Is leucine content in dietary protein the key to muscle preservation in older women?

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Loss of muscle mass and strength with aging is a serious problem that threatens physical function and independence in seniors. An adequate dietary protein intake is fundamental for muscle health because it provides the essential amino acids needed to replace those lost from catabolism and stimulates muscle protein synthesis and growth. Low protein intake is associated with accelerated muscle loss in older adults. Yet, a significant proportion of older adults, particularly women, do not meet the Recommended Daily Allowance for protein (1). Previous studies also suggest that the muscle protein anabolic sensitivity to dietary amino acids may be reduced with aging but can be restored by increasing the proportion of dietary leucine (2). Leucine is the essential amino acid that can directly activate the mechanistic target of rapamycin complex 1 (mTORC1) signaling pathway in skeletal muscle, thereby stimulating translation initiation and protein synthesis. On the basis of several acute studies, the dose of leucine necessary to achieve the maximal stimulation of muscle protein synthesis in older persons has been estimated to be ∼3–4 g/meal, which would correspond to ∼25–30 g protein/meal (1). NHANES data show that older adults achieve such an amount of protein intake only in one of the daily meals, dinner, when they tend to consume most of their daily protein intake (3). The other 2 meals contain suboptimal doses of protein (∼15 g) and leucine (<2 g), which, over time, may negatively affect skeletal muscle mass.

Previous studies have tested the efficacy of supplementing relatively low-protein meals with leucine to maximize muscle protein synthesis in older individuals (4, 5). In general, they found that the addition of 4–5 g leucine to regular meals could enhance muscle protein synthesis. However, supplementation with leucine may be cumbersome, expensive, and reduce appetite over the long term. These may become insurmountable problems in older women who tend to eat less protein than men, have lower disposable income, and a higher risk of polypharmacy.

In this issue of the Journal, Devries et al. (6) open the door to the intriguing possibility of improving the muscle anabolic response of healthy older women with a suboptimal dose of 15 g dietary protein by enhancing the leucine content of the protein meal with the use of a blend of high-quality proteins. In an extension of their previous study performed in men (5), they compared head-to-head in older women the efficacy of the leucine-enriched protein blend containing 4.2 g leucine with a control protein blend containing the same amount of total protein (15 g) but only 1.3 g leucine. The protein blends were administered 2 times/d for 6 d as part of a weight-maintenance diet that included a total daily protein intake of 1 g · kg⁻¹ · d⁻¹. In other words, the additional leucine was integrated into the habitual diet rather than supplemented. Twice during the 6 intervention days the participants performed resistance exercise on one leg. Primary outcomes were acute hourly and integrated daily changes in muscle myofibrillar protein synthesis in response to the protein blends in the nonexercised and the exercised leg muscle. The inclusion in the design of unilateral resistance exercise allowed the authors to determine the interaction between the differing amounts of leucine in the protein blends and the anabolic effect of exercise. However, it should be noted that exercise would also increase blood flow and leucine delivery to the nonexercised leg. Nonetheless, this was an important addition because aging reduces the muscle anabolic response to both resistance exercise and nutrition, and previous reports found that a combination of these 2 stimuli in older individuals can induce larger-than-expected increases in muscle protein synthesis (7). Devries et al. (6) found that a suboptimal protein dose with low leucine content produced a modest acute increase in myofibrillar protein synthesis at rest and a larger increase after resistance exercise, as expected. On the other hand, the leucine-enriched protein blend induced a much larger improvement in protein synthesis than the control blend, both in the nonexercised and the exercised leg. The acute hourly changes in muscle protein synthesis were sustained over time, with the leucine-enriched protein blend showing a superior efficacy in stimulating the integrated daily protein synthesis rate compared with the lower leucine content blend. Interestingly, the acute protein synthetic response was positively correlated with the amplitude of the plasma leucine peak after protein intake. It is probable that increased blood leucine availability resulted

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in a significant uptake of leucine into skeletal muscle, thereby amplifying the activation of mTORC1 signaling and resulting in higher muscle protein synthesis rates. However, muscle anabolic signaling was not reported in this article. It is noteworthy to highlight that resistance exercise with either nutritional intervention produced significant improvements in myofibrillar protein synthesis, which were magnified by the use of the leucine-enriched protein blend.

Overall, these results are encouraging and support the notion that in older women it is possible to stimulate muscle protein synthesis by integrating protein foods with high leucine content into the diet rather than supplementing leucine or essential amino acids. The big question is whether we can prevent muscle loss and sarcopenia by increasing the leucine content of the protein comprised in each individual meal within the constraints of a balanced diet. Because this was a short-term study, we cannot predict from the data of Devries et al. (6) whether a long-term diet including a leucine-enriched protein blend can prevent or reverse sarcopenia in older women. Studies of chronic leucine or essential amino acid supplementation for several months have so far yielded rather disappointing results with regard to their effects on muscle mass and strength (8, 9). The reasons may include compliance problems over long-term supplementation, an appetite-suppressant effect of higher leucine and amino acid intakes resulting in an overall decrease in food intake, adaptation to the supplement that reduces its efficacy over time, the need for longer intervention periods (years rather than months), the inclusion of individuals with baseline high protein intakes, or the need for better methods to measure muscle mass and function. However, if we consider that Devries et al. (6) used a food substitution, rather than a supplementation paradigm, to enhance the leucine content of a protein meal, the current results warrant following up with a prolonged randomized controlled trial aimed at determining the efficacy of the leucine-enhanced meal on body composition and physical function outcomes.

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