



QUALITY IN SPORT

eISSN 2450-3118 · Open Access · Peer-reviewed

Vol. 55 (2026) · Article 71118 · Published 16 May 2026

apcz.umk.pl/QS · Nicolaus Copernicus University in Toruń



Cite as: Mińkowski M, Oćwieja Z, Wyborska A, Fengler K, Jakubowska O, Kominiak D, Gascon Carreno M, Solecka K, Urbanik A, Pietrzak K. Creatine supplementation beyond skeletal muscles: cognitive and neuroprotective effects and underlying mechanisms – a narrative review. *Quality in Sport*. 2026;55:71118.

<https://doi.org/10.12775/QS.2026.55.71118>

ARTICLE TIMELINE

Received: 21.04.2026 **Revised:** 05.05.2026

Accepted: 05.05.2026 **Published:** 16.05.2026

INDEXING & EVALUATION

MEiN points: 20 **Unique ID:** 201398

Disciplines: Economics & Finance; Management & Quality Sciences

The journal has been awarded 20 points in the parametric evaluation by the Polish Ministry of Higher Education and Science (Annex to the announcement of 05.01.2024, No. 32553). Unique Journal Identifier: 201398. Scientific disciplines: Economics and Finance (Social Sciences); Management and Quality Sciences (Social Sciences).

Punkty Ministerialne z 2019 – aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398. Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych). © The Authors 2026.

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NARRATIVE REVIEW

Creatine supplementation beyond skeletal muscles: cognitive and neuroprotective effects and underlying mechanisms - a narrative review

HIGHLIGHTS

- ▶ Creatine supplementation produces small but consistent improvements in short-term and working memory.
- ▶ Benefits are most pronounced under metabolic stress: sleep deprivation, mental fatigue, hypoxia, and aging.

- ▶ Effects on attention and processing speed in healthy adults remain minimal and inconsistent.
- ▶ Mechanisms involve phosphocreatine buffering, ATP regeneration, mitochondrial support and antioxidant action.
- ▶ Creatine monohydrate has an excellent long-term safety profile in human studies.

AUTHORS & AFFILIATIONS

Mikołaj Mińkowski [MM]

ORCID: <https://orcid.org/0009-0001-2280-809X>

E-mail: mikolaj.minkowski@gmail.com

Wielospecjalistyczny Szpital Miejski im. Józefa Strusia w Poznaniu, Poznań, Poland

Dominika Kominiak [DK]

ORCID: <https://orcid.org/0009-0001-8212-4765>

E-mail: dom.k21@wp.pl

Szpital Wojewódzki w Poznaniu, ul. Juraszów 7/19, 60-479 Poznań, Poland

Zuzanna Oćwieja [ZO]

ORCID: <https://orcid.org/0009-0005-6357-6079>

E-mail: zuzannaocwieja@gmail.com

Centrum Medyczne HCP Szpital im. św. Jana Pawła II, Poznań, Poland

Marcel Gascon Carreno [MGC]

ORCID: <https://orcid.org/0009-0007-1754-2809>

E-mail: marczepan1@gmail.com

Centrum Medyczne HCP Szpital im. św. Jana Pawła II, 28 Czerwca 1956 r. 194, 61-485 Poznań, Poland

Agata Wyborska [AW]

ORCID: <https://orcid.org/0009-0003-1038-0107>

E-mail: agata.wyborska.x@gmail.com

Szpital Wojewódzki w Poznaniu, ul. Juraszów 7/19, 60-479 Poznań, Poland

Katarzyna Solecka [KS]

ORCID: <https://orcid.org/0009-0004-1053-2438>

E-mail: katarzynasolecka77@gmail.com

Uniwersytecki Szpital Kliniczny, ul. Przybyszewskiego 49, 60-355 Poznań, Poland

Karolina Fengler [KF]

ORCID: <https://orcid.org/0009-0008-7017-3915>

E-mail: fenglerkarolina@gmail.com

Uniwersytecki Szpital Kliniczny, ul. Przybyszewskiego 49, 60-355 Poznań, Poland

Agata Urbanik [AU]

ORCID: <https://orcid.org/0009-0005-7984-7515>

E-mail: a.urbanik21@gmail.com

Uniwersytecki Szpital Kliniczny, ul. Przybyszewskiego 49, 60-355 Poznań, Poland

Olga Jakubowska [OJ]

ORCID: <https://orcid.org/0009-0001-0655-3453>

E-mail: olgajak@onet.pl

Szpital Wojewódzki w Poznaniu, ul. Juraszów 7/19, 60-479 Poznań, Poland

Kamila Pietrzak [KP]

ORCID: <https://orcid.org/0009-0006-8223-1276>

E-mail: Kamila.pietrzak00@wp.pl

Centrum Medyczne HCP Szpital im. św. Jana Pawła II, 28 Czerwca 1956 r. 194, 61-485 Poznań, Poland

CORRESPONDING AUTHOR Mikołaj Mińkowski – mikolaj.minkowski@gmail.com

ABSTRACT

AIM: The aim of this narrative review was to gather and evaluate current evidence on the effects of creatine supplementation on cognitive function and brain health, with emphasis on mechanisms related to energy metabolism and potential neuroprotective properties.

MATERIALS AND METHODS: A narrative literature review was conducted using PubMed and Google Scholar, including randomized controlled trials, systematic reviews, and meta-analyses. The analysis focused on cognitive aspects such as memory, attention, and processing speed, as well as studies examining brain creatine metabolism, especially under conditions of increased metabolic demand.

RESULTS: Overall, the evidence suggests that creatine has small but fairly consistent effects on cognitive performance, mainly in short-term and working memory. Regarding attention and processing speed, current evidence suggests that although individual studies show varying degrees of effect, creatine supplementation does not have a significant positive impact on attention and processing speed. The benefits appear more noticeable in situations where the brain is under metabolic stress, such as sleep deprivation, mental fatigue, hypoxia, aging, or low baseline creatine levels. These effects are most likely linked to improved ATP availability, enhanced phosphocreatine buffering, and support of mitochondrial function.

CONCLUSIONS: Creatine may offer modest, context-dependent support for cognitive function, particularly when brain energy metabolism is challenged. While effects in healthy individuals seem limited, it may still be a safe and potentially useful option in specific populations. Further research is needed to better define its role and optimal use.

KEYWORDS creatine supplementation; cognitive function; brain energy metabolism; phosphocreatine system; neuroprotection; mitochondrial function; memory; aging brain; cognitive fatigue.

GRAPHICAL ABSTRACT

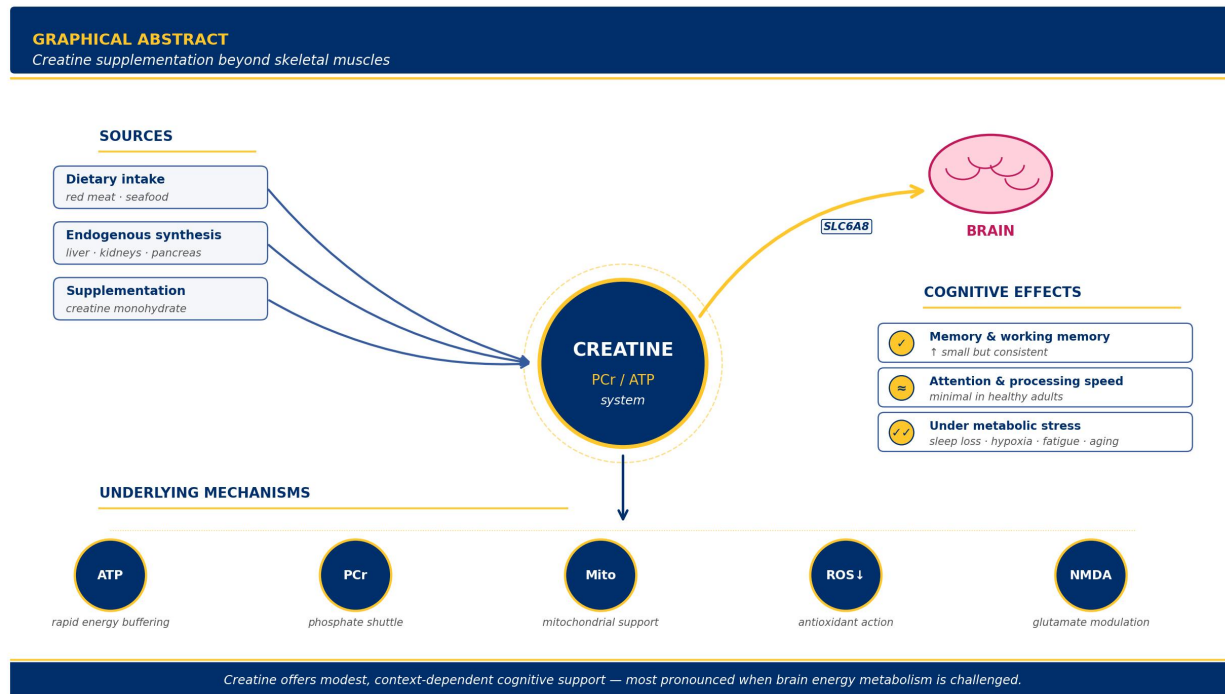


Figure 1. Graphical overview of creatine sources, brain transport (SLC6A8), cognitive outcomes, and underlying mechanisms of action discussed in this narrative review.

PLAIN LANGUAGE SUMMARY

Creatine is a natural substance found in our food and made by our body. It is best known as a supplement used by athletes to boost muscle energy and performance. In recent years, scientists have started to

investigate whether creatine can also benefit the brain, which is one of the most energy-hungry organs in the human body. This review summarises what current research tells us. Overall, creatine appears to give small but real improvements to short-term and working memory, and the benefits are clearer in situations where the brain is under strain — for example, after poor sleep, in older adults, at high altitude or after a head injury. In healthy young adults under normal conditions, the effects on attention and thinking speed are usually small. Creatine works by helping brain cells produce and recycle energy more efficiently and by supporting the mitochondria, the cell's 'power plants'. The supplement has a well-established safety record. More research is needed to identify who benefits most and what the best dose and duration are.

1. INTRODUCTION

1.1. Creatine as one of the most widely studied ergogenic aids

Creatine is widely perceived as one of the most extensively studied and commonly used ergogenic aids in sports nutrition. It is a naturally occurring, non-protein compound that can be obtained from the diet, primarily through the consumption of red meat and seafood [1]. In addition, it is endogenously synthesized in the liver, kidneys, and pancreas from glycine, arginine, and methionine [2]. The vast majority of creatine in the human body is stored in skeletal muscle (approximately 95%), while the remaining portion is found in tissues such as the brain, heart, and testes [1,3]. This distribution reflects the high and often fluctuating energy demands of these organs [3].

Interest in creatine supplementation increased rapidly in the early 1990s, following studies demonstrating its ability to improve high-intensity exercise performance and muscular strength [1]. Since then, a significant amount of research has confirmed its effectiveness in enhancing short-duration, high-intensity exercise capacity and promoting gains in lean body mass. As a result, creatine monohydrate is now considered to be one of the most well-established and evidence-based dietary supplements in sports science [4].

From a physiological standpoint, the ergogenic effects of creatine are mainly linked to its involvement in the phosphocreatine (PCr) system, which plays a pivotal role in cellular energy metabolism [2]. During periods of increased energy demand, phosphocreatine acts as a phosphate donor, allowing for the rapid regeneration of adenosine triphosphate (ATP) from adenosine diphosphate (ADP) through the creatine kinase reaction [3]. In practical terms, this system helps maintain energy availability during short, intense efforts, functioning as an instant energy supplier [2].

Although most of the previous research focused on skeletal muscle, in recent years more attention has been given to the role of creatine in other tissues with high energetic demands — particularly the brain [5].

1.2. Creatine metabolism in the brain

The brain is a highly energy-demanding organ that depends on a continuous and tightly regulated supply of ATP to maintain neuronal activity and effective synaptic transmission [6]. Therefore, creatine plays an important role in supporting cellular energy homeostasis in both neurons and glial cells [7].

Creatine is transported into the central nervous system by a specific sodium- and chloride-dependent transporter (SLC6A8), which enables it to cross the blood–brain barrier [7]. Once it reaches the brain, it becomes part of the phosphocreatine–creatine kinase system. This system functions not only as a rapid energy buffer, but also as a mechanism for intracellular energy transfer and a metabolic regulator [3].

Within the cell, the creatine kinase system facilitates the movement of high-energy phosphates from mitochondria, which produce ATP, to areas of increased energy demand, such as synapses [6]. Given the important role of mitochondria in neuronal metabolism, disruptions in their function have been strongly linked to the development of various neurological disorders [8].

Under these circumstances, creatine has attracted attention not only as a compound involved in energy buffering, but also as a potential modulator of mitochondrial function. Experimental evidence suggests that creatine supplementation may help stabilize mitochondrial activity, reduce oxidative stress, and support overall cellular energy balance [8]. In addition, findings from preclinical studies indicate that creatine may have neuroprotective effects, possibly through mechanisms related to improved energy availability and a reduction in the production of reactive oxygen species [9].

1.3. Why the cognitive effects of creatine are important

Although the human brain makes up only about 2% of total body mass, it is responsible for consuming approximately 20% of the body's total oxygen levels, meaning about one fifth of the body's total energy consumption, which highlights just how metabolically demanding it actually is [10]. Cognitive functions such as memory, attention, and executive functions are particularly sensitive to changes in energy availability, and even small disruptions can impair their performance [11].

Situations that increase metabolic stress, such as sleep deprivation, cognitive exhaustion, or hypoxic conditions, have been shown to negatively affect cognitive performance. One of the key reasons for this seems to be a reduced availability of ATP in neurons during these states [11]. Given its role in maintaining cellular energy balance, creatine supplementation has been proposed as a strategy to support cognitive performance under such conditions [12].

Another relevant aspect is cognitive fatigue, which occurs during sustained mental activity. It has been associated with decreased productivity and overall cognitive performance, by decreasing people's ability to inhibit responses, process information and concentrate [13]. This problem is particularly important not only in everyday functioning but also in sport, where cognitive fatigue predominantly affects physical, technical, tactical, and perceptual-cognitive dimensions of the athlete's performance [14].

With aging, these issues may become even more pronounced. It has been noticed that when people get older, mitochondrial efficiency starts to decline. In consequence, cerebral energy metabolism and phosphocreatine availability are also impaired [15]. These changes are thought to contribute to age-related impairments in memory, executive function and attention [15]. As a result, in recent years, there has been a spike in studies considering the potential role of creatine supplementation as a nutritional strategy to support cognitive health in older populations.

Several of the previous studies in this area suggested that creatine could improve aspects of cognitive performance, including working memory and certain measures of intelligence [12]. More recent reviews and meta-analyses indicate that while these effects are generally modest, they may be more noticeable in older individuals or in situations where cognitive demands are particularly high [15].

1.4. Aim of the review

This narrative review aims to examine the current evidence on how creatine supplementation may influence cognitive performance and brain function. It also explores the mechanisms that might explain these effects, with a particular focus on energy metabolism and potential neuroprotective properties. Finally, the review considers what these findings might mean in practice, both for athletic performance and for maintaining overall brain health.

2. RESULTS / REVIEW OF EVIDENCE

2.1. Creatine metabolism and energy homeostasis in the brain

Creatine plays a fundamental role in maintaining energy balance in the brain, mainly due to its involvement in the phosphocreatine–ATP system. This system acts as a rapid energy buffer, allowing ATP to be quickly regenerated in situations where energy demand is temporarily greater than supply [2,3]. Previous biochemical studies have shown that phosphocreatine levels can shift rapidly in response to changes in neuronal activity, which emphasizes its role as a short-term energy reserve [3]. Given that neurons have a very limited ability to store energy and depend largely on oxidative phosphorylation, a stable ATP supply is essential for maintaining synaptic function and proper ion balance.

In the central nervous system, creatine crosses the blood–brain barrier through the SLC6A8 transporter, as demonstrated in studies on both animals and humans, especially while examining creatine deficiency syndromes [7]. When a disruption in this transporter occurs, the process can lead to severe neurological impairments, including intellectual disability, which emphasizes how important creatine availability is for optimal brain function [7]. Once inside the cell, creatine is phosphorylated to phosphocreatine, forming a readily available substrate of high-energy phosphates that can be used during periods of increased energy demands [3].

At the cellular level, creatine kinase enzymes are located at strategic sites to couple areas of high energy expenditure to the efficient regeneration of ATP [8]. This system facilitates the transfer of high-energy phosphates from mitochondria to areas of the cell where ATP is most needed, particularly synapses [6]. Experimental studies using brain tissue and in vivo models suggest that disruptions in this system are associated with reduced synaptic efficiency and increased vulnerability to metabolic stress [6,8]. By helping to stabilize ATP levels and buffer energy fluctuations, creatine may help stabilize neuronal metabolism and protect against temporary energy deficits, which can negatively affect cognitive performance.

2.2. Effects of creatine on cognitive performance

Memory

There is a growing body of research that examines how creatine supplementation affects memory performance. A systematic review by Avgerinos et al. [16], which included six studies (281 individuals) and covered both young and older adults, found that creatine supplementation was associated with improvements in short-term and working memory, with stronger effects observed in older populations. Similarly, a more recent meta-analysis by Prokopidis et al. [33] identified 8 RCTs examining the effect of creatine supplementation compared with placebo on measures of memory in healthy individuals. They found small but statistically significant improvements in memory compared with placebo. Furthermore, subgroup analyses revealed a significant improvement in memory in older adults (66–76 years) compared with their younger counterparts (11–31 years), especially in tasks requiring rapid information processing or recall under cognitively demanding conditions.

On the other hand, in four studies that tested short-term memory improvements [12,27,28,29], only two of them showed beneficial effects of creatine intake [12,27]. Apart from short-term memory, McMorris et al. also assessed long-term memory and found it improved in the creatine group [27].

Individual studies generally support these findings, although the size of the effect varies. Differences in study design, such as supplementation dose, duration, and participants' baseline creatine levels, likely contribute to these inconsistencies [16].

Working memory and intelligence

One of the most frequently cited studies in this area is the randomized, double-blind, placebo-controlled crossover trial conducted by Rae et al. [12]. In their work, they tested the hypothesis that oral creatine supplementation (5 g/day for six weeks) would enhance intelligence test scores and working memory performance in 45 young adult, vegetarian subjects. They found that creatine supplementation had a significant positive effect ($p < 0.0001$) on both working memory (backward digit span) and intelligence (Raven's Advanced Progressive Matrices), both tasks that require speed of processing. This study suggests that enhanced energy availability may directly support higher-order cognitive processes.

On the other hand, subsequent studies have produced mixed results [16]. While some have shown similar improvements in working memory, others have reported no clear effects. This suggests that the benefits of creatine may depend on factors like diet (for example, vegetarian versus omnivorous), task difficulty, and baseline brain creatine levels.

Processing speed and attention

Beyond memory, creatine has also been investigated in relation to processing speed and attention. In the meta-analysis by Xu et al. [18], four studies were analysed, encompassing a total of 128 participants. They assessed the potential effects of creatine supplementation on attention scores. The result indicates that, although individual studies show varying degrees of effect, creatine supplementation does not have a significant positive impact on attention scores when considered as a whole.

Furthermore, when it comes to processing speed, after analysing four studies that included a total of 104 participants and assessed the potential effects of creatine supplementation on processing speed scores, the authors found that although individual studies show varying degrees of effect, creatine supplementation does not have a significant positive impact on processing speed scores when considered as a whole [18].

Nevertheless, not all trials have observed the same results. Inconsistencies may be explained by methodological differences, including the type of cognitive tests used and the duration of supplementation.

2.3. Creatine under conditions of cognitive stress

The cognitive effects of creatine appear to be more noticeable under conditions of increased metabolic stress. McMorris et al. [19] conducted a study to further explore that matter, creating 24-h sleep deprivation conditions. Subjects were divided into a creatine group and a placebo group. They took creatine monohydrate or a placebo, depending on their group, for 7 days immediately prior to the experiment. The study was double-blind. Subjects undertook tests of random movement generation (RMG), verbal and spatial recall, choice reaction time, static balance and mood state pre-test (0 h) and after 6, 12 and 24 h of sleep deprivation, with intermittent exercise. They found that at 24 h, the creatine group demonstrated significantly less change in performance from 0 h (Δ) in RMG, choice reaction time, balance and mood state than the placebo group, suggesting a protective effect of creatine against sleep loss-induced cognitive decline.

Mental fatigue provides another relevant example. Prolonged cognitive effort is known to reduce attention and executive function, as demonstrated in studies measuring cerebral oxygenated hemoglobin levels during mental fatigue. In a study by Watanabe et al. [20], using a double-blind placebo-controlled paradigm, the authors demonstrated that a dietary supplement of creatine (8 g/day for 5 days) reduces mental fatigue when subjects repeatedly perform a simple mathematical calculation. After taking the creatine supplement, the task-evoked increase of cerebral oxygenated hemoglobin in the brains of subjects measured by near-infrared spectroscopy was significantly reduced, which is compatible with increased oxygen utilization in the brain. This suggests that in such conditions, creatine may help sustain cognitive performance by supporting ATP availability and delaying the onset of fatigue-related impairments.

Hypoxic conditions provide another example of metabolic stress. Reduced oxygen availability limits ATP production, which can impair cognitive function. Turner et al. [21] conducted a study involving fifteen healthy adults. Participants were supplemented with either creatine or a placebo for seven days. They were then exposed to a hypoxic gas mixture containing 10% oxygen for 90 minutes, which induced a global oxygen deficit and led to impairments in several neuropsychological functions, particularly attentional capacity. However, the decline in cognitive performance observed under hypoxic conditions was attenuated in the creatine-supplemented group. Participants maintained better attention levels, as well as corticomotor excitability. One possible explanation is that increased phosphocreatine stores help sustain neuronal membrane potentials during metabolic stress, thereby supporting cognitive function. Overall, creatine monohydrate supplementation appears to increase brain creatine levels, enhance corticomotor excitability, and reduce attention deficits associated with severe oxygen deprivation.

Taken together, these observations suggest that creatine may be particularly beneficial when the brain is operating under suboptimal metabolic conditions, rather than during normal, well-rested states.

2.4. Creatine and the aging brain

As people age, mitochondrial efficiency and overall brain energy metabolism tend to decline, which can negatively impact cognitive performance [15]. Studies indicate that phosphocreatine levels in the brain may also decrease with age, potentially contributing to reduced cognitive efficiency.

As a result, creatine supplementation has been explored as a possible strategy to support cognitive function in older adults. A review by Rawson and Venezia [5] suggests that creatine may improve performance in tasks involving memory and processing speed in elderly populations. Oliveira and colleagues [26] found that dietary creatine intake is positively associated with visuospatial short-term memory, where participants who consumed greater than the median of 0.382 g/day displayed significantly higher forward and backward Corsi scores. For intervention studies, McMorris et al. [27] reported a positive effect of creatine supplementation on forward number recall, spatial recall (both forwards and backwards), and long-term memory, but not random number generation or backwards number recall. Notably, according to Marshall et al. [15], none of the studies that examined global cognition using the Mini Mental State Examination reported an association or change with creatine supplementation.

The majority of systematic reviews emphasize that older individuals may experience greater cognitive benefits compared to younger adults [16].

One possible explanation is that age-related reductions in creatine synthesis and mitochondrial function make older adults more responsive to supplementation. However, the number of high-quality clinical trials in this group is still relatively small, and more research is needed before firm conclusions can be drawn.

2.5. Neuroprotective effects

In addition to its role in energy metabolism, creatine has been widely studied for its potential neuroprotective effects. The review by Adhietty and Beal [8] acknowledged that creatine can support mitochondrial function and increase resistance to metabolic stress in neuronal cells. These effects are likely linked to improved ATP buffering and increased phosphocreatine availability.

Creatine has also been associated with reduced oxidative stress, partly by limiting the production of reactive oxygen species and helping stabilize mitochondrial membranes [8,21]. Preclinical studies have explored its potential role in neurodegenerative conditions such as Parkinson's disease, Huntington's disease, and Alzheimer's disease (AD), where mitochondrial dysfunction and oxidative damage are key factors. However, current evidence suggests that creatine supplementation is not efficacious in the treatment of AD. Studies regarding treatment of Parkinson's and Huntington's disease are still inconclusive. Further clinical trials of

creatine supplementation in Parkinson's and Huntington's disease, as well as more creatine studies utilizing animal and cell-culture models of these diseases, are warranted to fully understand and appreciate the exact mechanisms by which creatine exerts its neuroprotective effects [8].

Although the current literature on creatine use in mild traumatic brain injury (mTBI) is limited, several studies address the role of creatine in aspects of the neurometabolic cascade associated with a concussion or mTBI [11]. In one study, the authors used creatine supplementation (0.4 g/kg/day in an oral suspension administered by nasogastric tube or spoon) after severe TBI (Glasgow Coma Scale 3–9 on hospital admission) in children and adolescents (1–18 years of age). They reported decreased duration of post-traumatic amnesia, intubation and hospital stay, and elicited improvements in neurophysical, cognitive, personality/behavior and social aspects within 3 months of the injury [22]. In follow-up publications from the same cohort of patients, it was reported that creatine supplementation resulted in improvements in post-traumatic headaches, dizziness and fatigue [23], as well as dysarthria and lingual problems of understanding [24].

Creatine supplementation could play a protective role in mTBI when consumed prophylactically [11]. Sullivan et al. [25] found that mice injected with creatine (3 mg/g/day) for 3 or 5 days prior to a moderate controlled cortical contusion had a 21% and 36% reduction in cortical damage, respectively, compared to placebo at 7 days following injury.

2.6. Safety and dosage

Creatine supplementation is widely regarded as safe when used at recommended doses. Evidence-based research has consistently shown that creatine supplementation with recommended dosages (i.e. 3–5 g/day or 0.1 g/kg of body mass/day) effectively increases tissue creatine stores and is relatively well tolerated [4]. Moreover, in a review by Kreider et al. [1], it has been shown that short- and long-term supplementation (up to 30 g/day for 5 years) is safe and well tolerated in healthy individuals and in a number of patient populations ranging from infants to the elderly. Importantly, extensive research has not demonstrated harmful effects on kidney or liver function in healthy populations, even with long-term use [1,4].

A number of different forms of creatine (e.g. creatine salts, creatine complexed with other nutrients, creatine dipeptides, etc.) have been marketed as more effective sources of creatine than creatine monohydrate [30]. However, according to Antonio et al., there are no peer-reviewed published papers showing that the ingestion of equal amounts of other creatine forms increases creatine storage in muscle to a greater degree than creatine monohydrate. In fact, most studies show that ingestion of these other forms has less physiological impact than creatine monohydrate on intramuscular creatine stores and performance [4].

In a normal diet that contains 1–2 g/day of creatine, muscle creatine stores are about 60–80% saturated [1]. The most effective way to increase muscle creatine stores is to ingest 5 g of creatine monohydrate (or approximately 0.3 g/kg body weight) four times daily for 5–7 days [31]. Once muscle creatine stores are fully saturated, creatine concentration can generally be maintained by ingesting 3–5 g/day. This protocol is most effective, although lower daily creatine supplementation dosing strategies (i.e. 3–5 g/day) are also well established throughout the scientific literature for increasing intramuscular creatine stores. However, while effective, these non-loading creatine supplementation dosing strategies delay maximum intramuscular creatine storage [4]. Additionally, it is worth mentioning that higher levels of creatine supplementation for longer periods of time may be needed to increase brain concentrations of creatine [32].

That said, individual responses to supplementation may vary, and factors such as baseline diet, hydration status, and overall health should be taken into account when considering creatine use.

3. DISCUSSION

3.1. Interpretation of findings

Overall, the current evidence base suggests that the cognitive effects of creatine supplementation are generally modest, yet relatively consistent across different types of studies. The literature indicates statistically significant improvements in selected domains such as short- and long-term memory [8,12,16,27]. However, current evidence suggests that although individual studies show varying degrees of effect, creatine supplementation does not have a significant positive impact on attention and processing speed [18]. Regarding working memory and overall intelligence, current studies have produced mixed results, often depending on the prior state of brain metabolism [12,16].

It is also important to note that the benefits of creatine supplementation are not evenly distributed across populations. Greater benefits tend to be observed in individuals exposed to metabolic stress, older adults, victims of mTBI or those with lower baseline creatine levels, such as vegetarians or vegans [11,12,16,17,19,21]. In contrast, healthy, well-rested young individuals often show little to no measurable improvement, which may help explain the variability seen across randomized controlled trials [8,16].

Taken together, this suggests that creatine should be viewed not as a traditional cognitive enhancer, but rather as a compound that supports brain energy metabolism in conditions when brain energy metabolism is compromised.

3.2. Potential mechanisms

Several mechanisms may explain the effects of creatine on brain function, with ATP buffering being the most well-established. By increasing phosphocreatine availability, creatine enhances the brain's ability to rapidly regenerate ATP, which is especially important in neurons characterized by high and fluctuating energy demands [2,3]. Neurochemical studies indicate that even relatively small increases in brain creatine levels may influence energy dynamics during cognitively demanding tasks [20].

Beyond its role in energy metabolism, creatine may also provide protective effects at the mitochondrial level. Experimental research suggests that it can help stabilize mitochondrial membranes, improve the efficiency of oxidative phosphorylation, and reduce the production of reactive oxygen species [8,9,11,21]. These mechanisms may be particularly relevant in pathological conditions where mitochondrial dysfunction plays a central role.

Another possible pathway involves neurotransmission. Because synaptic activity requires a high energy supply, improved ATP availability may support neurotransmitter release and recycling processes. Although direct evidence in humans is still limited, findings from animal and cellular models suggest that creatine may indirectly support synaptic efficiency and neuronal communication [6,18,33,34].

3.3. Practical implications

From a practical perspective, the cognitive effects of creatine appear to depend largely on the context in which it is used. In athletes, creatine is already widely recognized for its benefits in physical performance. However, its potential to support cognitive function, especially under fatigue or competitive stress, is often overlooked, although it may represent an additional advantage [12,13]. This could be especially relevant in sports that rely heavily on rapid decision-making and sustained attention.

In students and individuals exposed to prolonged cognitive effort, creatine may help reduce some of the negative effects of sleep deprivation and mental fatigue [13,19]. However, given the relatively small effect sizes reported in the literature, it is still unlikely to function as a primary cognitive enhancer. Rather, it may serve as a supportive strategy that may offer benefits in demanding conditions.

In older adults, the current evidence appears to be more promising. Age-related declines in mitochondrial function and brain energy metabolism may increase sensitivity to creatine supplementation. This mechanism could explain the more consistent improvements observed in this group [5,15,26,27]. While further research is still needed, at this point, creatine may serve as a simple and accessible option to support cognitive health in aging populations.

3.4. Limitations of current research

Despite increasing interest in this area, several limitations of the current evidence base should be acknowledged. Many randomized controlled trials are based on relatively small sample sizes, which limits statistical power and increases differences in outcomes [16,35].

Another important issue is the diversity of study protocols. Differences in supplementation protocols, time of intervention, and participant characteristics such as age and condition, make it difficult to directly compare findings. In addition, the cognitive tests used across studies differ in their sensitivity and specificity, which may further contribute to inconsistent findings [33,35].

A further limitation is that relatively few studies directly measure changes in brain creatine levels, which makes it difficult to identify a clear physiological link between supplementation and cognitive outcomes. This highlights an important gap in the literature.

3.5. Future research directions

Future research should focus on addressing these limitations by adopting more standardized and rigorous study protocols. In particular, there is a clear need for larger randomized controlled trials with longer intervention periods, because most of the existing evidence is based on relatively short-term supplementation [18,35].

Incorporating neuroimaging techniques could also provide valuable insight into how creatine affects brain metabolism *in vivo*. Such methods may help determine whether the cognitive effects observed are directly linked to changes in brain creatine levels [36,37].

Another important area for future work is to establish optimal dosing strategies for cognitive outcomes. Although daily doses of 3–5 g are generally sufficient to saturate skeletal muscle, it remains unclear whether the same approach is effective for the brain, given the more limited transport of creatine across the blood–brain barrier [32,36].

4. CONCLUSIONS

Overall, the evidence reviewed here suggests that creatine supplementation has small but fairly consistent effects on certain aspects of cognitive function. As discussed in the mentioned literature, the most reliable improvements have been observed in short-term and working memory, with some studies indicating improvements in long-term memory. In contrast, its impact on attention and processing speed appears limited or largely insignificant when results are considered collectively [8,12,16,18,27,28].

A key observation across studies is that these effects are highly context-dependent. Benefits are more pronounced in situations characterized by increased brain metabolic demand, such as sleep deprivation, prolonged mental effort, hypoxia, aging, lower baseline creatine levels or mild traumatic brain injury [5,11,19,20,21]. On the other hand, healthy, well-rested young individuals often show minimal or no measurable cognitive benefit [16]. This pattern suggests that creatine should not be considered as a classical cognitive enhancer, but rather as a compound that supports brain energy metabolism, especially under conditions in which this system is challenged.

From a physiological perspective, the effects of creatine are most plausibly explained by its role in cellular energy metabolism. By increasing phosphocreatine availability, creatine helps maintain ATP supply during periods of elevated demand [2,3]. In addition, its potential to stabilize mitochondrial function and reduce oxidative stress may further contribute to preserving neuronal integrity and resilience [8,9,21]. Although these mechanisms are well supported experimentally, their translation into clear and consistent cognitive benefits in humans remains limited.

In practical terms, creatine appears to be a safe and accessible intervention that may offer additional benefits beyond its well-established role in physical performance. It may be particularly relevant for populations experiencing metabolic stress or age-related declines in brain energy function [1,4]. At the same time, the current evidence base has clear limitations, including small sample sizes, short intervention periods, and considerable variability in study design [16,35]. The lack of direct measurements of brain creatine further complicates interpretation of the underlying mechanisms.

Taken together, creatine supplementation represents promising, yet modest, context-specific support for cognitive function, particularly when energy availability is compromised. However, current evidence does not justify its use as a general cognitive enhancer. Future studies should focus on larger, well-controlled trials, longer supplementation periods, and the use of neuroimaging techniques to better understand how changes in brain creatine levels relate to functional outcomes [18,36,37].

5. DISCLOSURE

5.1. Author's contribution

Conceptualization, MM and AU; methodology, ZO and AW; software, MGC; check, KF, KS, AU and OJ; formal analysis, KP and ZO; investigation, DK and MGC; resources, AW and KP; data curation, KF; writing — rough preparation, MM; writing — review and editing, OJ, DK and KS; visualization, ZO and KF; supervision, MM; project administration, AU and MGC. All authors have read and agreed with the published version of the manuscript.

5.2. Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

5.3. Institutional Review Board Statement

Not applicable.

5.4. Informed Consent Statement

Not applicable.

5.5. Conflict of Interest

The authors declare no conflict of interest.

5.6. Data Availability Statement

No new data were created or analysed in this study. All findings reported are based on publicly available literature retrieved from PubMed and Google Scholar. Data sharing is therefore not applicable to this article. The full list of references is provided below and all cited articles are available through their respective publishers via the DOI links provided.

5.7. Acknowledgements

The authors thank the Nicolaus Copernicus University in Toruń and the affiliated Poznań clinical centres for institutional support during the preparation of this manuscript. The authors also acknowledge the editorial team of Quality in Sport for their valuable comments during the peer-review process.

5.8. CRediT Author Contributions (taxonomy)

Mapped to the CRediT (Contributor Roles Taxonomy, NISO Z39.104-2022):

- **Conceptualization:** MM, AU
- **Methodology:** ZO, AW
- **Software:** MGC
- **Validation:** KF, KS, AU, OJ
- **Formal analysis:** KP, ZO
- **Investigation:** DK, MGC
- **Resources:** AW, KP
- **Data curation:** KF
- **Writing – original draft:** MM
- **Writing – review & editing:** OJ, DK, KS
- **Visualization:** ZO, KF
- **Supervision:** MM
- **Project administration:** AU, MGC

Declaration of the use of generative AI and AI-assisted technologies in the writing process

In preparing this work, the authors used ChatGPT for the purpose of improving language and readability, text formatting and verifying bibliographic styles. After using this tool, the authors have reviewed and edited the content as needed and accept full responsibility for the substantive content of the publication.

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