

Omega-3 May Lower Alzheimer's Risk in High-Risk Individuals

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June 11, 2023

STORY AT-A-GLANCE

- › Research highlights the value of DHA bound to phospholipids – such as that found in krill oil – showing this particular form may reduce the risk of Alzheimer’s in those with the APOE4 gene
- › The APOE4 gene, which predisposes you to Alzheimer’s and lowers the typical age of onset, is thought to be present in about one-quarter of the population
- › People with the highest omega-3 blood levels are 18% to 21% more likely to live longer, healthier lives than those with the lowest levels. EPA was the most important factor; those with the highest levels of EPA were 24% less likely to experience unhealthy aging
- › In your brain, DHA stimulates Nrf2 (a transcription factor that regulates cellular oxidation protective genes) and heme oxygenase 1 (a protein produced in response to stress) and upregulates antioxidant enzymes
- › Getting an omega-3 index test is the best way to customize your dosage to ensure sufficiency, as requirements vary depending on your lifestyle. For optimal health, you’ll want an omega-3 index of 8% or higher

Editor's Note: This article is a reprint. It was originally published November 8, 2018.

More and more, scientists are confirming and validating recommendations to consume healthy dietary fats, and typically in far greater amounts than recommended by U.S.

dietary guidelines. Healthy fats are, in my view, so important for health, I've dedicated my last two books to this topic.

"**Fat for Fuel**" details how to implement a cyclical ketogenic diet high in healthy fats, low in net carbs and moderate in protein, delves even further into the specifics of dietary fats and how to discriminate between healthy and harmful ones.

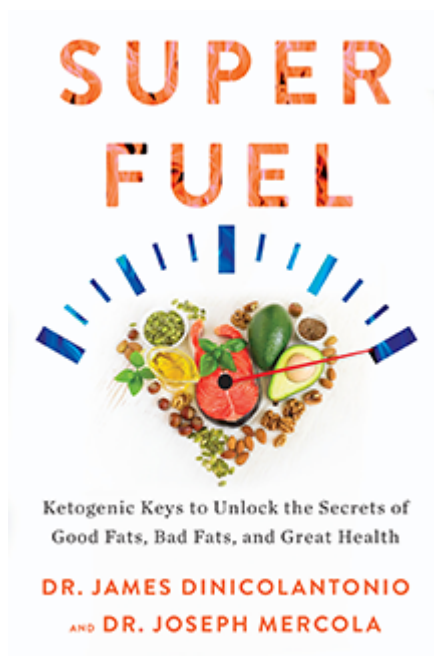
This is really crucial information, as unhealthy fats can do more harm than excess sugar. Unfortunately, if you pay attention to government dietary guidelines (or many conventional doctors), you'll be grossly misinformed about which types of fat to eat, and how much.

For example, in the past 100 years, our omega-6 intake has nearly tripled largely due to misleading or outright incorrect marketing and government health campaigns while our intake of omega-3 has decreased tenfold, causing a severe imbalance in our omega-3 to omega-6 ratio.

Hence, this was the incentive for writing "**Superfuel**" to set the record straight. A majority of the research for this book was compiled by **James DiNicolantonio**, Pharm.D., author of "**The Salt Fix**."¹ In a nutshell, "Superfuel" guides you back to a diet reminiscent of that during Paleolithic times, with particular focus on animal-based omega-3 fats, specifically those bound to phospholipids.

At that time, much of the omega-3 came from animal brains. Today, brains is unlikely to make the menu, but phospholipid-bound omega-3 can still be had from krill oil and fish roe.

To learn how fats are truly an extraordinary fuel for your body and brain, and why it's so vitally important to eat the right ones, be sure to order a copy of "**Superfuel**" today. All preorders will also receive three free gifts.



DHA Is Crucial for Cellular Health

The fats recommended by U.S. health authorities — primarily vegetable oils — are very high in processed (and hence damaged) omega-6 fats. One of the most significant dangers of vegetable oils is that the damaged fats are integrated into your cell membranes, including mitochondrial membranes, and once these membranes become dysfunctional it sets the stage for all sorts of complications and ill health.

For example, as DiNicolantonio explains in our interview, the inner membrane of your **mitochondria** contains a component called cardiolipin, which needs to be saturated in the omega-3 fat docosahexaenoic acid (DHA) in order to function properly.

Cardiolipin can be likened to a cellular alarm system that triggers programmed cell death (apoptosis) by signaling caspase-3 when something goes wrong with the cell. However, if the cardiolipin is not saturated with DHA, it cannot signal caspase-3, and hence apoptosis does not occur. As a result, dysfunctional cells continue to grow and may turn into a tumor. DHA is particularly crucial for brain health. In your brain, DHA:

- Stimulates Nrf2, a transcription factor that regulates cellular oxidation and reduction, and aids in detoxification

- Increases heme oxygenase 1, a protein produced in response to stress, including oxidative stress
- Upregulates antioxidant enzymes

All of this is important for optimal brain health and function. DHA and EPA are also actual structural elements that make up all of your cells, including those in your brain, so their importance really cannot be overstated.

However, the source of your DHA also matters. Industrially processed omega-3 fish oils can actually cause problems similar to those caused by excessive amounts of omega-6. This is a topic we examine at greater depth in "Superfuel."

About half of all fish oils also have problems with oxidation. So, when buying a fish oil supplement, you really need to look for a product that tests the hydro peroxide levels. The lower the level the better, but I recommend staying below 5%.

The Importance of Phospholipids

For years, I've recommended krill oil over fish oil if you don't regularly eat cleaner, small fatty fish such as anchovies and sardines. Krill has a number of benefits over fish oil, but one in particular has been highlighted in research, namely that of phospholipids.

While fatty acids (including DHA and EPA) are water soluble, they cannot be transported in their free form in your blood. They must be "packaged" into lipoprotein vehicles such as phospholipids.

In krill oil, the omega-3s DHA and eicosapentaenoic acid (EPA) are naturally bound to phospholipids, which makes them more readily absorbed by your body compared to fish oil, where the omega-3s are bound to triglycerides.

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

absorb DHA unless it's bound to phosphatidylcholine, and while krill oil contains phosphatidylcholine naturally, fish oil does not.

When you consume fish oil, your liver has to attach it to phosphatidyl choline in order for it to be utilized by your body, and this is yet another reason for its superior bioavailability. As the name implies, phosphatidyl choline is composed partly of choline, the precursor for the vital neurotransmitter acetylcholine, which sends nerve signals to your brain.

Choline is important to brain development, learning and memory. Since it plays a vital role in fetal and infant brain development, it's particularly important for pregnant and nursing women.

Research Highlights Value of Phospholipid-Bound DHA

Research² by Rhonda Patrick, Ph.D., highlights the value of DHA bound to phospholipids – such as that found in krill oil – showing this particular form may actually reduce the risk of Alzheimer's in those with the apolipoprotein E4 (APOE4) gene.

The APOE4 gene, which predisposes you to this degenerative brain disorder and lowers the typical age of onset, is thought to be present in about one-quarter of the population, so this information could prove invaluable for many. Having a single copy of the gene raises your risk two- to threefold. Being a carrier of both copies can raise your risk fifteenfold.

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. As explained by Patrick in her press release:³

"DHA promotes brain glucose uptake by regulating the structure and function of special proteins called glucose transporters located at the blood-brain barrier, the tightly bound layer of cells that limits passage of substances into the brain

...

DHA ... naturally occurs in a triglyceride form and a phospholipid form. Eating DHA-rich fish slows the progression of Alzheimer's disease and improves symptoms in APOE4 carriers. However, some evidence suggests that taking DHA supplements, which largely lack the phospholipid form, does not."

DHA in Phospholipid Form May Be Ideal

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 non-esterified 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. Patrick explains:⁴

"Whereas non-esterified DHA passes through the blood-brain barrier via passive diffusion, the phospholipid form, DHA-lysoPC, enters via a special transporter called Mfsd2a.

Previous studies have found APOE4 disrupts the tight junctions of the blood-brain barrier, leading to a breakdown in the barrier's outer membrane leaflet and a subsequent loss of barrier integrity. One end result of this loss is impaired diffusion of non-esterified DHA."

According to Patrick, people with APOE4 have a faulty non-esterified 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.

"When looking at the effects of DHA on cognitive function in people with APOE4-related Alzheimer's disease, it's important that researchers consider the

effects of DHA in phospholipid form, especially from rich sources such as fish roe or krill, which can have as much as one-third to three-quarters of the DHA present in phospholipids," Patrick says.⁵

"That's where we're most likely to see the greatest benefits, particularly in vulnerable APOE4 carriers."

Omega-3 Fats Linked to Healthy Aging

In other related news, researchers have again linked omega-3 intake to healthier aging. This prospective cohort study⁶ included data from more than 2,600 seniors collected between 1992 until 2015. Blood levels of omega-3 were obtained at the beginning and end of the study.

In that period, only 11% of participants experienced healthy aging, quantified as the number of years a person lives without physical or mental health problems or disability. Those with the highest omega-3 blood levels were 18% to 21% more likely to live longer, healthier lives.

Interestingly, EPA was found to be the most important factor in this study. Those with the highest levels of EPA were 24% less likely to experience unhealthy aging, compared to those with the lowest EPA levels.

Other omega-3s measured included the animal-based docosapentaenoic acid (DPA) and the plant-based alpha linolenic acid (ALA). DPA was the second-most important factor, while ALA, like DHA, had no significant impact on healthy aging. The researchers speculate that one of the reasons for these findings is omega-3s beneficial impact on heart health. For example:

- Two parallel studies^{7,8} published in 2008 found fish oil supplements worked better than placebo and the cholesterol-lowering drug Crestor in patients with chronic heart failure.

- Research published in 2016 found eating fatty fish and other omega-3 rich foods may lower your risk of a fatal heart attack by about 10%.^{9,10}
- Heart attack survivors who took 1 gram of marine-based omega-3 per day for three years were found to have a 50% reduced risk of sudden cardiac death.¹¹

EPA Also Lowers Heart Disease Risk

EPA specifically has also been linked to a lower risk for heart disease. A different study¹² involving a highly-processed form of EPA (a proprietary prescription formulation of fish oil called Vascepa) found it lowered cardiovascular health risks by 25% compared to a placebo containing mineral oil. This included heart attacks, strokes, bypass surgery and chest pain requiring hospitalization.

The drug trial was called REDUCE-IT and was done for five years. Perhaps the most unusual aspect of this trial is that they used a far higher dosage than is typically used in these types of studies. Participants received 4 grams of EPA per day, which is two to four times more EPA than typically given.

A 25% reduction in cardiovascular risk is typically what you see with the use of statins, and this significant reduction is believed to be a byproduct of EPA's ability to lower triglycerides. Now, while this study strongly supports the use of marine-based omega-3s, it's important to realize that Vascepa is a highly-processed form of omega-3.

With a price tag of \$2,500 a year, it's also one of your more expensive alternatives. Aside from being far less expensive, I still believe krill oil may be a superior choice, in part because it's bound to phospholipids, which increases absorption and may be particularly important for those at high risk for Alzheimer's. Krill also naturally contains astaxanthin, a very potent and powerful antioxidant, and the reason krill oil is far less prone to oxidation than fish oil.

Studies such as the REDUCE-IT trial do confirm and support health predictions made in "Superfuel," though, with a key point being that most people need far higher doses than previously thought. As suggested in the REDUCE-IT trial, an ideal dose appears to be

between 3 and 4 grams of DHA and EPA combined (although the only way to be sure is to measure your omega-3 blood level, which I'll discuss below).

To learn more about the ins and outs of omega-3 and omega-6 fats, be sure to order your copy of "Superfuel." Remember, all preorders will receive three free gifts, so place your order today.

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Your Blood Level, Not the Dosage, Is Key for Optimization

While identifying an ideal dosage is important, it's not the most crucial consideration. The fact that some studies have failed to find any health benefits from omega-3 suggests dosage is a flawed parameter. For example, a Cochrane Collaboration review¹³ concluded omega-3 supplementation has little to no discernible benefit for heart health or longevity.

One explanation for this is the fact that many nutritional studies look at dosage rather than blood levels. GrassrootsHealth vitamin D researchers have clearly demonstrated the importance of looking at achieved blood levels of a nutrient.

When studies look at dosage, no apparent [benefits of vitamin D supplementation](#) are found. However, when you look at people's blood level – the concentration of the nutrient in the body – truly dramatic effects are detected. A similar situation exists with omega-3, as the most important parameter is your blood level, known as your omega-3 index, not any particular dose.

The reason for this is because people metabolize nutrients at different rates, and while one may need a very small dose to achieve a certain blood level, another may need several times that dose. Requirements for omega-3 will also vary depending on your lifestyle; your intake of fatty fish, for example, and your level of physical activity.

For this reason, I recommend getting your omega-3 level tested on an annual basis, and to adjust your dosage based on what you need to achieve an omega-3 index of 8% or higher. So, while a general recommendation is to take 3 to 4 grams of omega-3 per day, the only way to really know whether this is too much or too little is to get tested. We offer a convenient, no doctor required, omega-3 index test for your convenience.

Sources and References

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