CPE article

Effects of Creatine and Resistance Training on Cognition in Older Adults

by Ranier Castillo

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Learning Objectives

After you have read this article, you will be able to:

- Discuss possible mechanisms linking muscular strength to cognition function.
- Describe emerging data regarding the potential beneficial effects of resistance training and blood-flow restriction on cognition function.
- Discuss varying research findings regarding the effects of creatine intake on cognition.

In the 21st century approximately 131,500,000 people—primarily older adults—are expected to exhibit some degree of cognitive loss, which can range from mild cognitive impairment (MCI) to dementia.[1] Interventions among individuals with MCI, a precursor for dementia, show greater success in improving patient outcomes compared with initiating interventions at later stages of cognitive loss.[2]

Currently, there are no pharmaceutical treatments for cognitive impairment;[3,4] however, holistic approaches, with the goal of preventing or delaying the susceptibility of dementia, are emerging as methods to support healthy aging. Early intervention is particularly important among those who carry a genetic risk factor, the e4 allele of the apolipoprotein E gene, or APOE4.[5]

While a high emphasis is placed in adopting a healthy diet and lifestyle, there is a need for more specific recommendations regarding resistance training (RT) and supplements that may benefit aging adults. Recent attention has focused on creatine supplementation, in addition to optimizing intake of essential nutrients through a balanced diet. A few studies provide preliminary support and potential mechanisms describing how RT and creatine may affect cognition. This review will summarize the findings of those studies and explain how these two interventions may benefit the aging brain.

Resistance Training

Exercise interventions, primarily aerobic exercise, demonstrate an effect of delaying or reversing neurodegenerative decline.[6] Some investigations also suggest a relationship between strength and cognition.[6] For example, handgrip strength, an indicator for muscular strength, has shown to be positively correlated with cognitive performance.[7,8]

Resistance Training and Cognition: Proposed Mechanisms

Possible mechanisms describing the relationships between muscular strength and cognition highlight neural and vascular connections between the brain and muscle that exhibit a significant decline of muscle mass and strength as individuals age.[9] Adults who do not actively work their muscles begin experiencing muscle decline starting as early as their thirties.[9] However, strength training exercises promote the maintenance of sympathetic nervous system (SNS) and the hypothalamus-pituitary-adrenal (HPA) axis activity.[6] This occurs, in part, through the activation of the SNS and subsequent release of adrenaline, noradrenaline, and cortisol.[6]

Adrenaline and noradrenaline are catecholamines, secreted by the adrenal medulla, that indirectly influence the brain's memory by binding to receptors within the brain.[10] When exposed to stress, cortisol is secreted and can then pass through the blood brain barrier (BBB) and directly influence cognition.[11] Results from prior investigations demonstrate how stress-related hormones exert positive effects on memory.[10] However, chronic secretion of these hormones may exert negative health outcomes, such as hypertension.[11]

Insulin-like growth factor 1 (IGF-1), a hormone secreted from the liver, is also secreted with RT and may improve cognition [12] This hormone crosses the BBB, interacting with the brain and promoting numerous functions such as neural proliferation.[12-14] Short-term and long-term resistance training regimens are associated with increased serum levels of IGF-1, while decreased levels of IGF-1 are correlated with decreased levels of cognition.[12, 15] Trejo et al[14] found that increased circulating IGF-1 increases development of hippocampal neurons, an area of the brain known for memory and spatial function.[10, 14] However, conflicting research show that increased neurons in the hippocampus show no significance in learning.[16, 17] Therefore, future studies are needed to further evaluate the effect of IGF-1 on cognition.

In addition, brain-derived neurotrophic factor (BDNF) plays a role in the regulation of neuron survival, neuron differentiation, and maintainance of long-term memory, thus combating memory decline.[18,19] However, limited human studies demonstrate increases of BDNF immediately post-exercise.[19,20] While further research is needed, findings from preliminary investigations indicate a possible mediating effect.

Application of Resistance Training

Moderate to vigorous intensity workouts have been shown to produce the most significant endocrine changes consistent with cognitive health.[19,22-24] Emerging data regarding blood-flow restriction (BFR) show increased efficiency during RT.[8] BFR occludes blood flow thereby restricting the muscle's access to oxygenated blood. RT with BFR have been shown to increase levels of IGF-1, BDNF, and cognitive function in older adults.[8,25]. While RT and BFR intervention studies on cognition are still novel, these findings provide initial insight on recommended RT intensity protocols for cognitive treatments.

Current recommendations by the American College of Sports Medicine (ACSM) emphasize the need to individualize training programs based on the individual's self-efficacy and physical fitness.[26] Particularly for older adults, it is important to take into consideration their susceptibility for frailty or conditions that may prevent them from performing high-intensity RT. Starting at a lower intensity may provide initial benefits until they increase their ability to perform higher level intensity exercises.[26]

Creatine

Creatine is a nitrogenous organic acid found in animal tissues.[27] There are two sources of creatine: dietary consumption of animal-based proteins and endogenous production.[27] According to the International Society of Sports Nutrition (ISSN)[28] and a combined group from the Academy of Nutrition and Dietetics, Dietitians of Canada, and ACSM, [29] creatine consumption and supplementation is safe and beneficial with intake at recommended levels. While creatine promotes the formation of adenosine triphosphate (ATP) during high-intensity exercise (i.e., ATP-PCr energy system), it also provides significant effects on cognition.

Creatine and Resistance Training

In older adults who are susceptible to muscle loss and frailty, creatine intake with resistance training is correlated with increases in lean muscle mass.[31] This translates to positive benefits for motor skills and other cognitive functions.[31] The mechanism of muscle gain and integrity is not fully understood yet,[32] but there is evidence suggesting that creatine is a mediator for IGF-1.[31,33] Also, creatine protects cells from oxidative damage by maintaining ribonucleic acid and mitochondrial integrity[27,33]

> "A decline in creatine levels of the brain is significantly related to conversions of MCI to dementia."

Creatine and Cognition

A decline in creatine levels of the brain is significantly related to conversions of MCI to dementia.[35] There are known impairments of motor skills and speech that are caused by creatine deficiencies, such as epilepsy and autistic behaviors.[36] Furthermore, creatine intake has been shown to exert benefits on individuals' mental tasks and memory.[27,37] While a higher level of cognitive improvement was seen among those with lower levels of creatine before interventions (i.e., vegetarians and elderly).[29], a meta-analysis conducted by Rae and Bröer[27] found that creatine consumption was not significant for treating demented populations. A counter to these findings proposed that the creatine dosage was too low to produce positive responses.[27]

Conclusion

There is evidence indicating that creatine and RT contribute to cognitive and muscle improvements. Brasure et al[38] found that a combination of diet, exercise, and cognitive training are the most effective method of preventing cognitive decline. According to ISSN,[28] the recommended safe amount of creatine is about 0.3 g per kilogram of body weight per day. After three consecutive days of intake at that dose, it is recommended to consume about 3 g to 5 g.[28] These findings suggest that creatine may aid in supporting both RT and cognition, while RT aids in cognition as well.

Sports dietitians can therefore play a critical role in older adults' physical and mental fitness by monitoring their creatine intake and referring clients to a certified exercise specialist for RT. This report invites future research to conduct interventions evaluating the potentially synergistic effects of RT and creatine on cognitive function in vulnerable populations, such as older adults. This may aid in the process of identifying dosage efficacy and the possible physiological mechanisms by which RT and creatine influence the brain.

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References

1. Shah H, Albanese E, Duggan C, et al. Research priorities to reduce the global burden of dementia by 2025. *Lancet Neurol*. 2016;15(12):1285-1294.
2. Hugo J, Ganguli M. Dementia and cognitive impairment: epidemiology, diagnosis, and treatment. *Clin Geriatr Med.* 2014;30(3):421–442.
3. Center for Disease Control. Subjective cognitive decline. Available at: https://www.cdc.gov/aging/data/pdf/Aggregated-2016-Cognitive-Infographic-508.pdf. Accessed May 5, 2019.
4. Langa KM, Levine DA. The diagnosis and management of mild cognitive impairment: a clinical review. *JAMA.* 2014;312(23):2551–2561.
5. Dumas JA. Strategies for preventing cognitive decline in healthy older adults. *Can J Psychiatry*. 2017;62(11):754-760.
6. Kennedy G, Hardman RJ, Macpherson H, et al. How does exercise reduce the rate of age-associated cognitive decline? A review of potential mechanisms. *J Alzheimers Dis*. 2016;55(1):1-18.
7. Fritz NE, Mccarthy CJ, Adamo DE. Handgrip strength as a means of monitoring progression of cognitive decline – a scoping review. *Ageing Res Rev*. 2017;35:112-123.
8. Törpel A, Herold F, Hamacher D, et al. Strengthening the brain: is resistance training with blood flow restriction an effective strategy for cognitive improvement? *J Clin Med.* 2014;7(10): 337.
9. Moon Y, Choi Y, Han S-H. Muscle profile and cognition in dementia patients with Alzheimer's disease. *Alzheimers & Dementia*. 2017;13(7).
10. Lupien S, Maheu F, Tu M, et al. The effects of stress and stress hormones on human cognition: implications for the field of brain and cognition. *Brain Cognition*. 2007;65(3):209-237.
11. Mcgaugh JL, Roozendaal B. Role of adrenal stress hormones in forming lasting memories in the brain. *Curr Opinion Neurobiol*. 2002;12(2):205-210.
12. Barha CK, Galea AL, Nagamatsu LS, et al. Personalising exercise recommendations for brain health: considerations and future directions. *Brit J Sports Med*. 2017;51(8):636-639.
13. Laron Z. Insulin-like growth factor 1 (IGF-1): a growth hormone. *Mol Pathol*. 2001;54(5):311–316.
14. Trejo JL, Carro E, Torres-Aleman I. Circulating insulin-like growth factor I mediates exercise-induced increases in the number of new neurons in the adult hippocampus. *J Neurosci.* 2001;21(5):1628-1634.
15. Stein AM, Silva TMV, Coelho FGM, et al. Physical exercise, IGF-1 and cognition: a systematic review of experimental studies in the elderly. *Dement Neuropsychol*. 2018;12(2):114–122.
16. Jaholkowski P, Kiryk A, Jedynak P, et al. New hippocampal neurons are not obligatory for memory formation; cyclin D2 knockout mice with no adult brain neurogenesis show learning. *Learning & Memory*. 2009;16(7):439-451.
17. Jedynak P, Jaholkowski P, Wozniak G, et al. Lack of cyclin D2 impairing adult brain neurogenesis alters hippocampal-dependent behavioral tasks without reducing learning ability. *Behav Brain Res*. 2012;227(1):159-166.
18. Bekinschtein P, Cammarota M, Medina JH. BDNF and memory processing. *Neuropharmacology*. 2014;76.
19. Marston K, Newton M, Brown B, et al. Intense resistance exercise increases peripheral brain-derived neurotrophic factor. *J Sci Med Sport*. 2017;20(10):899-903.
20. Walsh JJ, Scribbans TD, Bentley RF, et al. Neurotrophic growth factor responses to lower body resistance training in older adults. *Appl Physiol Nutr Metab.* 2016;41(3):315-323.
21. Rasmussen P, Brassard P, Adser H, et al. Evidence for a release of brain-derived neurotrophic factor from the brain during exercise. *Exper Physiol*. 2009;94(10):1062-1069.
22. Mavros Y, Gates N, Wilson, GC, et al. Mediation of cognitive function improvements by strength gains after resistance training in older adults with mild cognitive impairment: outcomes of the study of mental and resistance training. *J Am Ger Soc*. 2017;65(3):550-559.
23. Kierkegaard M, Lundberg I, Olsson T, et al. High-intensity resistance training in multiple sclerosis — an exploratory study of effects on immune markers in blood and cerebrospinal fluid, and on mood, fatigue, health-related quality of life, muscle strength, walking and cognition. *J Neurolog Sci*. 2016;362:251-257.
24. Li Z, Peng X, Xiang W, et al. The effect of resistance training on cognitive function in the older adults: a systematic review of randomized clinical trials. *Aging Clin Exper Res*. 2018;30(11):1259-1273.
25. Sardeli AV, Ferreira MLV, Santos LdC, et al. Low-load resistance exercise improves cognitive function in older adults. *Rev Bras Med Esporte*. 2018;24:125–129.
26. American College of Sports Medicine. *ACSM's Resources for the Personal Trainer,* 5th ed; 2018
27. Rae CD, Bröer S. Creatine as a booster for human brain function. How might it work? *Neurochem Int*. 2015;89:249-259.
28. Buford TW, Kreider RB, Stout JR, et al. International Society of Sports Nutrition position stand: creatine supplementation and exercise. *J Int Soc Sports Nutr*. 2007;4:6.
29. Thomas DT, Erdman KA, Burke LM. Position of the Academy of Nutrition and Dietetics, Dietitians of Canada, and the American College of Sports Medicine: nutrition and athletic performance. *J Acad Nutr Diet*. 2016;116(3):501-528.
30. Kreider R. Effects of creatine supplementation on performance and training adaptations. *Molec Cell Biochem*. 2003;244(1):89-94.
31. Chilibeck PD, Kaviani M, Candow DG, et al. Effect of creatine supplementation during resistance training on lean tissue mass and muscular strength in older adults: a meta-analysis. *Open Access J Sports Med*. 2017;8:213–226.
32. Jówko E, Ostaszewski P, Jank M, et al. Creatine and -hydroxy- -methylbutyrate (HMB) additively increase lean body mass and muscle strength during a weight-training program. *Nutrition*. 2001;17(7):558-566.
33. Sestili P, Martinelli C, Colombo E, et al. Creatine as an antioxidant. *Amino Acids*. 2011;40(5):1385-96.
34. Balsom PD, Soderlund K, Sjodin B, et al. Skeletal muscle metabolism during short duration high-intensity exercise: influence of creatine supple-

mentation, *Acta Physiologica. Scand*.1995;154:303-310.
35. Pilatus U, Lais C, Rochmont Adu M, et al. Conversion to dementia in mild cognitive impairment is associated with decline of N-actylaspartate and creatine as revealed by magnetic resonance spectroscopy. *Psych Res: Neuroimaging*. 2009;173(1):1-7.
36. Turner CE, Gant N. Chapter 2.2, The Biochemistry of Creatine. In: *Magnetic Resonance Spectroscopy*; 2014:91-103.
37. Watanabe A, Kato N, Kato T. Effects of creatine on mental fatigue and cerebral hemoglobin oxygenation. *Neurosci Res*. 2002;42(4):279-285.
38. Brasure M, Desai P, Davila H, et al. Physical activity interventions in preventing cognitive decline and Alzheimer-type dementia. *Ann Inter Med*. 2017;168(1):30.

CPE article

Common Indian Spices and Health Benefits

by Courtney Chramowicz, Saira Talwar, MS, and Susan Kundrat, MS, RDN, CSSD

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Learning Objectives
After you have read this article, you will be able to:

- Discuss the potential health benefits and recommended dosages of turmeric, ginger, fenugreek, and cinnamon.
- Discuss the potential safety issues and drug interactions of turmeric, ginger, fenugreek, and cinnamon.

Spices have been used for centuries to prevent and treat illness and enhance overall health and wellness. Four spices commonly used in India are turmeric, ginger, fenugreek, and cinnamon. This review highlights recent studies related to these spices and their proposed health benefits as follow-up to the *Healing Indian Spices: The Path to Wellness* session at the 2019 SCAN Symposium. As consumers seek natural, alternative options for preventing disease, managing illnesses, and staying fit and active, registered dietitians and other health professionals must be knowledgeable about the functional properties of herbs and spices.

Turmeric

Turmeric is often called the most commonly used spice in the world. Curcumin receives attention as the bioactive compound in turmeric, which has antioxidative and anti-inflammatory properties and is a spice native primarily to India.[1] Curcuminoids are typically extracted from fresh dried or powdered forms of the underground stems called rhizomes or leaves of the plant.[1] Curcumin, which is commonly mixed with bioavailability enhancers such as piperine, the principal plant alkaloid in black pepper, has been used for the management of arthritis, depression, gastrointestinal distress, dyslipidemia, muscle soreness, and acute on chronic stress.[2,3] In recent years, research and consumables have focused on including turmeric for these conditions. Curcumin has also been tested in conjunction with other medications and spices to further understand its potential health benefits.[4,5]

> "…the addition of curcumin has been shown to augment the improvements made by these drugs/ spices alone."[4,5]

Curcumin is believed to modify cellular signaling activity of the inflammatory cascade by affecting nuclear factor kappa-beta (NF- B) cells, proinflammatory cytokines (interleukins), cyclooxygenase 2 (COX-2), and 5-lipoxygenase (5-LOX) inhibitors. Daily et al reported that consumption of approximately 1,000 mg curcumin/ day for 8 to 12 weeks reduced inflammation and associated pain, relieving symptoms of osteoarthritis and rheumatoid arthritis.[6] Furthermore, when curcumin is used with certain drugs such as mesalamine (typically used for mild-to-moderate ulcerative colitis) or with other spices such as saffron (which possesses potential antidepressant effects), the addition of curcumin has been shown to augment the improvements made by these drugs/spices alone.[4,5] These health benefits were translated to another study that involved a healthy population who received 80 mg of a lipidated form of curcumin daily for 4 weeks. The noteworthy benefits reported included lowered triglycerides, reduced salivary amylase activity, and reduced beta amyloid