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Creatine: What Does It Really Do Beyond Muscle?

A physician's closer look at the science behind a popular supplement.

Creatine has achieved something unusual for a dietary supplement: a strong scientific reputation. Once associated primarily with bodybuilding and sports nutrition, it is now widely used by recreational athletes, older adults and people interested in maintaining muscle and physical performance. Its effects on skeletal muscle have been studied for decades, making it one of the better-researched supplements in common use.

The claims surrounding creatine, however, are expanding. It is increasingly promoted for memory, cognition, healthy aging, depression and brain health. Research is exploring its potential role during sleep deprivation and neurological disease, while a recent animal study reported that creatine prevented several inflammatory and neuronal changes in the brains of rats with chronic colitis.

Unlike many supplement trends, these ideas are not based on imaginary biology. The brain uses creatine, cerebral cells have substantial energy requirements, and the creatine-phosphocreatine system participates in maintaining cellular energy availability. There is also human research suggesting that supplementation may influence some aspects of cognition.

The harder question is how far this evidence takes us. Creatine's established reputation for muscle does not automatically establish it as a treatment for depression, a cognitive enhancer or a neuroprotective supplement. This makes it an unusually interesting subject for Signal & Noise™: there is clearly a signal, but its strength changes considerably depending on which claim is being made.

The Claim

The modern argument for creatine extends well beyond exercise performance. Advocates propose that increasing creatine availability may support cellular energy metabolism not only in skeletal muscle but also in the brain. From there, the proposed benefits include improved memory and cognition, greater resilience during periods of high cerebral energy demand, protection against age-related cognitive decline and potential effects on mood and neurological disease.

There are plausible mechanisms behind several of these ideas, and some are supported by human trials. Others remain largely experimental. The useful question is therefore no longer whether creatine simply "works," but what it works for and how confidently the evidence supports each increasingly ambitious claim.

Why It Might Work

Creatine participates in one of the body's important systems for rapidly buffering cellular energy. ATP provides immediately usable energy for cellular processes, but cellular ATP stores are limited. Phosphocreatine can donate a phosphate group to ADP through the creatine kinase reaction, helping regenerate ATP when energy demand changes rapidly.

This system is particularly important in tissues with substantial and fluctuating energy requirements. Skeletal muscle is the obvious example, but the brain also requires a continuous supply of energy to maintain ion gradients, neurotransmission and other neuronal processes. Creatine is present within the central nervous system, and neurons and glial cells participate in creatine metabolism.

This creates a credible rationale for investigating whether increasing creatine availability could influence brain function. Supplementation can alter brain creatine concentrations, although the increase appears smaller and less predictable than the rise achieved in skeletal muscle. The response may also vary according to baseline creatine status, diet, age and other physiological circumstances.

That distinction matters. Showing that creatine participates in brain energy metabolism establishes a mechanism through which an effect could occur. It does not demonstrate that taking additional creatine improves memory, prevents dementia or protects neurons from disease. Mechanistic plausibility is the beginning of the clinical question rather than its answer.

What the Human Evidence Shows

Research into cognition has now progressed far enough that the possibility of an effect deserves serious consideration. A 2024 systematic review and meta-analysis examined 16 randomized controlled trials involving 492 participants and reported improvements in memory, attention time and processing speed with creatine supplementation. Significant improvements were not demonstrated across every cognitive domain, including overall cognition and executive function.

An earlier systematic review and meta-analysis focused specifically on memory also reported a beneficial effect. Interestingly, subgroup analysis suggested that the effect might be greater in older adults than in younger participants. This raises the possibility that creatine supplementation may have different effects depending on underlying physiology rather than functioning as a universal cognitive enhancer.

The literature is not entirely consistent. Another 2024 systematic review concluded that supplementation can increase brain creatine but found the evidence linking this change to better cognition to be equivocal. Trials differ substantially in dose, duration, study population and the cognitive tests used, making broad conclusions difficult.

The largest individual randomized crossover study also illustrates the likely scale of the effect. In 123 participants receiving 5 grams of creatine daily for six weeks, the results were compatible with a small cognitive benefit rather than a dramatic enhancement of mental performance.

Taken together, the human evidence suggests a genuine but modest cognitive signal. Memory currently appears more promising than some other cognitive domains, and particular groups may respond differently. That is substantially more interesting than saying creatine has no effect on the brain, but it is also very different from describing creatine as a proven general-purpose cognitive enhancer.

Does the Context Matter?

One of the more interesting questions is whether creatine becomes particularly useful when cerebral energy demand is increased or creatine availability is relatively constrained. Researchers have therefore investigated populations and circumstances including aging, low dietary creatine intake and sleep deprivation.

This is biologically plausible. An intervention that produces little measurable improvement in a healthy, well-rested person whose cerebral energy requirements are being comfortably met could potentially behave differently when energetic demand rises or metabolic circumstances change. A 2026 systematic review examining older adults reported generally favourable findings, particularly involving memory and attention, while also emphasizing the limited number of high-quality clinical trials.

The emerging possibility is therefore not necessarily that everybody's brain performs better when given more creatine. It may be that the effect becomes more relevant under particular physiological circumstances. Establishing who benefits, under what conditions and by how much remains an important research question.

What About Depression?

Creatine has also been investigated as an adjunct to established treatments for depression, partly because altered cerebral energy metabolism has been proposed as one component of depressive illness. Several trials have produced encouraging results, but the evidence remains considerably less established than the evidence for exercise performance.

A 2025 meta-analysis of 11 trials involving 1,093 participants found a small-to-moderate reduction in depressive symptoms associated with creatine supplementation. However, the average improvement did not reach the authors' threshold for a clinically important difference, heterogeneity was substantial and the certainty of evidence was rated very low.

This is a useful example of how an emerging signal should be interpreted. There is enough evidence to justify further research, particularly into whether certain subgroups respond differently or whether creatine has value as an adjunct to established therapy. There is not enough evidence to regard creatine as an established treatment for depression.

The New Gut–Brain Finding

A recent study published in *Brain, Behavior, and Immunity* extends the creatine story into another area. Researchers induced chronic colitis in male and female rats and examined its effects on the hippocampus. Chronic intestinal inflammation was associated with increased inflammatory signalling and microglial activation in the brain, while hippocampal creatine concentrations fell in both sexes. Some measures of neuronal injury and altered electrophysiological function were particularly pronounced in male animals.

Creatine supplementation produced striking effects within this experimental model. It prevented colitis-associated microglial activation, restored hippocampal creatine concentrations towards control levels and prevented reductions in markers of neuronal integrity in the male animals in which those abnormalities occurred. Creatine also prevented several of the electrophysiological and ion-channel changes associated with chronic colitis.

The findings are scientifically interesting because they connect intestinal inflammation, immune signalling, cerebral energy metabolism and neuronal function. They provide another potential mechanism through which chronic inflammation outside the brain might influence brain physiology and suggest that creatine availability could modify part of that response.

What they do not demonstrate is equally important. These were rats with experimentally induced colitis, not people with Crohn's disease, ulcerative colitis, brain fog or cognitive impairment. The study measured biological and electrophysiological changes in brain tissue rather than demonstrating that creatine improves cognitive symptoms in people with inflammatory bowel disease. The findings provide a compelling reason for further investigation, but they are not yet a clinical indication for creatine.

Where Signal Becomes Noise

Creatine presents an unusual problem in health communication because the supplement already has substantial scientific credibility. With poorly studied supplements, biological plausibility is often exaggerated into evidence of benefit. With creatine, a different form of extrapolation can occur: strong evidence in one area can create an assumption that newer claims must be similarly well established.

The evidence actually exists on a gradient. Creatine's role in cellular energy metabolism is well established, and its effects on certain exercise and resistance-training outcomes are supported by a substantial body of research. Human cognitive research provides an increasingly credible but considerably more modest signal, particularly for memory. Research into depression remains preliminary, while neuroprotection and the inflammatory gut-brain effects highlighted by the recent colitis study remain much further from established clinical application.

The noise begins when those different levels of evidence are compressed into the statement that “creatine is good for the brain.” That phrase could mean anything from a small improvement in a memory test to prevention of dementia or protection against neurological injury. The first has some human experimental support; the latter claims require much stronger evidence.

What About the Kidneys?

Kidney safety remains one of the most persistent concerns surrounding creatine. Part of the confusion arises because creatine supplementation can increase serum creatinine, while serum creatinine is also routinely used to estimate kidney filtration. An increase in the laboratory value can therefore be interpreted as evidence that creatine has damaged the kidneys.

The physiology is more complicated. Creatinine is a breakdown product related to creatine metabolism, so supplementation can alter serum creatinine without necessarily reducing glomerular filtration. A 2025 systematic review and meta-analysis found a modest increase in serum creatinine associated with supplementation but no significant deterioration in measured glomerular filtration rate.

A larger 2026 meta-analysis reached a broadly similar conclusion. Creatine supplementation increased serum creatinine and consequently affected creatinine-based estimates of GFR, but the investigators did not find a significant deterioration when filtration was assessed using an alternative measured method, nor significant increases in albuminuria or proteinuria.

This does not mean that kidney health can be ignored or that creatine is appropriate for every person, particularly in the presence of established renal disease or other relevant medical circumstances. It does mean that an increase in serum creatinine during creatine supplementation should not automatically be interpreted as evidence of renal injury. The statements “creatine can raise creatinine” and “creatine damages healthy kidneys” are not equivalent.

Risks & Trade-offs

Creatine monohydrate is generally well tolerated in healthy adults at commonly studied doses. The most predictable effect is an increase in body mass, particularly early in supplementation, largely related to increased intracellular water associated with greater muscle creatine storage. For an athlete in a weight-sensitive sport this may matter; for someone taking creatine primarily for strength or preservation of muscle, it may not.

Gastrointestinal discomfort can occur, particularly with larger single doses, and product quality remains relevant because supplements are not all manufactured or independently tested to the same standard. People with established kidney disease, complex medical conditions or medications affecting renal function should not assume that safety data from healthy populations automatically apply to them.

There is also a more general trade-off that applies to many supplements. Creatine may be inexpensive and well studied, but taking it for a specific objective still makes most sense when the expected benefit corresponds to an outcome for which evidence actually exists. The evidential threshold for adding creatine to resistance training is different from the threshold for taking it specifically to prevent dementia.

What We Still Don't Know

Several important questions remain unresolved. We do not yet know which populations are most likely to experience meaningful cognitive benefits, whether differences in baseline dietary creatine explain some of the variability between studies, or whether higher brain creatine concentrations reliably translate into clinically important improvements in cognition.

Long-term neurological outcomes are even less certain. Evidence that creatine participates in brain energy metabolism and influences selected cognitive measures does not tell us whether supplementation reduces the incidence of dementia, protects against neurodegenerative disease or meaningfully modifies inflammatory neurological processes in humans.

The new colitis research adds another intriguing question: whether changes in creatine metabolism are part of the pathway linking chronic peripheral inflammation with altered brain function. That possibility is biologically interesting, but translating it from an experimental rat model into human disease will require clinical studies rather than further extrapolation from mechanism alone.

The Practical Takeaway

Creatine deserves its reputation as one of the better-supported supplements available, particularly for people undertaking resistance training or seeking to improve or preserve muscle performance. Its emerging role in brain health is also worth taking seriously. Human trials suggest that supplementation may produce modest benefits in some aspects of cognition, particularly memory, and research involving aging, mood and cerebral energetics provides reasonable grounds for continued investigation.

What the evidence does not currently justify is treating creatine as a proven neuroprotective supplement, a treatment for depression, a way to prevent dementia or a therapy for the neurological consequences of intestinal inflammation. The recent colitis study is fascinating precisely because it opens another scientific question; it should not be used to imply that the question has already been answered.

If someone asked me whether creatine is merely a gym supplement, I would now say no. Its biology and emerging human evidence clearly extend beyond skeletal muscle. If they asked whether everyone should therefore take creatine to protect their brain, I would be considerably more cautious. The science is becoming more interesting, but the strength of the evidence still depends very much on which benefit we are asking creatine to deliver.

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