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The influence of creatine on brain functioning – narrative review

Dominika Lewandowska,

ORCID https://orcid.org/0009-0002-4153-4634
E-mail: domi.lewandowska.dl@gmail.com

Dr. Anna Gostyńska Wolski Hospital

Marcina Kasprzaka 17, 01-211 Warsaw

Katarzyna Otrębska,

ORCID https://orcid.org/0009-0002-5169-5992

E-mail: kat.otrebska@gmail.com

Praski Hospital of the Transfiguration of the Lord,

al.“Solidarności” 67, 03-401 Warsaw, Poland

Aleksandra Makulec,

ORCID https://orcid.org/0009-0006-9990-7164

e-mail: omakulec@gmail.com

Medical University of Warsaw,

Żwirki i Wigury 63A, 02-091 Warsaw, Poland

Aleksandra Jóźwik-Szymańska
ORCID: https://orcid.org/0009-0005-7934-976X
email: ola444j@gmail.com
National Medical Institute of the Ministry of the Interior and Administration, Wołoska 137, 02-507 Warsaw, Poland

Natalia Kostecka,
ORCID https://orcid.org/0009-0009-6090-7484
email: kostecka.natalia@gmail.com
Grójec District Medical Center
Piotra Skargi 10, 05-600 Grójec, Poland

Laura Mikuła
ORCID: https://orcid.org/0009-0000-4827-2492
email: mikula.laura00@gmail.com
Czerniakowski Hospital
Stępińska 19/25, 00-739 Warsaw

Zuzanna Bogdan-Groszyk
ORCID: https://orcid.org/0009-0000-9211-0482
email: bgdn.zuzanna@gmail.com
Czerniakowski Hospital
Stępińska 19/25, 00-739 Warsaw

Aleksandra Szredzka
ORCID: https://orcid.org/0009-0007-8906-9379
email: aleksandra.szredzka@gmail.com
Dr. Anna Gostyńska Wolski Hospital
Marcina Kasprzaka 17, 01-211 Warsaw

Jan Kucharski

ORCID: https://orcid.org/0009-0006-3480-7998

e-mail: jkcharski@gmail.com

Praski Hospital of the Transfiguration of the Lord,

al.“Solidarności” 67, 03-401 Warsaw, Poland

Corresponding Author

Dominika Lewandowska, domi.lewandowska.dl@gmail.com

Abstract

Background: Creatine is a key component of cellular energy metabolism, with a well-established role in ATP resynthesis. Increasing attention has been directed toward its potential effects on brain function, including cognition, mood regulation, and neuroprotection.

Objective: To provide a narrative review of current evidence on the effects of creatine supplementation on brain function, with particular emphasis on cognitive performance, neurodegenerative diseases, and affective disorders.

Methods: A comprehensive literature review was conducted using PubMed, Scopus, and Web of Science databases. Included studies comprised randomized controlled trials, clinical trials, observational studies, and relevant experimental research assessing the impact of creatine on neurological and psychiatric outcomes.

Results: Creatine exerts its effects primarily through modulation of cellular bioenergetics, supporting ATP availability and mitochondrial function. Evidence indicates modest improvements in cognitive domains such as memory and processing speed, particularly under conditions of increased metabolic demand (e.g., sleep deprivation, cognitive fatigue). Data on neurodegenerative diseases are inconsistent; despite strong preclinical rationale, large clinical trials have not demonstrated significant therapeutic benefits. In affective disorders, especially depression, creatine shows potential as an adjunctive treatment, enhancing response to standard therapies. However, in bipolar disorder, supplementation may carry a risk of inducing manic or hypomanic episodes.

Conclusions: Creatine supplementation represents a biologically plausible, generally safe, and well-tolerated intervention with context-dependent effects on brain function. While it may provide modest cognitive benefits and potential support in depression, current evidence does not support its use as a primary therapeutic strategy in neurodegenerative diseases. Further

large-scale, well-designed studies are required to clarify its clinical utility in neuropsychiatric conditions.

Keywords: creatine, brain function, cognition, memory, processing speed, neurodegenerative diseases, depression, mood dissorders, mitochondrial function, ATP metabolism, neuroprocetion, supplementation

1. INTRODUCTION

In recent years, there has been growing interest in issues related to mental health and brain functioning, both in the general population and within the medical community. Increasing attention is being paid not only to the treatment of mental and neurological disorders, but also to strategies aimed at supporting cognitive functions, mood regulation, and overall mental performance. In this context, the identification of metabolic and nutritional factors that may influence central nervous system function has become particularly important. Creatine is an endogenous nitrogen-containing compound synthesized primarily in the liver, kidneys, and pancreas from arginine, glycine, and methionine. It plays a key role in adenosine triphosphate (ATP) resynthesis, especially under conditions of increased metabolic demand. Through a reversible reaction catalyzed by creatine kinase, phosphocreatine donates a phosphate group to adenosine diphosphate, thereby enabling the rapid regeneration of ATP. Although creatine is best known for its effects on skeletal muscle function, its significant role in the energy metabolism of neurons and glial cells provides the rationale for investigating its potential impact on brain function. [(1)] In recent years, an increasing number of studies have suggested that creatine supplementation may influence cognitive performance, mood, levels of mental fatigue, as well as regenerative processes within the central nervous system, including conditions such as stroke. At the same time, research findings remain inconclusive, and the mechanisms underlying creatine's action in the context of brain functioning are not yet fully understood.

The aim of this paper is to review the current state of knowledge regarding the effects of creatine on brain function, with particular emphasis on cognitive processes, mood disorders, post-stroke conditions, sleep quality, and the perception of fatigue.

2. MATERIAL AND METHODS

This study was conducted as a comprehensive narrative review of the available scientific literature examining the effects of creatine supplementation on brain function and mental health outcomes. A systematic literature search was performed using major electronic databases, including PubMed, Scopus, and Web of Science. The search strategy employed combinations of the following keywords: *"creatine supplementation," "brain function," "cognition," "neurodegenerative diseases," "mood disorders," "depression," "anxiety,"* and *"mental health."* Boolean operators (AND, OR) were used to optimize and refine the search results. The inclusion criteria comprised peer-reviewed clinical trials, randomized controlled trials, observational studies, and experimental studies that investigated the effects of creatine on neurological or psychiatric outcomes. Studies published in English and involving human participants were prioritized; however, selected animal studies were also included when they provided relevant insights into underlying mechanisms of action. Studies were excluded if they lacked relevance to central nervous system outcomes, focused exclusively on physical performance without assessing cognitive or psychiatric parameters, or did not provide sufficient methodological detail to allow for critical appraisal.

3. MECHANISMS OF ACTION

Creatine is an organic chemical compound that occurs naturally in the human body. The primary reservoir of creatine is skeletal muscle, which contains approximately 95% of the total creatine pool; the remaining 5% is distributed in cardiac muscle, smooth muscle, the brain, and the testes. [(2)] Within cells, creatine exists in two forms: free creatine and its phosphorylated form, phosphocreatine (PCr), which serves as a high-energy phosphate reserve. Creatine is transported to target tissues via a specific membrane transporter (SLC6A8), the expression of which has been demonstrated, among others, in neuronal cells and endothelial cells of the blood–brain barrier. [(3)] The primary mechanism of creatine action is based on its role in the creatine–phosphocreatine system, which enables the rapid resynthesis of adenosine triphosphate (ATP). This reaction is catalyzed by creatine kinase (CK) and involves the reversible transfer of a phosphate group from phosphocreatine to adenosine diphosphate (ADP), resulting in the regeneration of ATP. This mechanism is of particular importance in cells characterized by high and fluctuating energy demands, including neurons, where it contributes

to the stabilization of ATP levels and limits fluctuations in the ATP/ADP ratio. An important aspect of creatine's action is its influence on mitochondrial function. Evidence indicates that creatine participates in the regulation of oxidative phosphorylation and in the stabilization of the mitochondrial membrane potential, which translates into increased efficiency of ATP production. In addition, creatine reduces excessive generation of reactive oxygen species (ROS), thereby mitigating oxidative stress and protecting cellular structures from damage. These mechanisms are especially relevant in neural cells, which are highly sensitive to disturbances in oxidative and energetic homeostasis. Despite accounting for only approximately 2% of total body mass, the brain consumes nearly 20% of the body's total energy expenditure, underscoring the importance of the creatine–phosphocreatine system for its proper functioning. [(4)] Creatine plays a particularly significant role in tissues characterized by highly variable energy requirements, such as neurons. Dietary creatine constitutes an important supplement to the endogenous creatine pool and plays a significant role in maintaining systemic energy homeostasis. The primary dietary sources of creatine are animal-derived products, particularly meat and fish, in which creatine is present as a natural component of muscle cells. The highest concentrations of creatine are found in red meat and pelagic fish. The creatine content of raw meat products typically ranges from approximately 3 to 5 g/kg, although these values may vary depending on species, age of the animal, and the type of tissue. [(5)] [(6)]

4. CREATINE SUPPLEMENTATION

Creatine supplementation is one of the most extensively studied nutritional interventions, characterized by a well-established safety profile and clearly defined dosing strategies. Its use has been investigated not only in the context of physical performance, but also in neurological and psychiatric conditions.

Dosing strategies

The most commonly applied supplementation protocol consists of two phases: a loading phase followed by a maintenance phase. The loading phase typically involves the ingestion of 20 g of creatine monohydrate per day, divided into four equal doses, for a period of 5–7 days, leading to rapid saturation of tissue creatine stores. This phase is followed by a maintenance dose of 3–5 g per day, which is sufficient to sustain elevated creatine levels over time. [(7)]

Forms of creatine

Creatine is available in several supplemental forms, of which creatine monohydrate is the most extensively studied and clinically validated. Alternative formulations include creatine ethyl ester, creatine hydrochloride, buffered creatine, and creatine nitrate. Despite marketing claims,

current scientific evidence does not support the superiority of these alternative forms over creatine monohydrate in terms of bioavailability or efficacy. Notably, the majority of clinical trials investigating neurological or psychiatric outcomes have used creatine monohydrate, which therefore remains the reference standard.

Safety and adverse effects

Creatine supplementation is generally regarded as safe and well tolerated across a wide range of doses and supplementation durations. This favorable safety profile is supported by large-scale analyses of randomized controlled trials. Comprehensive reviews encompassing hundreds of clinical interventions have demonstrated no significant increase in the incidence of adverse effects in creatine-supplemented groups compared with placebo controls. Importantly, no dose–response relationship or association between supplementation duration and the risk of adverse events has been identified, even under conditions of higher dosing or long-term use. Reported side effects have been infrequent, mild, and nonspecific, most commonly including transient gastrointestinal discomfort or water retention within muscle tissue. Reports suggesting potential adverse effects of creatine on renal function, fluid–electrolyte balance, or muscle cramp incidence are not supported by the available clinical evidence. It should be emphasized that the majority of safety data pertain to creatine monohydrate, which remains the best-characterized and most extensively studied form of creatine [(8)]

Clinical considerations

The effects of creatine supplementation appear to be influenced by baseline creatine levels, metabolic status, and physiological demands. Individuals with lower endogenous creatine stores - such as vegetarians, older adults, or individuals experiencing metabolic stress - may derive greater benefit from supplementation. From a neuropsychiatric perspective, the therapeutic potential of creatine is most likely to be evident in conditions associated with impaired energy metabolism, rather than in healthy individuals with normal baseline brain function.

5. RESULTS

5.1. Creatine and Cognitive Function

Cognitive function comprises a set of mental processes that enable an individual to receive, process, store, and use information. These processes include both basic perceptual mechanisms and higher-order intellectual operations, such as reasoning and decision-making. Key cognitive domains include attention, memory, executive functions, processing speed, perception, and

language. The integrity of these processes is essential for everyday functioning. In recent years, interest in the effects of creatine on brain function has increased. Although creatine is commonly associated with improvements in physical performance, a growing body of evidence suggests that it may also have relevance in the modulation of cognitive function. The influence of creatine on cognition may be explained by several mechanisms. Creatine supplementation increases the availability of phosphocreatine in the brain, which may support the maintenance of stable ATP levels, particularly under conditions of elevated energy demand (e.g., intensive mental effort or stress). Another proposed mechanism involves the neuroprotective properties of creatine. [(9)] Current research indicates that creatine may affect neurotransmitter pathways in the brain not only indirectly through cellular bioenergetic regulation, but also directly as a neuromodulator, and potentially even as a novel type of neurotransmitter. Experimental data from recent years indicate that creatine is stored in synaptic vesicles and released in a manner dependent on action potentials and Ca^{2+} ions, thereby fulfilling key criteria for synaptic transmission.[(10)] Moreover, creatine has been shown to interact with major neurotransmitter systems, including the glutamatergic system (via modulation of the NMDA (N-methyl-D-aspartate) receptor and reduction of excitotoxicity), the GABAergic system (GABA_A - gamma-aminobutyric acid receptor), the serotonergic system (5-HT1A - 5-hydroxytryptamine receptor 1A - receptor), and adrenergic pathways, suggesting a broad regulatory effect on neuronal excitability. [(11)]. Creatine may also influence the glutamate–glutamine cycle by supporting glutamate conversion and reducing excessive glutamate concentrations, thereby limiting neurotoxicity associated with excessive excitatory transmission. [(12)] Consequently, through the integration of bioenergetic functions with modulation of neurotransmitter systems, creatine may stabilize synaptic activity and support neuronal homeostasis, which represents an important component of its neuroprotective action. These bioenergetic and neurochemical mechanisms may translate into measurable effects on specific cognitive domains, particularly those characterized by high energy requirements. Memory is one of the core cognitive functions, enabling the encoding, storage, and retrieval of information. Several forms of memory are distinguished, including short-term memory, working memory, and long-term memory, which involve distinct yet partially overlapping neural networks. Memory processes are highly energy-demanding, making them particularly sensitive to changes in ATP availability and mitochondrial function. Therefore, creatine - as a key element of cellular energy buffering - may play an important role in modulating memory processes. [(1)] A recent 2024 meta-analysis of randomized controlled trials demonstrated a statistically significant improvement in memory function following creatine supplementation. [(13)] This effect was

observed both in healthy individuals and in selected clinical populations. Attention and concentration represent another domain that may be influenced by creatine. In the aforementioned 2024 meta-analysis, creatine supplementation was shown to significantly improve reaction time and information-processing speed, although the strength of evidence for attention per se was rated as low to moderate. These findings suggest that creatine may enhance the efficiency of cognitive processes requiring rapid mobilization of energy resources, such as selective attention and sustained concentration. Available clinical data also indicate that creatine supplementation may affect information-processing speed. In an experimental study by Gordji-Nejad et al., a single high-dose creatine administration (0.35 g/kg) under conditions of partial sleep deprivation improved processing speed and overall cognitive performance. This effect was associated with changes in brain energy metabolism, including an increased phosphocreatine-to-inorganic phosphate ratio (PCr/Pi) and ATP levels, as well as stabilization of intracellular pH. These results suggest that creatine may support processing speed by increasing neuronal energy availability, particularly under conditions of increased metabolic burden such as sleep loss. [(14)] Overall, creatine may exert a limited effect on cognitive function, primarily through support of neuronal energy metabolism and neuroprotective mechanisms. Benefits appear to be most evident under conditions of increased brain energy demand, such as fatigue or aging. In healthy young individuals, the effects of supplementation remain relatively modest.

5.2. Creatine and Neurodegenerative Diseases

Particular attention has been directed toward the potential neuroprotective effects of creatine, including stabilization of mitochondrial function, reduction of oxidative stress, and inhibition of processes leading to neuronal cell death. Accordingly, its effects have been investigated in neurodegenerative diseases such as Parkinson’s disease, Huntington’s disease, and amyotrophic lateral sclerosis, as well as in acute conditions including ischemic stroke and traumatic brain injury. Despite promising preclinical findings - particularly in animal models - clinical results in humans remain inconclusive. In many cases, a meaningful therapeutic effect has not been confirmed, indicating the need for further research on efficacy, dosing, and central nervous system bioavailability of creatine. This section aims to summarize the current state of knowledge regarding the effects of creatine in selected neurological disorders and to discuss potential mechanisms of action in the context of neuroprotection. Alzheimer’s disease (AD) is a progressive neurodegenerative disorder whose pathogenesis involves complex interactions among β-amyloid accumulation, tau hyperphosphorylation, oxidative stress, and mitochondrial dysfunction. Increasing evidence suggests that disturbances in neuronal energy metabolism

represent one of the key features of the early stages of the disease. In this context, creatine - as an important component of the cellular energy-buffering system - has been proposed as a potential neuroprotective agent. The creatine–phosphocreatine system plays a fundamental role in maintaining ATP homeostasis in cells with high energy demand, such as neurons. In AD, mitochondrial efficiency and ATP production are reduced, which may impair synaptic function and exacerbate neurodegenerative processes. In theory, creatine supplementation may counteract these changes by increasing phosphocreatine availability and improving the efficiency of ATP regeneration.[(15)] In a pilot clinical study in patients with AD, creatine monohydrate supplementation (20 g/day for 8 weeks) was well tolerated, resulted in a significant increase in brain creatine concentrations (~11%), and was associated with improvements in selected cognitive outcomes. However, due to the single-arm design and small sample size, these findings are preliminary and require confirmation in randomized controlled trials. [(16)] Another condition investigated in the context of creatine supplementation is Parkinson's disease (PD). PD is a progressive neurodegenerative disorder characterized primarily by the loss of dopaminergic neurons in the substantia nigra and the presence of α-synuclein aggregates in the form of Lewy bodies. This results in characteristic motor symptoms, such as resting tremor, muscle rigidity, and bradykinesia, as well as numerous non-motor manifestations including cognitive impairment, depression, and sleep disturbances.[(17)] Oxidative stress, mitochondrial dysfunction, and impaired protein degradation pathways also play important roles in PD pathogenesis, contributing to progressive neuronal injury.[(18)] In a large, multicenter, randomized phase III clinical trial (NET-PD LS-1) involving 1,741 patients with early PD, creatine monohydrate supplementation (10 g/day) for up to 5 years did not affect disease progression compared with placebo. The trial was terminated early due to futility, and the results did not confirm earlier observations from preclinical studies and smaller clinical trials. [(19)] In a meta-analysis by Mo et al. (BMC Neurology, 2017), which included five randomized clinical trials involving 1,339 patients with PD, creatine supplementation showed no significant effects on motor function, activities of daily living, or overall Unified Parkinson's Disease Rating Scale (UPDRS) scores compared with placebo. [(20)] The limited efficacy of interventions targeting mitochondrial function and energy metabolism underscores the complexity of neurodegenerative mechanisms and highlights the need for alternative therapeutic strategies. In this context, increasing attention has been directed toward other neurodegenerative diseases with similar pathophysiological underpinnings, including Huntington's disease (HD), in which neuronal energy deficits and mitochondrial processes also play a central role. HD is an inherited, progressive neurodegenerative disorder with autosomal

dominant inheritance, caused by expansion of CAG repeats in the gene encoding huntingtin. This mutation results in a pathological protein that induces multiple cellular disturbances, including mitochondrial dysfunction, oxidative stress, transcriptional dysregulation, and excitotoxicity, leading primarily to degeneration of striatal neurons.[(21)] In a large randomized clinical trial (CREST-E) involving 553 patients with early HD, high-dose creatine supplementation (up to 40 g/day) for up to 4 years did not affect the rate of functional decline, leading to early termination of the study due to lack of efficacy.[(22)] In summary, creatine exhibits theoretical neuroprotective potential, primarily owing to its role in maintaining neuronal energy homeostasis and its effects on mitochondrial function and oxidative stress. However, despite promising preclinical findings, available clinical data in neurodegenerative diseases such as AD, PD, and HD remain limited and largely do not demonstrate a clinically meaningful therapeutic effect.

5.3. Creatine and Affective Disorders

Affective disorders, including unipolar depression and bipolar disorder, are among the most prevalent psychiatric conditions and constitute a major health and societal burden. Their pathogenesis is multifactorial and involves neurotransmission abnormalities, inflammatory processes, dysregulation of the hypothalamic–pituitary–adrenal axis, and disturbances in mitochondrial function and brain energy metabolism. Increasing evidence indicates that neuronal bioenergetic deficits may play a significant role in the development of depressive symptoms by affecting synaptic plasticity, neural network function, and mood regulation.[(23)] In this context, creatine - as a compound central to cellular energy buffering - has attracted interest as a potential adjunctive treatment for affective disorders. Depression is one of the most common mental disorders worldwide and is characterized by persistent low mood, loss of interest, and reduced energy, leading to substantial impairment in social and occupational functioning. Its course may be episodic or recurrent, and its etiology is multifactorial, involving interactions among biological, psychological, and environmental factors.[(24)] Recent clinical studies suggest that creatine may have an adjunctive effect in the treatment of depression, particularly as an add-on to standard therapy. In a randomized clinical trial, creatine supplementation as an adjunct to cognitive-behavioral therapy (CBT) resulted in a greater reduction in depressive symptoms compared with placebo, with good tolerability and safety.[(25)] In a randomized double-blind clinical trial by Lyoo et al. (PMID: 22864465), creatine was evaluated as an augmentation strategy in women with major depressive disorder receiving an SSRI. Compared with placebo, creatine supplementation was associated with a faster and greater reduction in symptom severity during the early phase of treatment. These

findings suggest a potential supportive role of creatine in SSRI-based antidepressant therapy; however, given the limited sample size, confirmation in larger clinical trials is required.[(26)] In addition to depression, affective disorders include bipolar disorder (BD), which is characterized by recurrent depressive episodes and episodes of mania or hypomania. The clinical presentation is heterogeneous and involves not only mood disturbances but also changes in psychomotor activity, cognitive function, and regulation of sleep and circadian rhythms.[(27)] As in depression, neurobiological abnormalities contribute to BD pathogenesis, including neurotransmitter dysregulation, inflammatory processes, and disturbances in mitochondrial function and brain energy metabolism. Accordingly, mechanisms implicated in the potential effects of creatine in depression may also be relevant to BD, providing a rationale for investigating its use in this group of disorders. In a randomized double-blind clinical trial conducted in patients with bipolar depression, adjunctive creatine supplementation (6 g/day) was associated with a greater reduction in depressive symptoms and a higher remission rate compared with placebo. However, cases of switching to hypomania or mania were reported, indicating a potential risk associated with creatine use in this population. [(28)] Clinical reports suggest that creatine supplementation may carry a risk of inducing manic or hypomanic episodes in patients with BD, which represents an important limitation to its potential therapeutic application in this patient group.[(29)]

6. Discussion

The present review synthesizes current evidence regarding the effects of creatine supplementation on brain function, with particular emphasis on cognitive performance, neurodegenerative diseases, and affective disorders. The available data indicate that the primary effects of creatine are mediated through modulation of cellular bioenergetics, with secondary influences on neurotransmission, oxidative stress, and neuroprotective mechanisms. Nevertheless, despite a biologically plausible and well-characterized mechanism of action, the clinical efficacy of creatine in disorders of the central nervous system remains inconsistent. One of the most robust and conceptually coherent findings concerns the role of creatine in supporting cerebral energy metabolism. The creatine–phosphocreatine system constitutes a fundamental buffer for ATP resynthesis, particularly in tissues characterized by high and fluctuating energy demands, such as the brain. This mechanism appears to be especially relevant under conditions of metabolic stress, including sleep deprivation, hypoxia, and increased cognitive load. In such circumstances, creatine supplementation may enhance phosphocreatine availability, stabilize ATP concentrations, and improve neuronal energetic efficiency. This observation may help

explain why the most consistent cognitive benefits are reported not under baseline conditions, but rather in states associated with increased energetic demand. With respect to cognitive function, the evidence suggests modest yet measurable benefits, particularly in domains such as memory and processing speed. Meta-analytic findings indicate a statistically significant improvements in memory performance following creatine supplementation, although the observed effect sizes are generally small to moderate. Effects on attention and executive functions are less consistent and often limited by methodological heterogeneity across studies. Importantly, the magnitude of cognitive effects appears to be influenced by baseline creatine levels, with greater benefits observed in individuals with lower dietary intake - such as vegetarians - or in conditions associated with cognitive fatigue. In contrast, in young and otherwise healthy individuals with normal baseline energy metabolism, the effects of supplementation appear limited. The potential neuroprotective role of creatine has been extensively explored in the context of neurodegenerative diseases. Preclinical studies provide strong evidence that creatine can mitigate mitochondrial dysfunction, reduce oxidative stress, and inhibit apoptotic pathways, thereby supporting neuronal survival. These findings established a compelling rationale for clinical translation. However, large-scale randomized controlled trials conducted in disorders such as Parkinson's disease and Huntington's disease have failed to demonstrate clinically meaningful therapeutic benefits. This discrepancy between preclinical and clinical outcomes likely reflects multiple contributing factors, including limited creatine penetration across the blood–brain barrier, suboptimal dosing strategies, the stage of disease at the time of intervention, and the multifactorial nature of neurodegeneration, which extends beyond bioenergetic dysfunction alone. In the domain of affective disorders, particularly unipolar depression, the available evidence appears more encouraging. Several randomized studies indicate that creatine supplementation may augment the effects of standard antidepressant treatments, such as selective serotonin reuptake inhibitors, resulting in faster and more pronounced symptom reduction. These effects may be related to the correction of neuronal bioenergetic deficits observed in depressive states, as well as to modulatory effects on neurotransmitter systems. Nevertheless, the current evidence base is limited by small sample sizes and considerable heterogeneity of study populations. Moreover, in bipolar disorder, the potential risk of triggering hypomanic or manic episodes represents a clinically significant concern, which substantially limits the therapeutic applicability of creatine in this patient group. An important theme emerging from this review is the context-dependent nature of creatine's effects. While its biological function is well established and mechanistically sound, its clinical impact appears to be strongly influenced by variables such as dosage, duration of

supplementation, baseline metabolic status, dietary intake, and the presence of underlying neuropathology. Furthermore, substantial variability in study design - including differences in cognitive outcome measures, supplementation protocols, and participant characteristics - limits comparability across studies and contributes to the observed inconsistency of findings. Several limitations of the current body of evidence must therefore be acknowledged. Many studies are characterized by relatively small sample sizes, short intervention periods, and a lack of standardized outcome measures. In addition, there is a notable scarcity of high-quality randomized controlled trials specifically focused on neuropsychiatric endpoints. Methodological heterogeneity further complicates interpretation and precludes firm conclusions regarding clinical efficacy. Future research should prioritize well-designed, large-scale randomized controlled trials employing standardized supplementation protocols and validated outcome measures. Particular emphasis should be placed on identifying subpopulations most likely to benefit from creatine supplementation, such as individuals with documented metabolic impairments, patients in early stages of neurodegenerative disease, or those with treatment-resistant depression. Further investigation into the pharmacokinetics of creatine within the central nervous system and strategies aimed at enhancing brain bioavailability may also be critical for optimizing therapeutic potential.

7. Conclusions

Creatine plays a central role in brain energy metabolism and represents a biologically plausible modulator of central nervous system function. Current evidence suggests that creatine supplementation may confer modest benefits in selected cognitive domains, particularly memory and processing speed, primarily under conditions of increased metabolic demand. Despite strong preclinical support for its neuroprotective properties, clinical data in neurodegenerative diseases remain inconsistent and do not confirm a significant therapeutic effect. In affective disorders - especially unipolar depression - creatine shows promise as an adjunctive treatment; however, the available evidence remains limited and requires further validation. The risk of inducing manic or hypomanic symptoms in bipolar disorder constitutes an important clinical consideration. Creatine supplementation is generally safe and well tolerated when administered within recommended dosing ranges. Overall, creatine should be regarded as a supportive, context-dependent intervention rather than a primary therapeutic strategy. Further high-quality clinical studies are necessary to clarify its role and clinical utility in neuropsychiatric conditions.

Keywords: creatine; brain function; cognition; memory; processing speed; neurodegenerative diseases; depression; mood disorders; mitochondrial function; ATP metabolism; neuroprotection; supplementation

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Author's Contribution:

Conceptualization: Dominika Lewandowska, Katarzyna Otrębska, Aleksandra Szredzka, Helena
Muszyńska;
methodology: Zuzanna Bogdan-Groszyk;
check: Jan Kucharski, Aleksandra Jóźwik-Szymańska, Aleksandra Makulec
data curation; Natalia Kostecka, Laura Mikuła
investigation: Dominika Lewandowska, Katarzyna Otrębska, Aleksandra Szredzka, Helena Muszyńska;
resources: Jan Kucharski, Aleksandra Szredzka, , Helena Muszyńska;
writing-rough preparation: Dominika Lewandowska, Aleksandra Szredzka, Helena Muszyńska;
writing-review and editing: Aleksandra Makulec, Aleksandra Szredzka, Helena Muszyńska;
visualization: Natalia Kostecka, Laura Mikuła, Katarzyna Otrębska;
supervision: Katarzyna Otrębska, Dominika Lewandowska, Aleksandra Jóźwik-Szymańska
project administrator: Dominika Lewandowska
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