International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Scholarly Publisher
RS Global Sp. z O.O.
ISNI: 0000 0004 8495 2390

Dolna 17, Warsaw,
Poland 00-773
+48 226 0 227 03
editorial_office@rsglobal.pl

ARTICLE TITLE	THE IMPACT OF CREATINE SUPPLEMENTATION ON COGNITIVE FUNCTION IN ELDERLY: A SYSTEMATIC REVIEW
ARTICLE INFO	Martyna Kaplińska, Dawid Siemieniuk, Aleksandra Kowalska, Hanna Wilska, Dominik Domoń, Dominika Domanowska, Adam Niedziela, Antoni Liebert, Natalia Klimek. (2025) The Impact of Creatine Supplementation on Cognitive Function in Elderly: A Systematic Review. *International Journal of Innovative Technologies in Social Science*. 3(47). doi: 10.31435/ijitss.3(47).2025.3516
DOI	https://doi.org/10.31435/ijitss.3(47).2025.3516
RECEIVED	20 June 2025
ACCEPTED	02 August 2025
PUBLISHED	06 August 2025
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

© The author(s) 2025.
This article is published as open access under the Creative Commons Attribution 4.0 International License (CC BY 4.0), allowing the author to retain copyright. The CC BY 4.0 License permits the content to be copied, adapted, displayed, distributed, republished, or reused for any purpose, including adaptation and commercial use, as long as proper attribution is provided.

THE IMPACT OF CREATINE SUPPLEMENTATION ON COGNITIVE FUNCTION IN ELDERLY: A SYSTEMATIC REVIEW

Martyna Kaplińska *(Corresponding Author, Email: Martyna.kaplinska@gmail.com)*
Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
ORCID ID: 0009-0004-1236-0166

Dawid Siemieniuk
National Medical Institute of the Ministry of the Interior and Administration, Wołoska 137, 02-507 Warsaw, Poland
ORCID ID: 0000-0003-1374-9822

Aleksandra Kowalska
Medical University of Lublin, Lublin, Poland
ORCID ID: 0000-0002-8205-8948

Hanna Wilska
Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
ORCID ID: 0000-0002-6483-5440

Dominik Domoń
Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
ORCID ID: 0009-0008-7631-4563

Dominika Domanowska
Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
ORCID ID: 0009-0002-2965-7754

Adam Niedziela
Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
ORCID ID: 0009-0002-6178-6484

Antoni Liebert
Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
ORCID ID: 0009-0004-8778-1803

Natalia Klimek
Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
ORCID ID: 0009-0004-3644-2529

ABSTRACT

Introduction: Age-related cognitive decline is a growing public health concern, affecting daily functioning and quality of life. Recent studies suggest that creatine supplementation may improve cognitive performance by supporting mitochondrial function and reducing oxidative stress. However, findings are mixed. This systematic review examines the effects of creatine supplementation on cognitive functions in older adults.

Methods: A systematic review was conducted following PRISMA guidelines. PubMed/Medline and EMBASE databases (2003–2025) were searched using the phrase "the effect of creatine supplementation on cognitive functions in the elderly." After screening 35 studies, four systematic reviews and meta-analyses met inclusion criteria. These studies assessed cognitive function through neuropsychological tests measuring memory, attention, executive function, and processing speed.

Results: Meta-analyses indicated favorable effects of creatine on memory and processing speed in older adults. Xu et al. reported significant improvements in memory (SMD = 0.31, 95% CI: 0.18–0.44) and processing speed (SMD = −0.51, 95% CI: −1.01 to −0.01), with no significant effect on global cognition or executive function. Prokopidis et al. found the most pronounced effects in adults aged 66–76. McMorris et al. highlighted inconsistencies across studies, while Stares et al. found no additional benefit when creatine was combined with resistance training.

Conclusions: Creatine supplementation may offer moderate cognitive benefits, particularly for memory and processing speed, in older adults—especially those with low baseline creatine or cardiovascular issues. Effects on global cognition and executive function appear limited. More high-quality, long-term randomized controlled trials are needed. Creatine's neuroprotective properties may support its use in cognitive health strategies, especially alongside physical activity and proper nutrition.

KEYWORDS

Creatine Supplementation, Cognitive Function, Aging, Memory, Executive Function, Neuroprotection

CITATION

Martyna Kaplińska, Dawid Siemieniuk, Aleksandra Kowalska, Hanna Wilska, Dominik Domoń, Dominika Domanowska, Adam Niedziela, Antoni Liebert, Natalia Klimek. (2025) The Impact of Creatine Supplementation on Cognitive Function in Elderly: A Systematic Review. *International Journal of Innovative Technologies in Social Science*. 3(47). doi: 10.31435/ijitss.3(47).2025.3516

COPYRIGHT

© The author(s) 2025. This article is published as open access under the **Creative Commons Attribution 4.0 International License (CC BY 4.0)**, allowing the author to retain copyright. The CC BY 4.0 License permits the content to be copied, adapted, displayed, distributed, republished, or reused for any purpose, including adaptation and commercial use, as long as proper attribution is provided.

Introduction.

Creatine (β-methylguanidinoacetic acid) is an organic compound containing structural elements of guanidine and acetic acid. It was discovered in 1832 by Michel Eugène Chevreul as a component of skeletal muscle(1). Creatine undergoes phosphorylation by the enzyme creatine kinase, converting into phosphocreatine. It is used for energy storage and release, as well as for muscle protein synthesis(2-4). Creatine supplementation by athletes has a confirmed significant impact on muscle tissue development, strength improvement, endurance, accelerated recovery, and increased IGF-1 synthesis. Additionally, there is growing interest in creatine supplementation and its impact on cognitive functions(5-8).

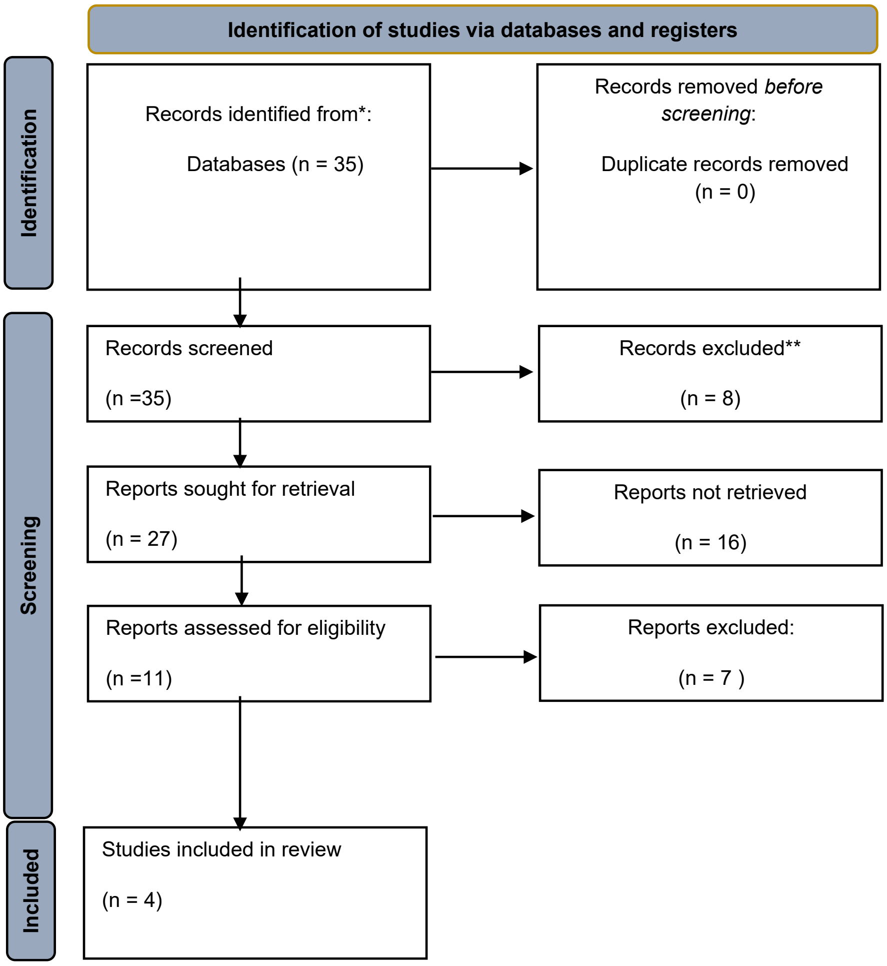
Cognitive impairments in the elderly (> 65 y.) population are becoming an increasing concern due to the aging of societies in developed countries. These impairments encompass deficits in a range of cognitive functions, including attention, memory, executive function, language, and processing speed. The impairment of these cognitive functions in the elderly significantly reduces quality of life, judgment, decision-making abilities, and worsens daily functioning and the performance of essential life activities(9). The age-related decline in cognitive functions, primarily associated with neurodegenerative diseases, is gradually becoming a public health issue(10).

There is an increasing number of publications in the literature on the impact of creatine supplementation on cognitive functions(11). The aim of this analysis is to gather available data from the literature and analyze it in terms of creatine supplementation and its impact on cognitive functions in the elderly population.

Material and Methods

The data for the analysis was selected using the PRISMA FLOW DIAGRAM. The search phrase used was: "the impact of creatine supplementation on cognitive functions in the elderly."

PRISMA 2020 flow diagram for updated systematic reviews which included searches of databases.



A literature review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. The databases PubMed/Medline and EMBASE were searched for the period 2003-2025 for systematic reviews covering the topic: the effect of creatine supplementation on cognitive abilities in older adults. Based on the above analysis, four articles were identified and will be analyzed in the following section of the publication.

Results

The following articles were included in the analysis:

1. Xu C, Bi S, Zhang W, Luo L. „The effects of creatine supplementation on cognitive function in adults: a systematic review and meta-analysis"(12).
2. McMorris T, Hale BJ, Pine BS, Williams TB. "Creatine supplementation research fails to support the theoretical basis for an effect on cognition: Evidence from a systematic review"(13).
3. Prokopidis K, Giannos P, Triantafyllidis KK, Kechagias KS, Forbes SC, Candow DG. "Effects of creatine supplementation on memory in healthy individuals: a systematic review and meta-analysis of randomized controlled trials"(14).
4. Stares A, Bains M. „The Additive Effects of Creatine Supplementation and Exercise Training in an Aging Population: A Systematic Review of Randomized Controlled Trials"(15).

The meta-analysis conducted by Xu et al.(12) included 16 RCTs with a total of 492 participants aged between 20.8 and 76.4 years. Among the studies, three specifically targeted older adults (aged ≥60 years), while the remaining 13 focused on adults (aged 18–59 years). Regarding sex distribution, three studies included only female participants, three included only male participants, and the remaining 10 included both male and female participants. In terms of health status, 13 studies focused on healthy individuals, while three studies targeted patients with specific conditions, such as fibromyalgia, mild cognitive impairment associated with Parkinson's disease, and chronic schizophrenia under treatment. All included studies provided objective measures of cognitive performance. The assessment covered various indicators including overall cognitive function, memory, executive function, attention, and processing speed. In all included studies, creatine monohydrate was used. Creatine supplementation showed a significant positive effect on memory (SMD = 0.31, 95% CI: 0.18–0.44, Hedges' g = 0.3003, 95% CI: 0.1778–0.4228) and attention span (SMD = −0.31, 95% CI: −0.58 to −0.03, Hedges' g = −0.3004, 95% CI: −0.5719 to −0.0289), as well as a significant improvement in processing speed (SMD = −0.51, 95% CI: −1.01 to −0.01, Hedges' g = −0.4916, 95% CI: −0.7852 to −0.1980). However, no significant improvements were found in overall cognitive function or executive function. Subgroup analyses indicated that creatine supplementation was more beneficial for individuals with medical conditions, those aged 18–60 years, and women. No significant differences were found between short-term (<4 weeks) and long-term (≥4 weeks) interventions in improving cognitive function. A low to moderate risk of bias was identified, and no significant publication bias was detected. The GRADE assessment indicates that the certainty of evidence for memory function is moderate, suggesting a reasonable level of confidence in the positive effects of creatine on memory. However, the evidence for processing speed, overall cognitive function, executive function, and attention is of low certainty, indicating that further research is needed to confirm these potential benefits.

The systematic review conducted by McMorris T et. al.(13), in addition to the overall assessment of creatine's impact on cognitive function, they specifically highlighted the effects in vegan and vegetarian populations. Rae et al. made very interesting observations(16). They examined the effect of creatine monohydrate on executive function performance in a group (N = 45) consisting of vegans (n = 18) and vegetarians (n = 27). They found a significant positive impact on executive functions (but did not assess non-executive functions). However, Benton and Donohoe (17) did not find any significant differences between omnivores and vegetarians after supplementation. As a result, they combined their data and did not report results specifically for vegetarians. Nevertheless, they noted that vegetarians taking creatine supplementation performed better in a memory recall test compared to omnivores taking the same supplement. Strangely, after creatine supplementation, omnivores actually performed worse on a short-term memory task than they did at baseline. This is very difficult to explain. It is important to note that, overall, there were no significant differences between omnivores and vegetarians in this study. Analyzing the group of older adults, similar to the case with vegans and vegetarians, studies conducted among older adults have consistently shown lower levels of total creatine in muscles compared to younger adults(18-20). However, with regard to the brain, longitudinal and cross-section studies show that total brain creatine content increases with age(21, 22). It is claimed that this aims to compensate for the decline in brain morphology and function associated with the aging process(23, 24). To understand the claims described above regarding the necessity of creatine supplementation in older adults, we must examine the empirical evidence concerning the interactions between brain health and cognitive abilities in older individuals. There is evidence suggesting that the brains of older adults show a reduction in structure, volume, size, white matter integrity, functional connectivity, and the number of dopaminergic receptors (23, 24): reduction in the number of mitochondria; changes in the size, shape, and structural composition of mitochondria; a decrease in mitochondrial oxygen consumption; and a reduced ability to synthesize ATP(25). Only two studies have investigated the effects of supplementation in older adults. McMorris et al. (13) found a significant improvement in three executive functions and one non-executive function, but two non-significant effects in other non-executive tasks. Alves et al. (26) found no significant effects on any variables (three executive functions and four non-executive functions). There were large differences in treatment protocols. McMorris et al. administered 4 × 5 g/day for 7 days, while participants in the Alves et al. study received 4 × 5 g/day for 5 days, followed by 1 × 5 g/day for 163 days. This suggests that participants in the Alves et al. study should have shown a greater positive effect (5). However, age also differed. McMorris et al.'s group had a mean age of 76.4 (SD 8.8) years, while the participants in Alves et al. had a mean age of 66.8, with a range of 60-80 years. Both of these factors may have influenced the results, but again, we really need to understand the total creatine content in the brain to explain the differences between the two studies.

Systematic review and meta-analysis of randomized controlled trials performed by Prokopidis K et. al.(14), showed very interesting results after analyzing 23 of RCTs. Almost half of the analyzed RCTs compared the effect of creatine supplementation with a placebo. This analysis assessed memory outcomes.

Memory was assessed using multiple evaluation tools in the included studies. The Rey Auditory Verbal Learning Test consists of 4 tasks assessing free and delayed recall memory, immediately after and 20 minutes following the presentation of a list of 12 words, respectively(27). The digit span test was used to assess short-term memory, where participants were asked to repeat sequences of digits both forward and backward(26). n this test, performance was assessed based on the number of digits participants were able to correctly recall. Additionally, current memory was evaluated through the participants' ability to correctly guess the mouse button press corresponding to an immediately displayed letter on the screen for 1 second(28). In the Sternberg memory task, participants were asked to memorize a set of 6 letters displayed on the monitor screen for 20 seconds(28). The letters were then displayed on the screen one at a time, and participants had to press a specific mouse button to indicate whether the letter displayed was present in the memorized set. The definitions of the measurements used to assess aspects of memory and complex memory using the Brief Battery of Cognitive Screening were not provided. The Corsi Block Test, a variation of the Corsi Block Tapping Test, was used to assess memory recall and the reproduction of the sequence of block positions on the screen. Additionally, the reverse Corsi Block Test was used to assess the recall of the sequence in reverse order. For the assessment of short-term memory using the phonological loop, a visual Digit Span Test was employed, where the goal was to recall as many digits as possible.

The main analysis showed that memory performance after creatine supplementation, compared to placebo, improved, although a moderate degree of heterogeneity was observed between the included RCTs (standard mean difference [SMD] = 0.29; 95% CI, 0.04–0.53; I2 = 66%; P = 0.02). A series of subgroup analyses showed that creatine monohydrate supplementation at low doses (≤ 5 g/day) (SMD = 0.24; 95% CI, -0.04 to 0.52; I2 = 38%; P = 0.09) or high doses (> 5 g/day) (SMD = 0.33; 95% CI, -0.07 to 0.74; I2 = 78%; P = 0.11) was not associated with an improvement in memory measurement outcomes. Furthermore, no differences were observed after supplementation in young adults (ages 11–31) (SMD = 0.03; 95% CI, -0.14 to 0.20; I2 = 0%; P = 0.72); however, in older adults (ages 66–76), increased memory performance was observed (SMD = 0.88; 95% CI, 0.22 to 1.55; I2 = 83%; P = 0.009). The duration of treatment also had no effect on the treatment outcomes (≤2 weeks, SMD = 0.33; 95% CI, -0.07 to 0.74; I2 = 78%; P = 0.11; >2 weeks, SMD = 0.24; 95% CI, -0.04 to 0.52; I2 = 38%; P = 0.09) Nor did sex have an impact on the treatment outcomes ([women and men, SMD = 0.26; 95% CI, -0.05 to 0.57; I2 = 69%; P = 0.10], [women, SMD = 0.39; 95% CI, -0.07 to 0.86; I2 = 62%; P = 0.10], [men, SMD = −0.12; 95% CI, -1.02 to 0.78; P = 0.79])(13, 26-30). A significant improvement in memory performance was observed after creatine monohydrate supplementation in powder form (SMD = 0.35; 95% CI, 0.05–0.66; I2 = 73%; P = 0.02), but no effect was found with capsule-form creatine monohydrate (SMD = 0.04; 95% CI, -0.30 to 0.39; I2 = 0%; P = 0.80). Additionally, study results showed significant improvement under non-stressful conditions (SMD = 0.43; 95% CI, 0.09–0.78; I2 = 75%; P = 0.01), while no changes were observed under stressful conditions (SMD = 0.03; 95% CI, -0.23 to 0.30; I2 = 1%; P = 0.80). Furthermore, in cohorts where the loss to follow-up was less than 15%, a significant improvement in memory was observed (SMD = 0.33; 95% CI, 0.04–0.62; I2 = 68%; P = 0.03), while no significant differences were found in cohorts where the loss to follow-up exceeded 15% (SMD = 0.02; 95% CI, -0.26 to 0.29; I2 = 0%; P = 0.90).

This meta-analysis also reveals that creatine monohydrate supplementation did not affect memory performance when higher doses were used (i.e., > 5 g/day). Although there is limited data examining the dose-response relationship of creatine on memory, the results suggest that the amount of endogenous creatine synthesis or dietary creatine intake may be sufficient to maintain adequate creatine stores in the brain(31) and that higher doses of exogenous creatine are not required, despite creatine's limited ability to cross the blood-brain barrier. Therefore, higher doses of creatine supplementation may not be necessary to optimize creatine content in the brain(32, 33) and (re)synthesis of ATP through mitochondrial creatine kinases(34). Currently, little is known about the impact of intervention duration. The subgroup analysis did not show significant differences between short-term studies (≤ 2 weeks) and long-term studies (> 2 weeks), but significantly longer studies are likely needed to demonstrate solid changes over time.

In the publication by Stares A et al.(15) The population of interest consisted of healthy older adults, arbitrarily defined as those aged 65 years. However, age-related declines in skeletal muscle mass, muscle strength, and BMD occur consistently after the fourth decade of life. Therefore, for study selection, this review included participants aged 48 years and older. Additional inclusion criteria included creatine supplementation, the presence of a true control group (without creatine supplementation), a physical training program, randomized controlled trials, and outcome measures in at least one of the following: strength, body composition, functional performance, endurance, and cognition. The present study included only one paper assessing cognitive function. The study examined the potential additive effects of daily creatine supplementation combined with 24 weeks of resistance training (RT) on a battery of cognitive and psychological outcomes. Although both the RT with creatine and placebo groups showed a reduction in scores on the Geriatric Depression Scale compared to their respective non-RT controls ($P < .0001$ and $P < .01$, respectively), no additional effect of creatine supplementation on mental status was observed compared to RT alone. Cognitive performance remained unchanged for all groups across all cognitive tests (data not shown). Previous studies have demonstrated the positive effects of creatine on depression(35), memory and spatial recall(29), and neuroprotection during unfavorable environmental condittions(36). The neuroprotective effect is believed to occur partly through the maintenance of mitochondrial bioenergetics and the reduction of oxidative stress(37). Since exercise alone has been shown to have neuroprotective properties in the brain, Alves et al. (26)aimed to investigate the potential additive effect of creatine combined with resistance training on mental health indicators, including emotional state and cognition. Although the study demonstrated positive effects of resistance training on emotional state, no creatine-specific effects were observed. The direct effects of creatine supplementation on the central nervous system are likely very limited due to the low efficiency of creatine in crossing the blood-brain barier. Although the study demonstrated positive effects of resistance training on emotional state, no creatine-specific effects were observed. The direct effects of creatine supplementation on the central nervous system are likely very limited due to the low efficiency of creatine crossing the blood-brain barrier. The effects may depend on baseline creatine levels in the brain and its turnover rate, which may also change throughout life. Moreover, previous studies have shown positive effects of creatine in the brain under stress conditions, suggesting that any cognitive benefits may occur in individuals with underlying deficiencies in brain energy metabolism or increased energy demand(36).

In the publication by Stares A et al.(15) The population of interest consisted of healthy older adults, arbitrarily defined as those aged 65 years. However, age-related declines in skeletal muscle mass, muscle strength, and BMD occur consistently after the fourth decade of life. Therefore, for study selection, this review included participants aged 48 years and older. Additional inclusion criteria included creatine supplementation, the presence of a true control group (without creatine supplementation), a physical training program, randomized controlled trials, and outcome measures in at least one of the following: strength, body composition, functional performance, endurance, and cognition. The present study included only one paper assessing cognitive function. The study examined the potential additive effects of daily creatine supplementation combined with 24 weeks of resistance training (RT) on a battery of cognitive and psychological outcomes. Although both the RT with creatine and placebo groups showed a reduction in scores on the Geriatric Depression Scale compared to their respective non-RT controls (P < .0001 and P < .01, respectively), no additional effect of creatine supplementation on mental status was observed compared to RT alone. Cognitive performance remained unchanged for all groups across all cognitive tests (data not shown). Previous studies have demonstrated the positive effects of creatine on depression(35), memory and spatial recall(29), and neuroprotection during unfavorable environmental condittions(36). The neuroprotective effect is believed to occur partly through the maintenance of mitochondrial bioenergetics and the reduction of oxidative stress(37). Since exercise alone has been shown to have neuroprotective properties in the brain, Alves et al. (26)aimed to investigate the potential additive effect of creatine combined with resistance training on mental health indicators, including emotional state and cognition. Although the study demonstrated positive effects of resistance training on emotional state, no creatine-specific effects were observed. The direct effects of creatine supplementation on the central nervous system are likely very limited due to the low efficiency of creatine in crossing the blood-brain barier. Although the study demonstrated positive effects of resistance training on emotional state, no creatine-specific effects were observed. The direct effects of creatine supplementation on the central nervous system are likely very limited due to the low efficiency of creatine crossing the blood-brain barrier. The effects may depend on baseline creatine levels in the brain and its turnover rate, which may also change throughout life. Moreover, previous studies have shown positive effects of creatine in the brain under stress conditions, suggesting that any cognitive benefits may occur in individuals with underlying deficiencies in brain energy metabolism or increased energy demand(36).

Discussion

The results of this systematic review indicate that creatine supplementation may have some positive effects on cognitive function in elderly individuals, particularly in memory and processing speed. However, the overall impact remains inconsistent across studies. The meta-analysis by Xu et al. demonstrated a significant improvement in memory and attention span, with a moderate effect size. On the other hand, the systematic review by McMorris et al. raised concerns regarding the variability in creatine's effects on different populations, particularly in vegetarians and omnivores. Some studies reported improvements in executive functions, while others failed to show any significant benefits.

One of the key findings of this review is that the beneficial effects of creatine supplementation on cognition appear to be more pronounced in populations with underlying medical conditions or in individuals with lower baseline creatine levels. This aligns with previous research suggesting that creatine acts as a neuroprotective agent by maintaining mitochondrial bioenergetics and reducing oxidative stress. However, its limited ability to cross the blood-brain barrier may explain why some studies found no significant improvements in overall cognitive function. Another notable observation is the potential dose-dependent effects of creatine supplementation. While Prokopidis et al. found a significant improvement in memory performance in older adults, they noted that higher doses (>5 g/day) did not yield greater benefits. This suggests that endogenous creatine levels or dietary intake may already be sufficient for cognitive function in some individuals, reducing the necessity for higher supplementation doses. Additionally, the effectiveness of creatine supplementation appeared to be influenced by the mode of administration, with powder-form supplementation yielding better results compared to capsules.

The study by Stares et al. explored the combined effects of resistance training and creatine supplementation, finding that exercise alone had a more significant impact on cognitive function than creatine supplementation. This further suggests that creatine's cognitive benefits might be context-dependent, possibly requiring additional physiological stressors or deficiencies to exert a noticeable effect. Despite these findings, there are several limitations to this review. Many studies included in the analysis had small sample sizes, limiting the generalizability of the results. Additionally, heterogeneity in study methodologies, including variations in supplementation duration, cognitive assessment tools, and participant characteristics, makes direct comparisons challenging. More rigorous and long-term studies are necessary to determine the optimal dosage, duration, and conditions under which creatine supplementation may have the most pronounced cognitive benefits.

Conclusions

Creatine supplementation shows promise as a potential intervention to enhance cognitive function in the elderly, particularly in areas such as memory and processing speed. However, the overall evidence remains mixed, with several studies failing to find significant improvements in executive function and general cognition. The greatest benefits appear to be observed in populations with medical conditions or those with lower baseline creatine levels, supporting its role as a neuroprotective agent.

Further research is needed to better understand the mechanisms underlying creatine's effects on brain function, particularly its interaction with age-related changes in mitochondrial metabolism and oxidative stress. Additionally, future studies should explore optimal dosing strategies, supplementation duration, and potential synergistic effects with other lifestyle interventions, such as exercise.

In conclusion, while creatine supplementation may hold potential as a cognitive enhancer in aging populations, it should not be considered a standalone intervention. A holistic approach that includes a healthy diet, physical activity, and other neuroprotective strategies remains essential for maintaining cognitive function in older adults.

REFERENCES

1. Twycross-Lewis R, Kilduff LP, Wang G, Pitsiladis YP. The effects of creatine supplementation on thermoregulation and physical (cognitive) performance: a review and future prospects. Amino Acids. 2016;48(8):1843-55.
2. Brosnan JT, da Silva RP, Brosnan ME. The metabolic burden of creatine synthesis. Amino Acids. 2011;40(5):1325-31.
3. Kreider RB, Stout JR. Creatine in Health and Disease. Nutrients. 2021;13(2).
4. Rackayova V, Cudalbu C, Pouwels PJW, Braissant O. Creatine in the central nervous system: From magnetic resonance spectroscopy to creatine deficiencies. Anal Biochem. 2017;529:144-57.
5. Dolan E, Gualano B, Rawson ES. Beyond muscle: the effects of creatine supplementation on brain creatine, cognitive processing, and traumatic brain injury. Eur J Sport Sci. 2019;19(1):1-14.
6. Joncquel-Chevalier Curt M, Voicu PM, Fontaine M, Dessein AF, Porchet N, Mention-Mulliez K, et al. Creatine biosynthesis and transport in health and disease. Biochimie. 2015;119:146-65.
7. Meftahi GH, Hatef B, Pirzad Jahromi G. Creatine Activity as a Neuromodulator in the Central Nervous System. Arch Razi Inst. 2023;78(4):1169-75.
8. Ostojic SM, Forbes SC. Perspective: Creatine, a Conditionally Essential Nutrient: Building the Case. Adv Nutr. 2022;13(1):34-7.
9. Lee Y, Kim JH, Lee KJ, Han G, Kim JL. Association of cognitive status with functional limitation and disability in older adults. Aging Clin Exp Res. 2005;17(1):20-8.
10. Kelley BJ, Petersen RC. Alzheimer's disease and mild cognitive impairment. Neurol Clin. 2007;25(3):577-609, v.
11. Avgerinos KI, Spyrou N, Bougioukas KI, Kapogiannis D. Effects of creatine supplementation on cognitive function of healthy individuals: A systematic review of randomized controlled trials. Exp Gerontol. 2018;108:166-73.
12. Xu C, Bi S, Zhang W, Luo L. The effects of creatine supplementation on cognitive function in adults: a systematic review and meta-analysis. Front Nutr. 2024;11:1424972.
13. McMorris T, Hale BJ, Pine BS, Williams TB. Creatine supplementation research fails to support the theoretical basis for an effect on cognition: Evidence from a systematic review. Behav Brain Res. 2024;466:114982.
14. Prokopidis K, Giannos P, Triantafyllidis KK, Kechagias KS, Forbes SC, Candow DG. Effects of creatine supplementation on memory in healthy individuals: a systematic review and meta-analysis of randomized controlled trials. Nutr Rev. 2023;81(4):416-27.
15. Stares A, Bains M. The Additive Effects of Creatine Supplementation and Exercise Training in an Aging Population: A Systematic Review of Randomized Controlled Trials. J Geriatr Phys Ther. 2020;43(2):99-112.
16. Rae C, Digney AL, McEwan SR, Bates TC. Oral creatine monohydrate supplementation improves brain performance: a double-blind, placebo-controlled, cross-over trial. Proc Biol Sci. 2003;270(1529):2147-50.
17. Benton D, Donohoe R. The influence of creatine supplementation on the cognitive functioning of vegetarians and omnivores. Br J Nutr. 2011;105(7):1100-5.
18. Forsberg AM, Nilsson E, Werneman J, Bergstrom J, Hultman E. Muscle composition in relation to age and sex. Clin Sci (Lond). 1991;81(2):249-56.
19. Gualano B, Rawson ES, Candow DG, Chilibeck PD. Creatine supplementation in the aging population: effects on skeletal muscle, bone and brain. Amino Acids. 2016;48(8):1793-805.
20. Rawson ES, Clarkson PM, Price TB, Miles MP. Differential response of muscle phosphocreatine to creatine supplementation in young and old subjects. Acta Physiol Scand. 2002;174(1):57-65.
21. Hultsch DF, Hertzog C, Small BJ, Dixon RA. Use it or lose it: engaged lifestyle as a buffer of cognitive decline in aging? Psychol Aging. 1999;14(2):245-63.
22. Forester BP, Harper DG, Jensen JE, Ravichandran C, Jordan B, Renshaw PF, et al. 31Phosphorus magnetic resonance spectroscopy study of tissue specific changes in high energy phosphates before and after sertraline treatment of geriatric depression. Int J Geriatr Psychiatry. 2009;24(8):788-97.
23. Li SC, Lindenberger U, Sikstrom S. Aging cognition: from neuromodulation to representation. Trends Cogn Sci. 2001;5(11):479-86.
24. Park DC, Reuter-Lorenz P. The adaptive brain: aging and neurocognitive scaffolding. Annu Rev Psychol. 2009;60:173-96.
25. Bertoni-Freddari C, Fattoretti P, Giorgetti B, Spazzafumo L, Solazzi M, Balietti M. Age-related decline in metabolic competence of small and medium-sized synaptic mitochondria. Naturwissenschaften. 2005;92(2):82-5.
26. Alves CR, Merege Filho CA, Benatti FB, Brucki S, Pereira RM, de Sa Pinto AL, et al. Creatine supplementation associated or not with strength training upon emotional and cognitive measures in older women: a randomized double-blind study. PLoS One. 2013;8(10):e76301.
27. Merege-Filho CA, Otaduy MC, de Sa-Pinto AL, de Oliveira MO, de Souza Goncalves L, Hayashi AP, et al. Does brain creatine content rely on exogenous creatine in healthy youth? A proof-of-principle study. Appl Physiol Nutr Metab. 2017;42(2):128-34.
28. Rawson ES, Lieberman HR, Walsh TM, Zuber SM, Harhart JM, Matthews TC. Creatine supplementation does not improve cognitive function in young adults. Physiol Behav. 2008;95(1-2):130-4.

29. McMorris T, Mielcarz G, Harris RC, Swain JP, Howard A. Creatine supplementation and cognitive performance in elderly individuals. Neuropsychol Dev Cogn B Aging Neuropsychol Cogn. 2007;14(5):517-28.
30. McMorris T, Harris RC, Swain J, Corbett J, Collard K, Dyson RJ, et al. Effect of creatine supplementation and sleep deprivation, with mild exercise, on cognitive and psychomotor performance, mood state, and plasma concentrations of catecholamines and cortisol. Psychopharmacology (Berl). 2006;185(1):93-103.
31. Brosnan ME, Brosnan JT. The role of dietary creatine. Amino Acids. 2016;48(8):1785-91.
32. Dechent P, Pouwels PJ, Wilken B, Hanefeld F, Frahm J. Increase of total creatine in human brain after oral supplementation of creatine-monohydrate. Am J Physiol. 1999;277(3):R698-704.
33. Pan JW, Takahashi K. Cerebral energetic effects of creatine supplementation in humans. Am J Physiol Regul Integr Comp Physiol. 2007;292(4):R1745-50.
34. Saks VA, Kongas O, Vendelin M, Kay L. Role of the creatine/phosphocreatine system in the regulation of mitochondrial respiration. Acta Physiol Scand. 2000;168(4):635-41.
35. Lyoo IK, Yoon S, Kim TS, Hwang J, Kim JE, Won W, et al. A randomized, double-blind placebo-controlled trial of oral creatine monohydrate augmentation for enhanced response to a selective serotonin reuptake inhibitor in women with major depressive disorder. Am J Psychiatry. 2012;169(9):937-45.
36. Turner CE, Byblow WD, Gant N. Creatine supplementation enhances corticomotor excitability and cognitive performance during oxygen deprivation. J Neurosci. 2015;35(4):1773-80.
37. Adhihetty PJ, Beal MF. Creatine and its potential therapeutic value for targeting cellular energy impairment in neurodegenerative diseases. Neuromolecular Med. 2008;10(4):275-90.