

# Top 9 Nutrients for Better Brain Health

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✓ Fact Checked

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## STORY AT-A-GLANCE

- › Nine nutrients that are vital for brain health and cognition are the marine-based omega-3 fats DHA and EPA, choline, phosphatidylserine, acetyl-L-carnitine, vitamins D and B12, MCT oil and probiotics
- › By using a lysophospholipid form of EPA (LPC-EPA), researchers were able to increase the EPA level in the brain of mice 100-fold. LPC-EPA also doubled the DHA level in the brain, whereas free EPA had no effect on DHA levels
- › Choline helps protect against Alzheimer's by reducing your homocysteine level, an amino acid associated with neurodegeneration and formation of amyloid plaques, and inhibiting microglia activation, which inhibits brain inflammation
- › Supplementing with 400 mg of phosphatidylserine increased the speed of calculations done in short-term memory by 20% in one study. In another, 300 mg/day improved cognitive function of geriatric patients
- › Low vitamin D is associated with poorer brain function, and increasing levels may help keep older adults mentally fit. Vitamin D has also been shown to improve a number of brain disorders, including dementia and Alzheimer's disease

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Like autism among children, Alzheimer's among seniors has reached epidemic proportions, with no slowdown in sight. On the contrary, evidence suggests the trend is

worsening. In 2022, Alzheimer's affects about 6.5 million Americans age 65 and older; of this number, 73% are over age 75. Alzheimer's is the fifth leading cause of death in the U.S.<sup>1</sup> The World Health Organization predicts that by 2050, 139 million adults worldwide will be living with dementia.<sup>2</sup>

It's important to realize that dementia is a lifestyle-predicated disease, and there are many strategies that will help prevent this kind of neurodegeneration. In essence, anything that will help optimize your mitochondria will also help prevent Alzheimer's.

Here, the focus is on specific nutrients shown to play an important role in brain health and cognition, starting with marine-based omega-3, which contains two long-chained fatty acids that are vital for brain health: docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA).

## **1. Marine-Based Omega-3 Fat: DHA**

The influence of marine-based omega-3 fats on physical and mental health has been the subject of intense research for decades, and there's compelling evidence they can help ameliorate a variety of psychiatric illnesses and degenerative brain disorders, including Alzheimer's.

In my book, "[Superfuel](#)," cowritten with James DiNicolantonio, Pharm. D., we explain how DHA is an essential structural component of your brain, and is found in high levels in your neurons, the cells of your central nervous system. When your omega-3 intake is inadequate, your nerve cells become stiff and more prone to inflammation as the missing omega-3 fats are substituted with omega-6 instead.

Once your nerve cells become rigid and inflamed, proper neurotransmission from cell to cell and within cells become compromised. Low DHA levels have been linked to memory loss and Alzheimer's disease, and some studies suggest degenerative brain diseases may potentially be reversible with sufficient DHA.

For example, in one study,<sup>3</sup> elderly volunteers suffering from memory deficits saw significant improvement after taking 900 milligrams (mg) of DHA per day for 24 weeks,

compared to controls. Another study<sup>4</sup> found significant improvement in verbal fluency scores after taking 800 mg of DHA per day for four months, compared with placebo. Furthermore, memory and rate of learning were significantly improved when DHA was combined with 12 mg of lutein per day.

I never previously realized this but DHA also stimulates one of the most important transcription factors that regulates cellular oxidation and reduction, and aids in detoxification, the Nrf2 pathway.<sup>5</sup> Additionally, it also increases heme oxygenase 1<sup>6</sup> (a protein produced in response to oxidative stress) and upregulates antioxidant enzymes – all of which are important for brain health.

In addition, DHA is a precursor for the signaling molecule protectin, which is synthesized in response to oxidative stress. (When found in your central nervous system it's referred to as neuroprotectin, or NPD1.) As explained in a 2011 paper in the journal *Nutrients*:<sup>7</sup>

*"NPD1 induces nerve regeneration, reduce leukocyte infiltration and maintains homeostasis through ageing by reducing pro-apoptotic and pro-inflammatory signaling. NPD1 is induced by oxidative stress and protects retinal and neuronal cells from oxidative stress-induced apoptosis.*

*Many mechanisms have been implicated, including suppression of the IL-1 $\beta$  induced stimulation of COX. The discovery of NPD1 offers new therapeutic opportunities for a range of neurodegenerative conditions, such as Alzheimer's disease. It also provides an exciting potential for DHA in helping to delay or minimize the 'normal' cognitive decline during ageing."*

## **2. Marine-Based Omega-3 Fat: EPA**

EPA, meanwhile, appears to be particularly beneficial in the treatment of depression,<sup>8</sup> as it helps lower levels of tumor necrosis factor alpha, interleukin 1 beta and prostaglandin E2 – three immune chemicals that tend to be elevated in those with depression.

A stumbling block has been to get sufficiently large amounts into your brain. To raise your brain level of EPA, you'd need to consume impractically large amounts of fish oil,

for example. One theory is that degradation by pancreatic enzymes renders the EPA incapable of passing the blood-brain-barrier.<sup>9</sup>

However, recent research<sup>10</sup> has discovered something really interesting. By using a lysophospholipid form of EPA (LPC-EPA), they were able to increase the EPA level in the brain of mice 100-fold. Even more remarkable, LPC-EPA also doubled the DHA level in the brain, whereas free EPA had no effect on DHA levels. The authors further noted that:

*"Only LPC-EPA increased EPA and DHA in retina, and expression of BDNF, CREB and 5-HT1A receptor in the brain. These novel results show that brain EPA can be increased through diet. Because LPC-EPA increased both EPA and DHA in the brain, it may help treat depression as well as neuroinflammatory diseases, such as Alzheimer's disease."*

Papasani Subbaiah, professor of medicine and biochemistry and molecular genetics in the UIC College of Medicine and corresponding author, told MedicalXpress:<sup>11</sup>

*"It seems that there is a transporter at the blood-brain barrier that EPA must pass through in order to get into the brain, but EPA in fish oil can't get through, whereas LPC-EPA can. You don't have to consume all that much LPC- EPA to have significant increases of EPA show up in the brain, so this could be a way to do rigorous studies on the effects of EPA in humans."*

## **The Importance of Phospholipid-Bound Omega-3**

There are a number of drawbacks to fish oil, and the lack of phospholipids is one of them. DHA and EPA are water insoluble and therefore cannot be transported in their free form in your blood. They must be packaged into lipoprotein vehicles such as phospholipids. This is primarily why the bioavailability of krill oil is so much higher than fish oil, because in fish oil, the DHA and EPA are bound to triglycerides.

When you consume fish oil, your liver has to attach it to phosphatidylcholine in order for it to be efficiently utilized by your body and brain. Phospholipids are also one of the principal compounds in high-density lipoproteins (HDL), which you want more of, and by

allowing your cells to maintain structural integrity, phospholipids help your cells function optimally.

Importantly, your brain cannot readily absorb DHA unless it's bound to phosphatidylcholine, and while krill oil contains phosphatidylcholine naturally, fish oil does not. As the name implies, phosphatidylcholine is composed partly of choline, the precursor for the vital neurotransmitter acetylcholine, which sends nerve signals to your brain, and choline itself is crucial for brain development, learning and memory, as you'll see in the next section.

Recent research<sup>12</sup> by Rhonda Patrick, Ph.D., also highlights the value of DHA bound to phospholipids, showing this form may actually reduce the risk of Alzheimer's disease in those with the apolipoprotein E4 (APOE4) gene, which lowers the typical age of onset of this degenerative brain disorder.

Two hallmarks of Alzheimer's are amyloid beta plaques and tau tangles, both of which impair normal brain functioning. Alzheimer's patients also have reduced glucose transport into their brains, and this is one of the reasons why plaque and tangles form and accumulate in the first place. According to Patrick,<sup>13</sup> DHA encourages your brain's uptake of glucose by regulating the structure and function of glucose transporters, proteins located at your blood-brain barrier.

While eating DHA-rich fish has been shown to slow the progression of Alzheimer's in APOE4 carriers, taking fish oil has not demonstrated the same efficacy. According to Patrick, this variation in response appears to be related to the different ways in which the two forms of DHA are metabolized and ultimately transported into your brain.

When the triglyceride form of DHA is metabolized, most of it turns into nonesterified DHA, while the phospholipid form is metabolized primarily into DHA-lysophosphatidylcholine (DHA-lysoPC). While both of these forms can cross the blood-brain barrier to reach your brain, the phospholipid form does so far more efficiently.

According to Patrick, people with APOE4 have a faulty nonesterified DHA transport system, and this may be why they're at increased risk for Alzheimer's. The good news is

that DHA-lysoPC can bypass the tight junctions, thereby improving DHA transport, and for those with one or two APOE4 variants, taking the phospholipid form of DHA may therefore lower their risk of Alzheimer's more effectively.

### **3. Choline Helps Fight Alzheimer's Disease**

Other recent research<sup>14</sup> demonstrates the importance of choline for brain health and prevention of neurodegenerative diseases such as Alzheimer's. Choline is a precursor to acetylcholine, a neurotransmitter required for the proper function of your brain and nervous system, playing a role in fetal brain development, memory, muscle control, mood and gene expression. As reported by Science Daily:<sup>15</sup>

*"The study focuses on mice bred to display AD-like symptoms. Results showed that when these mice are given high choline in their diet, their offspring show improvements in spatial memory, compared with those receiving a normal choline regimen in the womb.*

*Remarkably, the beneficial effects of choline supplementation appear to be transgenerational, not only protecting mice receiving choline supplementation during gestation and lactation, but also the subsequent offspring of these mice. While this second generation received no direct choline supplementation, they nevertheless reaped the benefits of treatment, likely due to inherited modifications in their genes."*

Choline helps protect against Alzheimer's by:

- Reducing your homocysteine level, an amino acid that has been shown to cause neurodegeneration and is involved in the formation of amyloid plaques, two hallmarks of Alzheimer's. Choline converts homocysteine into methionine, which has a number of beneficial effects.
- Inhibiting microglia activation. Microglia cells clear debris from your brain, and while this is a crucial function, in Alzheimer's the microglia have a tendency to become overactivated, causing inflammation in the brain that can result in the

death of neurons. By reducing activation of microglia, choline can help protect Alzheimer's patients from further brain damage.

## **4. Phosphatidylserine Boosts Cognitive Function**

Phosphatidylserine is another supplement that can help improve cognitive function<sup>16</sup> and protect against Alzheimer's disease.<sup>17</sup> Phosphatidylserine is an amino acid derivative that is highly prevalent in neural tissue and plays an important role in the cellular function in your brain.

While your body can synthesize it on its own, you can also get it through food (such as mackerel, cod, egg yolks and organ meats) and/or a phosphatidylserine complex supplement.<sup>18</sup> Phosphatidylserine has a unique structure that makes it both hydrophilic, meaning it's attracted to water and hydrophobic, or repelled by water.

With this structure, phospholipids are able to arrange themselves into a phospholipid bilayer – two parallel layers that form a major component of the human cell membranes. In brain cell membranes, the phospholipid bilayer acts as a "gatekeeper," regulating the entry beneficial substances, basically nutrients, water and oxygen, while eliminating metabolic waste.<sup>19</sup>

In one study,<sup>20</sup> supplementing with 400 mg of phosphatidylserine increased the speed of calculations done in short-term memory by 20% in a group of healthy adults. In another, it improved cognitive function of geriatric patients at a dosage of 300 mg per day for six months.<sup>21</sup>

Taken with DHA, it's also been shown to improve behavior and short-term auditory memory in children with ADHD.<sup>22</sup> In patients with Alzheimer's, phosphatidylserine helps inhibit amyloid beta and interferon-gamma-induced microglial activation.<sup>23</sup>

## **5. Acetyl-L-Carnitine Protects Against Neurotoxic Insults**

Acetyl-L-carnitine (ALCAR) has many beneficial effects on brain metabolism, protects against neurotoxic insults, and has been shown to benefit certain forms of depression. In one study,<sup>24</sup> healthy mice given ALCAR for 25 days at a dose of about half a gram per kilo, were found to have increased levels of the neurotransmitters noradrenaline and serotonin. According to the authors, this is "consistent with ALCAR's potential efficacy for depressive symptoms."

In another study,<sup>25</sup> ALCAR was found to improve the clinical condition of patients with degenerative cerebellar ataxia (a condition resulting in the loss of control of bodily movements). According to the authors, "statistically significant improvement of some symptoms and a slow progression of the disease in both groups of patients" were observed.

## **6. Vitamin D Protects Against Memory Loss**

Activated vitamin D receptors increase nerve growth in your brain, and researchers have also located metabolic pathways for vitamin D in the hippocampus and cerebellum, areas involved in planning, information processing and memory formation.

According to research<sup>26</sup> published in the Journal of Neurology, Neurosurgery and Psychiatry, low vitamin D is associated with poorer brain function, and increasing levels may help keep older adults mentally fit. Vitamin D has also been shown to improve a number of brain disorders, including dementia and Alzheimer's disease.<sup>27</sup>

In one six-year study,<sup>28</sup> those with severe vitamin D deficiency were more than twice as likely to develop dementia and Alzheimer's than those with higher levels. Even those with moderate deficiency had a 53% increased risk for all forms of dementia, and 69% increased risk for Alzheimer's specifically. According to the authors, "Our results confirm that vitamin D deficiency is associated with a substantially increased risk of all-cause dementia and Alzheimer disease."

The findings also suggest there's a threshold level of circulating vitamin D, below which your risk for dementia increases. This threshold was found to be right around 20 ng/mL



(50 nmol/L). Higher levels were associated with good brain health.

I recommend getting your vitamin D level tested twice a year, and taking whatever dosage required to achieve and maintain a vitamin D level between 60 and 80 ng/mL (150 and 200 nmol/L). Ideally, you'd want to raise your level by getting sensible sun exposure, but if you cannot, consider an oral vitamin D3 supplement balanced with magnesium and vitamin K2.

## **7. Vitamin B12 Deficiency Wreaks Havoc on Cognitive Function**

Vitamin B12 is another important player. Research<sup>29</sup> shows people with high levels of markers for vitamin B12 deficiency are more likely to score lower on cognitive tests and have a smaller total brain volume, which suggests a lack of B12 may contribute to brain shrinkage.

Mental fogging and problems with memory are two of the top warning signs that you have vitamin B12 deficiency, and this is indicative of its importance for your brain health.

Finnish researchers have also found that people who consume foods rich in B12 may reduce their risk of Alzheimer's in their later years.<sup>30</sup> For each unit increase in the marker for vitamin B12 (holotranscobalamin) the risk of developing Alzheimer's was reduced by 2%. Another study<sup>31</sup> found that supplementing with B vitamins, including B12, helps to slow brain atrophy in elderly people with mild cognitive impairment.

Vitamin B12 deficiency is widespread and many have trouble absorbing this nutrient properly from food sources. Blood tests for vitamin B12 are not always a reliable indicator of B12 status, so watching for symptoms of deficiency and increasing your dietary and supplemental intake is a practical alternative to blood testing.

B12 is available in its natural form only in animal food sources such as seafood, beef, chicken, pork, milk and eggs. If you rarely or never consume these animal products, you're at particularly high risk of B12 deficiency.

The good news is vitamin B12 supplementation is completely nontoxic and inexpensive, especially when compared to the cost of laboratory testing. I recommend an under-the-tongue fine mist spray, as this technology helps you absorb the vitamin into the fine capillaries under your tongue.

## **8. MCT Oil Boosts Brain Performance**

One of the primary fuels your brain needs is glucose, which is converted into energy. Your brain actually manufactures its own insulin to convert glucose in your bloodstream into the food it needs to survive.

If your brain's production of insulin decreases, your brain literally begins to starve, as it's deprived of the glucose-converted energy it needs to function normally. This is what happens to Alzheimer's patients – portions of their brain start to atrophy, or starve, leading to impaired functioning and eventual loss of memory, speech, movement and personality.

In effect, your brain can begin to atrophy from starvation if it becomes insulin resistant and loses its ability to convert glucose into energy. Fortunately, your brain is able to run on more than one type of energy supply. It can run on both glucose and ketones, and ketones are actually better.

Ketones are what your body produces (when it converts fat as opposed to glucose) into energy, and a primary source of ketone bodies are medium chain triglycerides (MCT). While coconut oil is one healthy option, MCT oil is a more concentrated source of ketones, so it tends to be more appropriate for clinical uses.

Most commercial brands of MCT oil contain a 50/50 combination of C8 and C10 fats (the "C number" stands for the carbon length of the MCT). My personal preference is straight C8 (caprylic acid), as it converts to ketones far more rapidly than do C10 fats, and will give you higher levels of ketones.

Ketones appear to be the preferred source of energy for the brain in people affected by diabetes, Alzheimer's, Parkinson's and maybe even ALS, because in these diseases,

certain neurons have become insulin resistant or have lost the ability to efficiently utilize glucose. As a result, neurons slowly die off.

The introduction of ketones may rescue these neurons and they may still be able to survive and thrive. In multiple studies, ketones have been shown to be both neurotherapeutic and neuroprotective. They also appear to lower markers of systemic inflammation. As noted by Mental Health Daily:<sup>32</sup>

*"In small scale human trials,<sup>33</sup> MCT supplementation boosted cognition in individuals with cognitive impairment and mild forms of Alzheimer's disease after just a single dose. While not everyone improved from the MCT treatment, those with certain genetics experienced notable improvement."*

## **9. Probiotics Feed Your Second Brain**

As your "second brain," the state of your gut also plays an important role in your neurological and psychological health. Probiotics have been shown to reduce symptoms of depression and decrease pathological hallmarks of Alzheimer's, including amyloid plaques and tangles. In one study,<sup>34</sup> the probiotic strain *L. plantarum* MTCC1325 was identified as having these "anti-Alzheimer's properties."

In another study,<sup>35</sup> published in *Frontiers in Aging Neuroscience*, 60 elderly patients diagnosed with Alzheimer's received either a placebo or a probiotic milk products containing *Lactobacillus acidophilus*, *Lactobacillus casei*, *Bifidobacterium bifidum* and *Lactobacillus fermentum* for 12 weeks.

At the beginning and end of the study, participants underwent a standardized cognitive assessment and a highly sensitive c-reactive protein test, which is a powerful marker of inflammation. As reported by neurologist Dr. David Perlmutter:<sup>36</sup>

*"The results of the study were stunning. The placebo group showed an increase in hs-CRP, the inflammation marker, by an impressive 45%. In the group taking the probiotic, on the other hand, hs-CRP didn't just stay the same, but actually declined by 18%, indicating a dramatic reduction in inflammation."*

***But here's the truly exciting news. Over the 12 weeks, the patients in the placebo continued to decline mentally, as you might expect. Their MMSE score dropped from 8.47 to 8.00, a substantial reduction.***

***But the group on the inflammation reducing probiotics actually demonstrated, not a decline in brain function, but an actual improvement, with their MMSE scores going from 8.67 up to 10.57, and that's a huge improvement. Again, not only was their mental decline stopped in its tracks, these individuals regained brain function!***

***The message here is that inflammation is directly determined by the health and diversity of our gut bacteria, and this has major implications in terms of brain health, function and disease resistance."***

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