



The Top Natural Nootropics And Brain-Boosting Supplements

Do you have any (or all) of these symptoms?



Brain-Related Fatigue | Feeling fatigued, exhausted, or sleepy after doing something mentally demanding.

Chronic Low Energy | Waking up feeling groggy, feeling tired throughout the day, relying on caffeine or stimulants to keep you alert.

Brain Fog | A type of cognitive dysfunction that includes memory problems, lack of ability to concentrate, and lack of mental clarity.

Anxiety or Depression | Persistent feelings of sadness, emptiness, guilt, hopelessness, worry, or pessimism.

Loss of Resiliency | Inability to handle and recover from stress.

Sleep Problems | Racing thoughts at bedtime or inability to fall asleep quickly, waking up in the night – sometimes repeatedly, insomnia

Whether you suffer from one or all of these issues, you must understand this critical truth:

These symptoms are NOT a normal thing, and they're NOT just a normal part of aging.

Here's the reality: These symptoms are present because you actually have damaged, inflamed, or dysfunctional neurons in your brain.

More specifically, you likely have at least one of the following going on in your brain:



Neuro Inflammation | Cells in your brain called microglia, which sort of function as your brain's immune system, are activated too frequently and become stuck in the 'on' position. As a result, they produce inflammatory compounds and oxidative damage.

Leaky Blood Brain Barrier | A shockingly common issue where the protective wall between your brain and bloodstream breaks down. When it becomes leaky, things get into the brain that shouldn't be there.

Mitochondrial Dysfunction / Shut Down | Mitochondria are your cellular energy generators AND danger sensors. But, mitochondria cannot be in both energy mode and cell defense mode. When your mitochondria are weak, they are constantly trying to 'sense danger' and can't produce energy. What would you then think if someone told you that taking a pill could make you feel smarter, sharper, and more creative? What if they told you a pill could maintain those feelings throughout your life? Would you call BS?

Those pills exist!

They're called nootropics and include an array of compounds that either improve cognitive function, particularly executive function, memory, focus, and the ability to work under stressful conditions, or prevent cognitive decline.

While the best-known examples include synthetic drugs like Adderall, modafinil, and piracetam, there are numerous herbs and naturally occurring molecules that possess similar properties while being vastly safer, especially with long-term use.

These brain-boosting supplements work through a variety of mechanisms to improve brain health and functionality [1–3]:

- Increase blood flow and nutrient delivery to brain cells.
- Reduce neuroinflammation and oxidative stress.
- Bolster mitochondrial function and energy production.
- Facilitate the removal of neurotoxins.
- Promote the growth of neurons.
- Improve neuronal communication and synaptic plasticity.
- Increase neurotransmitter signaling.

In this article, we'll overview some of the most potent and safe nootropics that you could pick up in any supplement shop or supermarket.

Botanicals

Botanicals are plants valued for their medicinal properties, flavors, or scents. Common herbs are probably the best-known example. They can be consumed as teas, tinctures, extracts, or in their natural state.

Rhodiola Rosea

BRAIN BOOSTING EFFECTS OF RHODIOLA ROSEA:





- Stabilizes mood
- Reduces anxiety and depression
- Improves cognitive performance
- Reduces feelings of exhaustion and irritability
- Functions as an antioxidant and anti-inflammatory
- Fast-acting

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Rhodiola is a medicinal herb traditionally used for enhancing mental performance and resilience to stress [140], effects that are due to the numerous ways rhodiola interacts with genes, signaling pathways, and molecular networks within neuronal cells to alter emotional behavior [141].



Specifically, rhodiola acts within the brain as a neuroprotective, cognitive enhancing, and mood stabilizing agent through reducing neuronal cell death and promoting regeneration, functioning as an antioxidant and anti-inflammatory, facilitating neurotransmission, and regulating several key mediators of the stress response within the hypothalamic-pituitary axis [142–144].

It's an incredibly powerful adaptogen, with effects noticed soon after regular supplementation. For instance, a large study of over 100 adults with chronic work- and life-related stress found that 400 mg/d of rhodiola rosea significantly reduced feelings of exhaustion, irritability, and anxiety in as little as three days [145]!



Other studies have found similar anti-stress and mood-boosting benefits.

- In first-year medical students, taking 100 mg/d for 3 weeks before exams improved mental performance by 50%, reduced mental fatigue by 42%, and increased general wellbeing by 8% [146]. Overall, exam scores after using rhodiola were 8.4% higher than after using a placebo.
- In young military cadets, a single dose of 370 mg taken an hour before cognitive tests improved general wellbeing, mental fatigue, and cognitive performance compared to placebo,

with no further improvement seen as the dose increased to 550 mg [147].

- In **adults with stress-related fatigue**, 140 mg/d for 1 month reduced feelings of burnout and improved cognitive performance [148].
- In a study of **working adults suffering from burnout**, a third of whom had been unsuccessfully treated for their stress in the past, 400 mg/d improved every aspect of quality of life and perceived stress after just 1 week, with further improvements seen after 12 weeks [149].



• In adults with **chronic fatigue syndrome**, 400 mg/d improved every aspect of fatigue after just 1 week, with further

improvements seen after 8 weeks [150]. Ultimately, 83% of the participants reported "very much" or "much" improved conditions, with every aspect of fatigue, stress, and global impairment being cut in half.



Rhodiola Rosea is a potent adaptogen that improves cognitive function and stress resilience, particularly in those with stressful lives.

Lion's Mane Powder

Lion's mane mushroom (also called Yamabushitake or Hericium erinaceus) is a medicinal mushroom that has been extensively studied for its neurohealth properties [151,152].

RESEARCH HAS SHOWN THAT LION'S MANE:





- Stimulates the production of Nerve Growth Factor (NGF), which promotes neuronal growth, development, and regeneration
- Restores levels of serotonin, noradrenaline, and dopamine levels in the brain that can be suppressed due to chronic stress
- Reduces inflammation throughout the body and within the brain
- Stimulates the expression of brain derived neurotrophic factor (BDNF), which has neuroprotective effects, plays a role in neuronal development
- Helps in the formation of neuronal connections important for memory and cognition

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Research has shown that lion's mane:

- Stimulates the production of Nerve Growth Factor (NGF) [153– 155], which promotes neuronal growth, development, and regeneration [156].
- Restores levels of serotonin, noradrenaline, and dopamine levels in the brain that can be suppressed due to chronic stress [157].
- Reduces neuroinflammation [157,158].
- Stimulates the expression of brain derived neurotrophic factor

(BDNF) [157], which has neuroprotective effects, plays a role in neuronal development, and helps in the formation of neuronal connections important for memory and cognition [159].

Studies in mice have demonstrated that these effects ultimately lend lion's mane cognitive-enhancing [160], neuroprotective [161], and mood-stabilizing properties [157]. Preliminary research in humans suggests the same:

In **overweight and obese adults**, 1500 mg/d for 8 weeks reduced feelings of anxiety by 27% and feelings of depression by 39%, while also increasing brain-derived neurotrophic factor (BDNF) [162]. These benefits were maintained for another 8 weeks after supplementation ceased.



Vigna et al. Evid Based Complement Alternat Med. 2019; 2019: 7861297.

In **older Japanese men with mild cognitive impairment**, 3000 mg/d for 16 weeks improved cognitive function by 12% compared to placebo [163].



Lion's mane is a medicinal mushroom with cognitiveenhancing, neuroprotective, and mood-stabilizing properties.

Bacopa Monnieri

BACOPA IS SHOWN TO:





- Reduces oxidative stress and increases antioxidant enzyme activity
- Reduces inflammation
- Neuroprotective
- Reduces β-amyloid deposition
- Increases the growth of nerve endings to enhance neuronal communication
- Increase blood flow and the delivery of oxygen and nutrients

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Bacopa monnieri is an Ayurvedic swamp plant (*Brahmi*) traditionally used for the enhancement of memory and cognition, as well as a general brain tonic. It's bioactive constituents, the bacosides, have numerous biological effects within the brain that facilitate this use [164–168]:

- Reduces oxidative stress and increases antioxidant enzyme activity
- Reduces inflammation
- Neuroprotective
- Reduces β-amyloid deposition
- Increases the growth of nerve endings to enhance neuronal communication
- Increase blood flow and the delivery of oxygen and nutrients



Abdul Manap et al. Drug Target Insights. 2019; 13: 1177392819866412

In **healthy elderly adults**, supplementing with 300 mg/d of bacopa for 12 weeks significantly improved reaction times, the continuity of attention, the quality of memory, and the speed of memory by 15– 30% compared to placebo [169]. Similar but less pronounced benefits were observed with 600 mg/d of bacopa, suggesting that more is not always better.



In **young medical students**, 300 mg/d of bacopa (50% bacosides) for 6 weeks significantly improved efficiency of attention, freedom from distractibility, and working memory [170].

In **healthy adults**, 300 mg/d of bacopa (50% bacosides) for 12 weeks significantly improved speed of visual information processing, learning rate, memory consolidation, and decreased anxiety compared to placebo [171].

In **healthy adults**, 300 mg/d of bacopa (50% bacosides) for 12 weeks significantly improved working memory and visual processing ability [172].

In **healthy elderly adults** (average 73 years), 300 mg/d of bacopa (50% bacosides) for 12 weeks significantly improved multiple measures of cognitive performance and mood state compared to

placebo, including memory, reaction time, depression, and anxiety [173].

In **healthy older adults** (>50 years), 300 mg/d of bacopa (50% bacosides) for 12 weeks significantly improved verbal learning, memory acquisition, and memory retention compared to placebo [174].

In those with **Alzheimer's disease**, 600 mg/d of bacopa (50% bacosides) for 6 months significantly improved various components of Mini-Mental State Examination Scale (MMSES), including orientation of time, place and person, attention, and their language ability in terms of reading, writing, and comprehension [175].

Bacopa Monnieri is an Ayruvedic herb shown to improve memory and cognitive function in healthy adults and those with Alzheimer's disease.

Ginkgo Biloba

THE BRAIN-PROTECTIVE EFFECTS OF GINKGO BILOBA





- Neuroprotective
- Improves memory and cognitive performance
- Works as an antioxidant
- Counteracts cognitive impairment
- Improves neuroplasticity
- Preserves brain receptors in aging adults

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Ginkgo biloba possesses an array of activities relevant to brain health and neurological function, with numerous studies showing that it is neuroprotective, an antioxidant, preserves brain receptors susceptible to age-related loss, counteracts cognitive impairment, enhances neuronal plasticity, and improves memory [176].



Singh et al. Neurotherapeutics. 2019; 16(3): 666-674.

The Asian Clinical Expert Group on Neurocognitive Disorders claims that ginkgo biloba should be part of the treatment, either alone or in combination with other drug therapies, for the management of Alzheimer's disease, vascular dementia, and behavioral and psychological symptoms of dementia [177].

A systematic review of 12 meta-analyses found that ginkgo biloba improves cognitive performance, activities of daily living, and clinical global impression in the treatment of dementia at doses greater than 200mg/day (usually 240mg/day) administered for at least 22 weeks (5 months) [178].

A systematic review that detailed the research finding positive and negative results with ginkgo biloba supplementation found that no benefit was seen when supplementation lasted less than 22 weeks (5 months), used less than 240 mg/d, and involved cognitively healthy adults [179].

Ginkgo Biloba impacts brain health in numerous ways, such as enhancing neuronal plasticity and being neuroprotective. Supplementation consistently improves cognitive function in those with dementia or neurodegenerative diseases.

Coffee Fruit (NeuroFactor)

4 BENEFITS OF COFFEE FRUIT (NEUROFACTOR)





- Powerful antioxidant
- Improves neuroplasticity
- Helps grow new neurons and prevents neurodegeneration
- Improves long-term memory

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NeuroFactor is a patented extract of the whole coffee fruit, including both the fruiting body and the coffee bean it contains. While many are familiar with the coffee bean and the joy it brings through brewing into a morning cup of Joe, the fruit contains powerful antioxidant compounds that benefit our brain and body [180,181].

Clinical studies in healthy adults have shown that 100 mg of NeuroFactor nearly doubles concentrations of brain-derived neurotrophic factor (BDNF) after 1–2 hours [182,183], beating out other forms of coffee bioactives, caffeine, and the phytochemicalrich grape seed extract.



BDNF is a key protein involved in brain health, well established to be critical for:

- Neuroplasticity (helps the brain adapt to new situations) [184].
- Neurogenesis (the growth, regeneration and creation of new neurons and synapses) [185,186].
- Long-term memory [187].
- Prevention of neurodegeneration [188].

Coffee fruit extract is a powerful stimulant of BDNF, which has several critical roles in the preservation of brain health with aging.

Polygala tenuifolia

POLYGALA TENUIFOLIA





- Improves memory and combats forgetfulness
- Supports neurotransmitters required for learning, memory, and mental health
- Promotes growth of new neurons in the brain
- Increases neuroplasticity and cognitive function

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Polygala tenuifolia is one of the fundamental herbs used in traditional Chinese medicine, used to improve memory and combat forgetfulness with aging [189]. There are several mechanisms through with Polygala tenuifolia may accomplish these goals:

- Inhibiting the breakdown of acetylcholine, dopamine, serotonin, and noradrenaline, neurotransmitters required for learning new information, memory storage, and overall mental health [190,191].
- Increasing the expression of brain derived neurotrophic factor (BDNF), which is fundamental for neuroplasticity and neurogenesis [192].

• Promoting the growth of new neurons in the brain [193].

In **healthy adults**, 300 mg/d of Polygala tenuifolia for 4 weeks improved spatial and verbal memory [194]. The participants also made fewer errors and scored better on a test measuring working memory.

In **elderly adults**, 300 mg/d of Polygala tenuifolia for 8 weeks improved cognitive function by 5–10% compared to placebo [195].

Polygala tenuifolia helps balance neurotransmitters within the brain, improving cognitive function in both young and elderly adults.

Pine bark extract (Enzogenol)







 Potent antioxidant and anti-inflammatory compound
Improves memory and focus

- Boosts brain function
- Boosts brain function

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Enzogenol is a patented pine bark extract containing over 80% proanthocyanidins, which are potent antioxidant and antiinflammatory compounds found naturally in many fruits and vegetables, but especially apples, grapes, red wine, blueberries, and chocolate [196].



In **older men**, 5 weeks of supplementation with 980 mg/d of Enzogenol improved working memory [197]. A 1g/d dose has also been shown to improve cognitive function in those with **traumatic brain injury** after 6 weeks [198].

Other studies have also documented cognitive improvements following supplementation with Pycnogenol, a pine bark extract containing ~70% proanthocyanidins.

- In **university students**, 8 weeks of supplementation with pycnogenol tended to improve test scores [199].
- In **healthy middle-aged adults**, 150 mg/d of pycnogenol for 12 weeks reduced oxidative stress by 30% while improving cognitive performance and mood [200].
- In older adults with high levels of oxidative stress, 100 mg/d of pycnogenol for one year reduced oxidative stress by 28% and improved cognitive function, attention, and memory [201].
- In adults with mild cognitive impairment, 100 mg/d of pycnogenol for 8 weeks improved cognitive function by 18% [202].

Pine bark extract has potent antioxidant and antiinflammatory effects within the brain that manifest as

Panax Ginseng

Panax ginseng has been a popular and widely-used traditional herbal medicine in Korea, China, and Japan for thousands of years. Numerous studies have found that supplementation prevents the death of vulnerable neurons, reduces neuroinflammation and oxidative stress, and slows disease progression of neurodegenerative diseases like Alzheimer's, Parkinson's, Huntington's, and ALS [203– 207].



Rokot et al. Evid Based Complement Alternat Med. 2016; 2016: 2614742.

It also possesses acute cognitive benefits. Several studies of healthy adults have reported that supplementing with 200–400 mg improves cognitive performance, reduces mental fatigue, and increases feelings of calmness during mentally demanding tasks (like testtaking) [208–210]. The benefits appear to be amplified when combined with ginkgo biloba [211].

Panax ginseng is a neuroprotective agent that has been shown to slow neurodegenerative disease progression with chronic use and acutely improve cognitive performance in the hours following supplementation.

Blueberry

Blueberries are a rich source of anthocyanins and pterostilbene (phytochemicals), and have been shown to increase the activity of nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) [212,213], neuropeptides that helps neurons grow, branch toward each other, and thus communicate better [214]. For these reasons, blueberries and their anthocyanins are being increasingly investigated as a means of combating neurodegenerative diseases [215].

Accordingly, blueberries have been shown to increase cognitive function and slow cognitive decline with aging.

- In older adults, blueberry juice improved learning and memory while reducing depression after 12 weeks of regular consumption [216].
- Consuming 390 mg of blueberry anthocyanins for 12 weeks improved brain perfusion and activation in brain areas associated with cognitive function in healthy older adults [217].
- Increases in brain activity have also been seen in those with mild cognitive impairment after regular supplementation with the equivalent of 1 cup of whole blueberries daily [218].
- Consuming 100 mg of blueberry extract for 3 months improved working and episodic memory in healthy older adults [219].
- Supplementing with 160 mg of anthocyanins improved memory and executive cognitive function after 16 weeks [220].
- In young and healthy adults, just 300 grams of mixed berries (1/4 blueberries and half the phytochemical content coming from the blueberries) improved cognitive function for 6 hours after consumption [221].
- A systematic review of human clinical trials found that six of seven studies reported improvements in cognition, including learning and memory, after anthocyanin-rich food consumption (like blueberries and bilberries) [222].

Blueberries are rich in anthocyanins that protect the brain from cognitive decline with aging and provide acute increases in cognitive function in the hours after eating them.

Vitamins and Minerals

It shouldn't come as a surprise that falling short on your micronutrient intake could set you up for long-term trouble with neurological health along with dozens of other problems. Yet, even if your diet is on-point with adequacy, there are certain compounds that you may not obtain enough of or obtain in the right form to maximize the benefits they offer.



Tocotrienols

Vitamin E tocotrienols are potent antioxidant molecules that incorporate into cell membranes and neutralize free radicals that would otherwise cause peroxidation of the phospholipids <u>(Serbinova et al. 1991; Serbinova and</u>

Packer 1994; Suzuki et al. 1993).

It's an incredibly important job, one that works synergistically with other antioxidants like vitamin C and glutathione to ensure the integrity of our cell membranes <u>(Chan 1993)</u>. Most of the vitamin E deficiency symptoms can be linked to unrestrained lipid peroxidation, such as the deterioration and our nerves that ultimately causes neuropathy and ataxia.

Supplementation with tocotrienols significantly increases their concentration in critically important organs like the brain, heart, and liver (Patel et al. 2012). Moreover, the concentrations achieved within the brain are precisely around the concentrations needed to prevent brain damage and neurotoxicity from excessive glutamate and other toxicants (Sen et al. 2004).



Because of their neuroprotective and antioxidant effects, an evergrowing body of research is looking into using tocotrienols for the prevention and treatment of Alzheimer's disease <u>(Chin and Tay</u> <u>2018)</u>. For example, a randomized controlled trial of individuals with active white matter lesions of their brains, a sign of neurodegeneration, found that 400 mg per day of mixed tocotrienols completely halted the loss of white matter and further brain deterioration after two years <u>(Gopalan et al. 2014)</u>. Comparatively, the white matter loss of the placebo group had increased by 23%!



Vitamin E is a generic term for eight structurally similar molecules, four tocopherols and four tocotrienols. While most vitamin E research focuses on just one of these eight molecules (alpha-tocopherol), it is becoming increasingly clear that the tocotrienols are superior antioxidants and anti-inflammatories that have potent neuroprotective effects.

Methyl B-Complex

Out of all the essential vitamins and minerals, the B-vitamins deserve special attention because without them, we wouldn't be able to turn the food we eat into cellular energy and our mitochondria couldn't function. The specific vitamins include:

- **Thiamine** (B1) is required to harvest energy from glucose and for the synthesis of energy-carrying molecules within mitochondria.
- **Riboflavin** (B2) is the central unit for flavoproteins, which are necessary for mitochondrial energy production and antioxidant defenses.
- **Niacin** (B3) is the central unit for NAD+ and NADP, which are necessary alongside flavoproteins for mitochondrial energy production and antioxidant defenses.
- **Pantothenic acid** (B5) is the central unit of coenzyme A, which plays a vital role in energy production and the metabolism of many nutrients.
- **Pyridoxal** (B6) is required for amino acid metabolism, gene expression, and the breakdown of homocysteine.
- **Biotin** (B7) is the central component of several enzymes involved in energy production, amino acid metabolism, gene expression, and cell growth.
- Folate (B9) is required for methylation reactions, DNA synthesis, and the breakdown of homocysteine.

• **Cobalamin** (B12) is necessary for the breakdown of certain amino acids and fatty acids, as well as for the breakdown of homocysteine and recycling of folate.

Aside from energy production, three of the B-vitamins are essential for another critically important job within the body: the breakdown of *homocysteine*, the excess of which has a diversity of harmful effects on our body, particularly when it comes to our cardiovascular system, brains, bones, and joints <u>(Kuo et al. 2005)</u>.

Moreover, individuals with chronic fatigue have significantly elevated levels of homocysteine in their cerebrospinal fluid that nourishes the brain and spinal cord, and the amount of homocysteine is directly related to one's fatigability — more homocysteine, more fatigue <u>(Regland et al. 1997)</u>. There's also a strong connection between homocysteine and neurodegeneration, with one analysis suggesting that lowering homocysteine levels in the elderly population could prevent 12–30% of all dementia and Alzheimer's disease cases <u>(Smith et al. 2018)</u>. Even if you don't yet have any mental health issues currently, elevated homocysteine increases your risk for cognitive problems down the road <u>(Zhou and Chen 2019)</u>.

All types of dementia	Alzheimer's disease	Vascular dementia	Cognitive impairment			
12%	15%	32%	6%			

Increased risk of cognitive decline per 5 µmol/L increase in homocysteine

The breakdown of homocysteine involves three B-vitamins: folate, vitamin B12, and vitamin B6. Folate is the most important and requires the most attention because we need a special form called 5-methyl-tetrahydrofolate, or methyl-folate for short, to break down homocysteine.

The reason it requires the most attention is because the only way our body can create methyl-folate is through the enzyme methylenetetrahydrofolate reductase (MTHFR). Yet, many people have genetic polymorphisms (a type of mutation) that impair the ability of this enzyme to function.

The two most common polymorphisms are $677C \rightarrow T$ and $1298A \rightarrow C$, both of which reduce MTHFR function to varying degrees (Weisberg et al. 1998; van der Put et al. 1998; Chango et al. 2000). For example, if having zero polymorphisms represents a completely functional enzyme, then being 677 TT can reduce enzymatic function by

70–80%, while being 1298 CC can reduce function by 40–50%.

GENOTYPE	677 CC (normal)	677 CT (heterozygous)	677 IT (homozygous)
1298 AA (normal)	100%	50–75%	20–30%
1298 AC (heterozygous)	60–90%	35–60%	_

1298 CC (homozygous)	50–60%				
The dathes () represent a lack of data due to the extreme rarity of these combination					

The dashes (—) represent a lack of data due to the extreme rarity of these combinations.

This means that you're going to have a hard time detoxifying homocysteine unless you directly consume methyl-folate to bypass this bottleneck process. While eating a diet rich in fibrous vegetables and legumes can help, since roughly 45–65% of their folate is in methyl-folate form <u>(Gorelova et al. 2017)</u>, many people need additional supplementation to keep homocysteine levels in check.

The amount of supplemental folate needed to maintain a healthy homocysteine range of 5–7 µmol/L is variable between individuals. The best thing to do is monitor your own homocysteine level and modify the dose of folate you take until homocysteine is in a healthy range. If you don't want to go to the trouble of doing regular blood work, just make sure to put emphasis on making sure you have more than adequate intake of folate (at least 400 micrograms of methylfolate per day) and other methylated B-vitamins.

Next up is vitamin B12, which we need to use folate in the breakdown of homocysteine. You'll find several forms of B12 on the market, including methyl-, adenosyl-, hydroxy-, and cyano- B12, but all of them are broken down into their core B12 molecule during digestion and absorption (Paul and Brady 2017).

Still, some studies have suggested that retention rates with methyland hydroxy- B12 are greater than that of cyano-B12, largely due to lower excretion [50,51]. Plus, there may be yet unidentified polymorphisms in B12 receptors and transporters that impact how someone responds to specific forms of B12 supplements. As such, it makes sense to supplement with methyl-, adenosyl-, or hydroxyforms of B12 — the forms that we naturally obtain in our diet -- rather than cyano-.

Lastly, for vitamin B6, all forms are turned into pyridoxal-5-phosphate (P5P), which is the only form of vitamin B6 that has biological activity within the body. That being said, supplementation with the pyridoxine form has been linked to the development of peripheral neuropathy when supplemented at more than 25 mg/d for months to years (van Hunsel et al. 2018), so we strongly recommend supplementing with P5P directly.

Lastly, while not a B-vitamin, it's worth mentioning that betaine (also called trimethylglycine) can also help break down homocysteine, and several studies have shown that supplementing upwards of 6 grams per day reduces homocysteine levels in a dose-dependent manner, where higher doses lead to greater reductions (McRae 2013; Olthof and Verhoef 2005; Olthof et al. 2003).
Elevated homocysteine concentrations and impaired methylation are strongly linked to cognitive decline with aging. To detoxify homocysteine and support optimal rates of methylation, we need ample intakes of riboflavin, folate, B6, B12.

For those with polymorphisms of the MTHFR enzyme, which reduce the activity of this enzyme responsible for making folate bioavailable, then supplementation of high-dose riboflavin and a specific form of folate called 5-methyl-THF become incredibly important.

Magnesium

Magnesium Taurate





Required for optimal nerve transmission

- Protects against cell death
- Prevents mitochondrial dysfunction
- Prevents migraines
- Improves anxiety and depression
- Slows development of and severity of Parkinson's and Alzheimer's
- Reduces risk of stroke

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Magnesium is required for over 300 enzymes to function properly [38]. We need it for our muscles to contract, to regulate blood pressure, for proper insulin signaling, and for the synthesis of DNA and proteins. Within the brain and nervous system, magnesium is required for optimal nerve transmission and protection against excitotoxicity (excessive excitation leading to cell death) [39,40].

In particular, one of the enzymes that relies on magnesium is ATP synthase, which is responsible for generating cellular energy (ATP) within mitochondria. Without magnesium, your mitochondria simply can't function efficiently [41,42], which matters because mitochondrial dysfunction is a central component of neurodegenerative diseases like Alzheimer's [43–46]. For example, those with Parkinson's disease have lower brain concentrations of magnesium than those without [47,48], and the extent of magnesium depletion correlates with symptom severity [49]. Similarly, those with Alzheimer's disease have lower brain concentrations of magnesium compared to those without [50–52].

But, not all forms of magnesium are the same. You'll find many types on the market, and the evidence is clear that magnesium taurate demonstrates a superior ability to enter into the brain and increase the brain's magnesium status.

One study compared the tissue distribution of magnesium 8 hours after taking equal amounts of magnesium citrate, malate, oxide, sulfate, and taurate [53]. It was shown that magnesium taurate increased brain magnesium concentrations 10–20% more than the other forms.



In another study, the tissue distribution of magnesium 24 hours after supplementation was compared between different doses (45, 135, and 405 mg) of magnesium citrate, glycinate, malate, and taurate [54]. Just 45 mg of magnesium taurate was enough to increase brain concentrations to the same extent as 405 mg of glycinate or citrate and was 23% more effective than 405 mg of magnesium malate.



Another form of magnesium not tested in these studies but touted for its neurological benefits is magnesium L-threonate. This form of magnesium was developed by Guosong Liu at Tsinghua University as a means of increasing brain magnesium concentrations in rats, but has only been compared to magnesium citrate and gluconate, showing marginal superiority [55].

Given the importance of magnesium in brain health, particularly magnesium concentrations within the brain, it makes sense to use the most bioavailable form: magnesium taurate. Magnesium plays a critical role in neurotransmission, neuroprotection, and energy production within the brain. Low brain concentration of magnesium has been linked to neurodegenerative diseases like Alzheimer's. The ideal supplemental form of magnesium for increasing brain concentrations is magnesium taurate.

Amino Acids and Peptides

Amino acids are a diverse group of nitrogen-containing molecules and the second most abundant component of the human body after water. When multiple amino acids join together, they form peptides and protein structures.

Our DNA holds the blueprint to create more than 25,000 proteinbased compounds that are involved in countless essential functions, including growth, movement, and the regulation of metabolism. From a neurological perspective, amino acids and peptides are also required for neurotransmitter synthesis and energy production within the brain.

L-Tyrosine

L-tyrosine is a conditionally essential amino acid that serves as the precursor molecule from which we create the catecholamines: dopamine, adrenaline, and noradrenaline. Your brain needs a

steady supply of tyrosine to make the catecholamines and keep your mental health at its peak [56,57], particularly if you are under a lot of stress [58].



Several clinical trials have shown that supplementing with 2–12 g/d of tyrosine improves cognition, alertness, and memory in stressful and demanding situations in otherwise healthy adults [59,60].

• In **healthy adults** who are up all day only to work through the night (24 hours of wakefulness), 10 grams of tyrosine significantly attenuated the cognitive decline caused by sleep loss [61].

- In **military cadets** undergoing a week of intense military combat training, 2 g/d of tyrosine better maintained their memory throughout [62].
- In **healthy adults** undergoing testing with loud and disruptive music playing, 5–10 grams of tyrosine an hour before the test significantly improved test-taking performance and the ability to focus [63].
- In **healthy adults** needing to multitask and frequently switch attention between tests, 11 grams of tyrosine improved testing accuracy and working memory [64].
- In **healthy adults** exposed to 90 minutes of cold water immersion, 10 grams of tyrosine taken beforehand improved working memory and information processing [65].
- In healthy adults, several studies using 2 grams of tyrosine have reported beneficial effects on working memory [66], deep thought [67], and cognitive flexibility [68].

L-tyrosine is a precursor to the catecholamines and supplementation can help maintain cognitive function when under high levels of stress that would otherwise drain

the brain of dopamine, adrenaline, and noradrenaline.

L-theanine

L-theanine isn't a stimulant; it's a naturally occurring amino acid found in tea that improves feelings of relaxation, tension, calmness, and anxiety in the hours following doses of 200–600 mg [233,234]. The reason we mention it here is because L-theanine synergizes with caffeine to enhance cognitive function while minimizing the potential for unfavorable side effects.

For example, one study compared the cognitive effects of 150 mg caffeine, 250 mg theanine, or the two combined, with testing conducted 30–90 minutes after supplementation [235]. Despite maintaining or improving the cognitive benefits from caffeine alone, the combination with L-theanine led to greater alertness, a better mood state, and less mental fatigue while minimizing the jitters and feelings of tension.



L-theanine is an amino acid found in tea that works synergistically with caffeine to improve cognitive function and minimize the potential for side effects.

Creatine

Creatine is a peptide we make within the liver and kidneys from the amino acids glycine, arginine, and methionine. While most of the body's creatine is stored in skeletal muscle, each and every cell in the body uses creatine in the form of phosphocreatine to regenerate ATP (cellular energy) near immediately. As such, creatine is a first-line energy supply.

To give an example of creatine's potent energy-generating properties, cellular ATP levels in working muscles during all-out exertion (e.g., leg muscles during sprints) barely decrease over the first 5–10 seconds, while 75–85% of phosphocreatine is used up [69].

In fact, it's the decline in phosphocreatine and consequential reduction in ATP supply that causes exercise intensity to decline so quickly when sprinting [70].

Supplementing creatine works, quite simply, through saturating phosphocreatine stores, so that there is more available for the immediate resynthesis of ATP when necessary. This is why creatine is

such a heavily researched ergogenic supplement for bolstering exercise performance, and studies clearly indicate that it is able to increase muscle strength, power output, and lean body mass [71– 75].

Yet, researchers are also starting to look into creatine's massive benefits for brain health and cognitive function by serving as an energy reservoir for neurons [76]. Many neurodegenerative diseases involve mitochondrial dysfunction and impaired energy production, so creatine saturation of brain stores can help protect neurons from further damage and disease progression [77–79].

There's also benefits on cognitive function in healthy adults, especially those with a low dietary intake of creatine, such as vegetarians and vegans (since creatine is found naturally in animal products only). Several studies have found that creatine supplementation increases brain creatine concentrations alongside memory, intelligence, and reasoning abilities [80,81].

For example, one study recruited young and healthy vegetarians and vegans to supplement with either 5 grams of creatine monohydrate or placebo for 6 weeks, at which point they took a 6week break and then started up again with the other supplement [82]. Creatine supplementation increased scores on a test of intelligence by 35% and scores on a test of working memory by 20%, with both scores declining when the participants stopped taking creatine.



Creatine is an essential molecule for energy production within the brain and supplementation can saturate creatine stores and improve cognitive function, particularly in those with a low dietary intake (e.g., vegetarians and vegans).

ALCAR

7 BRAIN-BOOSTING BENEFITS OF ALCAR





- Improves brain function, especially memory and attention
- Reduces oxidative stress
- Protects against β-amyloid neurotoxicity
- Reduces mental and physical fatigue
- Reduces depression more effective than antidepressant drugs! (And with far less side effects)
- Reduces pain and increases nerve conduction
- Prevents progression of brain-related disease

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Carnitine is an essential component of mitochondria, responsible for shuttling fatty acids across the mitochondrial membranes so that they can be used for energy production. Acetyl L-Carnitine (ALCAR) is a unique form of L-Carnitine that has incredible brain- and bodyboosting properties.

Why? Because supplementation is well-established to increase mitochondrial function and energy production [83,84], particularly within the brain thanks to ALCAR's ability to easily cross the blood-brain barrier [85–89]. It also protects against β-amlyoid neurotoxicity and reduces oxidative stress [90].

Notably, ALCAR concentrations slowly decline as cognitive impairment progresses, ultimately being 36% lower in Alzheimer's patients than healthy adults [91].



ALCAR concentrations decline with neurodegeneration

Collectively, these effects make ALCAR a game-changer for anyone with neurodegenerative disorders or dementia, or are on their way to developing them [92].

- A meta-analysis of 21 randomized controlled trials involving patients with mild cognitive impairment or Alzheimer's disease found that 1.5–3 g/d of ALCAR significantly improved cognitive function and prevented the progression of Alzheimer's after as little as 3 months [93]!
- Supplementing 1.5–2 g/d of ALCAR has also been shown to significantly improve cognitive function, particularly memory

Cristofano et al. PLoS One. 2016; 11(5): e0155694.

and attention, in older adults suffering from mild cognitive impairment or vascular dementia [94–96].

 In elderly adults suffering from excessive fatigue, 4 g/d of ALCAR improved cognitive function, reduced mental and physical fatigue, and improved the ability to function in daily life [97].



Malaguarnera et al. Arch Gerontol Geriatr. 2008; 46(2): 181-90.

Acetyl-L-Carnitine (ALCAR) increases mitochondrial function and energy production within the brain.
Supplementation has been shown to improve cognitive function in those with neurodegenerative disorders or dementia.

GABA

GABA





- Part of nucleic acids in DNA and RNA
- Critical for creation of brain phospholipids
- Induces nerve growth
- Increases learning
- Improves depression

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GABA is the most potent depressive neurotransmitter in human brains. It regulates many of the depressive and sedative actions in brain tissue and is critical for relaxation [98,99]. It is also critical for the regulation of neuronal communication, cognition, emotion, and memory [100–102].

Research has documented a relationship between lower levels of GABA in the brain and cognitive deficits in humans:

- Worse memory in patients with multiple sclerosis [103].
- Self-reported cognitive failures (inability to attend to relevant details while being distracted by irrelevant details) in healthy adults [104].

- Lower visuospatial IQ in post-graduate and doctoral students [105].
- Less empathy in healthy adults [106].
- Reduced resilience to stress and greater susceptibility to depression and anxiety [107].
- Susceptibility to addiction [108].

It's been suggested that higher GABA levels help reduce distraction in the brain, which makes it possible to react and make decisions more quickly [109]. A single dose of 800 mg of GABA has been shown to improve attention and task switching in healthy young adults [110,111].

GABA is a critical neurotransmitter for the regulation of neuronal communication, cognition, emotion, and memory, with supplementation helping improve attention and the ability to task-switch.

Cholinergics

Choline is an essential nutrient within the brain required for the synthesis of acetylcholine (the primary neurotransmitter involved in executive functions) and phosphatidylcholine (one of the most abundant and important structural components of cell membranes). Cholinergics are substances that increase brain choline concentrations and acetylcholine signaling.



It's well-established that choline within the brain plays a critical role in neuronal plasticity, membrane stability, signaling events, and neurotransmission [112]. It is, without a doubt, neuroprotective [113], and a low brain concentration is one of the primary contributors to vascular dementia and Alzheimer's disease [114,115].

In fact, if you take young adults and inhibit acetylcholine signaling, they demonstrate similar impairments to long-term and working memory as elderly adults suffering from cognitive decline [116]. Moreover, reductions in acetylcholine signaling set the brain up to be less plastic and more vulnerable from other insults like oxidative stress, inflammation, and injury [117].

For these reasons, Alzheimer's disease is currently treated with acetylcholinesterase inhibitors, a group of drugs that increase acetylcholine concentrations by inhibiting the enzyme that degrades it (acetylcholinesterase). Yet, there are several natural compounds that have similar effects.

Alpha-GPC

ALPHA-GPC HAS BEEN SHOWN TO:





- Protect neurons in the brain and support neurotransmission
- Increase dopamine and serotonin signaling in the brain
- Decrease risk of vascular dementia
- Be more effective than Alzheimer drug (Aricept) at improving cognition

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Alpha-glycerophosphocholine (Alpha-GPC) is a highly bioavailable source of choline for the brain. After ingestion, blood and brain

levels of choline and glycerophosphate (the molecule bound to choline in alpha-GPC) increase over 5–10 hours and remain elevated for more than a day [118].



As of 2007, alpha-GPC has been investigated in 14 clinical trials enrolling individuals with neurodegenerative disorders, vascular dementia, or stroke, and the results have been very positive [119]. For example, compared to drug therapy for Alzheimer's disease (the cholinesterase inhibitor called donepezil), 1200 mg/d of alpha-GPC was more effective at improving cognition over 6 months [119].



More recently, a series of publications from the ASCOMALVA study have been reported. This clinical trial recruited older adults with Alzheimer's disease to take either donepezil alone or with 1200 mg/d of alpha-GPC.

- After 1 year, alpha-GPC was shown to prevent the decline in cognitive function and progression in Alzheimer's disease seen in the drug-only group [120].
- After 2 years, these benefits simply became more pronounced [121]. The decline in cognitive function with alpha-GPC was 2.5to 4-fold less than with the drug alone. Alpha-GPC also reduced the extent of behavioral abnormalities [122].



Alpha-GPC is a potent source of choline for the brain that appears to be superior to conventional drugs for preventing cognitive decline with aging and in Alzheimer's.

CDP-choline

CDP-CHOLINE





- Promotes cell membrane health
- Improves memory and overall brain cognition
- Improves motor function
- Increases focus
- Reduces impulsive behavior
- Improves neuroplasticity (helps the brain adapt to new situations)

Like with alpha-GPC, CDP-choline is a bioavailable source of choline for the brain [123]. Unlike alpha-GPC, however, CDP-choline is the direct precursor for the synthesis of phosphatidylcholine [124], one of the most abundant and important structural components of cell membranes.



Research in humans has suggested that taking CDP-choline increases phosphatidylcholine synthesis within the brain [125], with one study showing that 500 mg/d takes 6 weeks to maximize increases in brain phospholipid concentrations, after which there is a plateau [126].

Several interventions have noted benefits of CDP-choline supplementation in both healthy adults and those suffering from cognitive decline.

- In **adolescents**, taking 250 or 500 mg/d of CDP-choline for 1 month improved motor function and attention [127].
- In healthy women, taking 250 or 500 mg/d of CDP-choline for 1 month improved attention performance and reduced impulsivity [128].

- A Cochrane Systematic Review of 14 double-blind, placebocontrolled trials of older adults with cognitive deficits like dementia reported that 600–1000 mg/d of CDP-choline was able to improve memory, correct abnormal behaviors, and increase the global impression that physicians have towards the participants [129].
- Two later studies involving older adults with dementia or Alzheimer's disease found that 1000 mg/d of CDP-choline plus a common Alzheimer's medication (acetylcholinesterase inhibitor) prevented the deterioration of cognition over 9 months compared to the drug alone [130,131].
- In older adults with mild vascular dementia, 1000 mg/d of CDPcholine doesn't just prevent a decline in cognitive function observed in a placebo group, but actually improves cognitive function relative to before supplementation started [132].

CDP-choline increases brain concentrations of phosphatidylcholine, one of the most abundant and important structural components of cell membranes, and has been shown to improve cognitive function in both healthy adults and those suffering from cognitive decline.

Huperzine A

4 BENEFITS OF HUPERZINE A





- Promotes learning
- Used for centuries to treatbrain-based illnesses
- Improves cognition, especially in people with Alzheimer's and vascular dementia
- Naturally occurring acetylcholinesterase inhibitor (primary class of drugs for treating Alzheimer's and dementia)

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Huperzine-A is an alkaloid derived from the moss *Huperzia serrata*, which itself has been used in traditional Chinese Medicine for centuries to treat neuronal- and cognitive-based illnesses [133]. It's a naturally occurring acetylcholinesterase inhibitor [134], meaning it prevents the breakdown of acetylcholine just like many Alzheimer's drugs do.

At least 20 randomized controlled trials have evaluated the efficacy of huperzine A in patients with Alzheimer's disease, with a metaanalysis showing improvements for cognitive function, daily living activity, and global clinical assessments with doses of 200–800 mcg (average: 370 mcg) over 8–36 weeks [135].



Other meta-analyses have reported that huperzine A improves cognition in those with vascular dementia [136], as well as in those with major depression [137]. It's effects are less pronounced in healthy adults without impaired cognitive function [138], even when combined with alpha-GPC [139], due to a ceiling effect whereby greater acetylcholine signaling doesn't confer additional benefits in those with proper signaling to begin with.

Huperzine A is a naturally occurring acetylcholinesterase inhibitor that improves cognition and functional capacities of those with Alzheimer's disease and other forms of dementia or cognitive impairment.

With all of this said, I'd like to tell you about our ultra-premium formula that we've designed specifically to boost brain health, and all that it encompasses -- from focus, to clarity, to mood support, to long-term brain health and neurotransmitter optimization. It's called UltraBrain and it includes most of the ingredients we just discussed.

INTRODUCING UltraBrain

We created a premium, next generation brain supplement that's packed with the nutrition your brain needs to heal and function at its full power.

ULTRABRAIN IS A FULL-SPECTRUM NOOTROPIC THAT:





- Restores your blood-brain barrier, keeping toxins OUT of your brain and letting IN key nutrients, like glucose and amino acids
- Increases mitochondrial function, ensuring they remain out of the cell danger response and stay in energy production mode
- Reduces inflammation and oxidative damage, helping your neurons fire more quickly and promoting proper cell function and communication
- Optimizes your entire brain, ensuring each part is working at maximum capacity
- Is safe and effective for everybody (and every brain), no matter the age or activity level
- Contains zero stimulants, junk, or fillers and uses only high quality, carefully sourced ingredients

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UltraBrain is a full spectrum nootropic that:

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- **Optimizes your entire brain**, ensuring each part is working at maximum capacity.
- Is safe and effective for everybody (and every brain), no matter the age or activity level.
- **Contains zero stimulants**, junk, or fillers and uses only high quality, carefully sourced ingredients.





THE PERFECT FORMULATION

15 Premium Ingredients in Effective Dosages

Suggested Use: Take 6 capsules per day. Use Ultrabrain 5 days a week and take 2 days off. (E.g. weekends off). Take UltraBrain with food, in one dose or two divided doses (e.g. 3 pills with breakfast and 3 pills with lunch). This is a potent supplement, so when initially starting, we suggest starting with only 2-3 pills per day and then working your way up to your optimal dose (up to 6 capsules per day), over the course of several days.

Supplement Facts

Serving size: 6 capsules

Servings Per Container: 25

Amount Per Serving		%DV
Rhodiola Extract (Rhodiola rosea) (3% salidrosides and 1% rosavins)	400 mg	**
Lion's Mane (Hericium erinaceus) (fruiting bodies)	600 mg	**
Alpha-GPC (50%)	150 mg	**
CDP-Choline (as Cognizin [®] Citicoline)	150 mg	**
Bacopa Extract (Bacopa monnieri) (leaf) (standardized to 50% bacopa glycosides)	300 mg	**
Ginkgo Extract (Ginkgo biloba) (24% flavone glycosides & 6% terpene lactones)	250 mg	**
CognatiQ [™] Whole Coffee Fruit Extract (Coffee Arabica)	100 mg	**
Huperzine A (from Huperzia serrata whole plant extract)	200 mcg	**
Acetyl-L-Carnitine	600 mg	**
Saffron Extract (Crocus sativus) (2% safranal)	30 mg	**
L-Theanine	200 mg	**
Agmatine Sulfate	500 mg	**
Polygala Tenuifolia (20:1 extract)	125 mg	**
Tyrosine (as N-Acetyl-L-Tyrosine)	300 mg	**
Magnesium (as Magnesium Taurate)	60 mg	**

** Daily Value (DV) Not Established Not a significant source of Vitamin A, Vitamin C, and Calcium.

Other Ingredients: Vegetable Capsules (cellulose).

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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 OR ILLNESS.

KEEP OUT OF THE REACH OF CHILDREN. DO NOT USE IF SAFETY SEAL IS DAMAGED OR MISSING. STORE IN A COOL, DARK PLACE. CONSULT YOUR PHYSICIAN IF YOU ARE PREGNANT OR LACTATING.

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Manufactured For: Energy Blueprint Labs 249 S Hwy 101 Suite 410 Solana Beach, CA 92075 theenergyblueprint.com

Why These Specific Nutrients?

We spent years combing through mountains of scientific studies, finding the ingredients *proven* to provide broad spectrum brain healing and support.

The result is a very carefully curated formulation that meets these unparalleled standards:

- Absolutely zero pseudo-science, fads, or false marketing. Pure science in every serving.
- Each ingredient is in its most potent, bioavailable form. Really nothing else can outperform these brain boosting compounds.
 Effective dosages in each and every serving. 1 scoop a day [OR X AMOUNT OF PILLS] is everything you need to help reverse cellular dysfunction and supercharge your mental capacity.

The specific stack of ingredients in UltraBrain work together to stimulate your brain in multiple ways:



Brain Clarity | Improve your memory, concentration, and focus. Remove your mental fog and clouded thoughts.



Brain Energy | Boost your alertness, stamina, and energy. Accomplish mentally demanding tasks and not feel tired.



Brain Strength | Handle and recover from stress better. Bounce back faster. Become less fragile and anxious.



Brain Balance | Maintain an even, joyful mood that easily feels and appreciates pleasure. Eliminate depression and anxiety and be happy, optimistic, and grateful.



BUY NOW From US\$ 74

UltraBrain was formulated to give you your youthful, alert, energetic brain back.

The 18 science-backed ingredients – in *effective* dosages in each serving – will help heal your brain, allowing your cognitive function to reach its full potential.

Even after just a few daily doses, you'll notice dramatic improvements in your mental performance and will be able to:

- Shut down neuroinflammation and increase mitochondrial health in the brain, supercharging your brain cell communication and stopping brain-related fatigue.
- **Repair neurotransmitter imbalances**, positively impacting your cognitive function and learning, your mood and ability to feel joy, your sense of relaxation and calm, your stress response and tolerance, and your energy and wakefulness.
- **Protect your blood-brain barrier**, keeping toxins out of your brain and preventing negative immune reactions.
- **Maintain steady blood sugar levels**, which will greatly reduce brain fog and anxiety. UltraBrain not only has zero sugars but it also has the proper amount of protein to help regulate your glucose.

- **Regulate your appetite.** Eating less will reduce inflammation and cellular damage and thus boost your brain health.
- **Minimize your caffeine dependence**, so you can correct your cognitive function and mood and significantly raise your baseline energy levels.
- **Develop metabolic flexibility**, helping your body seamlessly switch from burning calories from food to tapping into stored sources of fuel (ie body fat) when needed. Your body's capacity to easily shift like this is important for maintaining proper brain function and energy levels.

When your brainpower is optimized like this, you will be better able to:

- Make decisions quickly so you can work more efficiently and get your to-dos done in much less time!
- Sleep soundly through the night so you can bounce out of bed without the *need* for coffee.
- Handle bad news and stressful situations without anxiety or worry. Confidently tackle your problems, big or small.
- Be clear headed and able to concentrate for long periods of time.
- Recall all the important details of your life with ease (and without the need for post-it notes).
- Complete mentally challenging tasks with plenty of energy to spare. Now is the time to crack open that non-fiction book.

Custom formulated with 15 power-packed nutrients, UltraBrain is the ONLY supplement you need to heal

your brain and rewire it for lasting clarity, resilience, joy, and energy.

That's because each of the ingredients are scientifically proven to tackle *all* types of brain dysfunction.

Take it each day and heal damaged cells, reduce neuroinflammation, and repair faulty communication.

Take it each day and experience renewed mental strength and vitality – that you haven't felt in years.



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