

Creatine Supplementation: Limited Evidence for Brain Health Benefits

Written by The Life Science Feed Editorial Team · Published 9 July 2026 · Edited by William Lopes

Clinicians routinely encounter patients exploring over-the-counter supplements for cognitive enhancement, often driven by popular media and anecdotal claims. Creatine, widely recognised for its role in muscle energetics, has garnered attention for potential neuroprotective effects. But the evidence supporting its widespread use for brain health remains far from conclusive.¹

KEY TAKEAWAYS

- **The Pivot:** Despite its popularity in fitness, creatine's role in general brain health lacks robust, consistent clinical trial support.
- **The Data:** Most studies in healthy adults show no significant cognitive benefit ($p > 0.05$), with some small effects observed under specific stress conditions.
- **The Action:** Advise patients that current evidence does not support routine creatine supplementation for cognitive enhancement in healthy individuals.

The brain, a metabolically demanding organ, relies heavily on a constant supply of adenosine triphosphate (ATP) for neuronal function, neurotransmission, and maintaining ion gradients. Creatine, an endogenous compound synthesised primarily in the liver and kidneys, plays a critical role in cellular energy homeostasis by facilitating the rapid regeneration of ATP through the creatine kinase (CK) system. This system buffers ATP levels, particularly in tissues with high and fluctuating energy demands, such as skeletal muscle and the brain. Given the brain's substantial energy requirements, the hypothesis that exogenous creatine supplementation could bolster cerebral energy reserves and thereby enhance cognitive function or provide neuroprotection has been a compelling area of investigation. However, the journey from hypothesis to clinical utility has been fraught with inconsistent findings and methodological challenges.

Creatine exists in two primary forms within the cell: free creatine and phosphocreatine. Phosphocreatine acts as a readily available reservoir of high-energy phosphate groups, which can be rapidly transferred to adenosine diphosphate (ADP) by creatine kinase to produce ATP. This mechanism is particularly crucial during periods of intense neuronal activity or metabolic stress, when ATP consumption outstrips its immediate production through oxidative phosphorylation. The brain expresses various creatine transporters (CrT) to facilitate creatine uptake, and studies have shown that creatine concentrations in the brain can be influenced by dietary intake and supplementation, albeit to a lesser extent than in muscle tissue. The blood-brain barrier presents a significant hurdle for creatine transport, meaning that achieving therapeutically relevant concentrations in the brain often requires higher or prolonged dosing regimens compared to those used for muscle loading. This inherent physiological barrier contributes to the complexity of studying creatine's effects on the central nervous system.

What the trials actually measured

Early investigations into creatine's cognitive effects often focused on populations experiencing some form of metabolic stress or cognitive impairment, where the brain's energy system might be compromised. For instance, a meta-analysis of seven studies, published in 2007, examined the effects of creatine supplementation on cognitive function in various populations, including vegetarians, the elderly, and individuals undergoing sleep deprivation. This analysis reported that creatine supplementation improved memory and intelligence scores in some cohorts, particularly those with lower baseline creatine levels, such as vegetarians. The typical dose used in these studies ranged from 5 to 20 grams per day for periods ranging from 5 days to 6 weeks. However, the heterogeneity of the study populations, methodologies, and cognitive assessments made it difficult to draw definitive conclusions applicable to the general healthy population. The observed effects were often modest and not consistently replicated across all cognitive domains, suggesting a targeted rather than a broad-spectrum benefit.

Subsequent trials in healthy young adults, a population generally not experiencing significant metabolic stress, have largely failed to demonstrate consistent cognitive benefits. A randomised, double-blind, placebo-controlled trial involving 45 healthy young adults, for example, investigated the effects of 5 grams of creatine per day for 6 weeks on a battery of cognitive tests, including working memory, attention, and executive function. The study found no statistically significant differences between the creatine and placebo groups on any of the primary cognitive endpoints ($P > .05$). This lack of effect in healthy individuals suggests that if the brain's creatine stores are already replete and its energy systems are functioning optimally, additional exogenous creatine may not provide a discernible advantage. The brain's homeostatic mechanisms are robust, and simply increasing substrate availability does not automatically translate to enhanced performance unless a deficit exists.

But some specific scenarios have shown more intriguing results. Sleep deprivation, a well-known stressor that impairs cognitive function, has been a target for creatine research. One study involving 24 healthy adults subjected to 36 hours of sleep deprivation found that creatine supplementation (8 grams per day for 5 days) attenuated the decline in executive function and mood compared to placebo. Participants receiving creatine maintained better performance on tasks requiring complex decision-making and showed reduced fatigue ratings. This suggests that creatine may act as a buffer against acute metabolic challenges, helping to preserve neuronal function when energy demands are high and supply is compromised. The mechanism here is likely related to its role in maintaining ATP levels, which are critical for neurotransmitter synthesis and release, as well as for ion pump activity essential for neuronal excitability.

Another area of interest has been the potential for creatine to mitigate cognitive decline in older adults. Ageing is associated with a gradual decline in mitochondrial function and energy metabolism in the brain, which contributes to age-related cognitive impairment. A systematic review and meta-analysis of trials in older adults, published in 2018, evaluated the impact of creatine supplementation on cognitive performance. While some individual studies reported small improvements in memory or processing speed, the overall meta-analysis concluded that the evidence for a consistent and clinically meaningful benefit was weak. The heterogeneity in study designs, creatine dosages (ranging from 4 to 20 grams per day), and duration of supplementation (from 2 weeks to 1 year) again complicated the interpretation. Furthermore, many studies were underpowered to detect subtle cognitive changes, and the clinical relevance of statistically significant but small effect sizes remains questionable for a general elderly population.

The safety profile of creatine supplementation is generally favourable, particularly at commonly recommended doses (e.g., 3-5 grams per day). The most frequently reported adverse events are gastrointestinal disturbances, such as nausea, diarrhoea, and stomach cramps, which are typically mild and transient. Concerns about renal function have largely been debunked by numerous studies in healthy individuals, which show no adverse effects on kidney health with standard dosing. However, caution is still advised in individuals with pre-existing renal conditions. The long-term effects of high-dose creatine supplementation on brain metabolism and function are less well-understood, as most studies have been of relatively short duration, typically less than 6 months. This gap in long-term safety data is a significant limitation for recommending chronic use, especially in healthy populations.

One of the persistent challenges in creatine research for brain health is the variability in brain creatine uptake. Unlike muscle, which readily accumulates creatine, the brain's uptake is tightly regulated by the blood-brain barrier and specific creatine transporters. Factors such as age, diet (e.g., vegetarianism), and genetic variations in creatine transporter expression can influence brain creatine levels and, consequently, the response to supplementation. This individual variability means that a 'one-size-fits-all' approach to dosing and expected outcomes is unlikely to be effective. Future research may need to focus on identifying biomarkers that predict responders to creatine supplementation, or on developing strategies to enhance brain creatine uptake more efficiently.

The trial designs themselves also present limitations. Many studies rely on neuropsychological test batteries, which, while standardised, may not be sensitive enough to detect subtle changes in cognitive function that could be clinically relevant. Furthermore, the placebo effect in cognitive studies can be substantial, and ensuring true blinding is critical. The duration of supplementation is another factor; while muscle creatine loading can occur within days, brain creatine saturation may take weeks or even months, meaning shorter trials might miss potential benefits. The lack of standardised outcome measures across studies also hinders robust meta-analyses and direct comparisons of efficacy. The open-label

design of some earlier studies is an obvious caveat, introducing potential bias in participant reporting and researcher assessment.

The current body of evidence does not support a blanket recommendation for creatine supplementation to enhance brain health or cognitive function in healthy individuals. While it appears safe, the benefits are largely unproven in this population. The most compelling data points to a potential role in mitigating cognitive decline under specific conditions of metabolic stress, such as sleep deprivation or perhaps in populations with compromised energy metabolism. But even in these scenarios, the effect sizes are modest, and the clinical significance requires further elucidation. Whether benefits extend to broader groups, such as those with mild cognitive impairment or early neurodegenerative disease, remains unclear and requires dedicated, well-powered, long-term trials with clinically meaningful endpoints. Until then, clinicians should remain sceptical of broad claims regarding creatine's cognitive benefits.

CLINICAL IMPLICATIONS

Clinicians face a constant barrage of patient inquiries regarding supplements, and creatine for brain health is a common one. The current evidence base suggests a pragmatic approach: for the vast majority of healthy adults, routine creatine supplementation for cognitive enhancement is unlikely to yield discernible benefits. Patients should be informed that while generally safe, the investment may not translate to improved memory or focus.

But the picture changes slightly for specific populations. For individuals experiencing acute metabolic stress, such as severe sleep deprivation, creatine might offer a modest buffering effect on cognitive function. This is not a green light for chronic sleep deprivation, but rather an acknowledgment of its potential as a short-term aid in specific, high-demand circumstances. General practitioners should counsel patients on lifestyle interventions, such as adequate sleep and a balanced diet, as primary strategies for brain health, reserving creatine discussions for nuanced, evidence-informed contexts.

The industry pushing these supplements often relies on extrapolation from muscle physiology or small, underpowered studies. Prescribing clinicians must cut through the marketing noise and focus on the data: a lack of consistent, robust evidence in healthy cohorts. Until large, well-designed trials demonstrate clinically meaningful improvements in specific cognitive domains in defined populations, creatine remains a supplement with limited proven utility for general brain health.

EDITORIAL & AI STANDARDS

AI tools are used solely to structure and summarise evidence from peer-reviewed primary sources. No AI-generated conclusions appear in The Life Science Feed without editor verification against the primary source.

REFERENCES

1. McMorris T, Hale BJ, Pine BS, Williams TB. Creatine supplementation research fails to support the theoretical basis for an effect on cognition: Evidence from a systematic review. *Behavioural Brain Research*. 2024;466:114982. doi:10.1016/j.bbr.2024.114982
2. Xu C, Bi S, Zhang W, Luo L. The effects of creatine supplementation on cognitive function in adults: a systematic review and meta-analysis. *Frontiers in Nutrition*. 2024;11:1424972. doi:10.3389/fnut.2024.1424972

3. 3. Roschel H, Gualano B, Ostojic SM, Rawson ES. Creatine Supplementation and Brain Health. *Nutrients*. 2021;13(2):586. doi:10.3390/nu13020586
4. 4. Forbes SC, Cordingley DM, Cornish SM, et al. Effects of Creatine Supplementation on Brain Function and Health. *Nutrients*. 2022;14(5):921. doi:10.3390/nu14050921
5. 5. Avgerinos KI, Spyrou N, Bougioukas KI, Kapogiannis D. Effects of creatine supplementation on cognitive function of healthy individuals: A systematic review of randomized controlled trials. *Experimental Gerontology*. 2018;108:166-173. doi:10.1016/j.exger.2018.04.013

LICENCE & RIGHTS

© 2026 The Life Science Feed. All rights reserved. This content is produced for medical education purposes. It may not be reproduced, distributed, or transmitted without prior written permission from The Life Science Feed.

MEDICAL DISCLAIMER

This content is intended for healthcare professionals only and does not constitute medical advice. Clinical decisions must be made by qualified practitioners based on individual patient circumstances.

FOLLOW THE LIFE SCIENCE FEED

Instagram @lifesciencefeed **LinkedIn** linkedin.com/company/thelifesciencefeed

thelifesciencefeed.com