



Effects of Aging on Skeletal Muscle Hypertrophy

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Dietary protein intake

- Older adults have greater protein needs to compensate for anabolic resistance and hypermetabolic disease.
- Older adults may also have decreased intake due to age-related appetite loss, medical conditions, financial limits.
- Optimal intake of at least 1.0 to 1.5 g protein/kg BW/day is recommended; individual needs depend upon the severity of malnutrition risk.

Exercise

- Regular exercise helps maintain skeletal muscle strength and function in older adults.
- Resistance training has limited but positive effects on recovery of muscle in older people.
- A combination of resistance training and adequate dietary protein/amino acid intake for healthy muscle aging is recommended.

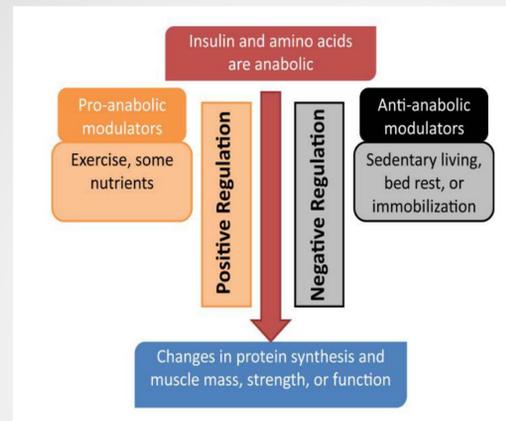
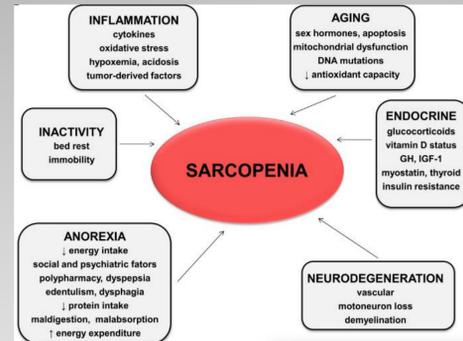
Abstract:

Context: Skeletal muscle is essential for proper bodily functions by playing key roles in strength and movement, and it accounts for roughly 50% of our total body mass.

Decreases in total muscle mass or mass-specific function would be expected to have a magnified negative impact. Sarcopenia, an age-dependent loss of motor nerves, leading by necessity to a coincident loss of muscle mass, would have exactly this kind of effect.

Results: This age-dependent disorder may be the result of aberrant mTOR signaling, irregular miRNAs content, malnutrition and lack of activity, and age-related inflammation. It may be possible to reduce the effects of sarcopenia via strength training, as well as increasing daily intakes of protein, essential amino acids, and fish oils. Combining the consumption of whey protein, which is high in leucine, and poly-unsaturated fatty acids with strength training resulted in increases in muscle mass and strength.

Objective: This review examines the existing causes and effects of age-related sarcopenia, as well as methods that might ameliorate problems associated with age-related sarcopenia.



Muscle Loss

The proximal cause of sarcopenia is the loss of motor neurons and their subsequent motor units due to lack of stimulus. In addition, detrimental changes in neuromuscular junction structure with aging may destabilize skeletal muscle. Loss of muscle mass may result from preferential decreased cross-sectional area of Type II muscle fibers.

Anabolic resistance: The inability of aged muscle to respond to anabolic stimuli. It can be attributed to age-associated changes in muscle and is believed to decrease the capacity for muscle growth. Older muscle may not respond sufficiently to exercise and nutrients. Chronic age-related inflammation may intensify anabolic resistance because inflammatory cytokines, like $TNF\alpha$, may inhibit muscle protein synthesis by interfering with mRNA translation. In one study, postprandial hyperaminoacidemia is decreased in older adults in comparison with younger adults, and greater doses of protein and leucine were required in order to compensate.

Autophagy: Incomplete autophagy may also play a role in the development of sarcopenia. This cascade has emerged as an important regulator of muscle growth and metabolism in response to growth factors, insulin, resistance exercise, and nutritional intake. Autophagic processes depend on the turnover rates of proteins to be activated. Inhibition of autophagy may exacerbate age-related deterioration of neuromuscular junctions and interrupt the homeostatic balance between anabolism and catabolism

mTOR: Overactive mTOR pathways, especially mTORC1, may increase the possibility of sarcopenia. Elevated mTORC1 during rest can attenuate anabolic responses, as unwarranted activation of this pathway may be linked to detrimental problems associated with aging. mTORC1 is activated by environmental nutrients and functions to promote mRNA translation and muscle protein synthesis with conditions favorable for growth. A potential result of excessive mTORC1 signaling is increased inflammation via nuclear factor kappa-light-chain-enhancer of activated B cells, or $NF\kappa B$, which is a downstream target of mTORC1

miRNAs: A potential cause of aging on muscle health may be miRNAs because they may enhance or repress mTOR signaling. MiR-496 inhibits translation of mTOR mRNA, and so reduces the activity of mTORC1. An additional RNA molecule that may lead to decreased muscle mass with aging is the long chain RNA Chronos. Chronos may have augmented activity with age, and might be involved in muscle mass loss with aging as it negatively regulates Bmp7 expression

**MiRNAs can also positively affect the mTOR signaling pathway and increase protein production. MiR-130a short interfering Chronos RNA (siChronos), and its actions significantly enhanced skeletal muscle hypertrophy. miR-27a/b can increase muscle size by inhibiting myostatin. Over expression of miR-27a reduced mRNA expression and increased muscle fiber cross-sectional area in mouse skeletal muscle.

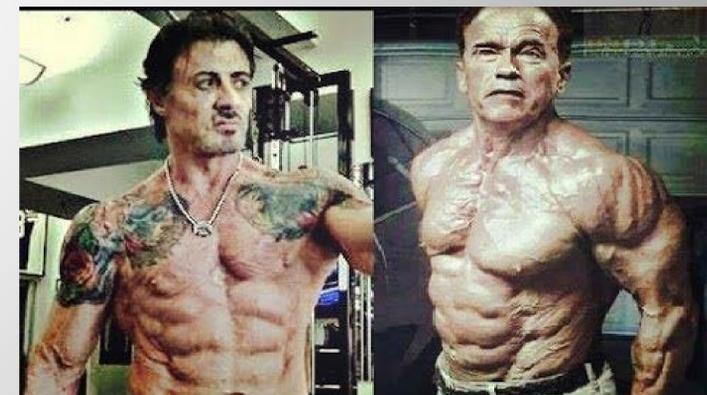
Interventions for Aged Muscle

Exercise: Exercise of various types and a well-balanced nutrition can improve day-to-day life and health and promote longevity. Exercise had a positive impact on gait speed, balance, and the chair rising test, all of which may be increasingly difficult to accomplish in elderly adults. Resistance exercise training improves muscle strength and stimulates muscle hypertrophy. Additionally, benefits of resistance training in older adults may result from blocking muscle degradation rather than up regulating muscle growth.

Protein Intake: Adequate nutritional intake and additional supplementation may further benefit increases in muscle mass in aged adults via increased muscle protein synthesis. Healthy older individuals should consume 1.2-2.5 g of protein per kg of body weight to preserve muscle mass and combat anabolic resistance.

Whey protein and EAAs: A popular and effective source because it promotes increase in skeletal muscle mass, strength, and functional capacity when in combination with resistance training. Whey is a complete, high quality protein based on its amino acids content and rapid digestibility. Compared to casein and soy, whey protein may stimulate muscle protein synthesis to a higher level during rest and exercise. A blend of proteins may combine to increase hyperaminoacidemia and also prolong hyperaminoacidemia better than any one protein supplement. This prolonged hyperaminoacidemia is important to support increased rates of muscle protein synthesis. In addition, increasing total essential amino acids intake, most importantly leucine, increases muscle protein synthesis by extending hyperaminoacidemia.

PUFAs: Poly Unsaturated Fatty Acids (PUFAs) have been linked with positive effects on metabolic function and other health benefits. They may increase the anabolic response to resistance training and whey protein supplementation. In combination with other supplements, PUFAs may decrease anabolic resistance associated with aging by boosting the anabolic response of muscle protein synthesis to hyperinsulinemia-hyperaminoacidemia. Their supplementation may be involved in down regulation of anabolic pathway inhibitors, and also up regulation of pathways that promote growth. While they are insufficient to elicit an anabolic response alone, their effects on muscle protein synthesis are enhanced when associated with the anabolic stimulus of amino acids administration



Conclusion

Sarcopenia is a serious problem the aged population may face if they are increasingly sedentary and malnourished. Recent data have demonstrated that regular strength training combined with increased protein intake can reduce effects of sarcopenia and promote health benefits in older adults. Anabolic resistance may decrease benefits of exercise for older adults and make sarcopenia a greater problem, but increasing protein intake and supplementing with poly-unsaturated fatty acids may enhance the anabolic response that normally results from exercise. An optimal protein source is whey protein because of its amino acids content, especially leucine, and its rapid digestibility. Because of this, it is quickly bioavailable and results in a rapid hyperaminoacidemic state. Sources rich in leucine are vital, as these sources increase hyperaminoacidemia to a greater level compared to low or no leucine. In addition, poly-unsaturated fatty acids may increase the anabolic response to strength training and protein intake, but do not have the same effect when taken alone. Although sarcopenia is a rising disorder in aging adults, its effects can be alleviated by increased strength training, and by increasing the intake of protein and other vital nutrients.

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 • Change in MPS flowchart: Bauer, J., G. Biolo, T. Cederholm, M. Cesari, A. J. Cruz-Jentoft, J. E. Morley, S. Phillips, C. Sieber, P. Stehle, D. Teta, R. Visvanathan, E. Volpi & Y. Boirie (2012) Evidence-based recommendations for optimal dietary protein intake in older people: a position paper from the PROT-AGE study group. *Journal of American Medical Directors Association*, 14, 542-559
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