



## **Evaluation of the Strength of Evidence for Supplementation Use for Healthy Cognitive Function**

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In recent years, research shows that nutrition and diet can affect cognitive performance both positively and negatively, and that environmental and cognitive enrichment can modulate the effects of nutrition and diet. Factors that have a positive effect on cognition include antioxidants, anti-inflammatory agents, and estrogen. Due to a high rate of oxygen metabolism, the brain accumulates oxidative damage with age. In rodents, antioxidants singly and in combination can improve cognitive function and reduce age-related cognitive decline. Recent studies also show that various fruits and vegetables (e.g., blueberries, spinach, etc.) can reduce age-related losses in motor function and cognition. In a higher mammalian animal model (the aged canine or dog), a diet enriched in antioxidants, mitochondrial cofactors, and fruits and vegetables produced both short and long-term improvements in cognition that were maintained over a three-year period.

Research in normal elderly humans is descriptive to date, but most studies suggest a positive effect of antioxidant supplementation on the maintenance of cognitive function. However, variable results have been reported due to a lack of placebo controlled clinical trials, and variable outcomes may be due to the range in age of subjects, the actual diet or supplements used, variability in dose, and environmental factors. Similar to antioxidants, supplementation with anti-inflammatory agents and postmenopausal use of estrogen in women appears to be associated with improved maintenance of cognitive function and a slowing in the rate of conversion to dementia. Treatment of mild to moderate Alzheimer's patients with high doses of vitamin E appears to slow the rate of decline as indicated by a delay in institutionalization, but did not improve cognitive function. In addition, another dietary supplement that has possible antioxidant characteristics and has been reported to improve age-related cognitive function is currently being used in a primary prevention trial.

Some dietary factors are associated with an increased risk for age-related cognitive dysfunction. Two of the primary factors appear to be high levels of cholesterol and homocysteine. Animals fed a diet rich in cholesterol show increased beta-amyloid deposition, and in humans, lowering the levels of cholesterol with statins appears to reduce the risk for Alzheimer's disease. Higher levels of homocysteine also are associated with increased risk for Alzheimer's disease, suggesting that dietary supplementation with folic acid may be protective.

It is unlikely, however, that diet alone is sufficient to maximize the maintenance of cognitive function with age. Indeed, recent studies suggest that exercise, environmental, and/or cognitive enrichment can lead to improvement and maintenance of cognitive function in animals and in humans. Both dietary supplementation and enrichment in combination may be better than either

one alone. In fact, in the aged canine, a combined treatment group maintained significantly higher levels of cognitive function over a three-year period than animals treated with either an antioxidant diet or enrichment alone.