Does Caffeine Help Decrease Beta-Amyloid in Alzheimer’s Disease?

Back-to-back studies published in the *Journal of Alzheimer’s Disease* show caffeine significantly decreased abnormal levels of beta-amyloid, the protein linked to Alzheimer’s disease, both in the brains and in the blood of mice exhibiting symptoms of the disease. Both studies build upon previous research by the Florida ADRC group showing that caffeine in early adulthood prevented the onset of memory problems in mice bred to develop Alzheimer’s symptoms in old age.

The just-published Florida ADRC study included 55 mice genetically altered to develop memory problems mimicking Alzheimer’s disease as they aged. After behavioral tests confirmed the mice were exhibiting signs of memory impairment at age 18 to 19 months – about age 70 in human years – the researchers gave half the mice caffeine in their drinking water. The other half got plain water. The Alzheimer's mice received the equivalent of five 8-oz. cups of regular coffee a day. That's the same amount of caffeine – 500 milligrams – as contained in two cups of specialty coffees like Starbucks, or 14 cups of tea, or 20 soft drinks.

At the end of the two-month study, the caffeinated mice performed much better on tests measuring their memory and thinking skills. In fact, their memories were identical to normal aged mice without dementia. The Alzheimer’s mice drinking plain water continued to do poorly on the tests.

In addition, the brains of the caffeinated mice showed nearly a 50-percent reduction in levels of beta amyloid, the substance forming the sticky clumps of plaques that are a hallmark of Alzheimer’s disease. Other experiments by the same investigators indicate that caffeine appears to restore memory by reducing both enzymes needed to produce beta amyloid. The researchers also suggest that caffeine suppresses inflammatory changes in the brain that lead to an overabundance of beta amyloid.

If larger, more rigorous clinical studies confirm that caffeine staves off Alzheimer's in humans, as it does in mice, this benefit would be substantial. Alzheimer’s disease attacks nearly half of Americans age 85 and older, and Alzheimer's and other dementias triple healthcare costs for those age 65 and older, according to the Alzheimer’s Association.

Journal articles cited:


2. Caffeine Suppresses Amyloid-β Levels in Plasma and Brain of Alzheimer’s Disease Transgenic Mice; Chuanhai Cao, John R Cirrito, Xiaoyang Lin, Lilly Wang, Deborah K Verges, Alexander Dickson, Malgorzata Mancarz, Chi Zhang, Takashi Mori, Gary W Arendash, David M Holzman, and Huntington Potter; *Journal of Alzheimer's Disease*, Volume 17:3 (July 2009).
Moderate Alcohol Intake Is Associated With Nearly 40% Lower Risk of Dementia

Moderate alcohol intake, especially wine, has been associated with reduced risk of dementia in middle aged adults. It is not known whether this association is also true for older adults or those with mild cognitive impairment (MCI).

Researchers sought to determine the relationship between alcohol intake and incident dementia in 3,069 community-living adults aged 75 years and older without dementia who were enrolled in the Ginkgo Evaluation of Memory Study (GEMS), an NIH-sponsored study of ginkgo biloba for prevention of dementia. At the beginning of the study, 2,587 of the participants were assessed to be cognitively normal and 482 had MCI.

Alcohol consumption was self-reported by study participants and categorized by the researchers as none, 1-7 drinks/week (light), 8-14 drinks/week (moderate), and more than 14 drinks/week (heavy). All types of alcohol were counted. The distribution of alcohol consumption per week was 0=42.6%; 1-7=38.2%; 8-14=9.4%; more than 14= 9.8%.

Participants were examined every six months for up to six years for changes in their memory or thinking abilities. If someone was suspected of having developed Alzheimer's or another dementia, they were thoroughly evaluated. There were 523 new cases of dementia during the follow up period of the study.

After adjustment for demographics, smoking, co-morbidities, depression, social activity, and baseline cognition, moderate alcohol intake (1-2 drinks per day) was associated with a 37% lower risk of dementia in participants with normal cognition at baseline but not in those with MCI.

For older adults who started the study with MCI, consumption of alcohol at any amount was associated with faster rates of cognitive decline; and those who were classified in the heavy drinker category (more than 14 drinks per week) were almost twice as likely to develop dementia during the study, compared to non-drinkers with mild cognitive impairment.

ICAD Presentations of DHA in AD and Age-Related Cognitive Decline

During the Alzheimer's Association's 2009 International Conference on Alzheimer's Disease in Vienna held in July 2009, researchers presented study results on recent and ongoing clinical trials.

Two of the most significant were the results of large studies of DHA, an omega-3 fatty acid. DHA (docosahexaenoic acid) is naturally found in the body in small amounts and is the most abundant omega-3 fatty acid in the brain. DHA oil is abundant in some marine microalgae,
which provide the DHA that makes fatty fish a good source of DHA. Dietary DHA is also available in foods enriched with algal DHA or fish oils, and dietary supplements. Previous animal studies and epidemiology in humans suggested that DHA may be beneficial in people with Alzheimer’s.

One of the trials was conducted by the Alzheimer’s Disease Cooperative Study (ADCS) supported by the National Institute on Aging (NIA), and the second by Martek Biosciences Corporation (Martek), the primary company that makes algal DHA for supplementation. The NIA trial lasted 18 months and was conducted in people with mild to moderate Alzheimer’s. Martek’s trial was six months, and the compound was tested in healthy people to see its effect on "age related cognitive decline" (ARCD). Both studies used Martek’s algal DHA.

The results of the ADCS trial show no evidence for benefit in the studied population. The Martek trial showed a positive result on one test of memory and learning but that study was in healthy older adults, not people with Alzheimer’s or another dementia. The results need confirmation, as is standard scientific practice.

Alzheimer’s Disease Cooperative Study 18-Month DHA Trial in Alzheimer’s Disease

Researchers from the ADCS led by Joseph Quinn, M.D., at Oregon Health and Science University, conducted a double-blind, randomized, placebo-controlled clinical trial comparing DHA and placebo in people diagnosed with mild to moderate Alzheimer’s. The trial took place at 51 research sites throughout the U.S. The average age of the participants was 76.

At the beginning of the trial, all 402 participants had a dietary DHA intake of less than 200 mg per day. Subjects were treated with DHA or placebo at a dose of two grams per day for 18 months. Those participants already taking approved Alzheimer’s drugs could continue taking them during the trial. Co-primary outcomes were rate of change on the Alzheimer’s disease assessment scale-cognitive (ADAS-cog) and rate of change on Clinical Dementia Scale-sum of the boxes (CDR-SOB). These two measures are the current standard tests used by FDA when assessing new Alzheimer’s drugs.

According to the researchers, treatment with DHA clearly increased blood levels of DHA, and also appeared to increase brain DHA levels, based on a measured increase of DHA in study participants’ cerebrospinal fluid (CSF). However, DHA treatment did not slow the rate of change on tests of mental function (ADAS-cog), global dementia severity status (CDR-SOB), activities of daily living (ADL), or behavioral symptoms (NPI) in the study population as a whole. There was no different treatment effect between the mild and moderate Alzheimer’s patients.

"These trial results do not support the routine use of DHA for patients with Alzheimer’s," Quinn said.

In a pre-planned exploratory data analysis, study participants were divided according to whether or not they carried the "e4" version of the "ApoE" gene. ApoE-e4 increases the risk of developing Alzheimer’s but does not appear to modify the rate of disease progression. In the people who had an ApoE-e4 gene, the researchers found no benefits of DHA treatment. In contrast, those without the ApoE-e4 gene who received DHA had a slower rate of decline on the primary test of mental function (the ADAS-cog). A trend in the same direction was seen on the Mini-mental state examination, another test of mental function.
"This is an intriguing exploratory result," said Quinn. "However it must be treated with appropriate caution. The finding requires further study for confirmation."

"One of the issues raised by this study – and other recent Alzheimer's and mild cognitive impairment therapy trials – concerns a possible interaction between certain therapies and genetic status. This issue needs to be explored more completely in future trials," Thies added.

**Memory Improvement with DHA Study (MIDAS)**

Researchers at Martek Biosciences Corporation examined the effects of algal DHA as a possible neuroprotective nutritional supplement for ARCD in their Memory Improvement with DHA Study (MIDAS).

Scientists led by Karin Yurko-Mauro, PhD, Associate Director of Clinical Research at Martek, conducted a randomized, double-blind, placebo-controlled, multi-center, six month study to determine the effects of 900 mg per day of algal DHA on improving cognitive functions in 485 healthy older people (average age=70) with mild memory complaint. The primary outcome measure was a change from baseline in CANTAB Paired Associate Learning (PAL), a visuospatial episodic memory test.

After six months, the researchers found that the study participants taking DHA supplements made significantly fewer errors on the PAL compared to when they started the study (-1.63 ± 0.76, p<0.03). Plasma phospholipid DHA levels doubled over the course of the study in those people taking the supplements, and correlated with the PAL response (p<0.04).

They also observed a significant decrease in heart rate in those taking DHA (change from baseline of -3.2 vs. -1 BPM, p<0.03) that was highly correlated with week 24 plasma levels (p<0.01). Blood pressure and body weight remained unchanged between groups. Plasma levels of Alzheimer's related proteins Abeta 1-40, 1-42 and hs-CRP were not significantly different.

The researchers observed no treatment-related serious adverse effects in the study, and the adverse effects profile for DHA was the same as for the placebo.

"In our study, healthy people with memory complaints who took algal DHA capsules for six months had almost double the reduction in errors on a test that measures learning and memory performance versus those who took a placebo," Yurko-Mauro said. "The benefit is roughly equivalent to having the learning and memory skills of someone three years younger."

Currently Enrolling Clinical Research Trials Conducted by the Alzheimer’s Disease Cooperative Study

GAP/IgIV Study

Intravenous (IgIV) has been approved and used successfully for over 20 years to treat a variety of autoimmune and immunodeficient diseases. Because it contains anti-amyloid antibodies, IgIV is being investigated in a Phase III study as a treatment for Alzheimer's disease. For more information, go to http://www.adcs.org/Studies/IGIV.aspx

Nerve Growth Factor Study (NGF)

A Phase II clinical study of Ceregene's CERE-110, a gene therapy product designed to deliver nerve growth factor (NGF) to the brain for the treatment of Alzheimer's disease (AD) is currently underway. This study is a randomized, double-blind, placebo-controlled trial and employs gene therapy to deliver nerve growth factor (NGF) directly into the brain.

Four research sites are able to screen participants or will be doing so shortly:

University of California, San Diego
University of California, Los Angeles
Georgetown University
Mount Sinai School of Medicine

For research site and further information: http://adcs.org/Studies/NGF.aspx