COGNITIVE SUPPORT NUTRIENTS

FOR COGNITION, MEMORY, AND BRAIN FUNCTION

Clinical Summary

Diet and nutrition are essential for the health and performance of the human brain. The overall composition of our diet as well as specific nutrients have been shown to have an impact on brain function in various experimental models and epidemiological studies.[1] Supplementing with neuroprotective nutrients such as citicoline, zinc, vitamin B6, vitamin B12, folate and carotenoids lutein and zeaxanthin have shown promise in improving cognitive function, memory, and brain health by modulating inflammation, reducing oxidative stress, optimising metabolic function, and providing key nutrients essential for brain structure.

Clinical Guide to Supplementation

Step 1: Assess 'Clinical Presentations of Poor Cognitive Health'

Step 2: Establish nutritional and lifestyle risk factors – See 'Additional Diet and Lifestyle Considerations'

Step 3: Consider evidence-based applications and mechanisms – See 'Clinical uses' and 'Mechanisms of action'

Step 4: Review side effects and drug-nutrient interactions – See 'Safety'

Clinical Presentations and Risk Factors

Clinical Presentations of Poor Cognitive Health

- Brain fog
- Mental fatigue and lack of mental stamina
- Short-term memory deficits
- Suboptimal attention and cognition
- Age-related cognitive decline
- Mood disorders such as depression and anxiety

Key Nutrient Considerations

- Citicoline
- Vitamin B6
- Folate
- Vitamin B12
- Zinc
- Lutein
- Zeaxanthin

Additional Diet and Lifestyle Considerations

Healthy diet: An overall healthy dietary pattern is important for preserving cognitive health into older age.[2]

Nutritional deficiencies: Low intakes of omega 3,[3,4,5] B vitamins,[6] Vitamin D,[7,8] choline,[9,10] vitamin C,[11,12] Magnesium,[13,14] CoQ10,[15] essential amino acids[16] and flavonoid rich fruits and vegetables[17,18] may affect mood and cognition.[19]

High homocysteine (Hcy) levels: Elevated Hcy is associated with cognitive impairment and cognitive decline.[20,21] MTHFR (C677T) polymorphisms, which can influence Hcy levels, may be associated with the risk of depression and poor cognitive function if B vitamin intake is inadequate.[22,23] Consider optimising B vitamin intake, especially B6, B12 and folate.

Chronic stress and sleep deprivation: Both chronic stress and sleep deprivation may adversely affect cognition.[24,25] Consider stress reduction strategies and sleep hygiene.

Lack of exercise: Physical activity has been shown to optimise cognitive function, potentially decelerating cognitive decline and attenuating neurodegeneration.[26,27]

Clinical Uses and Mechanisms

Clinical Uses

Support attention and memory: Citicoline supplementation has been shown to significantly improve mental energy, attention and memory in young, middle aged and older adults.[28,29,30] Lutein and zeaxanthin improve spatial memory, reasoning ability and complex attention.[31]

Promotion of cognitive performance and mental sharpness: Zinc,[32,33,34] citicoline,[35] lutein and zeaxanthin[36,37] supplementation improves cognitive function across a wide age range.

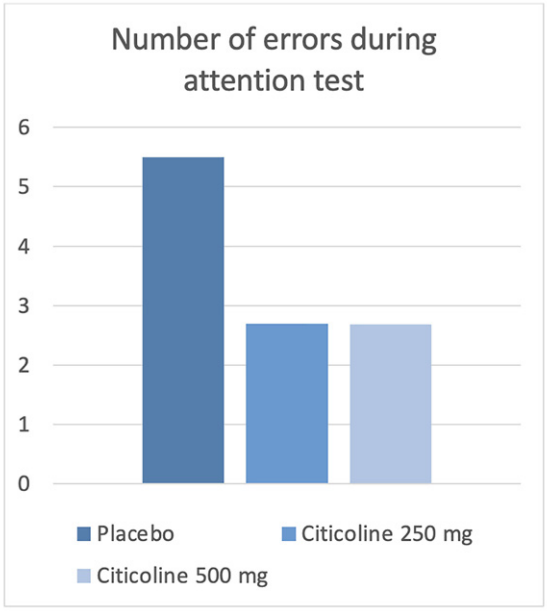
Prevention of age-related cognitive decline: Vitamins B6, folate, and B12 slow cognitive and clinical decline in people with mild cognitive impairment, particularly in those with elevated homocysteine levels.[38,39]

Improvement in mood and behaviour: Zinc,[40] vitamin B6[41] and citicoline[42] may improve mental health conditions such as depression and anxiety. Low levels of Vitamin B12[43] and folate[44,45] have been associated with higher incidences of depression and other mood disorders.

Reduces recovery time after acute ischemic stroke: Treatment with oral citicoline for moderate to severe acute stroke has been shown to be beneficial.[46,47]

Supports recovery from traumatic brain injury: Citicoline has shown to be an effective neuroprotective and regenerative agent in a variety of neurodegenerative disorders, brain ischemic conditions as well as traumatic brain injuries and its sequelae.[48,49,50,51,52,53]

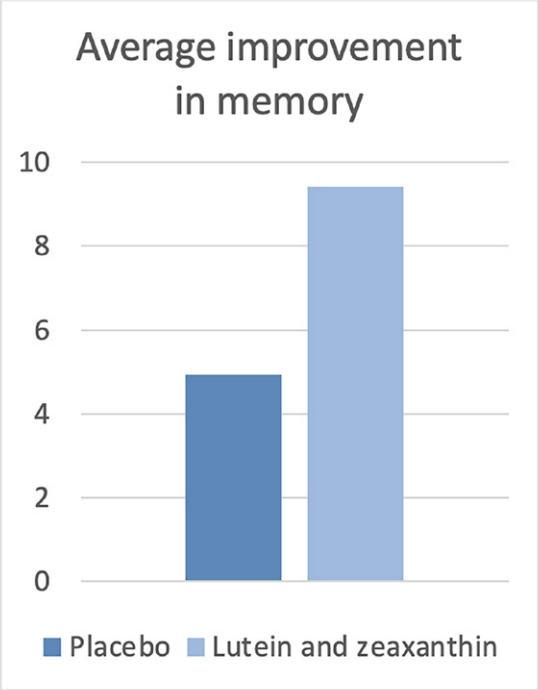
Image 1: Citicoline improves attention performance[54]



Sixty healthy adult women aged 40 - 60 received 250 mg citicoline, 500 mg citicoline, or placebo for 28 days. Citicoline significantly improved attention and ability to produce correct responses on the cognitive performance test.

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Image 2: Lutein and zeaxanthin improves memory[55]



Fifty-one young, healthy subjects received lutein (10 mg) and zeaxanthin (2 mg) or placebo for 1-year. Daily supplementation resulted in significantly improved in spatial memory, reasoning ability and complex attention.

Mechanisms of Action

Optimises neuronal function: Zinc is important for neuronal signalling and is found in high levels in the brain, particularly in areas involved in learning and memory.[56]

Improves brain function and structure: Citicoline is the precursor to phosphatidylcholine, one of the most important phospholipids in the nerve cell membrane. Phosphatidyl choline is essential for neuronal plasticity and increases new connections between nerve cells, required for cognitive functions.[57]

Supports neurotransmitter formation: Citicoline supports the formation of neurotransmitters, acetylcholine and dopamine. Increasing dopamine concentrations benefits short term memory (reading comprehension and solution-oriented thinking) and motor control (balance and reaction time).[58,59] Zinc and Vitamin B6 are important cofactors for the biosynthesis of several neurotransmitters (GABA and serotonin).[60,61,62]

Supports cellular energy: Citicoline enhances energy (ATP) synthesis and production in the brain.[63]

Provides anti-inflammatory and antioxidant properties: Folate,[64] zinc,[65] lutein and zeaxanthin[66] supplementation decreases pro-inflammatory cytokines and improve antioxidant capacity.

Reduces homocysteine levels: Homocysteine-lowering B vitamins (Vitamin B6, folate, B12) slow the rate of brain atrophy in elderly with mild cognitive impairment.[67]

Safety

Possible Side Effects

Supplementation of the combination of citicoline,[68,69] vitamin B6,[70,71] vitamin 12 and folate,[72] zinc,[73] lutein and zeaxanthin[74] is generally considered safe and well tolerated at the recommended dosage. However, higher intakes of some of these nutrients can lead to mild symptoms:

- **B12 deficiency and/or macrocytic anaemia, abdominal cramps, diarrhoea and nausea** may occur with intakes of ≥1-5mg/day of folate.[75,76]
- **Peripheral neuropathy** with intakes of ≥100mg/day of Vitamin B6 as pyridoxine hydrochloride.[77,78]
- **Flushing** might be experienced with daily intakes ≥50mg of Vitamin B3 as nicotinic acid.[79]

Caution is advised in people with renal impairment as zinc accumulation may occur.[80]

Interactions

Levodopa: Citicoline at high doses shows a levodopa-sparing effect. Thereby, citicoline may reduce the side effects of the drug (e.g., long term therapy for Parkinson's disease).[81] Possible beneficial interaction.

Methylphenidate: The efficacy of this drug is improved by zinc supplementation.[82] Possible beneficial interaction

Anticonvulsants: Reduced folate levels have been observed with long term use of this medication.[83,92] Beneficial interaction is possible, although medical supervision is required.

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