

# Memory Improvement with Docosahexaenoic Acid Study

## New Study By Martek Demonstrates Algal DHA Improves Memory and Learning

A new study in the current edition of *Alzheimer's & Dementia*<sup>1</sup>: The Journal of the Alzheimer's Association reported that healthy adults  $\geq 55$  years of age taking 900 mg algal docosahexaenoic acid/day (DHA) for six months demonstrated enhanced memory and learning skills compared to those taking a placebo.

Impairment of cognitive health can range from mild cognitive decline to dementia. With the dramatic aging of the US population the health, social and economic implications associated with cognitive decline are profound. Awareness of these factors prompted the CDC to identify cognitive health as a public health priority.<sup>2</sup> As many as 5.4 million older Americans have cognitive impairment without dementia. Of these, approximately 12% will develop dementia annually.<sup>3</sup> Many studies have shown an association of greater omega-3 fatty acid intake from fish and a reduction in the risk of dementia<sup>4</sup>, however few studies have directly tested the effects of omega-3s on cognitive decline.

### Why DHA?

A certain degree of memory loss and decline in cognitive function may be considered a normal part of aging. Brain health, including memory, is a high-ranking priority and often listed as one of the top health-related concerns of aging populations in the U.S. and other countries. Additionally, there is a growing awareness that certain aspects of healthy lifestyles may prevent or delay the expression of negative symptoms typically associated with aging including cognition. One of these aspects includes the addition of DHA to the diet. DHA is an integral component of all mammalian membranes. It is the major structural and functional omega-3 long-chain polyunsaturated fatty acid (n-3 LCPUFA) in the brain and retina throughout life.<sup>5</sup>

As a consequence, the presence of DHA at adequate levels in neural tissue is essential for optimal brain function during aging, as well as during other parts of life. DHA, the major omega-3 fatty acid found in the brain enhances cognition in infants.<sup>6</sup> Low plasma DHA levels have been associated with cognitive decline in patients with Alzheimer's disease and the aging adult. Martek Biosciences, a producer of the vegetarian source of the n-3 LCPUFA, docosahexaenoic (DHA) conducted a trial with algal DHA to discover its impact on age-related cognitive decline (MIDAS, clinicaltrials.gov).

Table 1 shows the details of the trial. This double-blind, randomized, placebo-controlled, multicenter trial evaluated the effects of supplementation on 485 healthy older adults. These subjects presented with mild memory complaints (Mini-Mental State Examination (MMSE)  $> 26$  and a Logical Memory (WMSIII) baseline score  $\geq 1$  SD below younger adults) and were randomly supplemented with either 900 mg of algal DHA per day or placebo. The Cambridge Neuropsychological Test Automated Battery, (CANTAB®) Paired Associate Learning (PAL) score was the primary measure of outcome. PAL is a validated test of visuospatial learning and episodic memory. In prior studies PAL successfully discriminated between healthy controls, mild cognitively impaired subjects and those with Alzheimer's disease.<sup>7</sup>

#### Goal

- Evaluate the effects of algal DHA on cognitive outcomes in healthy elderly ( $\geq 55$  yrs.) with a mild memory complaint

#### Trial Design

- Study Population: Age-related Cognitive Decline
- Multi-center (19 U.S. sites)
- Randomized, double-blind, placebo-controlled, parallel, stratified by age (55-69;  $>70$ )
- Oral Dose: 900 mg/day algal DHA or placebo (corn/soy)
- Study Treatment: 6 months
- Sample Size: 485 subjects
- Primary Endpoint: cognitive test of memory & learning as measured by the CANTAB™ Paired Associate Learning (PAL) test
- Secondary Endpoints: other cognitive tests, activity of daily living skills, plasma phospholipid fatty acid levels, safety and tolerability

Table 1: Study Description

### Results

All subjects were assessed for working memory, memory retention, attention, and executive function in order to determine the potential for algal DHA to affect cognition. After 24 weeks of DHA algal oil supplementation, performance on a memory and learning task (PAL 6 errors) was significantly improved in the algal DHA group compared to the group given a placebo, as shown in Figure 1. Algal DHA supplementation resulted in a significant two-fold reduction in the number of learning and episodic memory errors on the CANTAB® PAL 6 pattern test. The results indicate that 900 mg/day algal DHA supplementation for 6 months provided a benefit roughly equivalent to having the learning and memory skills of someone three years younger on this episodic memory task. This suggests that algal DHA supplementation may ameliorate early learning and memory deficits associated with cognitive aging.

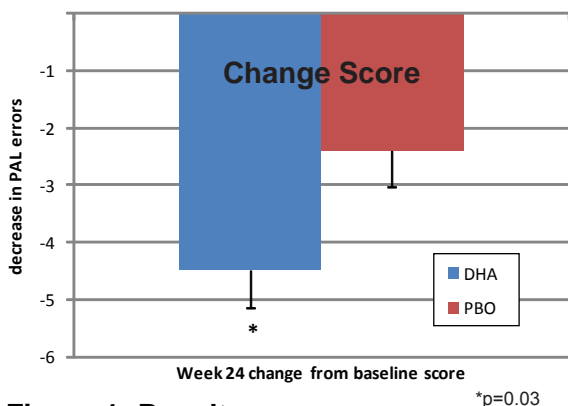


Figure 1: Results

## Blood Composition Relates to Cognitive Function

Blood levels of DHA serve as a great biomarker of DHA status.<sup>8</sup> Although DHA levels of various blood components is highly correlated with cardiac DHA<sup>9</sup>, direct correlation studies between DHA levels and brain tissue are complicated by lack of longitudinal studies in which brain samples can be obtained. However, a number of studies identify an association between omega-3 fatty acid intake with the risk of dementia or cognitive decline. Higher blood levels of DHA correlate with a reduced risk of cognitive decline. Levels of DHA in the brain of AD patients are notably lower compared to age-matched controls.<sup>10</sup>

In the current study, data showed that plasma DHA levels significantly increased (Figure 2) and were positively correlated with the improved memory scores in the algal DHA-supplemented study subjects, indicating enhanced DHA-related cognitive function. Changes in the other fatty acids correspond to well-known alterations with DHA supplementation including increased EPA and DPAn-6.<sup>11</sup>

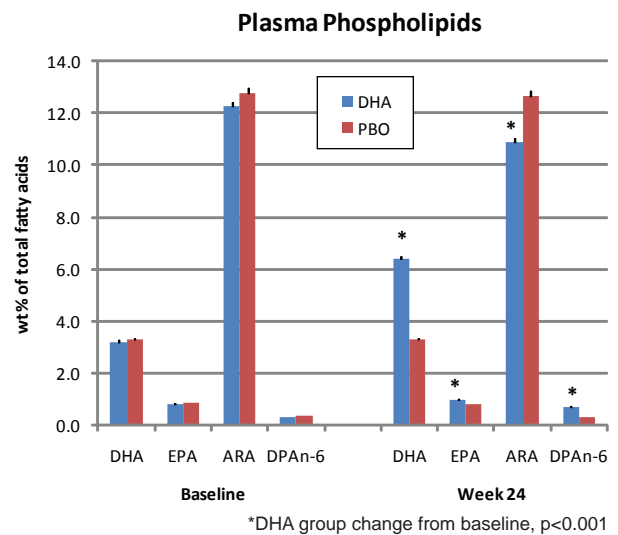


Figure 2: Plasma Results

## Other Benefits for Older Adults

One of the well-known benefits of long-chain omega-3 fatty acids is the beneficial effects on the cardiovascular system. DHA is known to lower triglyceride levels, increase HDL levels and decrease heart rate and blood pressure in some individuals. Figure 3 demonstrates that 900 mg algal DHA/day significantly decreased heart rate compared to placebo over the 24-week supplementation, providing a cardiovascular benefit which is consistent with previously published studies in humans.<sup>12</sup> Administration of 900 mg algal DHA/day was well-tolerated with no significant side effects.

Health statistics from the US National Center for Health Statistics indicate that sub-optimal intake of long-chain omega-3 fatty acids resulted in 84,000 deaths in 2005.<sup>13</sup> Fortunately, this is a modifiable risk factor. Quality of life issues are of concern in an aging population. Approximately 80 million baby boomers are nearing 65 years of age. This is a time when the risk of Alzheimer's disease and late life dementias doubles every 5 years.<sup>14</sup> Based on the findings of this large randomized, placebo-controlled, nutritional clinical study, 900 mg/day of algal DHA helps improve episodic memory and learning in older, healthy adults exhibiting mild memory complaints. This suggests that age related cognitive decline need not be considered an unchangeable consequence of aging.

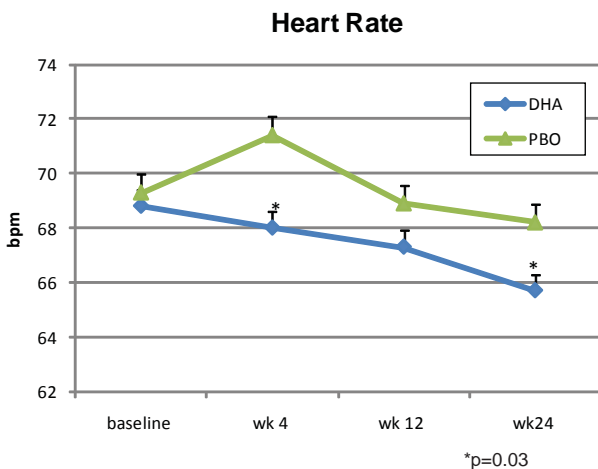


Figure 3: Heart Rate

## Conclusions

1. 900 mg/day algal DHA supplementation for 6 months resulted in a significant 2-fold reduction in the number of visuospatial learning and episodic memory errors and significant increases to verbal recognition memory scores.
2. DHA supplementation doubled plasma DHA levels. Higher plasma and red blood cell levels of DHA are associated with better cognitive function.
3. DHA supplementation significantly decreased heart rate compared to placebo over the 24-week supplementation, providing a cardiovascular benefit consistent with previously published studies in humans.

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