific order to support adaptation to resistance training. Adequate total daily protein intake is essential for muscle growth and recovery during resistance training [3, 4]. To make effective use of this intake, protein should also be distributed across meals in sufficient amounts to stimulate MPS. Kerksick et al. recommend approximately 20-40 g of high-quality protein per meal, with meals spaced about 3-4 hours apart [5]. However, the optimal amount may vary depending on individual needs and training conditions [6].

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Once daily protein needs and per-meal intake are met, protein timing becomes a secondary priority. Although consuming protein around exercise may support recovery, its additional benefits for long-term muscle adaptation remain uncertain when daily protein intake is sufficient [4]. Thus, nutritional planning should focus on meeting daily protein needs, ensuring adequate intake at each meal, and then considering the timing of consumption.

3.3. Revised duration of post-exercise anabolic sensitivity

The duration of enhanced MPS after resistance exercise does not necessarily reflect the length of time during which the muscle remains sensitive to protein intake. Phillips et al. reported elevated mixed-muscle protein synthesis for up to 48 h after exercise [2]. Nevertheless, these findings were based on only eight untrained adults tested under fasted conditions, which limits their application to other populations. Additionally, Tipton and Wolfe described exercise-related changes in protein metabolism lasting approximately 24–48 h, but this does not establish that increased sensitivity to dietary protein persists throughout this period [1].

Evidence from other populations remains more limited. Specifically, in young adults performing resistance training, van der Heijden et al. observed increased MyoPS during both the 0-2 h and 2-4 h periods after exercise [9]. However, as responses beyond 4 h were not measured, the duration of enhanced anabolic sensitivity remains unclear. Moreover, training status, age, and previous protein intake may affect the magnitude and duration of the response [3]. Thus, although exercise-related anabolic activity may persist beyond the immediate recovery period, the existing evidence does not demonstrate a consistent 48 h period of enhanced protein sensitivity across trained and untrained populations.

4. Molecular mechanisms and regulatory factors of muscle protein synthesis

4.1. The role of mTORC1 signaling in muscle protein synthesis

The mechanistic target of rapamycin complex 1 (mTORC1) is a central regulator of muscle protein synthesis, integrating signals from mechanical loading, amino acid availability, growth factors, and cellular energy status. Specifically, Zhang et al. describe how leucine sensing through Sestrin2 and arginine sensing via CASTOR1/2 regulate Rag GTPase-dependent recruitment of mTORC1 to the lysosomal surface [7]. Meanwhile, insulin and other growth factors stimulate mTORC1 through the PI3K–AKT–TSC2–Rheb pathway, while low energy levels activate AMP-activated protein kinase (AMPK), thereby inhibiting mTORC1 activity. In addition, mechanical loading provides another anabolic stimulus that converges on this signaling network. Once activated, mTORC1 regulates protein translation through downstream targets, including p70S6K and 4E-BP1.

In line with these mechanisms, Ji et al. Pointed out that whey protein supplementation combined with exercise increased the phosphorylation of AKT, mTOR, 4E-BP1, p70S6K, and rpS6 at 1-2 h post-exercise, whereas p70S6K and rpS6 phosphorylation decreased by 4–5 h [8]. Furthermore, myofibrillar FSR showed a dose-dependent increase with protein intakes ranging from 10 to 60 g. This suggests that nutrient availability and intracellular signaling contribute to muscle anabolism after exercise. However, acute changes in pathway phosphorylation alone cannot confirm long-term muscle growth or define a strict time limit for protein intake [3].

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4.2. Leucine regulation of mTORC1 signaling and its limits

Although leucine is essential for promoting MPS, current protein intake guidelines do not confirm a single leucine threshold for all individuals [5]. To further examine protein source, van der Heijden et al. compared the effects of 32 g of a plant-protein blend and an equal dose of whey protein in ten resistance-trained adults [9]. Although leucine levels differed between the plant blend and whey protein (2.5 vs. 3.2 g), and whey protein led to greater EAA availability in the blood (P = 0.04), post-exercise MyoPS was similar between the two groups, as shown in Table 2.

Table 2. Plasma EAA kinetics and myofibrillar protein synthesis after protein supplementation

Outcome	WHEY	BLEND	Significance
Supplement composition			
Leucine content (g/32 g protein)	3.2	2.5	—
EAA content (g/32 g protein)	14.5	12.0	—
Plasma EAA kinetics (0–4 h)			
Plasma EAA iAUC, 0–4 h	~44% higher than BLEND	Reference	P = 0.04
EAApeak (μmol·L^{-1})	2019 ± 509	1469 ± 247	P = 0.02
Time-to-peakEAA (min)	35 ± 11	63 ± 22	P = 0.01
Myofibrillar protein synthesis			
Basal MyoPS (%·h^{-1})	0.042 ± 0.020	0.043 ± 0.015	P = 0.92
MyoPS, 0–2h (%·h^{-1})	0.085 ± 0.037	0.080 ± 0.037	P = 0.93 (interaction)
MyoPS, 2–4h (%·h^{-1})	0.085 ± 0.036	0.086 ± 0.034	NS (interaction)
MyoPS, 0–4h (%·h^{-1})	0.084 ± 0.020	0.082 ± 0.031	P = 0.80 (interaction)

Note: Data from van der Heijden et al. [9]. Ten resistance-trained adults (8 men, 2 women) participated in a randomized, double-blind crossover study comparing 32 g of whey protein with a plant-protein blend. Plasma EAA analyses included nine participants, whereas MyoPS measurements included all ten. No significant between-condition differences in MyoPS were detected across the 0–2 h and 2–4 h periods. The reported P = 0.93 is the time × condition interaction across these periods, not a separate 0–2 h comparison. NS, not significant; iAUC, incremental area under the curve.

For longer-term outcomes, Jacob et al. studied 19 pre-frail or frail older women undergoing 12 weeks of resistance training with optimized protein intake (~1.2 g·kg^{-1}·d^{-1}) [10]. Although muscle protein synthesis and physical function improved, additional leucine supplementation (7.5 g/day) provided no significant benefit compared with an isonitrogenous alanine control. These findings show that leucine availability supports muscle anabolism but does not define a universal threshold for the anabolic response. Therefore, leucine targets should be viewed as practical guidelines rather than strict requirements for maximizing muscle growth.

5. Practical applications and future research directions

5.1. Implications for sports nutrition products

To support muscle recovery and adaptation, sports nutrition products should provide an adequate protein dose per serving and sufficient essential amino acids [5, 8]. These needs can be met by using

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whey protein or well-designed plant-protein blends. For instance, Van der Heijden et al. found that a blend of pea, brown rice, and canola proteins produced an acute MyoPS response comparable to whey protein at an equal protein dose [9]. This supports using complementary plant proteins in product formulation, although their long-term effects on muscle growth need further study.

In terms of product use and marketing, post-exercise protein supplements should be presented as a convenient way to meet daily protein needs rather than as necessary within a strict 1-2 h period [6]. Product labels and recommendations should therefore focus on protein content per serving, protein quality, amino acid composition, and ease of use. In addition, claims about the need for immediate post-exercise consumption should be avoided unless supported by sufficient evidence.

5.2. Precision nutrition and individual variability

The generalizability of current findings is limited by differences in participant characteristics and study designs. For example, Lak et al. investigated resistance-trained young males, with 31 of 40 participants completing the intervention (22.5% attrition), while van der Heijden et al. included only ten trained adults (eight men and two women) [4, 9]. In addition, the foundational 48 h time-course evidence was obtained from eight untrained participants under fasting conditions [2]. By contrast, Jacob et al. examined older women, but their study addressed a different nutritional intervention rather than protein timing [10] . Consequently, existing findings cannot establish whether the effects of protein timing are consistent across sex, age, and training status.

Future efforts should employ adequately powered, protein-matched randomized controlled trials (RCTs) with greater representation of women, older adults, and individuals with different training backgrounds. Such studies should standardize total protein intake, prior feeding conditions, and resistance-training protocols while comparing specific protein intake times. Moreover, long-term changes in muscle hypertrophy and strength should serve as primary outcomes, with acute MyoPS measurements providing complementary mechanistic evidence. These studies may clarify whether protein timing independently affects long-term muscle growth and strength in different populations.

6. Conclusion

This study shows that current evidence does not establish a universal 1-2 h post-exercise protein window. While acute MyoPS increases after exercise, immediate protein intake has not been shown to produce greater long-term muscle growth or strength than later intake. Besides, exercise-induced increases in muscle protein synthesis may persist for up to 48 h, but this does not indicate a uniform period of increased sensitivity to dietary protein. In practice, meeting daily protein needs and consuming adequate protein at each meal (approximately 20–40 g of high-quality protein) should take priority, while consuming protein close to exercise remains a convenient option. Leucine content can guide product formulation but should not be considered a universal threshold for muscle protein synthesis. Similarly, mTORC1 signaling helps explain interactions between exercise and nutrition but does not independently establish the benefits of specific protein timing strategies.

These conclusions are limited by differences in study design, feeding conditions, and participant characteristics, as well as the limited representation of different sexes, ages, and training statuses. Future randomized trials should compare clearly defined protein intake times while controlling total protein intake, feeding conditions, and training protocols. Long-term muscle growth and strength should be the main outcomes, with acute MyoPS measurements providing additional insight into the underlying mechanisms.

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