

Folic Acid May Improve Cognitive Performance

BY ROBERT FINN
San Francisco Bureau

Older adults who took 800 mcg of folic acid daily for 3 years showed significantly less cognitive decline than those who took placebo, according to a randomized, double-blind trial.

Three years of folic acid supplementation gave an individual the performance of someone 4.7 years younger for memory, 2.1 years younger for information pro-

cessing speed, and 1.5 years younger for global cognitive function, said Jane Durga, Ph.D., of Wageningen (the Netherlands) University and her associates (*Lancet* 2007;369:208-16).

According to the investigators, folic acid supplementation was associated with particularly good results in the most clinically relevant subtest, the one that measured delayed recall. After 3 years of supplementation, patients experienced an improvement in performance similar to

that of an individual 6.9 years younger.

In an accompanying editorial comment, Martha Clare Morris, Sc.D., and Christine C. Tangney, Ph.D., of Rush University Medical Center, Chicago, noted that normal levels of folic acid intake vary greatly across different regions, ethnic groups, ages, and socioeconomic circumstances (*Lancet* 2007;369:166-7).

In the United States and Canada, for example, grain is fortified with folic acid, and now less than 1% of the U.S. population

has an inadequate serum folate status. There is no such fortification in the Netherlands, where the study was conducted, and where the recommended dietary allowance (RDA) of folic acid is 300 mcg/day, lower than the U.S. RDA of 400 mcg/day.

In general, dietary folic acid intake is about 200 mcg/day in northern Europe but up to 559 mcg/day in Greece, where many eat the so-called Mediterranean diet. Before the fortification of grain began in

High Folate Intake May Lower AD Risk

High intake of folate decreased the risk of Alzheimer's disease in a predominantly Hispanic and African American cohort of elderly people, according to a recently published study.

There was a statistically significant association between AD risk and combined dietary and supplemental folate consumption, but not between AD and either type of folate alone, suggesting that cumulative intake from both sources is important in assessing Alzheimer's risk, wrote Dr. Jose A. Luchsinger of Columbia University, New York, and his associates.

These results are consistent with those of several previous studies of folate and AD risk, but conflict with the results of several others. "Definitive conclusions about the value of higher folate intake in the prevention of AD cannot be made at this time," Dr. Luchsinger and his associates said, adding that "the decision to increase folate intake to prevent AD should await clinical trials."

In what they described as the first published study of the issue in a cohort that was predominantly black and Caribbean Hispanic, the researchers assessed diet and cognitive status in 965 subjects in 1992-1994 and thereafter at 18-month intervals.

The subjects were Medicare recipients aged 65 years and older whose folate intakes were estimated using 61-item food frequency questionnaires. The group had a high prevalence of cardiovascular disease. A total of 192 developed AD over a mean follow-up of 6 years.

The risk of AD decreased with increasing intake of folate but not of vitamins B₆ or B₁₂, the investigators said (*Arch. Neurol.* 2007;64:86-92).

People with AD had a total folate intake "that was almost statistically significantly lower" than that in subjects without AD.

There was a "modest" correlation between folate intake and plasma homocysteine levels, suggesting that folate's ability to lower homocysteine may account for some of its effect on AD risk, Dr. Luchsinger and his associates said.

And since folate is derived primarily from vegetable sources, folate intake may be a marker of a healthier diet or of other socioeconomic or lifestyle factors, they noted.

—Mary Ann Moon

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the United States, mean folic acid intake was estimated at 275 mcg/day.

The study involved 818 individuals aged 50-70 years who are participating in the Folic Acid and Carotid Intima-Media Thickness (FACIT) trial, with a primary end point involving atherosclerotic progression. Age-related declines in cognitive performance were secondary outcomes. The patients were selected for high concentrations of plasma homocysteine, which is considered a risk factor for vascular disease. Folic acid supplementation is known to decrease homocysteine concentrations, Dr. Durga and her associates said.

Participants were excluded if they had

plasma total homocysteine concentrations less than 13 micromol/L or greater than 26 micromol/L (which may have been due to factors other than folate concentration). Patients were also excluded if they had renal disease, thyroid disease, or intestinal disease, or if they regularly used vitamin D supplements or drugs that could affect atherosclerotic progression.

Participants were given five cognitive

tests at baseline and again at the end of the study. Compared with those taking placebo, subjects taking folic acid scored significantly better on tests of memory and information-processing speed. There were no significant differences on sensorimotor speed, complex speed, or word fluency.

Global cognitive functioning, defined as an average of the five domains, improved significantly in the folic acid group.

After 3 years of supplementation, patients had an improvement in performance similar to that of an individual 6.9 years younger.

The groups did not differ on the Mini-Mental State Examination, a screening test for dementia.

It is unclear whether folic acid supplementation would result in a reduced incidence of dementia, the investigators noted. Some have argued that age-related cognitive decline is at the beginning of a continuum leading to dementia, but others have suggested that the cause of age-related cognitive decline differs from that of dementia. Similar trials in older populations, or in those with mild cognitive impairment or dementia, would be needed to address that question, Dr. Durga and her associates said. ■

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