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Effects of Creatine Supplementation on Central Fatigue, Cognitive Function and Recovery in Physically Active Individuals: A Narrative Review

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Abstract

Background. Creatine monohydrate is widely used to support high-intensity exercise, strength, power and repeated-effort performance. Recent evidence suggests that its role may also extend to brain bioenergetics, mental fatigue, cognition and recovery.

Aim. This review summarizes evidence from 2018-2025 on creatine supplementation in relation to central fatigue, cognition, fatigue resilience and recovery in active individuals.

Methods. A narrative search was conducted mainly in PubMed, with additional searches in Quality in Sport, Journal of Education, Health and Sport and Pedagogy and Psychology of Sport. Priority was given to reviews, meta-analyses, trials and mechanistic studies on creatine, fatigue, cognition, sleep, recovery and sports performance.

Results. Creatine may support selected cognitive outcomes, especially under increased energetic demand such as sleep deprivation, mental fatigue or high training load. Potential mechanisms include ATP buffering, the creatine-phosphocreatine system, brain high-energy phosphate metabolism and recovery support. Evidence also suggests possible benefits for muscle function, soreness and exercise-induced muscle damage, although findings vary by protocol and outcome measure.

Conclusions. Creatine monohydrate may be useful not only for high-intensity performance but also for selected cognitive and recovery-related outcomes. Direct evidence for reducing central fatigue remains limited, and further sport-specific trials are needed.

Keywords: creatine supplementation, creatine monohydrate, central fatigue, mental fatigue, cognitive function, sleep deprivation, recovery, physically active individuals

1. Introduction

Creatine monohydrate is among the most extensively investigated dietary supplements in sport, exercise, and health-related contexts. Its classical role is linked to the creatine-phosphocreatine system, which supports rapid adenosine triphosphate resynthesis during short-duration, high-intensity muscular work. For this reason, creatine supplementation has been associated with improvements in strength, power, repeated sprint ability, resistance training adaptations, and intermittent high-intensity performance [18,23,25,29,30]. These effects make creatine particularly relevant for athletes and physically active individuals involved in resistance training, team sports, sprint-based activities, combat sports, and other disciplines requiring repeated high-energy efforts.

Although the muscular effects of creatine are well established, current literature increasingly considers creatine as a compound with broader physiological relevance. Creatine is present not only in skeletal muscle but also in the brain, where energy availability is required for neuronal activity, neurotransmission, ion gradient maintenance, and cognitive processing [8-10,28]. The brain has high and continuous energy demands; therefore, disturbances in energy metabolism may contribute to impaired cognitive performance, increased perceived effort, reduced alertness, and greater susceptibility to fatigue. This provides a rationale for examining whether creatine supplementation may support brain bioenergetics, cognition, and fatigue resilience.

Central fatigue is a multifactorial reduction in the ability of the central nervous system to generate or maintain voluntary motor output during or after demanding effort [2,4]. In sport and exercise settings, central fatigue may interact with peripheral fatigue and influence endurance, technical accuracy, reaction time, decision-making, motivation, and perceived exertion [1-5]. Mental fatigue is not identical to central fatigue, but it is commonly used as a practical model to study how prolonged cognitive effort can impair physical and sport-specific performance [1,3,5].

The relationship between creatine and central or mental fatigue remains emerging. One of the most relevant studies examined whether creatine could counteract the mental fatigue-associated decline in visuomotor skills [6]. Creatine improved selected outcomes, but it did not fully prevent fatigue-related impairment in sport-specific psychomotor performance [6]. Therefore, creatine should not be presented as a proven central anti-fatigue agent, but rather as a potentially supportive nutritional strategy whose effects may depend on fatigue model, outcome domain, and energetic stress.

A more consistent line of evidence concerns cognition under increased energetic demand. Systematic reviews and meta-analyses suggest possible benefits of creatine for memory, attention time, and information processing speed, although results are not uniform across populations or test batteries [7,12,13]. Effects may be more pronounced when brain energy metabolism is challenged by sleep deprivation, prolonged cognitive workload, aging, low dietary creatine intake, or combined physical and mental stress [9,10,13,14].

Post-exercise recovery is another key concern for physically active individuals. Recovery includes restoration of muscle function, reduction of soreness, repair of exercise-induced muscle damage, replenishment of energy substrates, and readiness for subsequent training or competition. Creatine may theoretically support recovery through improved phosphocreatine availability, ATP resynthesis, cellular hydration, and possible anti-catabolic or anti-inflammatory effects [18-22,28]. However, findings differ across protocols, exercise models, populations, and outcome measures.

The present narrative review summarizes evidence from 2018-2025 on the effects of creatine supplementation on central fatigue, cognitive function, sleep-related fatigue resilience, and post-exercise recovery in physically active individuals. It also discusses mechanisms, practical implications, limitations, and future directions. By integrating evidence from sport performance, brain bioenergetics, sleep-related fatigue, and recovery research, this article provides a balanced overview of creatine as a nutritional strategy that may extend beyond traditional muscular performance outcomes.

For a journal focused on sport quality, health, and physical activity, this topic is important because supplementation decisions should be evaluated not only by short-term ergogenic effects, but also by broader consequences for recovery quality, fatigue management, cognitive readiness, and safe practical use. Physically active individuals often train while studying, working, traveling, or coping with insufficient sleep. Therefore, a review that integrates muscular, central, cognitive, and recovery-related outcomes may help clinicians, coaches, and practitioners interpret creatine supplementation in a more complete way.

2. Literature Search Strategy

This narrative review was designed to summarize current evidence on creatine supplementation, central fatigue, cognitive function, sleep-related fatigue resilience, and post-exercise recovery in physically active individuals. It was not intended to be a systematic review or meta-analysis; therefore, no formal risk-of-bias assessment, protocol registration, or quantitative synthesis was performed.

The primary search was conducted in PubMed for articles published between January 2018 and December 2025. Search terms were used in different combinations and included: creatine, creatine monohydrate, creatine supplementation, central fatigue, mental fatigue, cognitive function, memory, attention, brain, brain bioenergetics, sleep deprivation, sleep, recovery, exercise-induced muscle damage, muscle soreness, athletes, sports performance, and physically active individuals.

The main search structure was: (creatine OR creatine monohydrate OR creatine supplementation) AND (central fatigue OR mental fatigue OR cognitive function OR cognition OR memory OR attention OR brain OR sleep deprivation OR sleep OR recovery OR exercise-induced muscle damage OR athletes OR physically active individuals) AND 2018-2025. Priority was given to systematic reviews, meta-analyses, randomized controlled trials, narrative reviews, and mechanistic studies relevant to fatigue, cognition, sleep, recovery, performance, mechanisms, or safety.

Additional targeted searches were conducted in Quality in Sport, Journal of Education, Health and Sport, and Pedagogy and Psychology of Sport to identify thematically relevant publications recommended by the journal submission guidelines. These sources were used as supplementary references, whereas the core evidence synthesis was based primarily on PubMed-indexed literature. Supplementary APCz publications were used to provide journal-relevant context on creatine facts and myths [31], physical performance and muscle recovery [32], brain function [33], cognitive function and mood [34], and supplement use in fitness populations [35].

Articles were included if they were published between 2018 and 2025, were relevant to creatine supplementation or creatine metabolism, and addressed fatigue, cognition, sleep, recovery, or sport performance. Articles were excluded if they were unrelated to creatine, lacked relevance to the review question, focused exclusively on clinical populations without interpretive relevance, or fell outside the predefined publication period. The selected literature was grouped into central and mental fatigue, cognition and brain bioenergetics, sleep-related fatigue resilience, post-exercise recovery, mechanisms, performance, and safety.

Table 1. Summary of selected evidence on creatine supplementation, fatigue, cognitive function, sleep-related fatigue resilience, and recovery.

Study	Design / population	Protocol / focus	Main finding and relevance
Van Cutsem et al. [6]	Human intervention study; mental fatigue and visuomotor skills	Creatine loading protocol	Creatine improved selected outcomes but did not fully prevent fatigue-related psychomotor impairment.
Avgerinos et al. [7]	Systematic review of RCTs; healthy individuals	Various protocols	Creatine may improve selected cognitive outcomes, especially memory-related tasks.
Forbes et al. [9]	Narrative review; brain function and health	Various protocols	Creatine may influence brain creatine content and selected cognitive outcomes.
Candow et al. [10]	Review; brain health and function	Various protocols	Creatine may be most relevant when brain energy demand is increased.
Sandkühler et al. [11]	Randomized controlled trial; healthy adults	Creatine 5 g/day for 6 weeks	Only small or limited cognitive effects, supporting cautious interpretation.
Prokopidis et al. [12]	Systematic review and meta-analysis	Various protocols	Creatine improved memory performance in healthy individuals.
Xu et al. [13]	Systematic review and meta-analysis; adults	Various protocols	Possible benefits for memory, attention time, and processing speed; larger trials needed.
Gordji-Nejad et al. [14]	Experimental human study; sleep deprivation	Single high-dose protocol	Creatine altered cerebral high-energy phosphate metabolism and improved selected cognitive outcomes.
Cruz et al. [16]	Human study; naturally menstruating females	Creatine in resistance-training context	Improved total sleep duration after resistance training days.
Maaoui et al. [17]	Randomized crossover trial; physically active men	Creatine loading protocol	Improved subjective sleep quality, cognition, intermittent output, and soreness, but not all objective markers.
Northeast and Clifford [19]	Systematic review and meta-analysis	Various protocols	Examined effects on exercise-induced muscle damage markers.
Jiaming and Rahimi [20]	Systematic review and meta-analysis of RCTs	Various protocols	Creatine may influence recovery after exercise-induced muscle damage.
Doma et al. [21]	Systematic review and meta-analysis	Various protocols	Effects on damage markers may differ between acute and chronic contexts.
Yamaguchi et al. [22]	Double-blind randomized trial; eccentric exercise damage	Creatine monohydrate protocol	May support recovery, with possible sex- and age-related differences.
Kreider et al. [30]	Critical review; safety and regulation	Various protocols	Creatine monohydrate is the best-supported form for efficacy, safety, and bioavailability.

3. Creatine and Central Fatigue

Central fatigue involves reduced voluntary motor output or impaired ability to maintain neural drive during or after demanding physical or mental effort. Unlike peripheral fatigue, which is primarily related to processes within skeletal muscle, central fatigue involves neural drive, motor unit recruitment, neurotransmitter function, perceived effort, motivation, and brain energy metabolism [2,4]. In physically active individuals, central fatigue may contribute to impaired endurance, slower reaction time, poorer decision-making, reduced technical precision, and lower tolerance of repeated efforts [1,3,5].

Mental fatigue provides a useful model for studying central components of performance decline. It is commonly described as a psychobiological state caused by prolonged cognitive activity and may increase perceived exertion, impair attention, and reduce motivation [1,3]. In sport, these effects are important because performance often depends on attention, pacing, tactical decisions, and motor control, not only on muscle function.

Creatine has been proposed as a possible nutritional strategy for central fatigue resilience because the creatine-phosphocreatine system supports cellular energy buffering. In the brain, phosphocreatine contributes to rapid ATP regeneration required for synaptic transmission, ion transport, and maintenance of membrane potentials [8-10]. This mechanism is particularly relevant when central energy demand is increased, such as during prolonged cognitive effort, sleep deprivation, intense exercise, or combined physical and mental stress.

Direct evidence remains limited. Van Cutsem et al. examined whether creatine could combat the mental fatigue-associated decrease in visuomotor skills [6]. Creatine improved selected outcomes, including strength endurance and prolonged cognitive performance, but did not fully prevent the negative effects of mental fatigue on sport-specific psychomotor performance [6]. This suggests that creatine may support some components of fatigue resistance without eliminating the complex performance decrements caused by mental fatigue.

Interpretation requires caution because central fatigue cannot be reduced to brain energy availability alone. Neurotransmitter changes, sleep status, perceived effort, thermoregulation, afferent feedback from working muscles, psychological stress, and individual differences in training status may all contribute to central fatigue [2,4,5]. Moreover, many studies on creatine and cognition have been performed in healthy adults rather than athletes exposed to exercise-related fatigue [7,11-13].

Overall, creatine should not yet be described as a proven central anti-fatigue intervention. The available evidence supports a more cautious conclusion: creatine may contribute to fatigue resilience by supporting energy availability in muscle and brain, especially under conditions of high cognitive or physiological demand. Future trials should combine physical exertion with cognitive load, validated central fatigue measures, neuromuscular assessments, and sport-specific outcomes.

A further methodological challenge is that central fatigue is difficult to quantify. Studies may use voluntary activation, transcranial magnetic stimulation, perceived exertion, endurance performance, cognitive tests, or sport-specific motor tasks, but these outcomes do not measure the same construct. For this reason, future research should avoid relying on a single fatigue endpoint and should combine neurophysiological, perceptual, cognitive, and performance-based assessments. Such an approach would better reflect real sporting situations, where an athlete may experience simultaneous reductions in drive, attention, technical precision, and muscular output.

The practical implication is that creatine may be more relevant for maintaining performance quality during demanding conditions than for producing an obvious increase in resting central nervous system function. This distinction is important for responsible communication. In physically active populations, the most realistic hypothesis is not that creatine eliminates fatigue, but that it may slightly improve resilience when the central nervous system and skeletal muscle are both exposed to high energetic demand.

4. Creatine and Cognitive Function

The possible effect of creatine supplementation on cognitive function has become an important research topic. Cognitive processes such as memory, attention, executive control, reaction speed, and decision-making require continuous energy availability. Because the brain contains creatine and phosphocreatine, supplementation may theoretically influence cognition by supporting high-energy phosphate metabolism [8-10,13].

Systematic reviews suggest that creatine may benefit selected cognitive domains, but effects are heterogeneous. Avgerinos et al. reviewed randomized controlled trials in healthy individuals and reported possible improvements in memory-related and intelligence-related tasks, while emphasizing methodological limitations [7]. Prokopidis et al. found that creatine supplementation improved memory performance in healthy individuals, with stronger effects in some subgroups [12]. Xu et al. reported potential benefits for memory, attention time, and information processing speed, but also highlighted the need for larger controlled trials [13].

Several factors may explain variability. Baseline creatine status, habitual diet, age, sex, training status, dose, supplementation duration, and type of cognitive task may influence responsiveness. Individuals with lower dietary creatine intake may theoretically respond differently, although this requires further investigation in physically active populations. The cognitive domain assessed is also important; memory, attention, processing speed, and executive function may not respond similarly.

The concept of metabolic stress is central. In rested healthy adults performing simple tasks, brain energy availability may be sufficient and the effect of supplementation may be small. During sleep deprivation, prolonged cognitive work, mental fatigue, hypoxia, or combined physical and cognitive stress, central energy demand may increase, potentially making creatine more relevant [9,10,14]. This may explain why effects appear more promising under challenging conditions than under resting conditions.

The randomized controlled trial by Sandkühler et al. is important because it prevents overinterpretation. Healthy adults supplemented with creatine for six weeks showed only small or limited cognitive effects rather than broad improvement across tasks [11]. Thus, creatine should not be considered a universal cognitive enhancer.

By contrast, Gordji-Nejad et al. reported that a single high dose of creatine during sleep deprivation altered cerebral high-energy phosphate metabolism and improved selected cognitive outcomes [14]. This study is highly relevant because it links supplementation with both mechanistic markers and functional performance under central energetic stress. For physically active individuals, this may apply to contexts involving poor sleep, travel, competition pressure, academic or occupational workload, and heavy training.

In many sports, performance depends on cognition as well as physical output. Attention, anticipation, reaction time, decision-making, motor control, and concentration under fatigue may determine success. Although creatine may help preserve selected cognitive functions under stress, direct evidence for improved sport-specific decision-making or cognitive-motor performance remains insufficient. Future studies should use sport-relevant cognitive tasks and fatigue models.

Overall, creatine supplementation may support selected cognitive outcomes, especially memory, attention-related measures, and processing speed under increased energetic demand. Its strongest cognitive rationale concerns brain energy metabolism, but current evidence remains context-dependent. Creatine should therefore be described as a supplement with emerging cognitive relevance, not as a guaranteed cognitive enhancer.

Another important issue is transfer to sport-specific cognition. Standard laboratory tests often assess isolated domains such as memory or reaction time, whereas sport performance requires integration of perception, anticipation, tactical interpretation, emotional control, and rapid motor execution. A small improvement in processing speed may be meaningful in some sports, but it may be irrelevant if it does not translate into decision quality or technical execution under pressure. Therefore, future studies should include cognitive-motor tasks that resemble the demands of the target sport.

The interaction between cognition and recovery also deserves attention. Poor recovery and sleep loss may reduce cognitive flexibility, increase perceived exertion, and impair motivation to train. If creatine supports cognition only under energetic stress, then the most useful populations may be those exposed to repeated physical and mental demands rather than rested individuals in laboratory conditions. This interpretation aligns with the broader view of creatine as an energy-supporting compound rather than a stimulant.

5. Creatine, Sleep Deprivation and Fatigue Resilience

Sleep is essential for recovery, mood regulation, neuromuscular function, cognitive performance, and training readiness. Sleep restriction can impair attention, reaction time, decision-making, motivation, perceived exertion, and ability to tolerate repeated training stress. For physically active individuals, sleep-related fatigue connects central fatigue, cognition, and recovery.

Creatine has gained interest as a potential support strategy during sleep loss because the creatine-phosphocreatine system contributes to ATP resynthesis. During sleep deprivation, the brain may experience increased energetic stress and reduced ability to maintain attention and executive control. Creatine may help preserve function by supporting high-energy phosphate availability [8-10,14].

Gordji-Nejad et al. examined a single high dose of creatine during sleep deprivation and reported changes in cerebral high-energy phosphate metabolism together with improved selected cognitive outcomes [14]. This provides mechanistic and functional support for the hypothesis that creatine may be most useful when the brain is under metabolic stress. However, sleep deprivation models are not identical to real-world sport fatigue and should be interpreted cautiously. A complementary mechanistic study further indicated that high-energy phosphate metabolism during sleep deprivation may show hemispheric asymmetry, supporting the rationale for considering brain energetics in fatigue-related models [15].

The practical relevance is substantial. Athletes, students, recreational exercisers, shift workers, and tactical populations may experience combined physical training, cognitive workload, psychological stress, travel, competition demands, and insufficient sleep. In such situations, fatigue includes central and cognitive components, not only muscular tiredness. If creatine helps maintain brain energy availability during sleep loss, it may have value as an adjunct during periods of incomplete recovery.

Evidence directly examining sleep outcomes remains limited. Cruz et al. reported that creatine improved total sleep duration after resistance training days in naturally menstruating females [16]. Maaoui et al. examined creatine loading in physically active men and found improvements in subjective sleep quality, cognitive performance, intermittent high-intensity output, and soreness, although not all objective sleep or recovery markers changed [17]. These studies suggest possible interactions between creatine, training stress, sleep, and recovery, but the evidence remains early.

Creatine should not be viewed as a substitute for sleep. Adequate sleep duration, consistent sleep timing, sleep hygiene, recovery planning, and training load management remain primary strategies. Creatine may be considered only as a supportive nutritional strategy in periods of increased energetic demand, temporary sleep restriction, or combined cognitive and physical stress. More trials using objective sleep measures, cognitive testing, recovery markers, and sport-specific outcomes are needed.

From an athlete management perspective, the key question is not whether creatine can compensate for chronic sleep loss, but whether it can reduce the acute cognitive consequences of unavoidable sleep restriction. Examples may include travel across time zones, congested competition schedules, overnight duties in tactical populations, or periods of academic examination combined with training. In these cases, creatine may be one element of a broader recovery plan, but it should be combined with sleep extension whenever possible, adequate nutrition, and careful adjustment of training load.

6. Creatine and Post-Exercise Recovery

Post-exercise recovery is a multidimensional process that includes restoration of muscle function, replenishment of energy substrates, reduction of soreness, repair of exercise-induced muscle damage, normalization of inflammatory responses, and readiness for subsequent exercise. For physically active individuals, recovery affects training quality, adaptation, injury risk, and long-term performance.

Creatine may support recovery primarily through the creatine-phosphocreatine system. By increasing intramuscular creatine and phosphocreatine stores, supplementation may improve ATP resynthesis during repeated efforts and between exercise bouts [18,28-30]. This is especially relevant for resistance training, repeated sprint activity, intermittent team sports, and exercise requiring repeated explosive actions.

Exercise-induced muscle damage is one of the most studied recovery outcomes. It often occurs after unaccustomed, high-volume, or eccentric exercise and may involve soreness, temporary strength loss, impaired range of motion, swelling, inflammation, and increased creatine kinase or lactate dehydrogenase. Creatine may theoretically support recovery by improving energy availability, cell hydration, glycogen storage, membrane stability, and possible anti-catabolic or anti-inflammatory responses [18-22,28].

Systematic reviews and meta-analyses suggest that creatine may influence selected recovery outcomes, but findings are heterogeneous. Northeast and Clifford analyzed human trials on markers of exercise-induced muscle damage [19], while Jiaming and Rahimi focused on randomized controlled trials examining recovery after exercise-induced muscle damage [20]. These reviews support creatine as a recovery-related supplement, but do not justify the claim that it consistently accelerates all aspects of post-exercise repair.

A key issue is the distinction between functional recovery and biochemical markers. Strength recovery, power, range of motion, repeated-effort capacity, soreness, and perceived readiness are practically meaningful outcomes. Biochemical markers such as creatine kinase provide indirect information and vary widely between individuals. Therefore, biochemical data should be interpreted alongside functional and subjective measures.

Doma et al. highlighted a paradoxical pattern in the literature: effects on muscle damage markers may differ between acute and chronic exercise contexts [21]. This matters because elevated markers do not always indicate poor adaptation or impaired performance. In training, some muscle damage and inflammation may be part of adaptation. The goal of supplementation should be to support function and training continuity, not necessarily to suppress all markers.

Recent trials provide applied evidence. Yamaguchi et al. examined creatine monohydrate and recovery from eccentric exercise-induced muscle damage while considering sex and age differences [22]. Maaoui et al. reported improvements in soreness and intermittent high-intensity output after creatine loading, although not all recovery markers changed [17]. These findings reinforce the need for multidimensional recovery assessment.

Practically, creatine may be most useful during high training frequency, eccentric loading, resistance training, repeated high-intensity sessions, or short recovery intervals. It may help maintain muscle function, reduce perceived soreness in some contexts, and support subsequent performance [17-22]. However, recovery is also influenced by sleep, energy intake, protein and carbohydrate availability, hydration, psychological stress, menstrual cycle phase, injury status, and training load. Creatine should be considered an adjunct, not a standalone recovery solution.

Another practical point is that recovery should be evaluated over both short and long time scales. Acute studies may examine soreness or strength loss after a damaging protocol, whereas long-term training studies may reflect the ability to accumulate more high-quality work. Creatine could support both processes through different pathways: immediate phosphocreatine availability may influence repeated bouts, while improved training tolerance may contribute to chronic adaptation. These possibilities should be separated in interpretation.

Recovery research should also consider the athlete's broader context. A supplement that slightly reduces soreness may have limited value if sleep, energy intake, or training load are poorly managed. Conversely, in a well-controlled training environment, even modest improvements in repeated-effort capacity or perceived readiness may be meaningful. Therefore, creatine should be integrated into individualized recovery planning rather than treated as an isolated solution.

7. Mechanisms Linking Creatine with Fatigue, Cognition and Recovery

The potential effects of creatine on fatigue, cognition, and recovery can be understood through overlapping mechanisms. The most established mechanism is the creatine-phosphocreatine system, which supports rapid ATP resynthesis during high energetic demand [8-10,14,28]. In skeletal muscle, this improves the ability to maintain force or power during repeated intense efforts and may accelerate recovery between bouts [18,28-30].

A similar energetic rationale may apply to the brain, although brain creatine responses to supplementation appear less predictable than muscle responses. The brain requires continuous ATP availability for synaptic transmission, ion gradient maintenance, neurotransmitter cycling, and information processing. When cognitive demand increases or sleep is restricted, brain energy metabolism may become more stressed. Creatine may help buffer ATP availability, which could explain why cognitive effects are more likely under metabolically demanding conditions [9,10,13,14].

Creatine may also support recovery through cellular hydration and osmotic effects. Creatine uptake into muscle is associated with increased intracellular water, which may affect cell volume and potentially create an environment favorable to anabolic signaling and reduced protein breakdown [26,28-30]. It may additionally contribute to energy shuttling between ATP production and utilization sites, thereby improving energy transfer in tissues with rapidly changing demands.

Inflammation and catabolism are additional areas of interest. Some evidence suggests that creatine may modulate recovery-related inflammatory or anti-catabolic processes, but findings are not uniform [18-22,28]. Inflammation is also a normal part of training adaptation, so creatine should not be described simply as an anti-inflammatory supplement. Its role is better framed as possible support of recovery processes under specific conditions.

The common concept linking these mechanisms is energy availability under stress. In muscle, the stressor may be repeated high-intensity contractions. In the brain, it may be sleep deprivation or prolonged cognitive effort. In recovery, it may be restoration after damaging or repeated exercise. Thus, creatine is best understood as a supplement that may support energetic resilience, rather than as a stimulant or universal fatigue-reducing agent.

Table 2. Proposed mechanisms linking creatine supplementation with fatigue, cognition, and recovery.

Mechanism	Biological target	Potential effect	Practical relevance
Increased phosphocreatine availability	Skeletal muscle	Faster ATP resynthesis during repeated intense efforts	Strength, power, sprint, resistance and intermittent sports
ATP buffering	Muscle and brain	Stabilization of cellular energy availability	Physical and cognitive stress
Brain high-energy phosphate support	Central nervous system	Preservation of cognition under metabolic stress	Sleep deprivation, mental fatigue, travel, high workload
Cellular hydration	Skeletal muscle	Possible support of anabolic environment	Training adaptation and fat-free mass changes
Recovery modulation	Skeletal muscle	Possible effects on soreness, function, and damage markers	Eccentric exercise, resistance training, congested schedules
Anti-catabolic or inflammatory pathways	Muscle and systemic tissues	Possible moderation of excessive stress responses	Recovery outcomes; evidence remains mixed

These mechanisms are not mutually exclusive. For example, improved phosphocreatine availability may support repeated physical efforts, while better cellular energy buffering may also help maintain cognitive function during sleep restriction. Similarly, recovery outcomes may result from interactions between energy availability, training capacity, cell hydration, and perception of soreness. This complexity explains why some outcomes improve while others remain unchanged within the same study.

8. Practical Implications for Physically Active Individuals

Creatine monohydrate is the best-supported form of creatine in terms of efficacy, safety, bioavailability, availability, and cost-effectiveness [29,30]. For most healthy physically active individuals, a common strategy is 3-5 g/day. An alternative is a loading phase of approximately 20 g/day divided into smaller doses for 5-7 days, followed by 3-5 g/day [29,30]. Loading saturates stores more rapidly, whereas lower daily dosing may achieve similar saturation over a longer period.

Creatine is most useful for activities characterized by repeated high-intensity efforts, including resistance training, sprinting, repeated sprint sports, combat sports, team sports, and interval-based training [18,23,25-27]. Benefits for steady-state endurance are less consistent [24], although creatine may still be relevant in endurance sports involving surges, climbs, accelerations, or sprint finishes [25].

For cognitive function and central fatigue, recommendations should be cautious. Evidence suggests possible benefits for selected cognitive domains, especially under sleep deprivation or high cognitive load, but not broad enhancement across all tasks [7,11-14]. Creatine may be most relevant for individuals facing demanding training schedules, travel, academic or occupational stress, or temporary sleep restriction. It should not be promoted as a universal cognitive enhancer or as a replacement for sleep.

For recovery, creatine may be considered during high training frequency, resistance training, eccentric loading, repeated intense sessions, or short recovery intervals [18-22]. Potential benefits include better maintenance of muscle function, reduced soreness in some contexts, and improved repeated-effort capacity. Decisions should be based on functional outcomes, perceived recovery, and training quality rather than isolated biochemical markers.

Sex-specific and dietary factors require attention. Women remain underrepresented in creatine research, although recent studies address active females and naturally menstruating women [16,27]. Current evidence does not require separate universal dosing guidelines for women, but more research is needed. Individuals with low dietary creatine intake, including vegetarians and vegans, may theoretically respond differently, especially for cognitive outcomes, but this requires further study.

Creatine monohydrate is generally well tolerated in healthy individuals when used at recommended dosages [29,30]. Common concerns about kidney damage, dehydration, or muscle cramps are not supported in healthy populations using appropriate protocols [29,30]. Mild gastrointestinal discomfort may occur, especially with large single doses, and can often be reduced by dose splitting or taking creatine with meals. Individuals with kidney disease, serious medical conditions, pregnancy, or medications affecting renal function or fluid balance should consult a healthcare professional before supplementation.

Table 3. Practical implications and limitations of creatine supplementation for physically active individuals.

Area	Potential benefit	Evidence strength	Practical note
Resistance training	Strength, power, training volume, fat-free mass	Strong	Most established application
Repeated high-intensity exercise	Better repeated-effort performance	Strong to moderate	Relevant for sprint, team, combat and interval sports
Steady-state endurance	Limited direct benefit	Limited	May be more relevant for surges or sprint finishes
Cognitive function	Possible support for memory, attention, processing speed	Emerging	Effects appear context-dependent
Sleep deprivation	Possible preservation of selected cognitive outcomes	Emerging	Not a replacement for sleep
Central fatigue	Possible support of energetic resilience	Preliminary	Direct sport-specific evidence remains limited
Recovery	Possible effects on soreness and functional recovery	Moderate but heterogeneous	Functional outcomes should be prioritized
Safety	Generally well tolerated in healthy adults	Strong	Caution with kidney disease or relevant medical conditions

Implementation should be individualized. Practitioners should first clarify the goal of supplementation: increased strength, better repeated-effort capacity, support during heavy training, recovery from eccentric exercise, or possible cognitive support during sleep restriction. Monitoring should include performance, body mass, gastrointestinal tolerance, subjective recovery, sleep, and training quality. This is especially important in weight-class sports or endurance contexts where changes in body mass may influence competition strategy.

Product quality is also relevant. Athletes subject to anti-doping rules should choose supplements from reputable manufacturers and, where possible, products tested by independent certification programs. Although creatine itself is not prohibited, contamination risk exists for dietary supplements in general. This practical point is important when translating evidence into safe use in competitive sport.

9. Limitations and Future Directions

Several limitations should be considered. First, this article is a narrative review, not a systematic review or meta-analysis. Although the search was structured and focused on 2018-2025, no formal risk-of-bias assessment, protocol registration, or quantitative synthesis was performed.

Second, studies differ in design, population, dose, duration, timing, use of loading phases, training status, and outcome measures. Participants include healthy adults, recreationally active individuals, trained athletes, older adults, active women, and mixed samples. This heterogeneity limits direct comparison and the strength of practical conclusions.

Third, direct evidence regarding creatine and central fatigue in physically active individuals is limited. Much interpretation is based on mental fatigue, cognition, sleep deprivation, and recovery studies. These domains are related but not identical to exercise-induced central fatigue. Future work should combine validated fatigue measures, neuromuscular outcomes, cognitive testing, subjective measures, and sport-specific performance.

Fourth, cognitive outcomes vary across memory, attention, processing speed, executive function, reaction time, and cognitive-motor tasks. Effects may depend on whether participants are rested or exposed to metabolic stress, such as sleep deprivation, intense exercise, or prolonged cognitive work.

Fifth, recovery studies often use biochemical markers such as creatine kinase, lactate dehydrogenase, or inflammatory markers. These do not always correspond to functional recovery, soreness, perceived readiness, or performance. Future studies should prioritize meaningful outcomes such as strength recovery, repeated-effort performance, movement quality, soreness, sleep quality, and ability to complete subsequent training.

Future randomized, double-blind, placebo-controlled trials should include physically active and athletic populations, standardized creatine monohydrate protocols, objective and subjective sleep assessment, cognitive testing under rested and fatigued conditions, and sport-specific performance tasks. Research should also examine sex-specific responses, dietary creatine intake, menstrual cycle-related factors, vegetarian and vegan populations, and combined stress models involving sleep restriction, travel, academic or occupational stress, and congested training schedules.

Finally, the time frame of this review should be considered. Restricting the main search to 2018-2025 allowed emphasis on recent evidence, but older foundational studies contributed to the development of creatine research. The present review therefore prioritizes current interpretation rather than historical completeness. Future updates may be needed as new studies on brain creatine, sleep, female athletes, and sport-specific fatigue become available.

10. Conclusions

Creatine monohydrate is a well-established supplement with strong evidence supporting strength, power, repeated high-intensity exercise capacity, and resistance training adaptations.

Current literature also suggests possible relevance beyond skeletal muscle, particularly for brain bioenergetics, cognitive function, sleep-related fatigue resilience, and selected recovery outcomes.

Creatine may support selected cognitive outcomes under increased energetic demand, such as sleep deprivation, prolonged cognitive effort, or combined physical and mental fatigue. Mechanistically, this may relate to ATP buffering and high-energy phosphate metabolism. However, cognitive effects are not uniform, and creatine should not be described as a universal cognitive enhancer.

Evidence regarding post-exercise recovery suggests possible benefits for muscle function, repeated-effort capacity, and perceived soreness, especially after resistance, eccentric, or high-intensity intermittent exercise. Nevertheless, findings vary by protocol, exercise model, participant characteristics, and outcome measure. Biochemical markers of muscle damage should be interpreted cautiously and preferably alongside functional outcomes.

Direct evidence linking creatine supplementation with reduced central fatigue in physically active individuals remains limited. The most appropriate conclusion is that creatine may contribute to fatigue resilience by supporting energy availability in muscle and brain under high physiological or cognitive demand, but it cannot yet be considered a proven central anti-fatigue intervention. Further sport-specific randomized controlled trials are needed.

Disclosure

Author Contributions

Conceptualization, Katarzyna Kopeć and Julia Ceryn; methodology, Katarzyna Kopeć, Julia Ceryn and Anna Wicher; validation, Anna Wicher, Emilia Bolesta-Okuniewska and Konrad Borkowski; formal analysis, Julia Ceryn and Anna Wicher; investigation, Anna Wicher, Emilia Bolesta-Okuniewska, Konrad Borkowski and Maja Radziwon; resources, Aleksandra Marchwińska-Pancer, Oskar Pastuszek and Paweł Michalak; data curation, Julia Ceryn, Anna Wicher and Emilia Bolesta-Okuniewska; writing - original draft preparation, Katarzyna Kopeć, Julia Ceryn, Anna Wicher and Emilia Bolesta-Okuniewska; writing - review and editing, Konrad Borkowski, Maja Radziwon, Aleksandra Marchwińska-Pancer, Oskar Pastuszek and Paweł Michalak; visualization, Julia Ceryn and Konrad Borkowski; supervision, Katarzyna Kopeć; project administration, Katarzyna Kopeć and Julia Ceryn; funding acquisition, not applicable. All authors have read and agreed to the published version of the manuscript.

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No new data were generated or analyzed in this study. Data sharing is not applicable to this article.

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The authors declare no conflict of interest.

Declaration of the Use of Generative AI and AI-Assisted Technologies in the Writing Process

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