Topics: Brain function, cognitive performance with age, mild cognitive impairment (MCI), Alzheimer's Disease (AD), omega-3 fatty acids, docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), long chain polyunsaturated fatty acids (LC-PUFAs), fish, fish oil

Relevance to: Efalex Active 50+

STUDY 1

Reference: Chiu C, Su K, Cheng T, Liu H, Chang C, Dewey M, Stewart R, Huang S. The effects of omega-3 fatty acids monotherapy in Alzheimer's disease and mild cognitive impairment: A preliminary randomized double-blind, placebo-controlled study. Progress in Neuro-sychopharmacology & Biological Psychiatry 2008;32:1538-1544.

Objective: To determine the effect of EPA and DHA supplementation on cognitive performance in elderly adults with mild cognitive impairment (MCI) and mild or moderate Alzheimer's disease (AD).

Background: Population studies have shown that higher omega-3 LC-PUFA intake is associated with lower risk for MCI and AD. However, results of small, open supplementation trials in people with these conditions have been inconsistent.

Method: 23 people with mild or moderate AD and 23 with MCI were randomly and blindly assigned to take either 1.8 g/day of Omega-3 (1080 mg EPA + 720 mg DHA) or an olive oil placebo for 24 weeks. The following cognitive tests were performed at baseline and at weeks 6, 12, 18 and 24.

i) AD Assessment Scale (ADAS-cog) – a psychometric scale
ii) Clinician's Interview-Based Impression of Change Scale (CIBIC-plus) – assesses disease severity and progression of illness.
iii) Mini-Mental State Examination – to measure various aspects of cognitive function including orientation to time and place, naming, repeating, writing, copying, instantaneous recall, short-term memory, backward spelling and performing a 3 stage command.
iv) Hamilton Depression Scale (HDRS)

Blood fatty acids were assessed at baseline and weeks 12, 18 and 24.

Findings: CIBIC-plus improved in the treatment groups relative to placebo. ADAS-cog significantly improved in the MCI group compared to placebo. Higher blood EPA was associated with better cognitive outcome.

Conclusion: Omega-3 LC-PUFAs may improve general clinical function in patients with mild or moderate AD and MCI, but not their cognitive function. The cognitive effects of omega-3 LC-PUFAs might be favoured in patients with MCI more so than those with AD.

STUDY 2

Reference: Van de Rest O, Geleijnse JM, Dullemeijer C, OldeRikkert MGM, Beekman ATF, DeGroot CPGM. Effect of fish oil on cognitive performance in older subjects. Neurology 2008;71:430-438.

Objective: To determine the effect of EPA and DHA supplementation on cognitive performance in healthy elderly adults.

Background: Higher intake of omega 3 LC-PUFAs, EPA and DHA, is associated with reduced risk of cognitive decline. Numerous population studies have provided inconclusive results

and there have been no randomized supplementation studies completed in elderly people without dementia (i.e. healthy aging adults).

Method: 302 cognitively healthy (Mini-Mental State Examination score >21) adults aged 65 years or older were randomly and blindly assigned to take either 400 mg Omega 3 (226 mg EPA+ 176 mg DHA), 1800 mg Omega-3 (1093 mg EPA+847 mg DHA) or olive oil placebo for 26 weeks. Cognitive performance was determined at baseline and after 13 and 26 weeks to assess attention, sensorimotor speed, memory and executive function. The specific tests were as follows:

i) Word Learning Test –measures the storage and retrieval of newly acquired verbal material.
ii) The Forward Wechsler Digit Span Test – measures attention.
iii) The Backward Wechsler Digit Span Test – measures working memory.
iv) The Trail Making Test Version A – measures sensorimotor speed
v) The Trail Making Test Version B – measures concept shifting interference (executive function).
vi) The Stroop Color-Word Test – measures selective attention and susceptibility to behavioural interference.
vii) The Verbal Fluency Test – measures the ability to draw on one's encyclopedia memory in a strategy-based manner (executive, verbal reasoning).

Blood samples were taken at the same time points as the tests were performed for blood fatty acid status and APOE-4 allele presence was assessed.

Findings: Blood EPA/DHA increased by 238% and 51% in the high dose and low dose groups, respectively as compared with placebo. In general, cognitive test scores in all three groups improved, but changes were not significantly different among the groups and were probably mostly due to learning effects. People who carried the APOE-4 allele showed improvement following treatment with low and high dose EPA+DHA and men in the low dose group also improved compared to placebo.

Conclusion: Daily supplementation with EPA+DHA for 26 weeks did not significantly improve cognitive function in the population tested. However, results indicated that it may be more beneficial for men and those who carry the APOE-4 allele.

PRESS RELEASE

Two new studies in aging adults provide more knowledge about the effects of omega---3 fatty acids from fish to prevent cognitive decline.

In recent years, a number of studies have focused on potential benefits of regular consumption of fish containing omega-3 long chain polyunsaturated fatty acids (LC-PUFAs) to maintain or enhance brain function with respect to dementia and a few have looked at the impact on cognitive decline in normal, healthy aging adults. However, no randomized, double-blind, placebo-controlled clinical studies have confirmed that supplementation with omega-3 LC-PUFAs [eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)] could prevent mild cognitive impairment (MCI) or Alzheimer's Disease (AD). But two studies just published have provided some insight into those effects and have indicated where additional research is required.

The first study[1], led from Taipei City Hospital, Taiwan included 23 people with mild or moderate AD and 23 with MCI that took either 1.8 g/day of Omega-3 (1080 mg EPA + 720 mg DHA) or an olive oil placebo for 24 weeks. Cognitive tests were performed at baseline and at weeks 6, 12, 18 and 24 and included the AD Assessment Scale (ADAS-cog) and the Clinician's Interview-Based Impression of Change Scale (CIBIC-plus) which measures disease severity and progression of illness. Blood fatty acids were assessed at baseline and weeks 12, 18 and 24. Results showed that Omega-3 LC-PUFAs may improve general clinical function in patients with mild or moderate AD and MCI, but not their cognitive function. The cognitive effects of omega-3 LC-PUFAs might be more apparent in patients with MCI rather than those with AD.

The second study[2] from the Wageningen University, Radboud University and VU University, The Netherlands included 302 cognitively healthy adults aged 65 years or older that took either 400 mg Omega- 3 (226 mg EPA+ 176 mg DHA), 1800 mg Omega-3 (1093 mg EPA+847 mg DHA) or olive oil placebo for 26 weeks. Cognitive performance was determined at baseline and after 13 and 26 weeks to assess attention, sensorimotor speed, memory and executive function using a variety of tests and blood fatty acid status was assessed. Blood EPA/DHA increased by 238% and 51% in the high dose and low dose groups, respectively and compared with placebo. In general, cognitive test scores in all three groups improved, but changes were not significantly different among the groups and were probably mostly due to learning effects. However, men in the low dose group improved compared to placebo and people who carried the APOE-4 allele showed improvement following treatment with both doses of EPA+DHA. APOE is a gene that codes for a special protein which helps to transfer lipoproteins, fat-soluble vitamins and cholesterol into the lymph system and then into the blood stream. People with a particular form of APOE, called APOE-4 are prone to develop atherosclerosis, reduced cognitive ability and AD.

Results of both studies look promising, but indicate that further research is necessary. Both studies measured improvements in the placebo groups which masked the effects of the active. Hence, both groups of researchers indicated that olive oil may not be an appropriate choice for future studies. In addition, the treatment duration in both studies was relatively short to measure differences in cognitive decline that can sometimes take years to become apparent. Finally, genetic predisposition including gender and APOE-4 involvement, and the ramifications of disease severity at start of treatment on outcome, requires further investigation.

In 2007 two studies published in the *American Journal of Clinical Nutrition* suggested that regular intake of foods rich in EPA and DHA could prevent age-related cognitive decline. The first[3] showed that those who ate 10 grams or more of fish or fish products per day had significantly better test scores and a lower prevalence of poor cognitive performance
than did those whose intake was less than 10 g/day. The second study[4] showed that those with higher blood levels of EPA and DHA had less decline in sensorimotor speed and complex speed over the 3 years.

Two additional studies published earlier last year showed that men who consumed about 400 mg of omega-3 LC-PUFAs per day had less cognitive decline in a five year period than those who ate only about 20 mg per day of these nutrients[5] and that higher blood levels of omega-3 LC-PUFAs prevented deterioration in verbal fluency which was particularly apparent in people with high blood pressure and high blood triglyceride and/or cholesterol levels[6].

In November 2006, the Framingham Heart Study which followed 899 initially healthy volunteers with a median age of 76 years[7] showed that people who ate two or more servings of fish per week were 39 percent less likely to develop dementia, but those who ate less than that did not derive any benefit. Although oily fish contains many different fatty acids, it was only the DHA that was responsible for preventing dementia in this study.

All of these studies add to the growing body of information linking the benefits of DHA to brain function in aging people. Earlier population studies have shown that DHA levels are lower than normal in people with various forms of age related cognitive decline[8,9]. Other studies have shown that low DHA status is associated with the development of Alzheimer's disease[10] while high dietary fish intake[11] and specifically DHA intake[12] is associated with a lower

incidence of cognitive decline and Alzheimer's disease respectively. These studies clearly show low omega-3 LC-PUFA status is a risk factor for developing age related cognitive decline and demonstrate the importance of maintaining an adequate intake of these vital nutrients in adulthood to prevent mental deterioration. Small open, clinical studies providing DHA supplements have measured significant improvements in people with vascular dementia[13] and have shown they can delay the rate of cognitive decline in patients with very mild Alzheimer Disease[14]. Results of these latest studies combined with the fact that 24 million people worldwide currently have dementia[2] and that 80% of those with MCI are diagnosed with AD within 6 years[1], stresses the need for further research in this area.

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