

The Regulatory Role of Nutrients in Muscle Protein Synthesis (MPS) and Muscle Protein Breakdown (MPB) with Resistance Exercise

Jinchen Han^{1,*}

¹ Annie Wright Schools, Tacoma, 98403, United States

*Corresponding author: jinchen_han@aw.org

Abstract:

With the improvement of living standards nowadays, the body's health and physique have become a popular topic; the growth, maintenance, and health of muscles are achieved through the key process of muscle protein synthesis (MPS) and muscle protein breakdown (MPB). This paper discusses the important regulatory roles of macronutrients, amino acids, hormones, micronutrients, and vitamins in MPS and MPB, especially in the context of resistance exercise. Through a large review of the existing literature on the relationships between various nutrients and resistance exercise and muscle, this paper summarizes the complex interactions between all these nutrients and resistance exercise. This paper aims to provide comprehensive insights into the optimization of muscle hypertrophy and reduction of muscle atrophy, including an in-depth discussion of the importance of macronutrient intake during resistance exercise, the important role of amino acids, especially leucine, the associated effects of hormones such as insulin and testosterone, and the best timing and methods for the intake of these nutrients. This review demonstrates the indispensability and complementarity of each nutrient for muscle growth and building, provides practical advice for athletes such as powerlifters and bodybuilders, the declining elderly, and individuals seeking to enhance muscle health, fills existing research gaps, and provides valuable insights into the nutritional regulation of muscle protein metabolism.

Keywords: Resistance exercise; muscle protein synthesis (MPS); muscle protein breakdown (MPB); macronutrients; net muscle protein balance (NBAL).

1. Introduction

With the rapid development of science and technology and the gradual progress of human society toward civilization and advancement, people have begun to pay attention to how to maintain good physical health, especially athletes and the elderly. Muscles are often an indispensable core part of this, they support people's daily lives as necessary contractile force motors, and there is already a substantial body of research proves that a greater proportion of one's skeletal muscle to the total body weight will enhance one's recovery and resistance ability during severe disease, let alone it's role of being the largest metabolically active tissue and largest site for glucose processing in the body [1,2]. So, muscle growth and maintenance are unignorable under the topic of good physical health, and muscle protein synthesis (MPS) and muscle protein breakdown (MPB) are its key steps. These processes require resistance exercise and the following participation and regulation of nutrients, resistance exercise often stimulates more MPB, but not as much as it stimulates MPS; there is a balance between MPS and MPB, it's a dynamic

regulation that when MPS is greater than MPB, known as net muscle protein balance, a positive NBAL (difference between MPS and MPB), muscle hypertrophy happens, inversely, a negative NBAL means muscle atrophy is occurring [2,3]. This cycle also requires the important interactions of macronutrients, micronutrients, and hormones on MPS and MPB after resistance training, a functionally healthy body requires the development of an appropriate nutrition plan in conjunction with prescribed resistance training in order to have the most expected NBAL [2].

By clarifying how nutrients regulate MPS and MPB after resistance training and their significant effects on muscle growth, recovery, and general health, this study provides further suggestions for maximizing muscle gain, strength, function, and health. This paper reviews the literature and related studies, and further extends and develops insights on this basis. The regulation of MPS and MPB by macronutrients, amino acids, hormones, micronutrients, and vitamins under resistance exercise will all be covered in detail in this article. It will also suggest the optimal timing and technique for consuming nutrients to enhance muscle

protein metabolism. This article will provide practical advice based on current scientific evidence for athletes, older adults, and individuals seeking to optimize muscle health. With these goals, this review aims to fill existing research gaps in a comprehensive lecture on the relationship between all the nutrients and muscle gain and provide additional valuable insights into the nutritional regulation of muscle protein metabolism.

2. MPS and MPB

MPS is the process of building new proteins in muscle cells, it's mediated by the mammalian rapamycin Target 1 (mTORC1) signaling pathway and MPB is an unavoidable process of degrading existing muscle proteins into amino acids, the three systems of autophagy, calpain, and ubiquitin-proteasome need to be combined to complete the MPB [2]. These two processes are happening everywhere in the human body, for all proteins, it's the balance between MPS and MPB that determines the mass of human muscle [4]. Muscle hypertrophy occurs due to the accumulation of muscle protein, which means a positive NBAL, and there are a lot of factors that affect the NBAL, in short, the interaction between resistance training and nutrient intake results in a greater difference between MPS and MPB [4].

3. Macronutrients

Any topic related to MPS will include the word macronutrients, they play a significant role in the process of muscle protein synthesis, let alone as the main energy supply for basic human daily activities, these nutrients support human lives. Macronutrients include proteins that are comprised of aggregated amino acids; fats mainly structured with glycerol and fatty acids; and carbohydrates composed of the polymer of monosaccharides. Each of these macronutrients plays a specific role in MPS and MPB, mixed macronutrition meals can even double the efficiency of MPS, especially accompanying resistance training, maximizing the NBAL [5].

3.1 Protein

Protein is an essential structural component of all living matter, it's basic for muscle building, and it's the major building block; after resistance training, MPS and MPB can both be enhanced for 24-48 hours, and skeletal muscle maintains sensitivity to the anabolic effects of protein intake, during this period dietary protein acts as a key regulator to MPS, promote mRNA expression, myofibrillar and mitochondrial protein synthesis, improve adaptability to resistance training; also thanks to the Vitamins A, D, and E as well as the minerals selenium and zinc in protein-rich foods since they are responsible for the high MPS after a meal too [6,7]. MPS only significantly overruns MPB

when protein is digested afterward, leading to positive NBAL, skeletal muscle protein accumulated during this repetitive process, causing muscle hypertrophy [6]. One of the main reasons for the decline of physical fitness and resistance of skeletal muscle to various kinds of nutrition and exercise stimulation in the elderly is malnutrition, especially the lack of dietary protein intake, which is a great indication of the importance of sufficient protein intake [3]. More than these, it's been proven that higher protein ingestion accompanied by resistance exercise and a low-calorie diet is super efficient in cutting body fat and maintaining a lean physique shape [7].

3.2 Carbohydrate

Carbohydrates, the fuel of the body, there are three main kinds of carbs, simple sugars, complex carbohydrates, and glycoconjugate. Simple sugars are either monosaccharides or disaccharides, including glucose, fructose, and galactose, their main fate is to be converted into a glucose pool and finally produce ATP energy that cells use directly, extra glucose will be either stored as glycogen reserves or fat for future use. It is well known that glucose is so important, it's the basis of a functional body, especially since human brains are highly dependent on glucose to provide necessary energy; therefore, the importance of carbohydrate intake to store glycogen for human beings, particularly those who regularly exercise, is self-evident. The body's limited glycogen reserves will rapidly decline during high-intensity resistance training, leading to a gradual decline in exercise quality and an increase in MPB, and a high carbohydrate diet will increase the endogenous glycogen reserves, therefore, in order to quickly restore the body's glycogen reserves, the intake of carbohydrates after resistance training is needed [8]. Having carbohydrates on time after resistance training gives the body a quick boost of energy, improves the next exercise performance, and accelerates muscle repair, which means an enhancement of MPS and an inhibition of MPB [8]. The importance of dietary carbohydrate intake towards muscle growth is more than this, dietary fiber, a kind of complex carbohydrate, also plays a significant role in the process of muscle growth. There are two types of dietary fiber, soluble and insoluble, soluble dietary fiber (SDF) regulates and improves the gut microbiota, providing it with a major source of carbon and energy, SDF metabolizes it into beneficial products such as short-chain fatty acids (SCFAs) to prevent various gastrointestinal diseases [9]. Consuming SDF and combining it with insoluble dietary fiber promotes the metabolism and absorption of active substances, which is highly important in the context of resistance exercise with nutrient intake [9].

3.3 Fat

Fats are seen as enemies by many people since cutting weights is losing and burning body fat, but fats are actually indispensable construction parts and nutrients to the human body. Fats are a more efficient way to store calories than glycogen and function as basic body protection and thermal insulation. Dietary fats are the precursors of hormones and vitamins, they are the most concentrated source of energy, about 9Kcal per gram, they also carry the essential fatty acids as well as fat-soluble vitamins (A, D, E, K) and some phytochemicals which are all super helpful for the body's health. The absorbable forms of dietary fats are cholesterol, fatty acids, and glycerol. Cholesterol is a structural fat, the component of all cell membranes, the brain, and nerves; although it doesn't provide energy, it's needed by the body for producing vitamin D and steroid hormones, including a crucial sex hormone, testosterone, which is another determinant of muscle growth. For fatty acids, this paper mainly focuses on essential omega-3 polyunsaturated fatty acids since their great contribution towards muscle growth and maintenance. Multiple studies and research have demonstrated that omega-3 fatty acids obtained from fish oil can improve skeletal muscle mass and function, and even promote strength gains during resistance training, especially in middle-aged and older adults [1]. Omega-3 fatty acids also have anti-inflammatory properties, which can not be ignored in middle-aged and elderly people since inflammation is also often blamed for the loss of muscle function [10]. More importantly, dietary intake of high levels of unsaturated fatty acids, eicosapentaenoic acid(E-

PA), and docosahexaenoic acid(DHA) is associated with enhancing the key signaling pathway mTORC1 of MPS [1]; this puts dietary fat intake in an indispensable place in necessary nutrient intake in order to maximize NBAL, let alone omega family's other effects such as maintenance of healthy skin, normal growth and functioning of nerves and the brain, further emphasize the importance of fats, especially unsaturated fatty acids in daily dietary.

3.4 Synergistic Effect

The Interesting fact about all three macronutrients is that none of them can maximize the NBAL and support the body's health optimally by themselves alone. As Table 1 shows, multiple nutrients and resistance exercise work together as a whole, leading to a significantly increased postprandial MPS, the point of interaction of several nutrients to maximize the NBAL needs to be enhanced here. Combining carbohydrate and protein intake during resistance training will increase muscle glycogen reserves, improve muscle injury, and maintain better adaptability to the training, even enhancing strength [4,7,8]. Similarly, when fat and protein are consumed at the same time, the availability of amino acids from the protein source may also increase, although it is still not fully understood, the co-uptake of lipids and proteins does seem to have some effect on muscle anabolic metabolism after exercise, but it's already been proved that combining a high-protein diet rich in omega-3 with resistance training increases muscle strength and reduces inflammation in older men, this is a good illustration of the synergistic role of nutrients [4,10].

Table 1. Summary of the response of muscle protein metabolism to resistance exercise and nutrient intake [4].

Description	MPS	MPB	NBAL
Protein or amino acids alone	increase in rate	little to no change in rate or decrease in rate	increase in rate to more
Exercise alone	increase in rate	increase in rate	increase in rate
Amino acids plus exercise	Great increase in rate	little to no change in rate	Great increase in rate to more
Carbohydrates (insulin) alone	increase in rate	little to no change in rate	increase in rate
Carbohydrates (insulin) plus exercise	little to no change in rate	decrease in rate	increase in rate
Carbohydrates (insulin) plus amino acids following exercise	Great increase in rate	decrease in rate	Super significant increase in rate to more

3.5 Cautions

Finally, most importantly, any kind of macronutrients needs to be incorporated with resistance exercise together to achieve the goal of maximizing NBAL, as well as controlled in the correct amount to keep the physique healthy; excessive protein will be harmful to health and physique maintenance because it will end up a huge burden on the liver, stored as fat by the body and food protein sources are also good sources of fat; excess carbohydrates will also be stored as fat, the storing of too much fat can cause elevated blood lipids and obesity, increase the burden of the kidney, high blood cholesterol is highly related to heart disease, which is the leading cause of death for both men and women in America [11]. Excess of amino acids in the body is oxidized and disposed of, which won't help the body as well.

4. Amino Acids and Muscle Protein Metabolism

Proteins are comprised of amino acid strings, if going in-depth into protein and its effects on MPS and MPB, amino acids, especially essential amino acids(EAA) will be an inevitable topic. There are nine EAA, they are leucine, threonine, tryptophan isoleucine, lysine, phenylalanine, histidine, methionine, and valine [12]; leucine is the most noteworthy EAA in this group, the remarkable anabolic properties of leucine and its triggering effect on protein synthesis are the assets that keep it one of the most important nutrients to sit on [5].

Leucine's contribution to muscle growth can never be overstated, it is one of the decisive factors in human muscle growth and plays a mainstay role in all nutrients. Leucine's greatest credit goes to its activation of mTORC1. mTORC1 is significantly associated with MPS, as the indispensable regulator of protein synthesis, it caused phosphorylation of ribosome S6 kinase 1 (S6K1) and eukaryotic initiation factor 4E-binding protein 1 (4E-BP1), and ends up with eukaryotic extension factor 2 (eEF2) phosphorylation decreased, which can greatly affect DNA transcription efficacy, the translation of protein is activated by mTORC1, especially after high-intensity resistance exercise [12]. Not only that, Leucine can also induce a brief spike in plasma insulin within 30 minutes after ingestion, proving that it has important synergistic properties with other nutrients [5].

Besides these, leucine still contains more effects, as branch chain amino acid(BCAA), leucine's metabolite β -hydroxy- β -methylbutyrate(HMB), also plays a huge role in muscle anabolism, in particular, it has been proved that it can stimulate MPS and inhibit MPB [5]. Leucine metabolite HMB enhances MPS to a similar extent as leu-

cine, but it can also reduce MPB by inhibiting the well-known ubiquitin-proteasome system. Oral HMB can also cause MPB to decrease by about 57%, comparable to the same effect of insulin, this is probably why hyperaminoacidemia (mainly mediated by BCAAs) significantly inhibits the increase of MPB after exercise, ingestion of BCAAs after exercise reduces atrogen1 expression mainly attribute to leucine and it's metabolite HMB [2,5].

After ingesting EAA, muscle protein synthesis increases by about 60%, and with the increase of the utilization rate of amino acids, mainly EAA, the protein synthesis rate of human skeletal muscle will also increase rapidly with the strong effect; a significant increase in MPS in both young and old people with hyperaminoacidemia has been tested, strongly demonstrated the effectiveness of amino acids in enhancing MPS [1,12]. More than these, EAA and resistance training interact, and the benefits of many other nutrients are based on this, the role of amino acids in NBAL is even much greater than that of testosterone, the anabolic effect of this crucial sex hormone [4]. However, studies have also shown that the effect of amino acids on muscle anabolic metabolism can be clearly reflected even under a single intravenous injection of EAA phenylalanine, valine, and leucine, and MPS is strongly stimulated [5].

These are the reasons why protein that contains a higher portion of EAA and sufficient leucine especially will stimulate MPS better, the importance of these amino acids mostly constructs the importance of protein intake.

5. Hormones and Muscle Protein Metabolism

5.1 Insuline

Insulin is a hormone produced by the pancreas activated by carbohydrates, therefore they are inseparable in any topic related to MPS and MPB. Similar to the relationship between EAA and protein, the importance of insulin also partially constructs the importance of carbohydrate intake. When carbohydrates are digested, they will be broken down into simple sugars such as glucose and fructose, soon be absorbed by the blood and carry on to provide energy for the body; this process will increase the blood glucose level which will trigger the pancreas to release insulin to regulates the absorption of these glucose into the cells [13].

The main role of insulin is to regulate blood sugar/glucose levels, glycolysis, and gluconeogenesis, but under the topic of its regulation of MPS and MPB, there is much more about insulin [13]. Just like EAA-induced hyperaminoacidemia, insulin has a similar effect on MPB, hyperinsulinemia inhibits MPB increase after resistance exercise because insulin promotes the anti-catabolic action of mus-

cles [2,13]; enhancing NBAL by lowering MPB is one of the great contributions of insulin [2]. More than that, insulin is proven to increase the MPS at rest, especially when ingested from carbohydrates, its response also increases muscle accumulation of creatine, a compound that has been shown to improve athletic performance significantly, allow muscles to store water, and promote the enlargement of muscle fibers [4]. In the elderly, muscle anabolic resistance manifests as resistance to insulin-induced MPS stimulation, highlighting insulin's huge role in muscle growth and maintenance [3].

5.2 Testosterone

Testosterone is a sex hormone that can be naturally produced by the human body, in the testes for men and in smaller amounts in the ovaries and adrenal glands for women. Testosterone deserves to be another mainstay of muscle metabolism, it induces muscle fiber hypertrophy by increasing myoblast differentiation, increasing the number of satellite cells, proportionally increasing the number of muscle nuclei, and altering the ultrastructure of satellite cells [4]. Testosterone regulates changes in body composition by influencing the differentiation of mesenchymal-derived pluripotent stem cells [4]; testosterone also increases NBAL and muscle remodeling significantly and even eliminates amino acid losses in muscle protein metabolism [4]. With all these benefits, keeping the body producing testosterone becomes important, therefore, dietary fat intake is mentioned again since it provides the cholesterol the body needs to produce testosterone.

Compared to other nutrients, the effect of testosterone on muscle anabolism is amazing, the benefits are enormous, and this is why a large number of bodybuilders use steroids (synthetic testosterone), but this way of improving muscle mass through external drugs is definitely not advocated; the imbalance of hormones in the body, the increasing pressure on the heart, cardiovascular diseases are the huge cons that people can't ignore, heart attacks are often the cause of death for many athletes who do not control the dosage of external synthetic drugs.

6. Method and Timing of Nutrient Intake

The IOM recommendation for healthy macronutrient intake is 45%-65% total energy of carbohydrates, 10%-35% total energy of proteins, and 20%-35% total energy of fats.

0.8 grams of protein per kilogram of body weight is recommended, but the population that has regular resistance training in order to achieve muscle hypertrophy will benefit from higher protein intake, 1.5g-2.2g of protein per kilogram of body weight will be sufficient to support greater

muscle repair and growth, this can alter along the actual dietary mode [7,8,11]. High-quality protein must be emphasized here, it's proteins that contain greater amounts of EAA, especially leucine, and are highly digestible and without the presence of toxic materials such as protein digestion inhibitors or allergenic stimuli; such high-quality protein has the greatest effect on higher NBAL, most beneficial for muscle growth.

The influence of the source and timing of intake of nutrients on NBAL is also quite obvious, the significant role of co-intake of protein and carbohydrate during resistance training (especially longer than 70 min) has been mentioned above, and the intake of milk protein after resistance exercise leads to greater absorption of amino acids by the muscle circle compared to the intake of soy protein [4]; having more meals a day but less food at each is recognized as an effective way to maximize nutrient absorption, although protein supplementation takes precedence over any other nutrient after resistance training, the intake of carbohydrates after high-intensity resistance exercise day that rapidly stimulate the muscle glycogen replenishment should also pay attention to. 20 to 40 grams of high-quality protein every three to four hours can maximize MPS, all nutrient intake should be evenly distributed to allow the body to fully absorb and utilize, therefore maximizing the NBAL [8]; more techniques such as consuming about 30-40 grams of casein protein before bed have been shown to increase metabolism and MPS during sleep substantially [8].

High Glycaemic index (GI) carbohydrates are recommended as the effects of carbohydrates glycaemic index is mentioned above, the expectation is >70 [8]; carbon cycling is a great way to increase the effectiveness of strength/resistance training, consuming more carbon on high-activity days to provide the body with sufficient capacity and maximize muscle anabolic stimulation, while consuming 75% of the original carbon on low-activity days to ensure there won't be excess carbon that can turn into fat [14]. It is recommended to consume 1.2-1.5 grams of carbohydrates per kilogram of body weight per hour during longer resistance exercises, and 6-8 grams of carbohydrates per day for those who are bulking since heat surplus is the key to all nutrient intake [14]. The intake timing for carbohydrates should be pre-workout, during workout, post-workout, and throughout the day, combined with protein and other nutrients such as fish oil, trace elements, and vitamins to theoretically maximize the NBAL.

Fat is inevitably ingested in the daily intake of carbohydrates and protein, and the redundancy of carbohydrates and protein will also be converted into body fat. Therefore, the intake of dietary fat does not need to be deliberately increased when bulking, but the choice of fat intake

must be paid attention to. For example, the above-mentioned emphasis on the importance of intake of Omega-3 fatty acids and the great need for strict control of saturated fats and trans fatty acids, such as controlling the excessive intake of Animal fats, replacing them with PUFA such as vegetable oils; controlling the intake of FRY and puffed food such as chips and fried chicken, high in DHA and EPA such as fish and seafood that are high in omega-3 fatty acids, the Mediterranean diet is a good example of dietary fat intake, and still, cooperation with other nutrients maintain the principle of all nutrients intake.

The creatine mentioned above has been proven to be an A-Class supplement for body fitness, and its huge effect does not need to be overstated. For athletes and other people who pursue strength performance and muscle form, it is recommended to keep taking creatine monohydrate according to the instructions in order to maintain long-term stable muscle anabolic metabolism and water storage. However, the need for additional supplements other than protein powders such as fish oil capsules, vitamin tablets, and more branched-chain amino acid supplements remains to be justified.

However, each person's physical condition, training intensity, and goals are different, corresponding to some diet training and other plans are different, although still follow all the principles, it is still recommended to have a professional nutrition coach to help make a more detailed training and diet plan.

7. Conclusion

In summary, optimizing MPS and reducing MPB are essential for muscle growth, maintenance, and overall health. The interactions between resistance exercise and nutrient intake, particularly macronutrients, amino acids, and hormones, significantly affect these processes. Consuming protein rich in essential amino acids such as leucine is crucial for boosting MPS. Carbohydrates, particularly those with a high glycemic index, not only store the body's basic energy for activity and vitality, but also stimulate the release of insulin, help muscle repair and replenish glycogen, and inhibit MPB. Fats, especially omega-3 fatty acids, fight inflammation, enhance MPS, support muscle growth and function, and other nutrient branches such as cholesterol, vitamins, minerals, fiber, etc. are critical for maximizing NBAL, maintaining muscle growth and repair, maintaining good health and condition, and assisting in the absorption and utilization of various macronutrients. The synergistic effect of these nutrients, combined with resistance exercise, maximizes NBAL, leading to muscle hypertrophy and excellent athletic performance, and understanding the best times and methods

for nutrient intake will further enhance these results. This comprehensive review emphasizes the importance of a balanced nutrition plan that is tailored to individual needs, providing practical guidelines for athletes, seniors, and hobbyists seeking to maximize muscle, strength, and overall health, as well as educating the population about improving physical health and optimal nutritional intake. However, this review didn't dive deep into the long-term effects and changes of intake and supplement of various nutrient combinations, and there is still room for research on nutrient intake and recovery plans specific to each individual's physique and body, as well as different metabolic and absorptive capacities. Future studies can continue to refine personalized diet plans and long-term significance on this basis, to facilitate the in-depth study of this topic.

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