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The Impact of Oral Creatine Supplementation on Cognitive Functions and Mental Health in Healthy Individuals

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Abstract:

Introduction:

Dietary supplements have recently gained significant popularity, particularly among physically active individuals engaged in various sports disciplines. Typically associated with health and physique maintenance, these supplements are used to enhance physical performance and reduce recovery time following physical exertion. Regular supplementation enriches the diet with essential nutrients and improves athletic performance. [1] The diverse range of ingredients in these supplements determines their varied effects on the functions of different body systems and organs. They support the digestive and immune systems, improve musculoskeletal function, [2] slow down aging mechanisms, and positively impact the cardiovascular system. Additionally, products deemed acceptable in sports disciplines aim to boost immunity, promote muscle mass development, reduce excess body fat, and enhance the mental performance of those taking the supplements. [3]

One of the most commonly used supplements is creatine, highly popular among athletes, but also with multifaceted effects on the body.

There has been considerable interest in exploring the impact of creatine supplementation on brain function and other health aspects. Taking these supplements increases creatine stores in the brain, enabling the observation of numerous positive effects on cognitive factors and memory, particularly noticeable in older individuals or younger people experiencing periods of heightened energy demands on the brain. [4]

Aim of the study:

The purpose of this review is to analyze available research on the effects of creatine supplementation on the cognitive functions and mental health of healthy individuals and to highlight the potential positive impact of this supplementation on people suffering from sleep-related issues. Additionally, the primary myths surrounding the use of creatine supplements will be addressed.

Materials and Methods:

A comprehensive literature search was conducted using PubMed and Google Scholar databases. Keywords such as creatine supplementation, memory, depression, anxiety, side effects were used.

Keywords: creatine suplementation, memory, depression, anxiety, sleep deprevation, side effects, PTSD

Creatine: Short characteristics and Mechanism of Action

Creatine (β-methylguanidinoacetic acid), a compound classified as an organic substance, [5] is formed through the reaction of the amino acids arginine, glycine, and methionine. This process occurs predominantly in the kidneys and liver, although it can also take place in the brain.[6] The human body primarily absorbs creatine through the consumption of meat and as a dietary supplement.[7]

The primary function of creatine is to provide a rapid energy source essential for maintaining ATP homeostasis during periods of high energy demand. [8] Its mechanism of action involves transferring an N-phosphoryl group from PCr (phosphocreatine) to ADP (adenosine diphosphate), resulting in the formation of ATP (adenosine triphosphate) - an organic compound that serves as a multifunctional coenzyme and intracellular energy reservoir. ATP transports energy from mitochondria to the cytosol.[9] Additionally, creatine has been shown to contribute to the removal and inhibition of reactive oxygen species (ROS), which plays a significant role in preventing neurodegenerative diseases.[10]

Creatine and the Brain

Although the largest amounts of creatine are stored in skeletal muscles, the brain also accumulates significant quantities of this compound in a form specific to the brain and nervous tissue, known as BB-CK.[6] The brain's high metabolic activity necessitates substantial creatine levels, especially in individuals experiencing deficiencies.[11] A lack of creatine in the brain can lead to symptoms such as mental retardation, developmental delays (e.g., learning difficulties and seizures), and psychiatric disorders, all of which may be alleviated through creatine supplementation. [12]

Research indicates that creatine metabolism is crucial in certain neurological conditions by facilitating efficient ATP utilization through rapid or altered exchange mechanisms. Studies also highlight benefits for memory performance, particularly in spatial recall (forward and backward), number recall, and long-term memory.[13] [14]

Extensive research on creatine supplementation's effects on cognitive functions, such as memory, attention, and information processing speed, has revealed that creatine enhances memory performance by increasing energy supply through multiple pathways. The compound primarily supports ATP levels in brain cells by accumulating phosphocreatine (PCr) molecules, which provide energy to brain cells.[15]

Another cognitive benefit of creatine is its role in boosting acetylcholine synthesis, a neurotransmitter found in neuromuscular junctions, synapses, and various brain structures.[16] Creatine may also act as a neuromodulator, improving signal transmission between neurons, which enhances learning and information retention.[17] Studies have shown that creatine can enhance neurotransmission in the brain by accumulating in synaptic vesicles, from which it is released into the synapse upon stimulation.[18] Although creatine supplementation has not significantly improved concentration, it does offer benefits for information processing speed.[19] It is particularly useful in complex tasks and enhances cognitive processing through increased cellular metabolism and efficiency, which can benefit students and older individuals whose cognitive functions decline with age.[20] [21] [22]

While creatine does not directly enhance overall executive functions, it positively impacts specific types that require substantial cognitive effort. However, research on its direct influence on sustained attention is limited and inconclusive due to small sample sizes and a lack of studies.[23]

Numerous analyses of creatine supplementation provide information about the variability of its effects across different population groups. For individuals with various diseases, creatine may serve as an additional element of treatment or prevention, particularly in cases of neurodegenerative disorders that result in cognitive impairments.[24] [25]

Age and Dosage

Stratified analysis indicates no significant benefits of creatine supplementation for adults aged 18–31. However, individuals over 60 years old experience noticeable memory performance improvements.[26] Further studies are needed to substantiate these findings.

Regarding supplementation duration, research shows no additional benefits from extending supplementation beyond two weeks. Studies have demonstrated that a two-week supplementation period significantly enhances memory performance, with similar results observed in cognitive function tests conducted after shorter supplementation durations. This suggests that substantial benefits can be achieved within a few weeks, and prolonged supplementation does not significantly enhance outcomes. [14] [21] [27]

Sleep Issues and Creatine

Numerous studies on creatine supplementation in sleep disorders demonstrate significant improvements in cognitive functions related to disrupted brain bioenergetics. [28] [29] [30] One study highlighted the positive effects of creatine supplementation in individuals deprived of sleep for 24 hours, resulting in improved mood, task performance, and decision-making accuracy.[31] Similar research indicated that creatine supplementation mitigated the loss of higher executive functions during sleep deprivation.[31] [32]

Mental Health Impacts:

Depression

The prevalence of mental disorders, particularly depression and anxiety, has increased. Many patients with these conditions fail to adhere to psychiatric recommendations, often denying the existence of an illness that affects their functioning.[33]

Research across various populations has shown a strong correlation between creatine supplementation and depression-related conditions.[34] [35] For instance, magnetic resonance spectroscopy studies have linked low prefrontal cortex creatine levels to mood disorders, including depression, particularly among women with lower creatine concentrations in the brain. [36] [37]

One study involving women with depression demonstrated increased brain PCr levels following the supplementation of 10g of creatine, alleviating symptoms in patients resistant to selective serotonin reuptake inhibitors (SSRIs). These findings underscore the significant impact of creatine supplementation on creatine kinetics, mood, and well-being. [38]

Anxiety Disorders

Generalized anxiety disorder (GAD), often leading to post-traumatic stress disorder (PTSD), is another common psychiatric condition. Research has investigated creatine supplementation's effects on reduced creatine levels in the white matter of patients with PTSD.

In one study, a 52-year-old woman with PTSD, depression, and fibromyalgia experienced significant improvements after four weeks of creatine monohydrate supplementation. The same group of participants, both male and female, showed notable reductions in depressive and PTSD symptoms and improved sleep quality. These individuals had shown resistance to psychiatric medications before creatine supplementation. [39] [40] [41]

Are There Side Effects?

Many of studies suggest that creatine supplementation may cause short-term water retention, increasing intracellular volume. [42] However, other research indicates no impact on total body water, both intracellular and extracellular, compared to total muscle mass in long-term supplementation. Therefore, creatine supplementation does not necessarily lead to water retention. [43] [44]

Additionally, concerns about creatine’s adverse effects on kidney function have been debunked. [45] Research shows that appropriate creatine dosage does not impair renal function. Instead, potential side effects were often confused with interactions involving other medications, undiagnosed kidney conditions, concurrent dietary supplements, or improper creatine dosing. [46]

Discussion

Currently, creatine supplementation is not widely used as an adjunct or complementary treatment for brain disorders, except in cases with documented creatine synthesis deficiencies. [38] Existing knowledge on creatine supplementation primarily focuses on muscle mass and workout performance enhancement.[47] [48]

Recent advancements in neurology, psychiatry, and metabolic disorder research have sparked interest in creatine’s therapeutic potential for various conditions. [49]

Further studies using sensitive and standardized methodologies are needed to elucidate its impact on executive functions, attention, and memory. Research should also address creatine’s efficacy across age groups and establish appropriate supplementation strategies for different populations.

Disclosure:

Author's contribution

Conceptualization: Kinga Furtak; Methodology: Katarzyna Kamińska-Omasta; Software: Bartosz Omasta; Check: Kuba Borys Romańczuk and Daria Rybak; Formal analysis: Olga Krupa and Magdalena Agata Czerska; Investigation: Olga Krupa and Szymon Przemysław Stolarczyk; Resources: Magdalena Agata Czerska and Zofia Martyna Wójcik; Data curation: Paulina Dorota Pietrukaniec; Writing -through preparation:Kinga Furtak ; Writing -review and editing: Katarzyna Kamińska-Omasta and Kuba Borys Romańczuk; Visualization: Szymon Przemysław Stolarczyk and Zofia Martyna Wójcik; Supervision: Paulina Dorota Pietrukaniec; Project administration: Olga Krupa and Daria Rybak; Receiving funding -no specific funding.

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