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High homocysteine levels may double risk of dementia, Alzheimer's disease

NIH/NATIONAL INSTITUTE ON AGING

People with elevated levels of homocysteine in the blood had nearly double the risk of developing Alzheimer's disease (AD), according to a new report from scientists at Boston University. The findings, in a group of people participating in the long-running Framingham Study, are the first to tie homocysteine levels measured several years before with later diagnosis of AD and other dementias. The report, which appears in the February 14, 2002, issue of The New England Journal of Medicine, provides some of the most powerful evidence yet of an association between high plasma homocysteine and later, significant memory loss.

The relationship between AD and the amino acid homocysteine is of particular interest because blood levels of homocysteine can be reduced, for example, by increasing intake of folic acid (or folate) and vitamins B6 and B12. The therapeutic use of these compounds is being explored as scientists try to understand better homocysteine's role in AD or other types of dementia as well as its possible link to various forms of heart disease.

The dementia/AD study is being conducted by Philip A. Wolf, M.D., Boston University (BU), and colleagues at BU and Tufts University, who authored the new findings. The study was supported by the National Institute on Aging (NIA), part of the National Institutes of Health (NIH). The researchers were also funded by NIH's National Institute of Neurological Disorders and Stroke (NINDS). The Framingham Heart Study is supported by the NIH's National Heart, Lung, and Blood Institute (NHLBI).

"The Framingham population gave us the perfect opportunity to look at homocysteine levels in a group of people without memory problems over a period of several years, well before any evidence of dementia," Wolf pointed out. "This is the clearest demonstration yet of the relationship between elevated homocysteine levels and dementia," he noted.

"The evidence is beginning to mount regarding homocysteine's role in dementia," according to Neil Buckholtz, Ph.D., chief of the Dementias of Aging program at the NIA. "The good news is that we may have found a potential risk factor for AD that is modifiable. We don't know yet whether reducing homocysteine levels will reduce dementia risk, but this is something that can and will be tested in clinical trials." Buckholtz noted that the NIA-sponsored Alzheimer's Disease Cooperative Study, a nationwide consortium of research centers, is already planning a clinical trial of folate and vitamins B6 and B12 to test whether reducing homocysteine levels with high doses of these vitamin supplements can slow the rate of cognitive decline in people diagnosed with AD. Wolf and colleagues followed 1,092 people in a "dementia-free" group of the Framingham cohort. Participants

in this group, whose average age was 76, were enrolled in the study between 1976 and 1978. Plasma homocysteine levels were measured between 1979 and 1982 and between 1986 and 1990. Researchers also considered age, sex, vascular risk factors other than homocysteine, and plasma levels of folate and vitamins B6 and B12 of the participants. Information from the participants was also available on the late-onset AD genetic risk factor APOE-e4.

From the 1986-1990 examinations through December 2000, some 111 people developed dementia, including 83 diagnosed specifically with AD. Elevated homocysteine levels (defined as greater than 14 mmol/liter) doubled the chance that a participant would develop AD and each 5 mmol/liter elevation increased the risk of AD by 40 percent. The analysis showed further that people with consistently high levels of homocysteine throughout the period of the study were at highest risk for dementia and AD. The researchers also examined whether the earlier levels of homocysteine, measured between 1979 and 1982, had any relationship to the development of dementia or AD later on; this analysis, too, linked elevated levels at least 8 years prior to a later diagnosis of dementia and AD. The association between homocysteine and AD was found to be strong and independent of other factors, such as age, gender, APOE genotype, and other known or suspected risk factors for dementia and AD.

There was no direct association in this study between the serum levels of folate and vitamins B6 and B12 and the development of dementia among the participants. As the relationship between these B vitamin levels, homocysteine, AD, and cardiovascular disease continues to be studied, scientists speculate that consuming adequate amounts of B vitamins by diet or supplementation might help reduce levels of homocysteine in some individuals. Findings from the NHLBI-supported DASH (Dietary Approaches to Stop Hypertension) study suggest that a diet rich in green leafy vegetables, low-fat dairy products, citrus fruits and juices, whole wheat bread, and dry beans can significantly lower levels of homocysteine. The Food and Drug Administration (FDA) now requires the addition of folic acid to enriched breads, cereals, flours, corn meals, pastas, rice, and other grain products. "Although there is no evidence that actually reducing homocysteine levels will prevent AD or cardiovascular disease, a healthy diet low in fat and rich in nutrients is always a good idea," says BU's Wolf.

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The NIA leads the Federal effort to support and conduct basic, clinical, and social and behavioral studies on aging and AD. It supports the Alzheimer's Disease Education and Referral (ADEAR) Center, which provides information on AD research, including clinical trials, to the public, health professionals, and the media. ADEAR can be contacted toll free at 1-800-438-4380 weekdays or by visiting the website www.alzheimers.org. Press releases, fact sheets, and other materials about aging and aging research can be viewed at the NIA's general information website, www.nia.nih.gov.

The NHLBI is the nation's leading supporter of biomedical research on diseases of the heart, blood vessels, and lung; sleep disorders; and on the management of blood resources. The Institute's Framingham Heart Study began in 1948 as the first long-term population-wide epidemiological study and has led to such medical breakthroughs as identifying the risk factors for heart disease, including high blood cholesterol and high blood

pressure. Information about Framingham is available online at www.nhlbi.nih.gov/about/framingham. NHLBI press releases, fact sheets, and other materials are available on the NHLBI website at www.nhlbi.nih.gov.

The National Institute on Aging is a component of the National Institutes of Health, U.S. Department of Health and Human Services

Media Contact

Vicky Cahan
cahanv@nia.nih.gov
301-496-1752

http://www.nih.gov/nia