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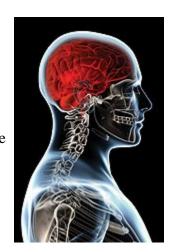
Cover Story

Omega-3 Fatty Acids Increase Brain Volume

By Julius Goepp, MD

The cardioprotective power of **omega-3 fatty acids** has been thoroughly documented in clinical literature. Less well known is their <u>paramount</u> role in optimizing many facets of brain function, from depression, cognition, and memory to mental health.

Recent research has opened up a new horizon in our understanding of omega-3s' profound ability to halt age-related decline and pathology, shattering the long-held medical belief that brain shrinkage and nerve cell death is progressive and irreversible. Omega-3s have been shown to possess antidepressant and neuroprotective properties. One recent landmark study found that aging humans who consumed more omega-3s had <u>increased</u> gray matter brain volume and that <u>most</u> new tissue development was observed in the part of the brain associated with *happiness*.1



Similar findings appeared in the prestigious journal *Lancet*.2 In one of the largest studies of its kind, scientists analyzing the diets of **12,000** pregnant women found that children of those who consumed the <u>least</u> omega-3 were 48% more likely to score in the <u>lowest</u> quartile on IQ tests.

In this article, the latest research on these essential fatty acids' importance to the growth, development, and function of the human brain is detailed. You will learn about their intrinsic power to preserve cognition and memory and *reverse* age-related loss of brain function. You will also discover exciting findings on their unique capacity to combat multiple forms of mental illness, neuropsychiatric disorders, and aberrant behavior, from **Alzheimer's disease** and **aggression** to **bipolar disorder** and **depression**.

Key Nutrient from the Cradle to the Grave

Approximately 8% of the brain's weight is comprised of omega-3 fatty acids 3—the building block for an estimated 100 billion neurons.4 Docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) play a host of vital roles in neuronal structure and function, protecting them from oxidative damage, inflammation, and the cumulative destruction inflicted by other chronic insults.5,6

Embedded in the omega-3-rich neuronal membrane are numerous proteins and complex molecules required for electrochemical transmission and signal reception.4 Scientists have recently shown that the precise balance of fatty acids in brain cells helps determine whether a given nerve cell will be protected against injury or inflammation, or whether it will instead succumb to the injury.7



Omega-3s accumulate in the human brain during fetal development. The amount of the omega-3 DHA has been closely tied to intelligence and cognitive performance in infancy and childhood.8 But the omega-3 content of brain cell membranes involved in essential memory-processing areas *diminishes* with advancing age and in certain chronic brain disorders.9

These findings have led scientists to suspect a role for omega-3 deterioration in development of typical age-related cognitive decline such as that seen in Alzheimer's and chronic disease. 10

Early developmental deficits in brain content of omega-3s have been associated with poor brain maturation and neurocognitive dysfunction.11 These are manifested especially in the area of attention, increasing the risk for attention-deficit/hyperactivity disorder (**ADHD**) and other behavioral disturbances.8 Later in life, declining levels of DHA and EPA may contribute to development of aggression, anxiety, depression, schizophrenia, dementia, and a variety of other mental health and even criminal conditions.12-17

Scientists are having great success at *reversing* many of the fundamental age-related decreases in brain function correlated with omega-3 deficiency.10 ADHD and related conditions can be prevented or mitigated by supplementing infants and nursing mothers with DHA.8,18 Young rats supplemented with DHA show increased *plasticity*, or flexibility of function, in their developing brain cells, with highly invigorated development of synapses, the electrochemical junctions where nerve signals are relayed.9 In aged rats, omega-3 supplementation *reverses* age-related neuronal changes and maintains learning and memory performance that arise from powerful antioxidant and anti-inflammatory effects.9

A remarkable animal study has just revealed that omega-3 fatty acids halt the age-related loss of brain cell receptors vital to memory production, and show potential for increasing neuronal growth.19

A Natural Crime Fighter?

Recent findings suggest that some criminal and aggressive behaviors are closely correlated with low serum omega-3 levels, which are linked to lower levels of altruism, honesty, and self-discipline.13 These effects may be related to alterations in serotonin turnover, which controls impulsivity and aggression-hostility behaviors.13

There's solid data indicating that optimal omega-3 intake at all ages is a promising avenue for subduing aggression and hostility.20,21 For example, 1.5 grams of omega-3 supplementation (containing **840 mg EPA** and **700 mg of DHA**) in autistic children with severe tantrums, aggression, or self-injurious behavior produced significant improvements compared with placebo, without adverse effects.22 And stressed but otherwise healthy volunteers given 1,500 mg/day of DHA reported a significantly improved rate of stress reduction compared to a no-treatment group, suggesting an adaptogenic role for omega-3s (adaptogens help the body respond to imposed stress in a variety of ways).23

In a group of substance abusers, supplementation with 2,225 mg EPA and 500 mg DHA for 3 months produced significant decreases in anger and anxiety scores compared to placebo recipients.16 Amazingly, the two nutrients complemented each other, with EPA increases being most robustly associated with lowered anxiety scores, and DHA increases with lowered anger scores. Similarly, in young adult prison inmates, multi-supplements featuring omega-3s produced significant reductions in antisocial, violent, aggressive, and transgressive (rule-breaking) behavior.24,25

More Potent than Prozac®

Large epidemiological studies repeatedly demonstrate that depressed people have significantly reduced levels of DHA and EPA in red blood cell membranes or serum.26,27 One autopsy study revealed lower amount of omega-3s in the brains of those who'd suffered depression compared to those who did not. 28 Low omega-3 status is frequently found in people who have attempted or committed suicide.29-31 In fact, seasonal variations in blood levels of omega-3s have been shown to closely parallel similar variations in violent suicide deaths.7 Patients with deficient omega-3 status also had reduced expression of the vital transporter complex responsible for moving *serotonin* at nerve cell junctions.7

People who get more omega-3s actually have bigger, more functional brains.

In fact, the serotonin-related benefits of omega-3 supplementation are powerful enough to stand up to a head-to-head comparison with fluoxetine (Prozac®), a common and highly effective member of the selective serotonin reuptake inhibitor (SSRI) category of modern antidepressants.32 In that study, 50% of subjects responded well to fluoxetine alone, 56% to EPA supplementation (1,000 mg), and an impressive 81% in people who took both forms of treatment.32

WHAT YOU NEED TO KNOW: REVERSE BRAIN AGING

- Lipids comprise a significant portion of the brain. Of these lipids, omega-3 fatty acids are particularly important.
- Omega-3 fatty acids exert profound anti-aging effects on brain structure and function, from cognition and memory to mental health and Alzheimer's prevention.
- They have recently been associated with increased volume of the brain's gray matter, especially in those regions associated with happiness, and they boost intelligence through enhanced function from birth onwards.
- They support brain cell structure, increase the production of vital neurotransmitters, and blunt oxidative and inflammatory damage.
- Ranges of **1,000-3,000 mg** of **EPA** and **1,000-1,500 mg** of **DHA** have been shown to yield significant improvements in symptoms of depression, aggression, and other mental disorders, as well as protection against early cognitive decline and even early Alzheimer's disease.



At doses above 2,000 mg, results are uniformly dramatic. Double-blind, placebo-controlled trials are revealing substantial superiority of omega-3 therapy to placebo, using standard depression assessment scales.33 Numerous other studies are further validating these dramatic effects on depression in a host of other contexts: depressive symptoms were alleviated in patients with Parkinson's disease, and in pregnant women with major depressive disorder. 34,35 A particularly powerful effect was shown in middle-aged women experiencing psychological distress and depressive symptoms during the menopausal transition.36 In one Israeli study, omega-3 supplementation in children with major depression provided significant improvement across all indices of measurement.37

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A Novel Intervention for Bipolar Disorder

Bipolar disorder, formerly known as manic-depression, continues to be a perplexing condition for psychiatrists. In bipolar disorder, patients may "cycle" between periods of profound depression and periods of elation and excessive activity (mania). But some cycle rapidly, and others more slowly, while some patients who meet criteria for the conditions have little or no manic component at all.



As with depression, cell membrane deficiencies in omega-3s are associated with bipolar disorder, and people with higher seafood intakes appear to be relatively protected against bipolar symptoms.38,39 An autopsy study of the brains of people with bipolar disorder revealed significant deficits in DHA content of brain cell membranes, with concomitant elevations of

inflammatory products that would have been suppressed by normal levels of omega-3s.40

Omega-3 fatty acids are showing encouraging results in treating some patients with bipolar disorder. In one study, patients supplemented with 9,600 mg omega-3 fatty acids daily showed significantly longer periods of remission than did placebo recipients, and the treatment was well-tolerated.41 A study using MRI scanning revealed profoundly favorable cell membrane alterations in brain tissue induced by very high dose omega-3 supplementation (approximately 9,700 mg daily).42 In general omega-3s appear to be more successful at managing the depressive phases of bipolar disorder than the manic phases,25,43-46 a feature they share with many prescription medications. Several small studies demonstrated that supplementation could also reduce the frequency of manic episodes. One dramatic example is a 2009 study of children with bipolar disorder, in which both manic and depressive symptoms were significantly mitigated by combined DHA (1,560 mg daily) and EPA (360 mg daily) supplementation for 6 weeks, according to clinician ratings as well as parent ratings.47

Most studies showing the greatest effectiveness in bipolar disorder involve combinations of DHA and EPA.48 And as we saw with depression, higher daily doses, on the order of **1,000-1,500 mg** of **DHA** and up to **2,000-3,000 mg** of **EPA**, are optimal for bipolar management.49

Cognitive Decline and Alzheimer's Disease

Omega-3 intake is strongly associated with many different measures of cognition and memory in numerous epidemiological studies, and there's compelling evidence for potent neuroprotection over long time periods. 5,50-52 Insufficient omega-3 intake is strongly correlated with diminished adaptability of brain synapses and impaired learning and memory.53 People with lower omega-3 levels may be more likely to suffer from a host of cognitive impairments including dyslexia, ADHD, and cognitive decline.54-56

Laboratory and animal studies shed light on these observations, suggesting that omega-3 treatment and supplementation may enhance brain function through increased production of the membrane-rich *neurites* required for new synapse formation.57,58 Other protective and cognition-enhancing effects include improved neuronal cell membrane characteristics resulting in enhanced neurotransmission, increased synaptic release of vital neurotransmitters such as serotonin, and neuroprotection from inflammation and oxidant-related damage including those induced by antipsychotic medications.51,53,59 DHA is also protective against several risk factors for dementia including head trauma, diabetes, and cardiovascular disease.51

In healthy adults, increased omega-3 intake is positively associated with greater brain volume in regions associated with emotional arousal and regulation of behavior. People who get more omega-3s have bigger, more functional brains.1 A 2009 study found that omega-3-supplemented adults made fewer risk-averse decisions, but did not show increased impulsiveness.60

In other words, the omega-3 group appeared better able to take appropriate risks in problem-solving, without dangerous impulsivity—skills that are especially relevant in people with depression, who often withdraw and become fearful of even everyday risk taking.



Alzheimer's disease remains one of the most intransigent of age-related neuropathologies. Oxidative damage and inflammation underlie the progressive loss of memory and disorientation that typify the disease, resulting in the term "inflammaging" to describe the complex events that lead to clinically important symptoms. 61,62 Omega-3s have been shown to favorably *alter* some of the characteristic changes associated with the disease.

DHA (1,700 mg daily combined with 600 mg EPA) in Alzheimer's patients significantly reduced levels of inflammatory cytokines circulating in their blood, suggesting that some of the brain tissue inflammation might be mitigated.63,64 Omega-3 supplementation, again with 1,700 mg DHA and 600 mg EPA, in Alzheimer's patients with mild-to-moderate disease improved appetite and produced significant beneficial increases in body weight after 6 and 12 months of treatment, while

placebo patients showed no change in weight.65 These findings have led to calls by experts for increased use of omega-3s as a preventive strategy—calls made all the more urgent by the observation that supplementation is most effective in slowing or *reversing* mild Alzheimer's disease and early age-related cognitive decline. 66-69

The molecular basis for this early intervention strategy lies in the cellular pathology at the core of Alzheimer's: omega-3 treatment of cultured brain cells suppresses many of the early signs of damage triggered by the inflammatory Alzheimer's protein known as beta-amyloid.70 And animal studies suggest that oral supplementation with DHA may enhance the formation of new synapses and their vital dentritic spines, all of which can improve cognitive function.58 In fact, learning and memory in animal models of Alzheimer's are improved by DHA supplementation, and in humans fewer learning errors were made by people with age-related cognitive decline after six months on DHA (900 mg daily).66

Summary

An estimated 8% of brain matter is composed of omega-3s. Omega-3 fatty acids exert profound anti-aging effects on brain structure and function, from cognition and memory to mental health and Alzheimer's prevention. They have recently been associated with increased volume of the brain's gray matter, especially in those regions associated with happiness, and they also boost intelligence through enhanced function from birth onwards. They support brain cell structure, increase the production of vital neurotransmitters and blunt oxidative and inflammatory damage. Ranges of **1,000-3,000 mg** of **EPA** and **1,000-1,500 mg** of **DHA** have been shown to yield significant improvements in symptoms of depression, aggression, and other mental disorders, as well as protection against early cognitive decline and even early Alzheimer's disease.

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