

Nootropic support for cognition, mood, and brain tissue structure and function

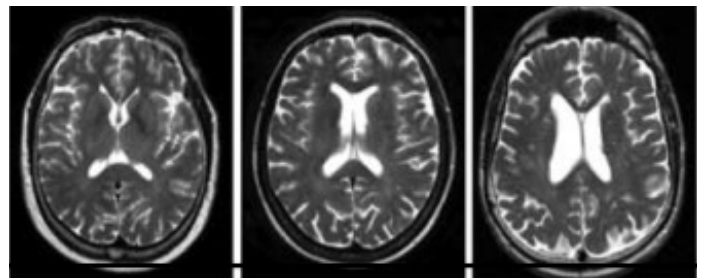
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Brain Vitale™ contains a comprehensive array of brain-supportive nutrients formulated to optimize brain function and help prevent or partially reverse age, injury or disease-related cognitive and neurological decline while stimulating new brain cell formation.* It provides building blocks for the regeneration of brain phospholipids, crucial structural components of neuronal synapses. Brain Vitale™ also provides precursors to the brain neurotransmitter acetylcholine (ACh), and improves production and receptor function for various other neurotransmitters. It is formulated to help boost brain cell energy production, reduce age-related mitochondrial decline, and provide antioxidant protection.*

Benefits include*:

- Improved cognition, mood and memory
- Support for recovery from brain and nerve injuries (stroke, concussion, sciatica & various neuropathies)
- Potential symptom improvement and reduced progression of various neurodegenerative conditions, such as Alzheimer's, Parkinson's, ALS or multiple sclerosis



MRI images of brain tissue shrinkage with aging (from left to right)¹¹⁶

Brain-Derived Neurotrophic Factor (BDNF)

BDNF is a protein that stimulates the development, differentiation, and protection of neuronal survival in the central and peripheral nervous systems and is strongly linked to cognitive and mental health.¹¹⁸ BDNF influences mood, memory and may affect sleep.

Blood BDNF levels decline during aging; decreased levels may be associated with depression and brain cell loss. Animal studies demonstrate that BDNF has antidepressant effects; in humans suffering from depression, blood levels of BDNF are lower than in healthy controls. Additionally, alterations in BDNF have been identified in various chronic neurodegenerative diseases.¹¹⁸

The total number of brain cells typically declines with aging. It was previously thought that there were no nutritional interventions capable of stimulating BDNF production enough to support the addition of new brain cells. Evidence now exists for ALCAR and coffee fruit concentrate (NeuroFactor™) as effective in boosting BDNF, thus potentially supporting brain regeneration.¹¹⁹

The ingredients in Brain Vitale™ provide benefits through complementary and synergistic mechanisms of action:

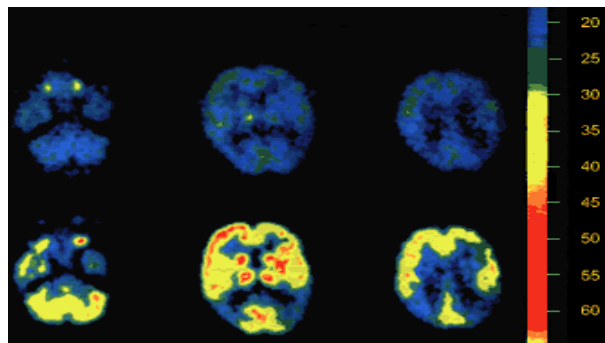
Citicoline or CDP-choline is a substance found in every cell of the body and is especially vital to brain health. Studied as Cognizin®, citicoline has been shown to support healthy brain activity.⁶³ Citicoline is broken down during intestinal absorption into two compounds: 1) Choline, which crosses the blood-brain barrier (BBB) and may be used for ACh production or formation of phosphatidylcholine, as part of brain cell phospholipids,^{57,60,63} and 2) Cytidine, which boosts synthesis of cytidine triphosphate (CTP), a cofactor for the reaction incorporating choline into phosphatidylcholine. Thus, citicoline supplies precursors for the synthesis of phospholipids, major constituents of brain tissue that support neuronal communication.^{57,59,61,65} This mechanism of action represents a unique property of citicoline compared to glycerophosphocholine GPC, which can significantly benefit brain tissue maintenance, especially after long term supplementation.

Coffee Fruit Concentrate (as NeuroFactor™) is an extract from the whole coffee cherry, including the flesh of the berry that surrounds the coffee bean, and contains several distinctive compounds not found in coffee beans themselves. In clinical studies, NeuroFactor™ has been shown to substantially stimulate production of brain-derived neurotrophic factor (BDNF), raising its plasma levels by 37%-54%.^{118,119} One study showed a 206% increase in BDNF contained in structures called exosomes, which cross the BBB.¹¹⁸ This increase was not observed in subjects taking brewed coffee, green coffee bean extract, natural coffee caffeine, grape seed extract, or chlorogenic acid, which attests to the unique ingredients found in the coffee berry. This coffee fruit concentrate contains only 0.7% caffeine, which translates into 0.7mg per 100mg dose.

Glycerophosphocholine (GPC) is a naturally occurring source of choline contained in small amounts in various foods and in all human cells. GPC is a water-soluble molecule and has been proven to be a more clinically effective source of choline than choline or phosphatidylcholine (PC) from diet or supplements. Following GPC ingestion, the plasma level of choline rises rapidly and remains elevated for up to ten hours. A high plasma concentration gradient of choline stimulates its transport through the BBB with high efficiency. This increases choline reserves inside neurons, where it is used for synthesis of PC and ACh.

Acetyl-L-Carnitine (ALCAR) is a derivative synthesized in humans from L-carnitine, which itself is synthesized from the amino acids lysine and methionine or derived in small amounts from foods (especially meat and dairy products). ALCAR is actively transported across the BBB and is thought to influence the cholinergic system as a cholinergic receptor agonist and to promote synthesis of ACh by providing the acetyl ligand.⁹⁵ Thus, it complements compounds that provide the choline component of ACh, such as GPC or citicoline. ALCAR supports cellular energy production by facilitating fatty acid transport into mitochondria and was shown to stabilize cell membrane fluidity and reverse age-related decline in mitochondrial function.^{93,120,121}

Phosphatidylserine (PS) is a crucial component of cell and mitochondrial membranes, making it essential for optimal brain function. PS has a unique role in supporting neurotransmitter release and receptor function, as well as intracellular signaling, all of which enhance communication between brain cells. PS is also regarded for helping to modulate elevated cortisol, which may have detrimental effects on brain health over the long term.



One study evaluated brain activity in patients with probable Alzheimer's disease, assessed by glucose consumption on PET scan, before (upper images) and after (lower images) supplementing with 500 mg/day of PS for three weeks. Results show a significant increase in glucose consumption after PS supplementation.¹¹³

Ginkgo biloba has been used in Chinese medicine therapeutically for over 5000 years. More than 500 scientific studies with standardized ginkgo biloba extracts have shown this compounds to improve microcirculation to brain cells, thus it may help to improve cerebral insufficiency syndrome,^{123,130-132} enhance memory in young and older individuals;¹³⁰⁻¹³² alleviate symptoms of Alzheimer's and dementia,^{124,127,129} balance catecholamine, serotonin and cortisol levels;¹²⁵ and protect the brain from stress-induced neuronal death.¹³⁰⁻¹³²

When studied individually, the ingredients in Brain Vitale™ have been shown to*:

Support brain function and healthy cognition:

- Help increase brain energy consumption by supporting mitochondrial function^{61,63,65,71}
 - Increased brain energy consumption may slow the progression of Alzheimer's disease or dementia, and/or reduce some of its symptoms, including brain volume shrinkage^{48,79-84,96,100-107,113}
 - Improve cognition and social behavior in patients with Alzheimer's,^{4,9,16,17} vascular/age-related dementia,¹⁰⁻¹² and Parkinson's disease²²⁻²⁵
 - Improve memory and general mental function, especially in the elderly and those with cognitive impairment associated with excessive alcohol intake^{72,75,112}
- Support focus and attention;^{60,66,67,69} help reduce errors while on task^{67,69}
- Improve memory/mental focus,^{1,2,3,15} and reaction time^{51,52} in the young and elderly
- Improve sleep patterns in patients with Parkinson's disease⁸⁵
- Counteract age-dependent reduction in number of brain cells⁴⁹ and ACh receptors⁵⁰
- Improve EEG patterns in healthy subjects; lessen slow wave ("delta") activity that becomes more prevalent with aging or pathologic brain decline²⁰

Support brain and neuronal repair and recovery:

- Support brain DNA synthesis and repair^{57,60,63}
- Improve brain recovery from stroke,⁵⁻⁷ cranial injury⁵⁶ and anesthesia³⁹
- Increase speed of recovery from stroke⁷⁸
- Repair blood brain barrier tissue damaged by hypertension³³
- May be beneficial for conditions necessitating myelin repair¹
- Protect neural structures from free radical damage⁶³
- Improve neuronal cell survival and proliferation¹¹²
- Increase speed of nerve healing and prevent nerve function loss in animal models of sciatic nerve injury⁸⁶

Modulate acetylcholine and other neurotransmitters, and enhance mood:

- Boost ACh production and release from neurons and likely other types of cells^{22,23}
- May compensate for ACh decline⁵⁴ due to aging or estrogen deficiency⁴¹ (as in natural/surgical menopause, oral contraceptive use)
- Increase production of dopamine, norepinephrine, serotonin and GABA^{18,30,60,61,63,70,71}
- Relieve depression, likely through increased brain energy^{76,77,108}
- Improve symptoms of ADHD¹¹⁴ and seasonal affective disorder¹¹²

Improve muscle function, growth hormone and testosterone production, and modulate cortisol:

- Boost growth hormone production in the young and elderly^{8,27,28,55}
- Increase fat oxidation⁵⁵ and muscle strength,^{26,28} improve reaction time,^{51,52} and possibly as a result, improve balance, especially in the elderly
- Help normalize elevated cortisol induced by exercise^{109,110} or mental stress^{115,117}
 - Optimize testosterone levels in men who exercise¹¹¹ (possibly explained by elevated cortisol suppressing testosterone)
- Support immune function by reducing the influence of cortisol on depressing the immune response¹¹¹

Potential synergy of Brain Vitale™ with pharmaceutical drugs*

Brain Vitale™ is not likely to interfere negatively with pharmaceutical drugs prescribed for improving brain function. On the contrary, it may enhance their benefits due to its effects on the metabolism of various neurotransmitters. For example, GPC and citicoline may enhance the effect of acetylcholinesterase inhibitors due to their stimulation of acetylcholine synthesis and release in the synaptic cleft, where these pharmaceutical drugs delay its breakdown. This may be of particular benefit to those who experience limited benefit (in efficacy and duration) from this class of drugs.²³ Studies show that GPC, citicoline, PS or ginkgo may enhance dopamine, serotonin or GABA production in the brain, thus Brain Vitale™ may enhance the action of reuptake inhibitors of any of these neurotransmitters. In addition, the neuronal membrane improvements brought about by GPC, citicoline and PS are likely to enhance neurotransmitter receptor function, which will likely further enhance the effects of psychotropic drugs.

Brain structures and processes involved in neuronal communication

The figure below illustrates the 12 aspects of neuronal communication that may be improved by particular Brain Vitale™ ingredients.*

- 1. Blood brain barrier:** CDP-choline, GPC, PS, Ginkgo biloba
- 2. Blood circulation to and inside the brain:** Ginkgo biloba
- 3. New brain cell formation:** Neurofactor™, ALCAR, GPC, PS, Citicoline
- 4. Reduction of brain cell death:** GPC
- 5. Cell membrane of pre-synaptic and post-synaptic neurons:** Citicoline, GPC, PS, ALCAR
- 6. Cellular uptake (entry):** GPC, Ginkgo biloba
- 7. Neurotransmitter synthesis:** GPC, Citicoline
- 8. Mitochondrial function:** ALCAR, PS, GPC and mitochondrial cell membranes: Citicoline, GPC, PS
- 9. Oxidative stress:** Ginkgo biloba, Citicoline
- 10. Neurotransmitter storage & release in the synaptic cleft:** GPC, ALCAR, Citicoline
- 11. Neurotransmitter receptors function:** Citicoline, GPC, PS, Ginkgo biloba
- 12. Intracellular signaling from various neurotransmitters:** Citicoline

Brain Vitale™ nutrients cross the blood brain barrier:

Choline, Serine, ALCAR, Citicoline metabolites, Ginkgo biloba

1. BLOOD BRAIN BARRIER

- 2. Blood circulation to and inside the brain**
- 3. New brain cell formation**
- 4. Reduction of brain cell death**

5. Cell membrane of pre-synaptic neuron

6. Cellular uptake (entry)

8. Mitochondrial function & mitochondrial cell membranes

7. Neurotransmitter Synthesis

9. Oxidative stress

10. Neurotransmitter storage & release in the synaptic cleft

Synaptic space:

While in the synaptic space, neurotransmitters act on receptors of neurons and are subsequently either broken down or taken back by presynaptic neurons.

Most psychotropic drugs act in this space to inhibit re-uptake of various neurotransmitters in order to prolong their action.

5. Cell membrane of post-synaptic neuron

11. Neurotransmitter receptors function

12. Intracellular signaling from various neurotransmitters

8. Mitochondrial function and mitochondrial cell membranes

9. Oxidative stress

Supplement Facts

Serving Size 2 capsules
Servings Per Container 60

Amount Per Serving	% Daily Value
Acetyl-L-Carnitine HCl	500 mg *
Citicoline (as Cognizin®)	250 mg *
Glycerophosphocholine (from soy lecithin)	200 mg *
Coffee Fruit Concentrate (as NeuroFactor™) (Coffea arabica)(whole fruit)	100 mg *
Phosphatidylserine (from sunflower lecithin)	100 mg *
Ginkgo (Ginkgo biloba)(leaf) [standardized to contain 24% ginkgo flavonoglycosides and 6% terpene lactones]	100 mg *

*Daily Value not established.

Other Ingredients: Cellulose (capsule), silicon dioxide, dicalcium phosphate, vegetable stearate.



Recommended Use:

- As a dietary supplement, take two capsules per day with meals, or as directed by your health care practitioner.
- Adequate intake of DHA is critical in achieving the goals of Brain Vitale™ for brain function and regeneration since DHA is an essential component of neuronal membranes. Consider combining with OmegAvail™ Ultra DHA, OmegAvail™ Hi-Po, CogniAid™ and/or additional GPC, based on individual clinical considerations.

For a list of references cited in this document, please visit:

http://catalog.designsforhealth.com/assets/itemresources/Brain_Vitale_References.pdf

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*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

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