Skeletal muscle memory: Recall for healthy aging

Learn about the critical role of skeletal muscle in overall health, and the importance of maintaining muscle mass as we age to support longevity and combat age-related conditions

Skeletal muscle tissue is critical for locomotion, breathing, and as a storage site for carbohydrates and fats. The largest deposits of amino acids in the body are stored in skeletal muscle, serving to mitigate disease risks and improve outcomes should an infection, hospitalization, or surgical procedure occur. [1-7] Retention of muscle size as we get older is essential for whole-body health and is one of the most important factors to living years spent in good health, known as 'healthspan'. [8]

An unavoidable outcome of aging is the natural loss of skeletal muscle size and inability to perform daily activities due to a process called sarcopenia – a term derived from the Greek language meaning 'flesh' (sarx) and 'loss' (penia). [9] In sedentary (inactive) individuals, the onset of sarcopenia can start before middle age and leads to performance and metabolic dysfunction. Maintenance of muscle health is closely linked to survival during the aging process and is therefore paramount to maintaining mobility and self-reliance with aging.

Accruing muscle mass – hypertrophy – has gained popularity with the rise of bodybuilding and 'competitive fitness' and is an increasingly desired outcome of gym patronage. Fortunately for those who choose to lift weights, muscular function is among the greatest predictors of healthspan and lifespan. [10,11] The health benefits of weightlifting that improve long-term quality of life include high muscular function, preserving the muscle-to-brain connection (i.e., innervation), and maintaining fast contracting and powerful muscle fibers. [12] Collectively, these benefits can serve to enable reactive movements such as quickly recovering balance to prevent a fall. Falls in older age are one of the leading causes of loss of mobility and mortality. [13] Falls result in a rapid healthspan decline and loss of independence due to further loss of muscle mass and function. These risks can be altogether mitigated through early adoption of a muscle-centric approach to fitness. A rebound in muscle health becomes harder to accomplish with age; however, increasing the size and performance of our muscles at any age may offer a type of 'memory' for our muscle cells to recall when we inevitably experience injury, illness/disease, or a shift in life priorities.

Skeletal muscle has a 'memory' to recall prior exercise adaptations

The internal environment of skeletal muscle is influenced by volume and the type of external stimulation. In fact, all living organisms are governed by the SAID principle (Specific Adaptations of Imposed Demands). The SAID principle gives rise to the varied adaptations associated with different modes of exercise (i.e., resistance, endurance, concurrent). Resistance training (e.g. barbells, dumbbells, cable assisted machines, etc.) uses progressively heavier weights and/or increasing volume to increase muscle size and function, while endurance training (e.g. running, cycling, swimming, etc.) uses long duration low-resistance repeated movements to drive metabolic changes in muscle that increase energy production capacity via the addition of mitochondria (the powerhouse of the cell). Concurrent exercise is the combination of both resistance and endurance training that benefits muscle growth and energy production.

Regardless of training type, exercise alters the cellular and molecular characteristics of skeletal muscle. Changes to these characteristics after exercise training serve as a biological 'save point' for skeletal muscle health. In short, some changes to the skeletal muscle environment after exercise training are 'stored' within specialized cellular (i.e., muscle fiber nuclei, or myonuclei) and molecular (i.e., epigenetic) components. The imprint exercise training leaves on these components in muscle serves as a blueprint for future skeletal muscle adaptation. The current evidence for this 'muscle memory' is most compelling for resistance training. [(14-16)] It is currently unclear how long 'muscle memory' might last; however, it may serve to kickstart the biological machinery for improved muscle health upon resuming exercise training. In other words, past exercise training rewires the cellular and molecular components of muscle to create a tissue that is more adaptive to future training after periods of inactivity (i.e., injury, illness, hospitalization, etc.)

Exercise demands specific changes that become imprinted in our cells as an efficient progress-saving feature

If we consider our DNA as the overall blueprint for all things created in the body, the blueprint then guides the instruction manual for each specific job at each stage of the building process. To drive efficient work patterns, the blueprint can be highlighted, bolded, and otherwise bookmarked for easier navigation. Each time we exercise, we signal for very specific instructions to be called upon to build healthier muscle tissue. To make the process more efficient, our DNA is chemically tagged through a process called 'methylation'. DNA methylation serves to signal an exercise-related gene to turn on or off with training. Recent evidence from our lab and others suggests that two to three months of disuse does not erase DNA methylation changes in muscle caused by previous exercise training prior to disuse. [(14,17,18)] If epigenetic 'muscle memory' lasts longer than a few months, it could have important implications for muscle adaptive potential in old age, when muscle becomes harder to build and maintain.

Concluding remarks

Aging is an inevitable lifelong process, but we can improve our healthspan by limiting the loss of bodily function through consistent exercise. Perfect consistency is not realistic, and as such, we should rest assured that our efforts are not lost during these brief lapses that happen to us all. Thankfully, it seems muscles have a built-in 'auto- save' feature for these setbacks that can reduce negative consequences and help return to a healthier state more efficiently. Starting the building process earlier allows more time and capitalizes on younger muscle's high level of plasticity (i.e., muscle's ability to respond and adapt to stimuli). Even when adopting an active lifestyle later in life, there is still sufficient muscle plasticity to limit setbacks and promote muscle health. Still, an active lifestyle that incorporates resistance training is one of the best ways to take advantage of ‘muscle memory’ and may promote youthful characteristics even in old age.

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References

1. de Hoogt PA, Reisinger KW, Tegels JJW, Bosmans JWAM, Tijssen F, and Stoot JHMB. Functional compromise cohort study (FCCS): sarcopenia is a strong predictor of mortality in the intensive care unit. World J Surg. 2017. Epub 2017/12/30. doi: 10.1007/s00268-017-4386-8. PubMed PMID: 29285609.
2. Cosquéric G, Sebag A, Ducolombier C, Thomas C, Piette F, and Weill-Engerer S. Sarcopenia is predictive of nosocomial infection in care of the elderly. Br J Nutr. 2006;96(5):895-901. Epub 2006/11/10. PubMed PMID: 17092379.
3. Wolfe RR. The underappreciated role of muscle in health and disease. Am J Clin Nutr. 2006;84(3):475-82. Epub 2006/09/09. PubMed PMID: 16960159.
4. Carey EJ. Sarcopenia in solid organ transplantation. Nutr Clin Pract. 2014;29(2):159-70. Epub 2014/02/18. doi: 10.1177/0884533613520619. PubMed PMID: 24531627.
5. Kirk PS, Friedman JF, Cron DC, Terjimanian MN, Wang SC, Campbell DA, Englesbe MJ, and Werner NL. One-year postoperative resource utilization in sarcopenic patients. J Surg Res. 2015;199(1):51-5. Epub 2015/05/21. doi: 10.1016/j.jss.2015.04.074. PubMed PMID: 25990695; PMCID: PMC4604009.
6. Krell RW, Kaul DR, Martin AR, Englesbe MJ, Sonnenday CJ, Cai S, and Malani PN. Association between sarcopenia and the risk of serious infection among adults undergoing liver transplantation. Liver Transpl. 2013;19(12):1396-402. Epub 2013/10/24. doi: 10.1002/ lt.23752. PubMed PMID: 24151041; PMCID: PMC3870151.
7. Sheetz KH, Waits SA, Terjimanian MN, Sullivan J, Campbell DA, Wang SC, and Englesbe MJ. Cost of major surgery in the sarcopenic patient. J Am Coll Surg. 2013;217(5):813-8. Epub 2013/10/15. doi: 10.1016/j. jamcollsurg.2013.04.042. PubMed PMID: 24119996; PMCID: PMC3809011.
8. Seals DR, Justice JN, and LaRocca TJ. Physiological geroscience: targeting function to increase healthspan and achieve optimal longevity. J Physiol. 2016;594(8):2001-24. Epub 20150311. doi: 10.1113/ jphysiol.2014.282665. PubMed PMID: 25639909; PMCID: PMC4933122.
9. Rosenberg IH. Sarcopenia: origins and clinical relevance. J Nutr. 1997;127(5 Suppl):990s-1s. doi: 10.1093/jn/127.5.990S. PubMed PMID: 9164280.
10. Araújo CGS, Kunutsor SK, Eijsvogels TMH, Myers J, Laukkanen JA, Hamar D, Niebauer J, Bhattacharjee A, de Souza ESCG, Franca JF, and Castro CLB. Muscle Power Versus Strength as a Predictor of Mortality in Middle- Aged and Older Men and Women. Mayo Clin Proc. 2025;100(8):1319-31. Epub 20250430. doi: 10.1016/j. mayocp.2025.02.015. PubMed PMID: 40304660.

11. Srikanthan P and Karlamangla AS. Muscle mass index as a predictor of longevity in older adults. The American journal of medicine. 2014;127(6):547-53. Epub 20140218. doi: 10.1016/j.amjmed.2014.02.007. PubMed PMID: 24561114; PMCID: PMC4035379.
12. Lavin KM, Roberts BM, Fry CS, Moro T, Rasmussen BB, and Bamman MM. The importance of resistance exercise training to combat neuromuscular aging. Physiology. 2019;34(2):112-22. Epub 2019/02/07. doi: 10.1152/physiol.00044.2018. PubMed PMID: 30724133.
13. de Souto Barreto P, Rolland Y, Vellas B, and Maltais M. Association of Long-term Exercise Training With Risk of Falls, Fractures, Hospitalizations, and Mortality in Older Adults: A Systematic Review and Meta-analysis. JAMA internal medicine. 2019;179(3):394-405. doi: 10.1001/jamainternmed.2018.5406. PubMed PMID: 30592475; PMCID: PMC6439708.
14. Seaborne RA, Strauss J, Cocks M, Shepherd S, O'Brien TD, van Someren KA, Bell PG, Murgatroyd C, Morton JP, Stewart CE, and Sharples AP. Human skeletal muscle possesses an epigenetic memory of hypertrophy. Sci Rep. 2018;8(1):1898. Epub 20180130. doi: 10.1038/ s41598-018-20287-3. PubMed PMID: 29382913; PMCID: PMC5789890.
15. Serrano N, Dupont-Versteegden EE, and Murach KA. Muscle memory theory: A critical evaluation. J Physiol. 2025;603(17):4705-11. Epub 20250806. doi: 10.1113/ jp289597. PubMed PMID: 40768525.
16. Sharples AP and Turner DC. Skeletal muscle memory. Am J Physiol Cell Physiol. 2023;324(6):C1274-c94. Epub 20230508. doi: 10.1152/ajpcell.00099.2023. PubMed PMID: 37154489.
17. Wen Y, Dungan CM, Mobley CB, Valentino T, von Walden F, and Murach KA. Nucleus type-specific DNA methylomics reveals epigenetic "memory" of prior adaptation in skeletal muscle. Function. 2021;2(5):zqab038. Epub 20210805. doi: 10.1093/ function/zqab038. PubMed PMID: 34870208; PMCID: PMC8636928.
18. Seaborne RA, Strauss J, Cocks M, Shepherd S, O'Brien TD, Someren KAv, Bell PG, Murgatroyd C, Morton JP, Stewart CE, Mein CA, and Sharples AP. Methylome of human skeletal muscle after acute & chronic resistance exercise training, detraining & retraining. Scientific Data. 2018;5(1):180213. doi: 10.1038/sdata.2018.213

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