Examine.com

Memory & Focus Supplement Guide

Written by the editors of Examine.com

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Medical Disclaimer

This guide is a general-health document for adults over 18. Its aim is strictly educational. It does not constitute medical advice. Please consult a medical or health professional before you begin any exercise-, nutrition-, or supplementation-related program, or if you have questions about your health.

This guide is built on scientific studies, but study outcomes are never homogeneous: individual results do vary. If you engage in any activity or take any product mentioned herein, you do so of your own free will, and you knowingly and voluntarily accept the risks. While we mention major known interactions, it is possible for any supplement to interact with other supplements, as well as with foods and pharmaceuticals.

A product may not contain the exact compounds and amounts listed on its label. Before you decide whether to take it, investigate it and its manufacturer. More than isolated compounds, herbs are prone to batch-to-batch variability, which can alter their efficacy and safety.

For evidence supporting the claims mentioned in this guide, please visit Examine.com.

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How to Use This Guide

The Examine.com team has been publishing research on nutrition and supplementation since March 2011. Drawing from all we've learned, we've designed this Stack Guide to help you figure out which supplements can help you reach your health goal, and which can hinder you or just waste your money.

Core supplements have the best safety-efficacy profile. When used responsibly, they are the supplements most likely to help and not cause side effects.

Primary options may provide substantial benefit, but only in the right context. A primary option is not for everyone, but if you read the entry and find that you meet the criteria, consider adding the supplement to your stack.

Secondary options have less evidence for their effects. They could work or be a waste of money. Keep them in mind, but think twice before adding them to your stack.

Promising supplements are backed by tradition or by mechanistic, animal, epidemiological, or anecdotal evidence, but not yet by convincing human trials.

Inadvisable supplements are either potentially dangerous or simply ineffective, marketing claims notwithstanding. Do not add them to your stack. At best, they'll be a waste of money; at worst, they can cause you harm.

Now that you've been presented with various supplements worthy of your interest, the time has come to combine them based on your objective. We'll guide you in **assembling your stack**.

Then comes the **FAQ**, in which we cover common questions that may arise when assembling your stack.

Lastly, we include information on **precautions and troubleshooting**.

With all this combined, you should be able to identify and assemble the supplement stack best suited to your objective.

Core Supplements

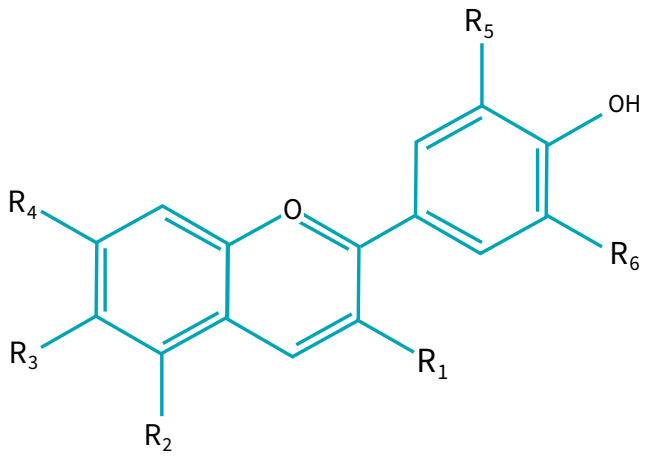
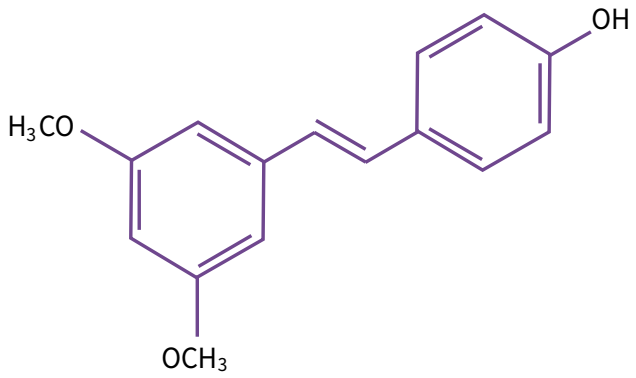
Blueberries

Why they're a core supplement

The anthocyanins and pterostilbene in blueberries can protect the brain and influence its activity. Anthocyanins are also the probable reason why blueberries can increase the activity of *neuronal growth factor* (NGF), a neuropeptide that helps neurons grow, thus branch toward each other, thus communicate better. The human studies were in senior citizens, but the mechanistic and animal evidence suggest that the brain of younger people could also benefit.

Blueberries do not interact negatively with pharmaceuticals: Safe and readily available, they are the ideal core supplement for a *Memory & Focus* stack.

Figure 1: The differences between Anthocyanins and Pterostilbene

Anthocyanins	Pterostilbene
	
Pigments that often give a red, purple, or blue color to the plants that have them	A derivative of resveratrol, the antioxidant found in red wine
Some have antioxidant or anti-inflammatory properties	May possess antioxidant and anticancer properties
More than 635 anthocyanins have been identified	Can help reduce blood glucose and improve insulin sensitivity

How to take them

Studies support the following protocols:

- Blueberry anthocyanins: 500–1,000 mg/day.
- Blueberry powder: 5.5–11 g/day (≈ 38.5–77 mg of anthocyanins).
- Fresh blueberries: 60–120 g/day (≈ 120–240 mg of anthocyanins).
- Blueberry juice: 500 mL/day. Blueberries should be the first ingredient of the juice. Any juice made primarily from sugars, with added flavoring, will not provide the same benefits to memory or focus.

Primary Options

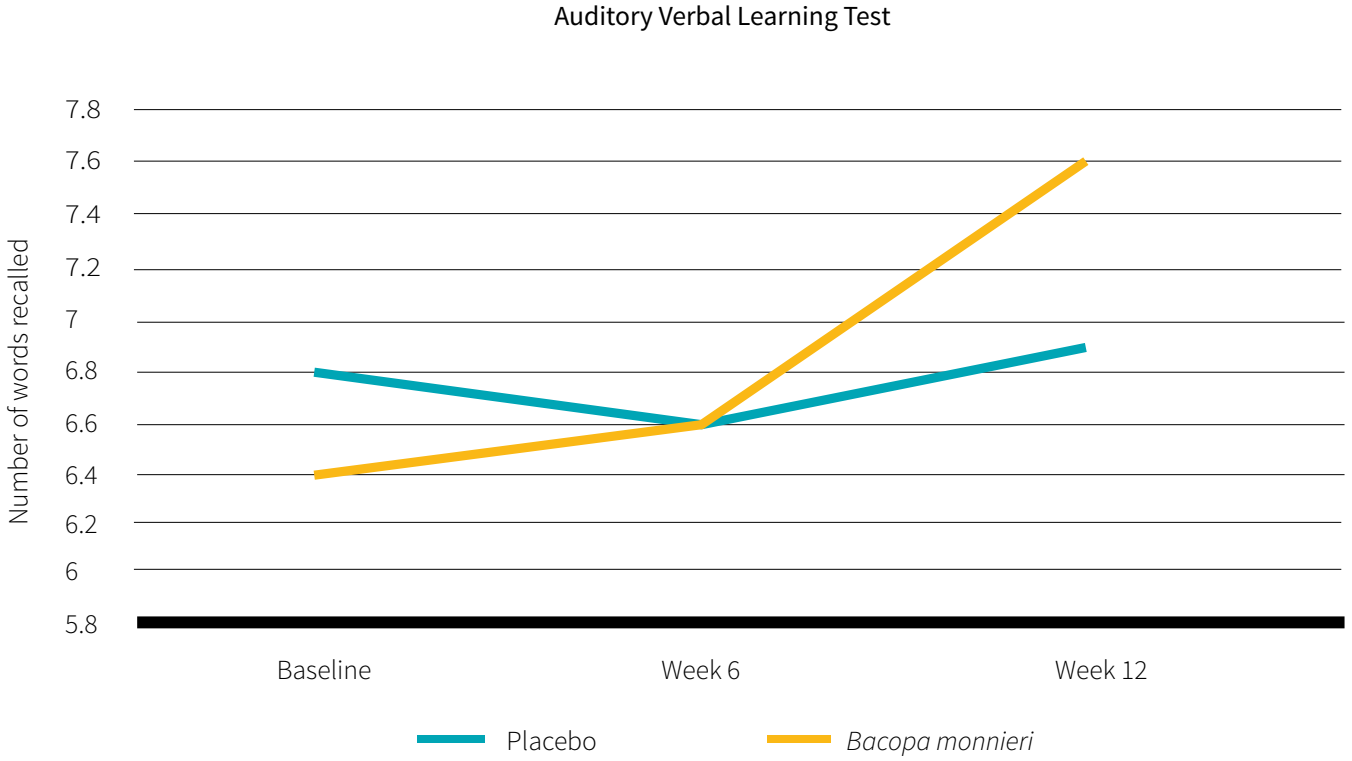
Bacopa Monnieri

Why it's a primary option

Bacopa monnieri is a swamp plant used in traditional Indian medicine to improve memory and cognition. While most effective for elderly people, it can provide benefits for all age groups, but only after one month of supplementation.

Figure 2: Bacopa monnieri's memory-enhancing effects

Extended supplementation with *Bacopa monnieri* may be able to enhance memory recall. During an Auditory Verbal Learning Test (AVLT), the group taking Bacopa monnieri was able to recall more words read off to them from a list of 15 words.



Source: Calabrese et al. *J Altern Complement Med*. 2008 Jul.

Bacopa monnieri reliably improves working memory (your RAM, so to speak, which determines how much information you can keep at the forefront of your mind). Further research is needed to determine if it can affect verbal fluency, word processing, and attention span.

Bacopa monnieri is not a core supplement because more research is needed to ascertain that it does not interact negatively with pharmaceuticals.

How to take it

Take a dose once a day with food. Take 150 mg of bacosides, the active compound in *Bacopa monnieri*, so about 300 mg of an extract with a 55% bacoside content. To supplement the leaf powder, assuming a 10–20% bacoside content, take 750–1,500 mg. Further research is needed to determine the efficacy and safety of higher doses.

Caffeine with Theanine

Why it's a primary option

Theanine is an amino acid with relaxing, but not sedating, properties. It neither interacts with sedative neurotransmitters nor causes feelings of fatigue. It can reduce the overexcitability often caused by caffeine without impairing caffeine's stimulatory effect. In fact, the improvements in concentration (focus and attention span) induced by caffeine and theanine respectively have been shown to be synergistic.

Even though coffee is a popular beverage worldwide, caffeine is not innocuous. Regular consumption leads to tolerance and often to dependence and withdrawal. Moreover, caffeine interacts dangerously with monoamine oxidase inhibitors (MAOIs), a kind of antidepressant, and several other pharmaceuticals, notably tizanidine.

Caffeine can also decrease blood lithium levels. Suddenly eliminating all caffeine from your diet can cause lithium levels to rise. If you are on lithium, keep your day-to-day caffeine intake roughly the same; if you wish to stop taking caffeine, talk with your doctor about slowly weaning yourself from it.

How to take it

Take 200 mg of both caffeine and theanine (400 mg total) some 30 minutes before you need increased focus and attention.

People not used to caffeine should start with 50 mg of caffeine and 100 mg of theanine. Conversely, veteran coffee drinkers may need more than 200 mg of caffeine to experience its cognitive benefits, in which case the accompanying dose of theanine becomes 300 mg (even higher doses of theanine may not be dangerous, but neither have they shown greater benefits).

Supplementing caffeine on an empty stomach can increase the rate of absorption, but it can also cause stomach upset.

With its half-life of 5 to 6 hours, caffeine can disrupt sleep when consumed in the evening. Even if it doesn't prevent you from falling asleep, caffeine will impair the *quality* of your sleep.

Caffeine should be cycled based on its stimulatory effects. Should it no longer provide noticeable benefits, stop supplementation for 2 to 4 weeks to reset tolerance.

Secondary Options

Atypical Caffeine Sources (Guarana, Yerba Mate)

Why it's a secondary option

Both guarana (*Paullinia cupana*) and yerba mate (*Ilex paraguariensis*) contain caffeine but also unknown bioactive compounds, so avoid those herbs if you take amphetamines (e.g., Adderall).

Preliminary evidence suggests that both herbs have cognitive benefits beyond those conferred by their sole caffeine content, but further research is needed to confirm this effect.

How to take it

Different batches can contain different amounts of caffeine and other bioactive compounds, so always start with very low doses.

Some 30 minutes before you need increased focus and attention, take 200 mg of theanine with either 50–75 mg of **guarana** (assuming a 9% caffeine content) or 1 g of **yerba mate** leaf powder (about 17.5 mg of caffeine).

Both herbs may be supplemented as teas, but this makes accurate dosing difficult. Too high of a dose can lead to excessive stimulation and cardiac complications, such as arrhythmia.

Cholinergics

Why they're a secondary option

A supplement is said to be cholinergic when it increases the activity of acetylcholine, a major neurotransmitter associated with memory and attention span. Cholinergics have been studied in the context of old-age dementia; they have been shown to slow cognitive decline, but further research is needed to ascertain their effects on cognition in younger people.

Both alpha-GPC and CDP-choline can provide the brain with the choline it needs to produce more acetylcholine (choline bitartrate is much cheaper, but little of it seems to reach the brain). CDP-choline is also a source of uridine, which can increase the rate of neuronal growth and turnover.

Huperzine-A can inhibit acetylcholinesterase, an enzyme that breaks down acetylcholine. Its half-life exceeds 24 hours, so it accumulates in the body when taken daily, which is problematic since long-term studies are scarce. There is a possibility that, over time, the body could adapt by producing more acetylcholinesterase, which would lead to reduced acetylcholine levels and a withdrawal period after huperzine-A supplementation has ceased. While the doses used in the studies (0.2–0.99 mg) were deemed safe in the short term, long-term supplementation cannot be recommended.

How to take them

To supplement with **alpha-GPC**, take 300–600 mg once a day with a meal. A higher dose (1,200 mg) can benefit people with dementia. Pairing alpha-GPC with uridine might provide synergistic benefits.

To supplement with **CDP-choline**, take 250–500 mg twice a day (i.e., 500–1,000 mg/day). To supplement with **CDP-choline** for its pro-uridine content, take 500–1,000 mg twice a day (i.e., 1–2 g/day).

Creatine

Why it's a secondary option

Creatine is an important source of fuel for cells, especially neurons. A genetic developmental disorder called "creatine transporter defect" (CTD) can cause a creatine deficiency and result in severe cognitive impairment. CTD can be treated with creatine supplementation.

More research is needed to determine whether creatine supplementation can benefit cognition in people who are not deficient. While most people produce enough creatine naturally to prevent cognitive complications, vegans and vegetarians might benefit from supplementation more than omnivores.

How to take it

Take 2–5 g of **creatine monohydrate** (other forms of creatine may be more *expensive*, but studies have not found them to be more *effective*). Active people should supplement closer to the high end of this range, though 2 g is technically sufficient to provide cognitive benefits.

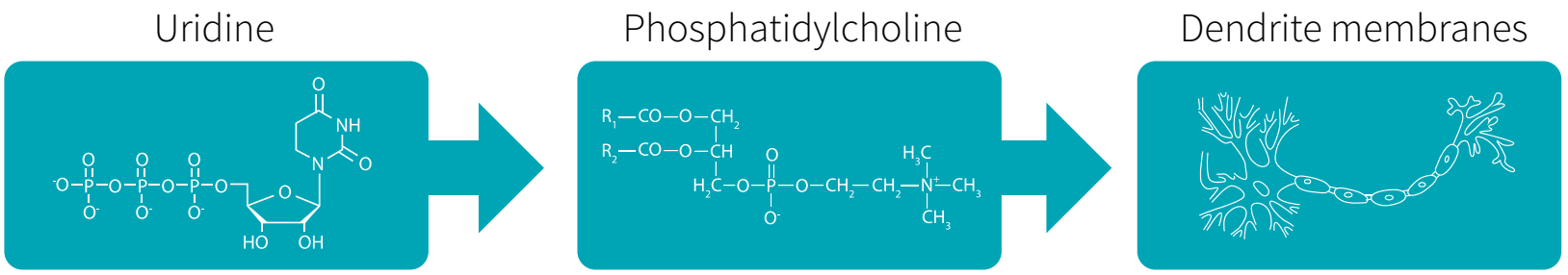
Should you find yourself particularly sensitive to creatine's digestive side-effects, which include nausea and cramping, try drinking more water. You can also split your daily dose and take it with meals. Finally, you could try micronized creatine monohydrate, which also has the advantage of being more soluble.

Uridine

Why it's a secondary option

Uridine is required to create neuronal membranes; it can also increase the rate of neuronal growth and turnover. There is little uridine in food. While the body can synthesize enough to satisfy its basic needs, preliminary evidence suggests that supplementation can benefit cognition.

Figure 3: How uridine could benefit cognition: mechanistic chart



Uridine has only been shown to be safe in the short term; more research is needed before long-term supplementation can be recommended. On the bright side, the benefits to cognition appear to be lasting (if new neurons are formed thanks to additional uridine, they do not just die off when supplementation is discontinued).

Uridine is thought to be synergistic with blueberry and *Bacopa monnieri*, though more research is needed to confirm this, too.

How to take it

Uridine is usually supplemented through uridine monophosphate (**UMP**), which is ⅔ uridine. The standard dosage for uridine is 250–500 mg twice a day (i.e., 500–1,000 mg/day), which translates as 375–750 mg of UMP twice a day (i.e., 750–1,500 mg/day).

Other options include triacetyluridine (TAU) and CDP-choline. Following oral supplementation, both appear to be effective in reaching the human brain.

If **TAU** is indeed seven times more bioavailable than an equimolar amount of uridine, as one study noted, then much lower doses could be used: 35–70 mg twice a day (i.e., 70–140 mg/day). Research on this compound is still scarce, however, which makes it hard to recommend.

As for **CDP-choline**, it is a source both of cytidine, which the body converts into uridine, and of choline, which the brain converts into acetylcholine. To supplement CDP-choline for its pro-uridine content, high doses are required: 500–1,000 mg twice a day (i.e., 1–2 g/day).

Further research is needed to determine if taking uridine with food is more effective than taking it on an empty stomach.

Inadvisable Supplements

Coleus Forskohlii with *Artichoke Extract*

Long-term potentiation (LTP) refers to a persistent strengthening of synapses. Chemically induced long-term potentiation (CILTeP) refers to the initiation of LTP through the use of compounds that increase cell levels of cyclic adenosine monophosphate (cAMP). Elevated cAMP levels in brain cells are associated with improved cognition, memory formation, and muscle contractions.

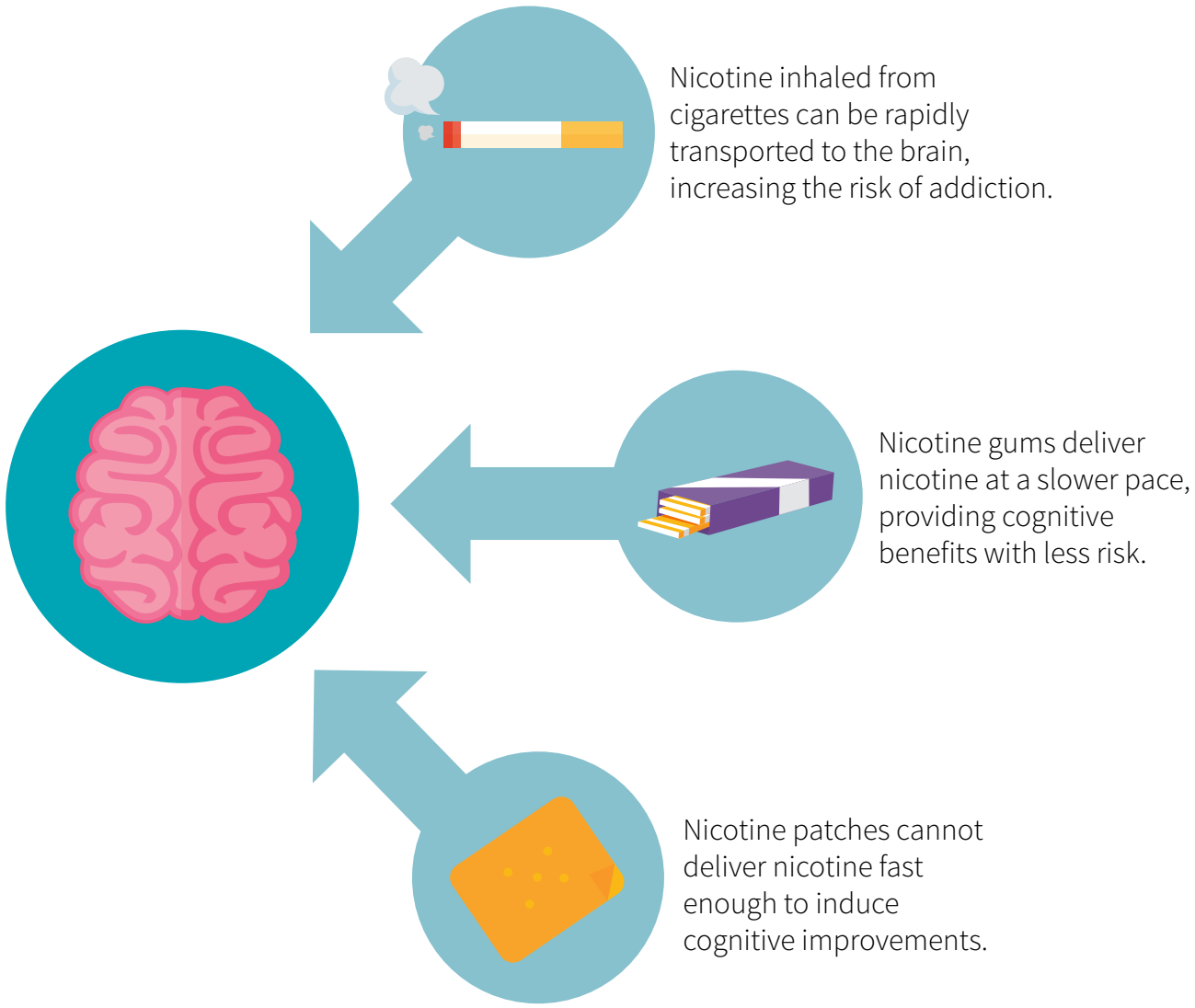
The standard CILTeP stack combines forskolin (the bioactive in *Coleus forskohlii*), to increase cAMP production, with luteolin (the bioactive in artichoke extract), to inhibit cAMP deactivation. However, there is no evidence to suggest that this combination works. Forskolin and luteolin are flavonoids, which tend to be poorly absorbed. Most probably, neither compound reaches the brain to exert its desired effect.

Though forskolin and luteolin work in isolated brain cells, real-world supplementation does not increase cAMP levels. This "CILTeP stack" does not belong in any stack designed to improve memory and focus.

Nicotine

Nicotine's addictive properties vary depending on the dose taken and the speed at which it enters the bloodstream. When inhaled, nicotine reaches the blood quickly, which makes this delivery method especially addictive. At the other end of the spectrum, patches are the least addictive delivery method, but they act too slowly to provide an acute stimulatory effect.

Figure 4: A model showing the benefits of nicotine on mental function



When it comes to speed of delivery, nicotine gum holds the middle ground. Chewing nicotine gum while working on a mentally demanding task (2 mg of nicotine at a time, no more than 10 mg in one day) has theoretical advantages. Making this a daily habit, however, would allow tolerance to develop, and only ceasing supplementation entirely (for a couple of weeks) would allow sensitivity to return. Increasing the dose instead would, sooner or later, lead to nicotine withdrawal. Even the minimum dose, taken regularly, is potentially addictive, and thus potentially harmful.

Of course, tobacco is still the most noxious source of nicotine, and not just because it contains some thirty carcinogens. As noted above, when inhaled, nicotine reaches the blood quickly, which makes it especially addictive. In addition, several other compounds in tobacco, such as monoamine oxidase inhibitors (MAOIs), amplify the addictive effects of nicotine. Finally, the acquired need to suck on something contributes to the addictive properties of cigarettes, cigars, and smoking pipes (and thumbs, for little children).

Assembling Your Stack

Incorporating Core Supplements

The only core supplement in the *Memory & Focus* stack is the humble ***blueberry***.

Choose one of the following protocols:

- Blueberry anthocyanins: 500–1,000 mg/day.
- Blueberry powder: 5.5–11 g/day.
- Fresh blueberries: 60–120 g/day.
- Blueberry juice: 500 mL/day.

Blueberries can be swapped for other dark berries. If you select the "juice" option, make sure your juice is made of actual berries, not of berry-flavored sugars!

The above protocols are recommended for most people; their efficacy and safety are backed by a significant body of evidence. Follow one of them for a couple of weeks before you consider making any modification, such as adding one of the following options.

Incorporating Options

For people who want to improve their long-term memory formation

Take the core blueberries, as described above. Take *Bacopa monnieri* (150 mg of bacosides) with a meal. Twice a day, take either:

- 500–1,000 mg of CDP-choline (i.e., 1–2 g/day).
- 150–300 mg of alpha-GPC (i.e., 300–600 mg/day) with 375–750 mg of UMP (i.e., 750–1,500 mg/day).
- 150–300 mg of alpha-GPC (i.e., 300–600 mg/day) with 35–70 mg of TAU (i.e., 70–140 mg/day).

For people who want to improve their attention span

Take the core blueberries, as described above. Take 200 mg of both caffeine and theanine (400 mg total) some 30 minutes before you need increased focus and attention.

People not used to caffeine should start with 50 mg of caffeine and 100 mg of theanine. Conversely, veteran coffee drinkers may need more than 200 mg of caffeine to experience its cognitive benefits, in which case the accompanying dose of theanine becomes 300 mg (even higher doses of theanine may not be dangerous, but neither have they shown greater benefits).

Caffeine should be cycled based on its stimulatory effects. Should it no longer provide noticeable benefits, stop supplementation for 2 to 4 weeks to reset tolerance.

If you drink tea (*Camelia sinensis*) several times a day, you may not need to supplement theanine. Similarly, caffeine can be consumed as pills but also through coffee, tea, energy drinks, etc. You could try replacing 200 mg of caffeine by either 50–75 mg of guarana (assuming a 9% caffeine content) or 1 g of yerba mate leaf powder (about 17.5 mg of caffeine), but neither option is recommended, and both should be avoided if you take amphetamines (e.g., Adderall).

Others options

People who don't frequently eat meat can add creatine (5 g taken with a meal) to any stack.

Caffeine can be consumed as pills but also through coffee, tea, energy drinks, etc. You could try replacing 200 mg of caffeine by either 50–75 mg of guarana (assuming a 9% caffeine content) or 1 g of yerba mate leaf powder (about 17.5 mg of caffeine), but neither option is recommended, and both should be avoided if you take amphetamines (e.g., Adderall).

FAQ

Can I add to my stack a supplement not covered in this guide?

Supplement your current stack for a few weeks before attempting any change. Talk to your doctor and research each potential new addition in advance. Check for known negative interactions with other supplements in your current stack, but also for synergies. If two supplements are synergistic or additive in their effects, you might want to use lower doses for each.

Can I modify the recommended doses?

If a supplement has a recommended dosage range, stay within that range. If a supplement has a precise recommended dose, stay within 10% of that dose. Taking more than recommended could be counterproductive or even dangerous.

Should I take my supplements with or without food? And at what time?

Answers are provided in each supplement entry whenever the evidence permits. Too often, however, the evidence is either mixed or absent. Besides, a supplement's digestion, absorption, and metabolism can be affected differently by different foods. Fat-soluble vitamins (A, D, E, K), for instance, are better absorbed with a small meal containing fat than with a large meal containing little to no fat.

Starting with half the regular dose can help minimize the harm a supplement may cause when taken during the day (e.g., tiredness) or in the evening (e.g., insomnia).

Why are the anthocyanin dosages all over the place?

Some studies used pure anthocyanins, others blueberry powder, yet others fresh blueberries. The dosages in this guide are based on those studies. The dosages for blueberry powder and fresh blueberries are not extrapolated from their anthocyanin content, which can vary fivefold between varieties (the numbers in this guide are therefore approximations).

The optimal range for pure anthocyanins seems to be 500–1,000 mg, but studies have found benefits from doses as low as 100–200 mg. If you want to get 500–1,000 mg of anthocyanins through fresh berries, you most certainly can, but you're looking at 250–500 g of berries, and that can be a lot to buy and consume on a daily basis.

Can I replace blueberries with other anthocyanin-rich foods?

Most studies are on blueberries, and the total amount of anthocyanins does not tell the whole story, for different *kinds* of anthocyanins can be found in different amounts in different berries. Studies on cognition have reported benefits from blue-purple anthocyanins, notably cyanidin and delphinidin, whereas red anthocyanins, such as pelargonidin, lack the same scientific backing.

So dark berries (blueberries, blackberries, elderberries …) can be considered interchangeable for the purpose of enhancing cognition, whereas red berries (strawberries, raspberries …), although also rich in anthocyanins, are not suitable alternatives.

Blue-purple anthocyanins can be found in foods other than dark berries, such as purple cauliflower, purple potatoes, and purple rice, but keep in mind that some blue-purple plants, such as beetroot, derive their color from betalains, not from anthocyanins.

What's the difference between anthocyanins and anthocyanidins?

Anthocyanins contain anthocyanidins. To be more precise, an anthocyanidin is simply an anthocyanin without its sugar molecule(s).

Can fish oil improve memory and focus?

Preliminary evidence suggests that fish oil may benefit cognition, but more research is needed before supplementation can be recommended for this specific purpose. Including more fatty fish in your diet may nevertheless be a good, healthy idea. Cod, salmon, and sardines are the best fish to eat, since they have high levels of omega-3 fatty acids but low levels of mercury. If you cannot change your diet and want to supplement fish oil, you can take a 1-g gelule daily.

Why are there no racetams in this stack?

While racetams (e.g., piracetam, aniracetam, oxiracetam) are thought to improve cognition, they are not recommended in this guide because they are pharmaceuticals and because human evidence is lacking. Further research is needed on their long-term safety and efficacy.

Precautions and Troubleshooting

Stack components are seldom studied together. The safest way to add supplements to your daily routine is one at a time, at least a couple of weeks apart, to better assess the effects (and side effects) of each new addition. Start at half the regular dose for a week, then slowly increase to the regular dose if you are not experiencing the desired effects.

Any supplement that can affect the brain, especially supplements with a stimulatory or sedative effect, should first be taken in a controlled situation. Do not take a dose, least of all your first dose, before events such as driving or operating heavy machinery, where impaired cognition may be a risk for your safety and the safety of others.