Psychiatr. Pol. ONLINE FIRST Nr 400: 1–10
Published ahead of print 11 June 2026
www.psychiatriapolska.pl
ISSN 0033-2674 (PRINT), ISSN 2391-5854 (ONLINE)
DOI: https://doi.org/10.12740/PP/OnlineFirst/220253

The impact of creatine on brain functions

Tymoteusz Borowski[1], Maria Zimoń[1], Magdalena Piegza[1,2]

[1] Student Scientific Association, Department of Psychiatry, Faculty of Medical Sciences in Zabrze, Medical University of Silesia in Katowice, Tarnowskie Gory, Poland

[2] Department of Psychiatry, Faculty of Medical Sciences in Zabrze, Medical University of Silesia in Katowice, Tarnowskie Gory, Poland

Summary

As an endogenous compound essential for energy homeostasis, creatine holds a fundamental role in the bioenergetics of the brain, an organ with high metabolic requirements. This review provides a synthesis of current knowledge on the impact of creatine on the functions of the central nervous system (CNS). The brain, which is capable of de novo creatine synthesis, demonstrates an increase in its internal concentrations following supplementation; however, this effect is less significant than in muscle tissue and is constrained by the blood-brain barrier, among other factors. The development of effective CNS-targeted dosing strategies remains a subject of ongoing research. An overview of the literature suggests that creatine supplementation may beneficially influence cognitive performance, particularly under conditions of elevated metabolic demand like stress or sleep deprivation, with the potential to enhance memory and mitigate fatigue. Nonetheless, findings from the cited research are inconsistent due to methodological heterogeneity and a common failure to directly measure brain creatine levels. Reports on creatine's antidepressant properties are particularly encouraging, with preclinical and initial clinical studies pointing to its potential utility (e.g., via the mTORC1 pathway) in augmenting mood disorder treatments. Moreover, the authors examine the use of creatine in chronic fatigue syndrome, where evidence supports improvements in physical performance and reductions in pain intensity, although its effect on generalized fatigue remains ambiguous.

Key words: depression, cognitive functions, creatine

Introduction

Creatine, chemically identified as 2-[carbamimidoyl(methyl)amino]acetic acid or methyl guanidoacetic acid, is a naturally occurring nitrogenous organic acid present in animal tissues. Its initial discovery is credited to Michel Chevreul in 1832, with its chemical structure being detailed by Justus von Liebig in 1847. The name "creatine" is derived from the Greek *kreas* (meat), a reference to its original source, muscle tis-

sue, from which it was isolated through alkalization. Notably, Justus von Liebig, also regarded as a foundational figure in biochemistry, funded a significant portion of his research by manufacturing and selling a popular meat extract containing approximately 8% creatine [1]. This demonstrates that its potential as a dietary supplement was recognized even by its earliest investigators.

For several decades, the consequences of creatine monohydrate intake, including its effect on muscle concentrations and subsequent impact on physical performance, have been thoroughly studied. It was first noted in the 1990s that consuming creatine monohydrate results in about a 20% increase in its intramuscular content [2].

The primary biological function of creatine is to facilitate the rapid regeneration of adenosine triphosphate (ATP) when its consumption is high. This occurs via the transfer of a phosphoryl group from phosphocreatine to adenosine diphosphate (ADP), a reaction catalyzed by creatine kinase (CK). The creatine-phosphocreatine system thereby serves as a crucial 'energy buffer,' playing a key role in maintaining ATP homeostasis in tissues with high metabolic rates [3].

In a manner analogous to its role in muscle, elevating creatine levels in the brain may also yield certain advantages. The brain contains a minor fraction of the body's total creatine, estimated at under 5%, while muscle tissue constitutes the main reservoir, holding as much as 95% [4]. Despite this, the brain exhibits an exceptionally high metabolic rate, and creatine is vital for its energy metabolism processes, similar to its function in skeletal muscle. Evidence supporting this notion includes the presence of creatine kinase isoforms within the CNS, as well as the occurrence of psychiatric disorders resulting from creatine deficiency in the brain. Such deficiency may arise from rare, inherited disorders of creatine synthesis or transport, including creatine transporter deficiency caused by mutations in the *SLC6A8* gene, which leads to severe neurodevelopmental impairments and does not respond to creatine supplementation. In certain acquired psychiatric conditions, including depression, a secondary reduction in brain creatine levels has also been reported, and supplementation with creatine monohydrate has been investigated as a potential approach for partially alleviating some symptoms [5].

The impact of creatine supplementation on brain function is governed by multiple potential mechanisms. As an organ with substantial metabolic activity, the brain accounts for roughly 20% of the body's basal energy expenditure, despite comprising only 2% of total body mass. Its proper functioning – including maintaining membrane potentials, conducting action potentials, and ensuring signal transmission – is therefore contingent upon a constant energy supply [6]. In circumstances of accelerated brain ATP turnover (e.g., during complex cognitive processing) or disrupted bioenergetics (e.g., hypoxia, sleep deprivation, or various neurological diseases), an external supply of creatine helps to preserve stable brain ATP levels [7].

Aim, material, and methods

This paper is a review aimed at organizing the current knowledge regarding the impact of creatine supplementation on brain function, based on studies published be-

tween 2002 and 2025 and indexed in the PubMed database. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) protocol was used to present the data selection and analysis process. Data collection was conducted from April to June 2025, limited to publications in the English language. The time frame covered the years 2002–2025, which allowed for the inclusion of current 21st-century scientific findings in the discussed area. Both review and original research articles were included, focusing on the effects of creatine supplementation on: brain creatine/phosphocreatine levels, cognitive functions, depressive symptoms, and symptoms of chronic fatigue syndrome. The literature search in the PubMed database yielded 2,807 articles using the following phrases: "brain creatine," "creatine and depression," "creatine and cognitive function," and "creatine and Chronic Fatigue Syndrome." After a thorough analysis of the articles, 34 papers were ultimately qualified for inclusion (Figure 1).

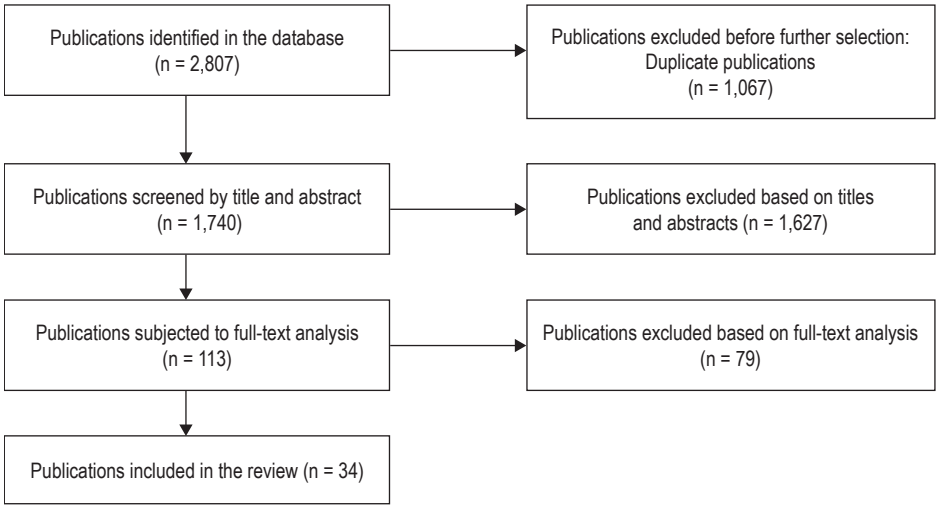

Figure 1. **The diagram illustrates the selection of publications utilized in this review**

The impact of exogenous creatine on brain creatine levels

Creatine is made available to the body through both dietary intake and endogenous synthesis in organs like the liver, pancreas, and kidneys. Daily creatine consumption from food is variable but is estimated to be 1 to 4 grams for individuals who regularly consume meat. The primary dietary sources are meat and fish, containing an average of 3 to 5 grams of creatine per kilogram of raw tissue. Skeletal muscle cannot synthesize creatine de novo and thus readily uptakes it from both internal production and external dietary sources. The brain, conversely, can produce its own creatine and does not seem to depend on synthesis from other organs or on dietary intake [8].

It has been suggested that muscle creatine levels might decline with advancing age, though this could be a consequence of reduced physical activity rather than the aging process itself. Similarly, brain creatine levels may also fall with age, but this could be attributed to decreased neuronal activity or specific pathological states. Moreover, recent research indicates that healthy young and older adults can possess comparable brain phosphocreatine concentrations [9].

It has been shown that while a vegetarian diet, which is low in creatine, leads to a decrease in muscle creatine content [10], no significant differences in brain phosphocreatine levels have been observed between vegetarians and omnivores [11].

In contrast to the well-defined supplementation protocols for increasing skeletal muscle creatine, an optimal dosing regimen for effectively elevating its levels in the brain remains largely unestablished. This is due to a scarcity of data from studies directly measuring the influence of supplementation on creatine content within brain tissue.

Although the direct measurement of muscle creatine is feasible through biopsy analysis, its assessment in the brain is more complex. Techniques like proton (^{1}H-MRS) and phosphorus (^{31}P-MRS) magnetic resonance spectroscopy are utilized for this purpose [12]. The limited accessibility and high expense of this methodology, however, have constrained the number of studies conducted. Furthermore, creatine content appears to be highly region-specific within the brain, complicating direct comparisons between studies that have measured it in different areas [12]. Nevertheless, available data indicate that supplementation leads to an increase in brain creatine/phosphocreatine concentrations; however, the relative magnitude of this increase is smaller than that typically observed in skeletal muscle. It is estimated that brain creatine levels rise by approximately 10%, whereas increases of up to around 20% may be observed in skeletal muscle. This disparity represents one of the factors contributing to the lack of a clear consensus regarding optimal creatine dosing strategies in the context of effects on the CNS [2].

Several factors may explain the different uptake dynamics of creatine in muscle versus brain tissue. The brain may engage in a compensatory response to creatine ingestion by downregulating its endogenous synthesis, thereby maintaining a homeostatic level despite supplementation [13]. Additionally, the permeability of the blood-brain barrier to circulating creatine is thought to be restricted, likely due to a low expression of the creatine transporter on the astrocytes that form the barrier [14]. It is therefore theorized that higher doses or longer durations of supplementation might be required to increase brain creatine levels. Interestingly, some reports suggest that guanidinoacetic acid (GAA), a natural precursor to creatine, might be more effective at raising brain creatine content than an equivalent dose of creatine itself [15]. Accordingly, GAA may represent a promising pharmacological approach for modulating creatine levels in the central nervous system, potentially exceeding the effectiveness of creatine supplementation alone.

The influence of creatine on cognitive functions

Despite numerous reports of positive outcomes, direct comparisons across studies of creatine supplementation are hindered by significant methodological variations. These differences involve study populations, cognitive assessment tools, and the specifics of dosing regimens and duration. Still, the collective body of evidence suggests that creatine supplementation can exert a beneficial influence on select cognitive domains in various research contexts.

For instance, creatine supplementation has been shown to improve cerebral oxygen utilization and reduce mental fatigue during repetitive computational tasks [16]. Notably, the effects of creatine often become more apparent under conditions of heightened physiological stress, such as during hypoxia or sleep deprivation combined with physical exercise. It is also hypothesized that more cognitively demanding processes, due to their greater energy needs, might be more responsive to increased creatine availability [17].

The data on the effects of creatine supplementation on cognitive function in older adults are inconsistent. While some studies have reported improvements [18], others have failed to confirm its efficacy, either as a standalone intervention or when combined with exercise training [19]. A major limitation of many of these studies is the lack of brain creatine measurements. This makes it difficult to determine whether the observed age-related cognitive decline results from neurodegenerative processes or if the supplementation protocol was simply inadequate to significantly elevate brain phosphocreatine levels. This issue warrants further investigation.

A prevailing hypothesis is that vegetarians may respond differently to creatine supplementation than meat-eaters [20]. In some studies, a stronger effect of supplementation on memory performance has been observed in vegetarians compared with individuals consuming a mixed diet [21]. However, it should be emphasized that the observed differences may have resulted not from improvements in the vegetarian group but rather from a deterioration of the assessed parameters in the control group, which substantially limits the possibility of unambiguous interpretation of these findings. Moreover, available neurochemical data indicate comparable baseline brain creatine concentrations in individuals consuming meat and in vegetarians, which challenges the assumption of differential responsiveness of these groups to creatine supplementation [22]. Consequently, current evidence does not provide strong support for the hypothesis of diet-dependent differences in cognitive responses to creatine supplementation, and this issue requires further, methodologically rigorous investigation.

The enhancement of cognitive processes is also highly relevant for athletes. Performance in many sports relies on motor control, decision-making, coordination, and reaction time, all of which can be adversely affected by fatigue. In this setting, creatine might serve an ergogenic function by theoretically mitigating fatigue and thereby supporting performance. Indeed, creatine has been demonstrated to effectively buffer the adverse effects of sleep deprivation on throwing accuracy among rugby players [23]. In contrast, no effect on passing accuracy was noted in non-stressed soccer players [24]. This may suggest that creatine supplementation is most beneficial under conditions of

cognitive strain, such as sleep deprivation. Unfortunately, these studies also did not analyze brain creatine levels, making it impossible to definitively link the observed effects to biochemical changes in brain tissue.

Antidepressant properties of creatine

Population-level research has identified a link between dietary creatine consumption and depression risk in adults [25]. Furthermore, direct clinical investigations using proton magnetic resonance spectroscopy (^{1}H-MRS) have shown that reduced creatine levels in the prefrontal cortex are associated with depressed mood and greater symptom severity [26].

Animal studies point to a possible sex-dependent effect of creatine on depressive symptoms, with greater efficacy observed in female rats compared to males [27]. However, creatine, when used in conjunction with other antidepressant drugs, appears to offer benefits in male rodents as well [28]. Creatine has also been examined in other clinical models where depression is a frequent secondary outcome of a primary disease or its treatment. For example, in a murine model of epilepsy, dietary creatine not only lessened seizure severity but also reduced depressive-like behaviors [29]. Antidepressant effects have also been shown in mice treated with amyloid β1-40, a model for Alzheimer's disease-related depression [30]. Moreover, chronic corticosterone administration, linked to behavioral changes that lead to depressive disorders, can be counteracted by even a single dose of creatine, which can induce morphological changes that ameliorate these symptoms [31]. It has been suggested that the antidepressant effects of creatine in animal models are associated with the activation of the mTORC1 signaling pathway (mechanistic Target of Rapamycin Complex 1), which plays a key role in the regulation of synaptic neuroplasticity, similarly to the mechanisms observed with fast-acting antidepressant agents such as ketamine [32].

Thus far, only a handful of human clinical trials have evaluated creatine supplementation for the treatment of recurrent depressive disorders, bipolar disorder, and depression co-occurring with methamphetamine use disorder [33]. With few exceptions, most of these trials have yielded promising outcomes. They have investigated both creatine as a monotherapy and as an adjunctive treatment with appropriate pharmacotherapy. Significant improvements in mood-related measures were observed, assessed using scales such as the HDRS (Hamilton Rating Scale for Depression), MADRS (Montgomery–Asberg Depression Rating Scale), and the Young Mania Rating Scale, which correlated with increases in brain creatine/phosphocreatine levels, particularly in the frontal lobe, as measured by magnetic resonance spectroscopy (^{1}H-MRS or ^{31}P-MRS) [34]. This relationship indicates a link between the brain pharmacokinetics of creatine in the central nervous system and the clinical outcome.

An analysis of both preclinical findings and the limited small-scale human studies suggests that creatine supplementation may play a role in the management of various forms of depressive disorders. Nonetheless, there is a well-founded need for more numerous, larger-scale studies with more participants.

Creatine in chronic fatigue syndrome

Chronic fatigue syndrome (CFS) is a condition of unknown etiology that presents with persistent fatigue for over six months, alongside a cluster of symptoms including muscle and joint pain, cognitive difficulties, sleep disturbances, and anxiety. The potential of creatine supplementation to improve the functioning of individuals with CFS has recently come under investigation.

It is hypothesized that disordered creatine metabolism or a deficiency may be a significant factor in the pathogenesis of this condition. Studies have linked urinary creatine concentration to the severity of pain and fatigue in patients with fibromyalgia – a pain syndrome that frequently co-occurs with CFS [35]. Additionally, differences in creatine levels across various brain regions have been noted in CFS patients compared to healthy controls [36]. While the precise role of these findings in the disease's pathogenesis is not yet fully understood, it has been proposed that supplementation with creatine or its precursor (GAA) could lessen CFS symptoms by increasing creatine content in the brain.

Following this premise, several studies have assessed the effect of creatine supplementation on patients with CFS. Initial research reported improvements in depressive symptoms, pain scores, sleep quality, and overall quality of life following creatine supplementation, although it was also noted that these effects might wane after discontinuing the supplement [37]. Numerous studies indicate that creatine may have a beneficial effect on physical performance and reduce pain, which are common co-occurring symptoms in CFS, however, it does not appear to exert a significant impact on the primary symptom of the disorder, namely generalized, centrally perceived fatigue [38, 39].

Recapitulation

Creatine is a compound of considerable potential for optimal brain function, stemming from its essential role in cerebral bioenergetics. While the brain possesses the capacity for endogenous synthesis, supplementation can increase phosphocreatine levels in the CNS; this effect is, however, limited, which brings up questions about the most effective dosing strategies.

Potential cognitive advantages, particularly noted under conditions of metabolic stress, are marked by inconsistent results, making it difficult to draw uniform conclusions. As a result, formulating consistent conclusions and determining an optimal dosing regimen for the central nervous system is challenging. This is primarily due to the considerable heterogeneity of the available studies and the frequent lack of direct measurements of brain creatine levels. In studies that did not employ magnetic resonance spectroscopy, the assessment of cognitive function does not allow for a definitive determination of whether the administered creatine dose effectively increased its availability in the central nervous system, which substantially limits the interpretation and comparability of the findings.

Initial data on creatine's antidepressant properties appear promising, as preclinical and a few clinical trials indicate a beneficial effect in reducing the intensity of depres-

sive symptoms, partly through the mTORC1 pathway; however, these findings require much deeper validation. There is also preliminary interest in the use of creatine for chronic fatigue syndrome. Available research points to improvements in some symptoms accompanying CFS, but its effect on the key aspect – the generalized feeling of fatigue – remains ambiguous.

The key conclusion arising from the analysis of the material presented by the authors of this review is that, despite multiple indications suggesting a potentially beneficial effect of creatine on brain function, there is currently a lack of strong and conclusive scientific evidence supporting its efficacy in the treatment of central nervous system disorders. Most of the available data are derived from studies with small sample sizes, animal models, or indirect observations, which substantially limits the ability to draw definitive clinical conclusions. Consequently, creatine cannot currently be considered a therapy of established efficacy. The current state of knowledge regarding the effects of creatine on brain function remains at the stage of intensive investigation, and the available evidence is limited and associated with a considerable degree of uncertainty. Methodological hurdles and an incomplete understanding of the involved mechanisms restrict the ability to formulate definitive conclusions and recommendations. Further rigorous research, especially randomized controlled trials that incorporate neuroimaging, is imperative to fully assess the clinical potential of creatine.

References

1. Wallimann T. *Introduction – Creatine: Cheap Ergogenic Supplement with Great Potential for Health and Disease*. In: Salomons GS, Wyss M, editors. *Creatine and Creatine Kinase in Health and Disease* [Internet]. Dordrecht: Springer Netherlands; 2007 [cited 2025 May 17]. p. 1–16. Available from: https://doi.org/10.1007/978-1-4020-6486-9_1
2. Dolan E, Gualano B, Rawson ES. *Beyond muscle: the effects of creatine supplementation on brain creatine, cognitive processing, and traumatic brain injury*. Eur J Sport Sci. 2019 Feb;19(1):1–14.
3. Hall M, Trojian TH. *Creatine supplementation*. Curr Sports Med Rep. 2013;12(4):240–4.
4. Sahlin K, Harris RC. *The creatine kinase reaction: a simple reaction with functional complexity*. Amino Acids. 2011 May 1;40(5):1363–7.
5. Salomons GS, Van Dooren SJM, Verhoeven NM, Marsden D, Schwartz C, Cecil KM, et al. *X-linked creatine transporter defect: An overview*. Journal of Inherited Metabolic Disease. 2003;26(2–3):309–18.
6. Turner CE, Byblow WD, Gant N. *Creatine Supplementation Enhances Corticomotor Excitability and Cognitive Performance during Oxygen Deprivation*. J Neurosci. 2015 Jan 28;35(4):1773–80.
7. Hammett ST, Wall MB, Edwards TC, Smith AT. *Dietary supplementation of creatine monohydrate reduces the human fMRI BOLD signal*. Neuroscience Letters. 2010 Aug 2;479(3):201–5.
8. Braissant O, Bachmann C, Henry H. *Expression and Function of Agat, Gamt and CT1 in the Mammalian Brain*. In: Salomons GS, Wyss M, editors. *Creatine and Creatine Kinase in Health and Disease* [Internet]. Dordrecht: Springer Netherlands; 2007 [cited 2025 May 17]. p. 67–81. Available from: https://doi.org/10.1007/978-1-4020-6486-9_4

9. Lukaszuk JM, Robertson RJ, Arch JE, Moyna NM. *Effect of a defined lacto-ovo-vegetarian diet and oral creatine monohydrate supplementation on plasma creatine concentration*. J Strength Cond Res. 2005 Nov;19(4):735–40.
10. Solis MY, Artioli GG, Otaduy MCG, Leite C da C, Arruda W, Veiga RR, et al. *Effect of age, diet, and tissue type on PCr response to creatine supplementation*. J Appl Physiol (1985). 2017 Aug 1;123(2):407–14.
11. Solis MY, Painelli V de S, Artioli GG, Roschel H, Otaduy MC, Gualano B. *Brain creatine depletion in vegetarians? A cross-sectional 1H-magnetic resonance spectroscopy (1H-MRS) study*. British Journal of Nutrition. 2014 Apr;111(7):1272–4.
12. Rawson ES, Venezia AC. *Use of creatine in the elderly and evidence for effects on cognitive function in young and old*. Amino Acids. 2011 May 1;40(5):1349–62.
13. Merege-Filho CAA, Otaduy MCG, de Sá-Pinto AL, de Oliveira MO, de Souza Gonçalves L, Hayashi APT, et al. *Does brain creatine content rely on exogenous creatine in healthy youth? A proof-of-principle study*. Appl Physiol Nutr Metab. 2017 Feb;42(2):128–34.
14. Béard E, Braissant O. *Synthesis and transport of creatine in the CNS: importance for cerebral functions*. Journal of Neurochemistry. 2010;115(2):297–313.
15. Ostojic SM, Ostojic J, Drid P, Vranes M. *Guanidinoacetic acid versus creatine for improved brain and muscle creatine levels: a superiority pilot trial in healthy men*. Appl Physiol Nutr Metab. 2016 Sep;41(9):1005–7.
16. Watanabe A, Kato N, Kato T. *Effects of creatine on mental fatigue and cerebral hemoglobin oxygenation*. Neurosci Res. 2002 Apr;42(4):279–85.
17. Roschel H, Gualano B, Ostojic SM, Rawson ES. *Creatine Supplementation and Brain Health*. Nutrients. 2021 Feb 10;13(2):586.
18. McMorris T, Mielcarz G, Harris RC, Swain JP, Howard A. *Creatine supplementation and cognitive performance in elderly individuals*. Neuropsychol Dev Cogn B Aging Neuropsychol Cogn. 2007 Sep;14(5):517–28.
19. Alves CRR, Merege Filho CAA, Benatti FB, Brucki S, Pereira RMR, de Sá Pinto AL, et al. *Creatine supplementation associated or not with strength training upon emotional and cognitive measures in older women: a randomized double-blind study*. PLoS One. 2013;8(10):e76301.
20. Rae C, Digney AL, McEwan SR, Bates TC. *Oral creatine monohydrate supplementation improves brain performance: a double-blind, placebo-controlled, cross-over trial*. Proc Biol Sci. 2003 Oct 22;270(1529):2147–50.
21. Benton D, Donohoe R. *The influence of creatine supplementation on the cognitive functioning of vegetarians and omnivores*. Br J Nutr. 2011 Apr;105(7):1100–5.
22. Yazigi Solis M, de Salles Painelli V, Giannini Artioli G, Roschel H, Concepción Otaduy M, Gualano B. *Brain creatine depletion in vegetarians? A cross-sectional 1H-magnetic resonance spectroscopy (1H-MRS) study*. Br J Nutr. 2014 Apr 14;111(7):1272–4.
23. Cook CJ, Crewther BT, Kilduff LP, Drawer S, Gaviglio CM. *Skill execution and sleep deprivation: effects of acute caffeine or creatine supplementation – a randomized placebo-controlled trial*. J Int Soc Sports Nutr. 2011 Feb 16;8:2.
24. Cox G, Mujika I, Tumilty D, Burke L. *Acute creatine supplementation and performance during a field test simulating match play in elite female soccer players*. Int J Sport Nutr Exerc Metab. 2002 Mar;12(1):33–46.
25. Bakian AV, Huber RS, Scholl L, Renshaw PF, Kondo D. *Dietary creatine intake and depression risk among U.S. adults*. Transl Psychiatry. 2020 Feb 3;10(1):52.

26. Faulkner P, Paioni SL, Kozhuharova P, Orlov N, Lythgoe DJ, Daniju Y, et al. *Relationship between depression, prefrontal creatine and grey matter volume*. J Psychopharmacol. 2021 Dec 1;35(12):1464–72.

27. Allen PJ, D'Anci KE, Kanarek RB, Renshaw PF. *Sex-specific antidepressant effects of dietary creatine with and without sub-acute fluoxetine in rats*. Pharmacology Biochemistry and Behavior. 2012 Jun 1;101(4):588–601.

28. Kanekar S, Ettaro R, Hoffman MD, Ombach HJ, Brown J, Lynch C, et al. *Sex-Based Impact of Creatine Supplementation on Depressive Symptoms, Brain Serotonin and SSRI Efficacy in an Animal Model of Treatment-Resistant Depression*. International Journal of Molecular Sciences. 2021 Jan;22(15):8195.

29. Warrington TP, Bostwick JM. *Psychiatric Adverse Effects of Corticosteroids. Mayo Clinic Proceedings*. 2006 Oct 1;81(10):1361–7.

30. Rosa JM, Pazini FL, Cunha MP, Colla ARS, Manosso LM, Mancini G, et al. *Antidepressant effects of creatine on amyloid β1–40-treated mice: The role of GSK-3β/Nrf2 pathway*. Progress in Neuro-Psychopharmacology and Biological Psychiatry. 2018 Aug 30;86:270–8.

31. Pazini FL, Cunha MP, Azevedo D, Rosa JM, Colla A, de Oliveira J, et al. Creatine Prevents *Corticosterone-Induced Reduction in Hippocampal Proliferation and Differentiation: Possible Implication for Its Antidepressant Effect*. Mol Neurobiol. 2017 Oct 1;54(8):6245–60.

32. Pazini FL, Rosa JM, Camargo A, Fraga DB, Moretti M, Siteneski A, et al. *mTORC1-dependent signaling pathway underlies the rapid effect of creatine and ketamine in the novelty-suppressed feeding test*. Chemico-Biological Interactions. 2020 Dec 1;332:109281.

33. Kious BM, Kondo DG, Renshaw PF. *Creatine for the Treatment of Depression*. Biomolecules. 2019 Sep;9(9):406.

34. Forbes SC, Cordingley DM, Cornish SM, Gualano B, Roschel H, Ostojic SM, et al. *Effects of Creatine Supplementation on Brain Function and Health*. Nutrients. 2022 Jan;14(5):921.

35. Malatji BG, Meyer H, Mason S, Engelke UFH, Wevers RA, van Reenen M, et al. *A diagnostic biomarker profile for fibromyalgia syndrome based on an NMR metabolomics study of selected patients and controls*. BMC Neurol. 2017 May 11;17(1):88.

36. Mueller C, Lin JC, Sheriff S, Maudsley AA, Younger JW. *Evidence of widespread metabolite abnormalities in Myalgic encephalomyelitis/chronic fatigue syndrome: assessment with whole-brain magnetic resonance spectroscopy*. Brain Imaging Behav. 2020 Apr;14(2):562–72.

37. Leader A, Amital D, Rubinow A, Amital H. *An Open-label Study Adding Creatine Monohydrate to Ongoing Medical Regimens in Patients with the Fibromyalgia Syndrome*. Annals of the New York Academy of Sciences. 2009;1173(1):829–36.

38. Alves CRR, Santiago BM, Lima FR, Otaduy MCG, Calich AL, Tritto ACC, et al. *Creatine supplementation in fibromyalgia: a randomized, double-blind, placebo-controlled trial*. Arthritis Care Res (Hoboken). 2013 Sep;65(9):1449–59.

39. Ostojic SM, Stojanovic M, Drid P, Hoffman JR, Sekulic D, Zenic N. S*upplementation with Guanidinoacetic Acid in Women with Chronic Fatigue Syndrome*. Nutrients. 2016 Feb;8(2):72.

Corresponding author:
Tymoteusz Borowski
e-mail: s87908@365.sum.edu.pl