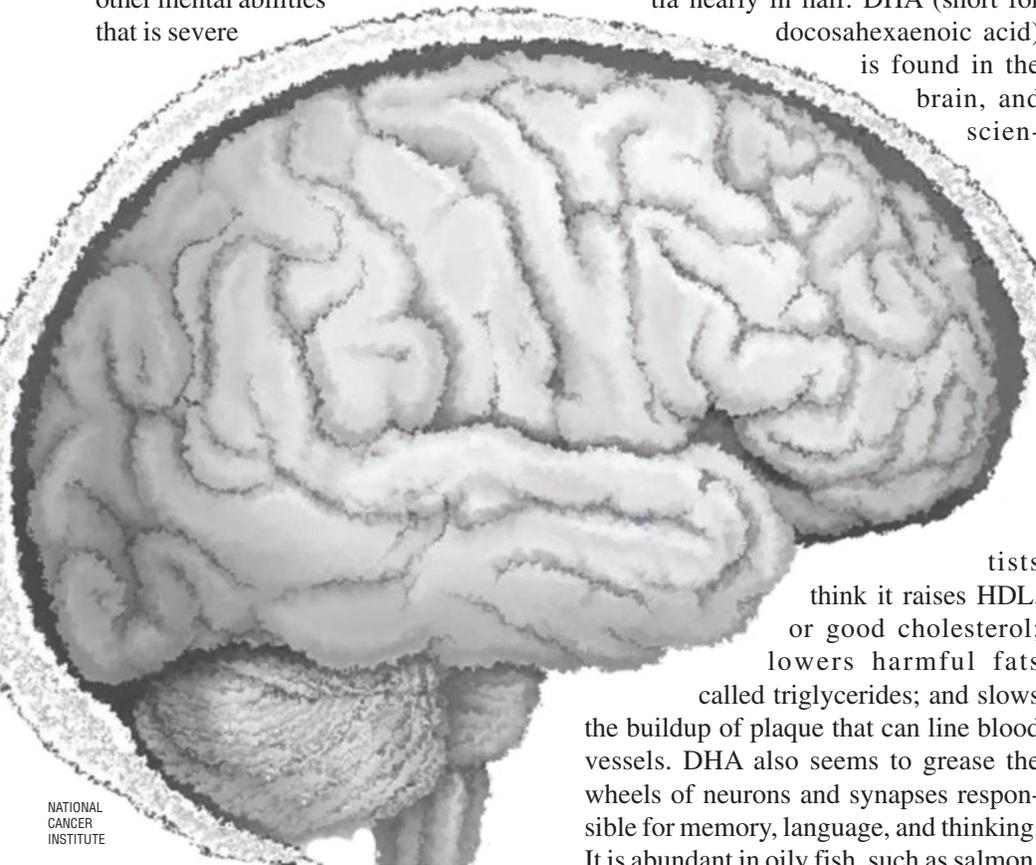


# Food Discoveries for **Brain Fitness**

Eating a nutrient-dense breakfast has long been touted as a way to boost the brain's memory and creativity. Now, Agricultural Research Service studies are showing that eating a healthful diet over a lifetime can improve the condition of the brain as people reach their twilight years. "Dementia" is a general term for a loss of memory and other mental abilities that is severe



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enough to interfere with daily life. It is caused by physical changes in the brain. While Alzheimer's disease is the most common type of dementia, there are other forms, including mild cognitive impairment.

## Reducing Alzheimer's Risk

Every 70 seconds, someone develops Alzheimer's disease, says the Chicago, Illinois-based Alzheimer's Association. Direct and indirect costs of Alzheimer's and other dementias to Medicare, Medicaid, and businesses amount to more than \$148 billion each year. To understand links between inadequate nutrition and

brain degeneration, scientists use different approaches that involve cell culture, animal model, and human clinical studies.

A long-term study headed by physician Ernst Schaefer found that people who ate the greatest amount of oily fish rich in an omega-3 fatty acid, DHA, on a weekly basis appeared to cut their odds of dementia nearly in half. DHA (short for docosahexaenoic acid) is found in the brain, and scien-

tists think it raises HDL, or good cholesterol; lowers harmful fats called triglycerides; and slows the buildup of plaque that can line blood vessels. DHA also seems to grease the wheels of neurons and synapses responsible for memory, language, and thinking. It is abundant in oily fish, such as salmon, tuna, mackerel, and herring.

Schaefer is the director of the Lipid Metabolism Laboratory at the Jean Mayer USDA Human Nutrition Research Center on Aging (HNRCA) at Tufts University in Boston, Massachusetts. He and colleagues analyzed the DHA blood levels of the nearly 900 men and women, ages 55 to 88, participating in the Framingham Heart Study. All participants were free of dementia at the beginning of the 9-year study.

The researchers ranked the participants into four groups, or "quartiles," based on highest to lowest DHA blood levels. Participants with plasma DHA levels in the upper quartile experienced a significant

47-percent lower risk of developing dementia compared with participants with levels in the lower three quartiles. There was also a significant correlation between plasma DHA levels and both fish intake and DHA intake.

Participants who ate the greatest amount of oily fish averaged about three servings a week, which is equivalent to an average daily DHA intake of 180 milligrams. The study suggests that relatively higher oily-fish consumption over time correlates with a lower incidence of dementia in people over 75, according to Schaefer.

The study appears in a 2006 issue of the *Archives of Neurology*.

## Genetics Still a Barrier

While ARS researchers are reporting links between various food components and reduced risk of different forms of dementia, other research studies have shown that the risk of developing some cognitive problems is inherited. For example, people who carry the APOE epsilon 4 (APOE e4) gene variant (about 20 percent of the population) are known to have a greater chance of developing Alzheimer's disease and all-cause dementia.

Former HNRCA neuroepidemiologist Tina Huang compared links between types of fish intake and dementia in relation to the APOE genetic status of 2,547 study volunteers. Huang and colleagues looked at the APOE e4 status of each study participant, all of whom were dementia-free at the beginning of the 8-year study. They found that those with the APOE e4 allele did not enjoy a significant oily-fish-eating benefit found among other study participants.

Consuming fatty fish more than twice per week (compared to less than once per month) was associated with a reduced Alzheimer's risk by just over 40 percent. It was also associated with a lower risk of dementia by nearly 30 percent. Consuming lean fried fish did not show a protective effect. Further, linking oily, or fatty, fish—but not lean fried fish—with a reduction in dementias supports the idea that DHA

The study suggests that relatively higher oily-fish consumption over time correlates with a lower incidence of dementia in people over 75.



is the primary protective nutrient in fish. “We only found a protective effect with fatty [non-fried] fish,” says Huang.

The study results were published in *Neurology* in 2005.

### Brain-Boosting Food Nutrients

Other HNRCA researchers are adding to a limited but growing body of evidence of a link between vitamin D and cognitive function. Metabolic pathways for vitamin D, for example, have been found in the hippocampus and cerebellum, areas of the brain involved in planning, processing, and forming new memories. This suggests that vitamin D may be implicated in cognitive processes.

In a study of more than 1,000 participants receiving home care, the researchers evaluated associations between measured vitamin D blood concentrations and neuropsychological tests. Elders requiring home care have a higher risk of not getting enough vitamin D because of limited sunlight exposure and other factors.

The participants, ages 65 to 99 years, were grouped by their vitamin D status, which was categorized as deficient, insufficient, or sufficient. Only 35 percent had sufficient vitamin D blood levels. They had better cognitive performance on the tests than those in the deficient and insufficient categories, particularly on measures of “executive performance,” such as cognitive flexibility, perceptual complexity, and reasoning. The associations persisted after taking into consideration other variables that could also affect cognitive performance.

The study appears in the *Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* in 2009.

### Challenging B’s Brain Power

Several of the B vitamins have long been known to nourish the brain. B12 is essential for brain and nerve cell function, B6 is essential to nerve tissue, and folate (a B vitamin) is essential to cell and tissue growth. Now, HNRCA neurobiologist and

lead author Aron Troen and physician Irwin Rosenberg are reporting that a B-vitamin deficiency may cause cognitive impairment. Rosenberg heads the Nutrition and Neurocognition Laboratory.

The researchers fed a group of mice a diet deficient in all three vitamins—B12, B6, and folate—and found that the mice had lower cognitive function.

The authors theorize that a deficiency of B vitamins induces a metabolic disorder that manifests with dysfunction of the brain’s blood vessels and circulation, as well as with high homocysteine levels.

The elevated levels of homocysteine and reduced levels of B vitamins that were associated with blood supply-related cognitive impairment in the mice mimic conditions that are associated in older adults with an increased risk for Alzheimer’s disease. The findings provide a much-needed model system in which to study the role of the brain’s blood vessel network and circulation in cognitive function, according to Troen.

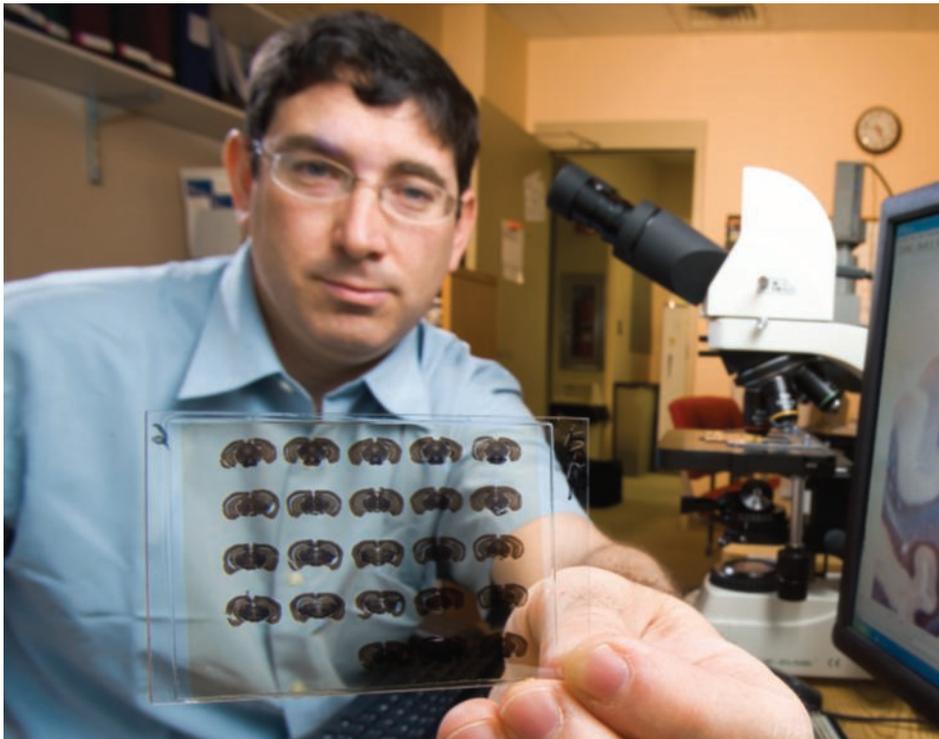
The study is in a 2008 issue of *Proceedings of the National Academy of Sciences*.

### Folate Findings in Latino Study

The B vitamins and their role in preventing decline in brainpower are also being newly explored through human nutrition studies conducted by university researchers and ARS nutrition scientist Lindsay H. Allen. The investigations, led by Mary N. Haan of the University of California-San Francisco, are part of the multiyear Sacramento (California) Area Latino Study on Aging (SALSA). Begun in 1996, the study attracted nearly 1,800 Hispanic seniors, ages 60 to 101, as volunteers.

The research “is needed,” Allen says, “because many studies of B vitamins and brain function have given inconsistent or conflicting results.” Allen directs the ARS Western Human Nutrition Research Center in Davis, California, just outside Sacramento. Scientists from the University of California-Davis (UCD), the UCD Medical Center, and Kaiser Permanente

STEPHEN AUSMUS (D934-1)



Neurobiologist Aron Troen reported that a B-vitamin deficiency may cause cognitive impairment. Here, Troen is examining brain images to assess diet-induced changes.



DHA, an omega-3 fatty acid, is abundant in oily fish, like salmon. Physician Ernst Schaefer (left) reported that higher oily-fish consumption may cut odds of dementia over time. Here, Schaefer visits with Elizabeth Ventura, owner of a fish market in Boston.

Division of Research in Oakland also collaborated in the studies.

The analysis of volunteers' blood samples showed that lower levels of folate were associated with symptoms of dementia and poor brain function—also called “cognitive decline”—as determined by standard tests of memory and other factors. The impairments were detectable even though very few (less than 1 percent) of the volunteers were actually deficient in folate.

Volunteers with higher concentrations of folate in their red blood cells had lower risk of impaired cognitive function and dementia. Even so, having low plasma folate at the outset of the study did not increase volunteers' risk of further cognitive decline or dementia during the next 5 years of the research.

In women, but not men, low levels of folate were associated with symptoms

of depression. In fact, female volunteers whose plasma folate levels were in the lowest third were more than twice as likely to have symptoms of depression as volunteers in the highest third. This finding provides new evidence of an association between lower blood folate and depression. Depression is already known to affect brain function.

#### New Assignment for HoloTC?

In related research with another nutrient—vitamin B12—the scientists determined that holotranscobalamin (holoTC), a protein that carries this vitamin in the bloodstream, might be key to a new approach for detecting cognitive decline earlier and more accurately.

The SALSA team found a correlation between cognitive decline, greater depression, and a low holoTC-to-vitamin B12 ratio in plasma, suggesting the possible

value of this ratio as a convenient, reliable biomarker. In particular, depressed volunteers whose holoTC-to-B12 ratios were in the lowest third, meaning they had relatively less holoTC, were more than three times more likely to have symptoms of cognitive decline.

The scientists have published these and other findings in the *American Journal of Clinical Nutrition*, *Clinical Chemistry and Laboratory Medicine*, and the *Journal of Nutrition, Health, and Aging*.

These findings add to the body of evidence of how healthful components in foods help protect the brain against disease.—By **Rosalie Marion Bliss** and **Marcia Wood**, ARS.

*This research is part of Human Nutrition, an ARS national program (#107) described at [www.nps.ars.usda.gov](http://www.nps.ars.usda.gov).*

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Technician Ivor Asztalos (front, left) runs an immunoassay on plasma samples from the Framingham Heart Study. Assay results are being reviewed by postdoctoral fellow Thomas van Himbergen (center) and Ernst Schaefer.