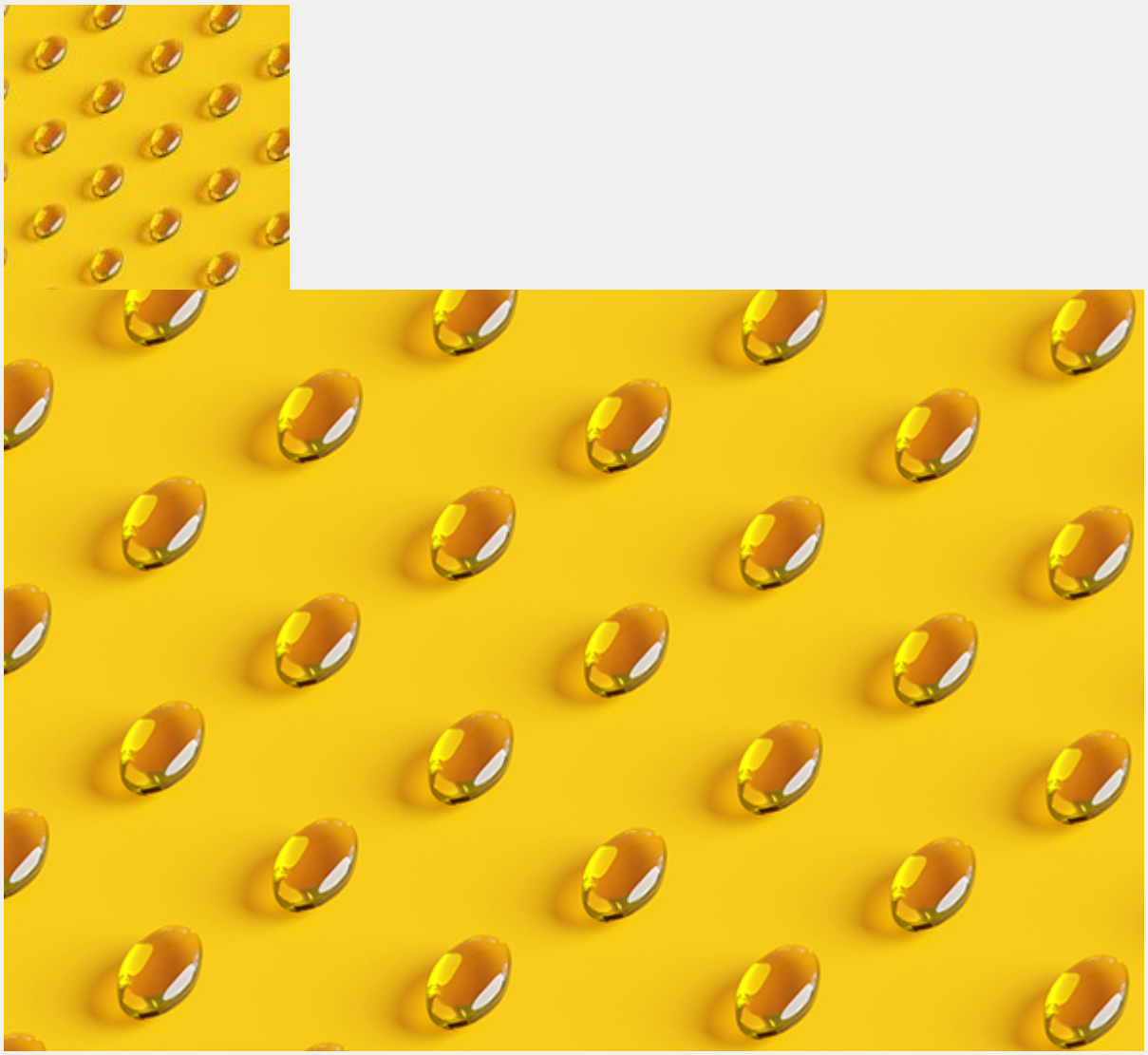
# The brain benefits of omega-3s from cradle to grave



Recently, a patient shared with me that her doctor had told her to stop taking fish oil supplements: “They’re a waste of money,” he admonished.

When it comes to the brain, that’s dead wrong.

A pioneering study was just published that demonstrates the brain-protective impact of fish oil supplementation: “ω-3 PUFA for Secondary Prevention of White Matter Lesions and Neuronal Integrity Breakdown in Older Adults”

Allow me to translate. White matter lesions (WMLs) are little bright spots that are frequently seen in brain MRIs of older individuals. Their extent corresponds with the likelihood that the person is destined for cognitive decline or Alzheimer’s disease. They are like the brain equivalent of age spots on your hands; WMLs are signs of circulatory impairment, loss of myelin coating of nerve fibers, deposits of cellular debris, inflammation, and destruction of axons—the tendrils that establish connections in the brain. They are almost ubiquitous in the elderly, but their extent predicts the likelihood of eventual dementia.

I see them often on MRIs: Radiologists dutifully report “White matter hyperintensities are identified”. It’s almost expected past a certain age.

It's already been shown that blood levels of omega-3s impact the presence of WMLs; in fact, higher levels of omega-3s are associated with a 40% reduction in the probability for WMLs among older adults, and even predict less executive cognitive function decline in older adults without dementia.

In medical research, we call this an "association". It's a hint that there *might* be a protective effect of giving fish oil supplements to at-risk individuals. The researchers in the current study sought to demonstrate the feasibility of converting a mere association into a practical action plan.

They recruited subjects 75 years and older without dementia but who already had moderate levels of WMLs; they also had low blood levels of Omega-3s, suggesting they weren't eating a lot of oily fish or taking fish oil supplements, increasing the chance they might respond to boosting. They then dutifully took fish oil pills daily for three years. Repeat MRIs were performed on the subjects.

The experiment "failed"; there was little change in the WML volume of consumers of fish oil vs. their placebo comparators: *"Although the ω-3 group had less annual WML accumulation than the placebo group, the difference was not statistically significant."*

But—and this is a big but—in the subgroup of subjects who carried an APOE4 gene, there was a significant protective effect of fish oil supplements.

This is actually clever slicing and dicing by the researchers, because often studies fail to reveal benefits—or dangerous side effects—among large heterogeneous cohorts of experimental subjects; nevertheless, certain *sub-groups* are impacted (different strokes for different folks).

For example, most people lose double-digit pounds on the new weight loss drugs, so the studies granting them approval tout astounding *average* results. But an unhappy minority find their weight barely budges (believe me, I've seen them).

Focusing on subgroups can pick up signals that might be missed when looking at a population as a whole.

Genetic alleles like APOE4 act in pairs. People with one APOE4 allele and one normal one—approximately 15-25% of the population—have an estimated two-to-three-fold higher likelihood of developing Alzheimer's disease. People with a double-hit of APOE4—2% of the population—have a 91% chance of eventually developing Alzheimer's.

In this study, only 28 participants (28%) carried an APOE4 genetic allele. It doesn't state whether they were homozygous carriers or heterozygous but if they had had a double APOE4 it might have been hard to recruit a non-demented subject over 75!

And it was precisely in those high-risk APOE4 carriers that the brain benefits of Omega-3s were seen. This is often obscured in studies that look at relatively well individuals—kind of like testing the survival advantages of wearing seat belts in safe low-mileage drivers. It's hard to pick up a statistically significant signal unless you were to look at thousands of subjects. In this study, a scant *90 subjects* completed the protocol! Which makes it even more surprising and impactful that a subset of APOE4 carriers attained the challenging threshold of statistically significant benefits.

It's validating of the proposition that our genes are *not deterministic*—they are not our destiny and are more or less guided in their expression by environmental

factors—*epigenetics* at work. Diet and lifestyle shape the expression of genetic liabilities in Alzheimer's, just as they do even among carriers of the dreaded BRCA genes that promote breast cancer.

When it comes to brain protection, the question often arises, "Which is more important, EPA or DHA?" They're found in various ratios in Omega-3 formulas. In this study, researchers used a balanced formula, containing both. This study involved *"treatment with 1.65 g of ω-3 PUFA (975 mg of EPA and 650 mg of DHA)".*

Interestingly, the study authors differentiate among the effects of each:

*" . . . these findings suggest that an EPA-dominant formula may provide some benefit in APOE4 carriers with no dementia and WMLs, and DHA-dominant formulas may benefit noncarriers of APOE4 with mild-to-moderate AD."*

As usual, as in many recent studies that claim to downplay the efficacy of fish oil interventions, inadequate dosage and duration may have underestimated the impact of supplementation in lower-risk users. Studies lasting decades are prohibitively expensive, and long-term adherence is hard to enforce. Maybe the subjects, already aged 75+, should've started fish oil capsules long before they had significant WMLs? Lifelong supplementation may offer the key to prevention.

And the amount of Omega-3 used in this study was *just two* high potency fish oil pills per day. It was thought by the researchers that this was the right amount to boost blood levels of Omega-3 to levels shown protective against WMLs. But maybe more would've yielded more robust results?

Nevertheless, it's a small trail-blazing study indicating the potential for Omega-3s to stave off dementia. The study authors deservingly conclude:

*"These results will enable improved study design and sample size calculations for future efforts of a relatively cheap, safe, and well-tolerated therapy for primary and secondary dementia prevention."*

Add to this a plethora of research showing fish oil benefits throughout the lifecycle:

- Mothers' levels of Omega-3s improves kids' IQ
- Fish oil helps kids with ADHD
- Fish oil vs. autism
- Fish oil reduces violence and aggression
- Omega-3 for anxiety and depression
- Fish oil displays a protective effect against suicide
- Omega-3 improves processing speed in middle-aged adults
- Access to Omega-3-rich fish and shellfish may have paved the way for better brain capacity in human evolution

We can only conclude that it's a safe bet that supplementation with Omega-3s is a recipe for lifelong brain health.