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THE EFFECTS OF CREATINE SUPPLEMENTATION ON MUSCLE AND COGNITIVE FUNCTION IN OLDER ADULTS: A REVIEW OF RANDOMIZED CONTROLLED TRIALS

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ABSTRACT

Background; Aging is associated with a progressive decline in muscle mass and muscle strength, which significantly affects physical performance and quality of life in older adults. The aging process may also contribute to the deterioration of cognitive function. Creatine supplementation has been proposed as a potential intervention to support muscle and cognitive function in older adults.

Objective: The aim of this study was to evaluate the effects of creatine supplementation on muscle mass, muscle strength, and cognitive function in older adults.

Methods: A review of randomized controlled trials (RCTs) was conducted using the PubMed database. The literature search was performed in May 2026 and included studies published between 2000 and 2026. Studies involving adults aged ≥ 60 years who received creatine supplementation either alone or in combination with resistance training were included in the analysis.

Results: Based on 13 randomized controlled trials, creatine supplementation was shown to increase muscle strength, lean body mass, and overall muscle function in older adults. The greatest benefits were observed when creatine supplementation was combined with regular resistance training. Evidence regarding cognitive function remains inconclusive, although some studies reported potential benefits in selected cognitive domains.

Conclusion: Creatine supplementation, particularly when combined with resistance training, may represent an effective strategy for improving muscle mass and strength in older adults. Although evidence regarding cognitive outcomes remains inconclusive, some findings suggest potential benefits for cognitive function. Further RCTs are needed to clarify these effects.

KEYWORDS

Creatine, Aging, Older Adults, Resistance Training, Muscle Strength, Cognitive Function, Sarcopenia

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1. Introduction

1.1. Biological Basis of Creatine

Creatine is an endogenous nitrogen-containing compound that occurs naturally in the human body and is also obtained through dietary intake, primarily from meat and fish. Although it is not a proteinogenic amino acid, its biosynthesis involves the amino acids glycine, arginine, and methionine and occurs predominantly in the liver, kidneys, and pancreas (Wyss & Kaddurah-Daouk, 2000; Brosnan & Brosnan, 2007).

Approximately 95% of the body's total creatine pool is stored in skeletal muscle, while the remaining fraction is distributed among other tissues, including the brain (Kreider et al., 2017). Within cells, creatine exists both in its free form and as phosphocreatine, which is generated through a reaction catalyzed by creatine kinase (Wallimann et al., 2011).

The primary physiological role of creatine is to maintain cellular energy homeostasis through the phosphocreatine–ATP system. Phosphocreatine serves as a reservoir of high-energy phosphate groups, enabling the rapid regeneration of ATP from ADP, particularly during short-duration, high-intensity anaerobic exercise (Kreider et al., 2017; Wallimann et al., 2011).

In addition, creatine plays a crucial role in intracellular energy transport through the creatine kinase system, which links sites of ATP production, such as mitochondria, with sites of ATP utilization. This mechanism facilitates the efficient transfer of high-energy phosphate groups between cellular compartments and partially compensates for the limited diffusion capacity of ATP and ADP within the cell (Wallimann et al., 2011).

The literature also highlights the involvement of creatine in the regulation of mitochondrial function, the attenuation of oxidative stress, and the stabilization of cellular membranes, all of which may contribute to cellular protection against damage (Wallimann et al., 2011).

1.2. Aging: Sarcopenia and Cognitive Function

Sarcopenia is a progressive muscle disease characterized by the age-related decline in skeletal muscle mass, muscle strength, and physical performance. It predominantly affects older adults and is associated with an increased risk of falls, fractures, physical disability, loss of independence, and mortality (Cruz-Jentoft et al., 2019). As the global population continues to age, sarcopenia has become a major public health concern due to its substantial impact on healthcare systems and quality of life among older individuals.

Aging is also accompanied by a gradual decline in cognitive function, including impairments in memory, attention, processing speed, and executive functioning (Harada et al., 2013). These changes may adversely affect daily functioning, social participation, and overall well-being in older adults.

At the cellular level, age-related cognitive decline has been linked to disturbances in cerebral energy metabolism, including mitochondrial dysfunction, increased oxidative stress, and reduced ATP production (Camandola & Mattson, 2017). These alterations may compromise neuronal function and contribute to the development of cognitive impairment associated with aging.

1.3. Creatine as a Potential Intervention in Older Adults

Creatine supplementation combined with resistance training has been shown to significantly increase lean body mass and muscle strength in older adults compared with placebo (Chilibeck et al., 2017; Forbes et al., 2021).

Randomized controlled trials have demonstrated greater improvements in muscle strength and lean body mass among participants receiving creatine supplementation together with resistance training compared with individuals performing resistance training alone or receiving creatine supplementation without structured exercise (Gualano et al., 2014).

Beyond its effects on muscle function, creatine may also influence cognitive performance. Due to its role in cellular energy metabolism, creatine has been proposed as a potential intervention capable of supporting brain function, particularly in tissues characterized by high energy demands. Systematic reviews have reported potential improvements in short-term memory and reasoning ability following creatine supplementation; however, findings regarding other cognitive domains remain inconclusive (Avgerinos et al., 2018).

1.4. Current State of Knowledge

Current evidence indicates that creatine supplementation contributes to significant improvements in muscle mass and muscle strength in both older adults and physically active individuals (Chilibeck et al., 2017; Forbes et al., 2021). Numerous studies have demonstrated that these benefits are particularly evident when creatine supplementation is combined with resistance training.

The strongest and most consistent evidence relates to the effects of creatine on muscle function. In contrast, the available data regarding cognitive function are less conclusive, and study findings remain inconsistent. While some investigations have reported improvements in memory and other cognitive domains, others have failed to demonstrate significant benefits, highlighting the need for further research in this area (Avgerinos et al., 2018; Prokopidis et al., 2023).

1.5. Research Gap and Study Objective

Despite the growing body of evidence regarding creatine supplementation, important gaps in the current literature remain, particularly with respect to older adults. Previous studies and meta-analyses have consistently demonstrated the beneficial effects of creatine on muscle mass and muscle strength. However, the evidence concerning its effects on cognitive function remains inconclusive, with considerable variability observed across studies.

Therefore, the aim of the present review was to evaluate the effects of creatine supplementation on muscle and cognitive function in older adults based on evidence derived from randomized controlled trials.

2. Methodology

2.1. Search Strategy

A literature search was conducted using the PubMed database to identify studies investigating the effects of creatine supplementation in older adults. The search was performed in May 2026 and included articles published between 2000 and 2026.

The following keywords were used in the search strategy: “creatine supplementation,” “older adults,” “aging,” “muscle strength,” “cognitive function,” and “randomized controlled trial.”

2.2. Inclusion Criteria

The following studies were included in the analysis:

1. Randomized controlled trials (RCTs).
2. Studies involving participants aged ≥ 60 years.
3. Studies investigating creatine supplementation.
4. Studies assessing muscle function and/or cognitive function.

2.3. Exclusion Criteria

The following studies were excluded:

1. Studies involving athletes or younger populations.
2. Non-randomized studies.
3. Animal studies.
4. Studies that did not assess muscle or cognitive function.

2.4. Study Selection

After applying filters restricting the search results to randomized controlled trials, a total of 222 publications were identified. Titles and abstracts were subsequently screened, and studies that did not meet the predefined inclusion criteria were excluded. Following full-text assessment, 13 studies were deemed eligible and were included in the final analysis.

2.5. Data Extraction

Data extracted from the selected studies included the first author, year of publication, number of participants, supplementation protocol, duration of the intervention, and outcomes related to muscle and cognitive function.

Table 1. Characteristics of the Studies Included in the Analysis

Author (Year)	Population	Intervention	Duration	Main Findings
Amiri (2023)	Older adults	Creatine + resistance training	10 weeks	Increased muscle strength, reduced oxidative stress, and improved quality of life
Gualano (2014)	Older women	Creatine + resistance training	24 weeks	Increased muscle strength and lean body mass (LBM)
Candow (2015)	Healthy older adults	Creatine + resistance training	12 weeks	Increased muscle strength and muscle mass
McMorris (2007)	Older adults	Creatine supplementation	2 weeks	Potential improvement in cognitive function, particularly under conditions of increased energy demand

Author (Year)	Population	Intervention	Duration	Main Findings
Candow et al. (2021a)	Older adults	Creatine + resistance training	12 months	Increased bone and muscle density and cross-sectional area
Fernández-Garrido et al. (2026)	Older adults	Creatine + resistance training	16 weeks	Improved physical and cognitive function
Gotshalk (2002)	Older men	Creatine supplementation	1 week	Improved muscular performance
Candow (2014)	Older adults	Creatine + resistance training	12 weeks	Increased muscle strength; no differences between pre- and post-exercise supplementation
Candow (2019)	Older adults	Creatine + resistance training	8 months	No effect on bone mineral density (BMD)
Candow et al. (2021b)	Older men	Creatine + resistance training	12 months	Increased muscle strength and muscle mass
Aguiar (2013)	Older women	Creatine + resistance training	12 weeks	Increased muscle strength and physical performance
Bernat (2019)	Older men	Creatine + high-velocity resistance training	8 weeks	Improved physical function
Chilibeck (2005)	Older men	Creatine + resistance training	12 weeks	Increased bone mineral density

2.6. Quality Assessment

The methodological quality of the included studies was evaluated based on commonly accepted criteria for assessing randomized controlled trials, including randomization procedures, blinding, and completeness of outcome reporting.

3. Results

3.1. Effects on Muscle Function

The vast majority of studies demonstrated that creatine supplementation combined with resistance training resulted in significant increases in muscle strength and lean body mass in older adults (Amiri et al., 2023; Gualano et al., 2014; Candow et al., 2015).

These effects were observed in both short-term and long-term interventions, including studies with intervention periods of up to 12 months (Candow et al., 2021b).

3.2. Effects on Cognitive Function

The effects of creatine supplementation on cognitive function remain less conclusive. McMorris et al. (2007) reported improvements in short-term memory among older adults; however, these findings have not been consistently replicated across all studies.

More recent evidence suggests that combining creatine supplementation with resistance training may have beneficial effects on selected cognitive domains. Nevertheless, these findings require further confirmation in future randomized controlled trials (Fernández-Garrido et al., 2026).

3.3. Additional Metabolic Effects

Evidence from individual studies has also reported that creatine supplementation may contribute to reductions in oxidative stress and improvements in antioxidant defense mechanisms (Amiri et al., 2023).

4. Discussion

4.1. Interpretation of Findings

Creatine supplementation combined with resistance training has been shown to significantly increase both muscle strength and lean body mass in older adults, as demonstrated by numerous randomized controlled trials and pooled analyses (Chilibeck et al., 2017).

The synergistic interaction between creatine supplementation and physical exercise appears to be a key factor underlying these effects. Available evidence suggests that creatine supplementation alone produces substantially smaller benefits compared with its use in conjunction with regular resistance training (Rawson & Venezia, 2011).

The effects of creatine supplementation on cognitive function remain less clear. While some studies have reported improvements in short-term memory and selected cognitive domains, the available findings are inconsistent and require further confirmation through well-designed randomized controlled trials (Avgerinos et al., 2018).

4.2. Mechanisms of Action of Creatine

The creatine kinase–phosphocreatine system serves as an intracellular energy buffer and plays a central role in the regulation of cellular energy metabolism. Through the phosphocreatine shuttle, ATP can be rapidly regenerated from ADP in tissues characterized by high energy demands (Wallimann et al., 2011).

Creatine supplementation increases intramuscular phosphocreatine stores, thereby enhancing the capacity for high-intensity exercise and enabling greater training workloads. Consequently, this may contribute to greater gains in muscle strength and muscle mass over time (Kreider et al., 2017).

In addition to its effects on skeletal muscle, creatine may exert antioxidant properties and support central nervous system function by improving neuronal energy metabolism. These mechanisms have been proposed as potential contributors to the beneficial effects of creatine on cognitive function and healthy aging (Arazi et al., 2021; Forbes et al., 2022).

4.3. Comparison with Existing Literature

The findings of the present review are consistent with the current body of evidence demonstrating the beneficial effects of creatine supplementation on muscle strength and lean body mass in older adults, particularly when combined with resistance training (Chilibeck et al., 2017).

The effects of creatine on muscle function have been well documented, whereas its influence on the central nervous system remains less clearly established. Available evidence suggests potential improvements in short-term memory and selected aspects of cognitive function; however, study findings remain inconsistent (Avgerinos et al., 2018).

4.4. Limitations

A major limitation of the available literature is the substantial heterogeneity among studies, including differences in participant characteristics, supplementation protocols, and resistance training interventions. Additional heterogeneity arises from the varying designs of studies investigating cognitive outcomes. For example, the study conducted by McMorris et al. assessed the effects of creatine supplementation under conditions of disrupted energy homeostasis associated with sleep deprivation, which may limit the generalizability of its findings to the broader population of older adults.

Another limitation is the relatively small number of studies examining cognitive outcomes, as well as the lack of standardization in the neuropsychological tests used to assess cognitive function (Avgerinos et al., 2018).

4.5. Clinical Implications

Creatine supplementation combined with resistance training has been shown to increase lean body mass and muscle strength in older adults. These effects may help counteract the progression of sarcopenia and contribute to improvements in quality of life among older individuals (Chilibeck et al., 2017).

Current evidence also indicates that creatine is generally safe and well tolerated in healthy individuals when consumed at recommended doses (Kreider et al., 2017).

4.6. Future Research Directions

Further research is required to better characterize the effects of creatine supplementation in humans and to identify populations that may derive the greatest benefit from its use.

Particular attention should be given to the standardization of creatine dosage, supplementation duration, and methods used to assess cognitive function in future studies.

5. Conclusions

Numerous studies have demonstrated the beneficial effects of creatine supplementation on muscle strength and lean body mass in older adults. The combination of creatine supplementation and regular resistance training appears to be particularly effective in enhancing these outcomes.

Although the evidence regarding cognitive function remains inconclusive, some studies suggest that creatine supplementation may exert beneficial effects on short-term memory and selected cognitive domains.

Current evidence also indicates that creatine is a safe and well-tolerated supplement in healthy individuals when consumed at recommended doses.

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