

Vitamin B12 May Slow Brain Aging

Liam Davenport | May 11, 2016

Individuals with increased levels of circulating homocysteine have faster rates of brain changes associated with aging than other people, whereas higher levels of vitamin B12 are associated with slower rates of brain aging, new research suggests.

Babak Hooshmand, MD, PhD, Center for Alzheimer Research–Aging Research Center, Karolinska Institutet, Stockholm, Sweden, and colleagues found that total brain volume losses were lower in individuals with higher baseline vitamin B12 levels, whereas the opposite was true of those with increased homocysteine levels.

"Vitamin B12 and tHcy [total homocysteine] might be independent predictors of markers of brain aging in elderly individuals without dementia," the investigators write.

They add, "[I]f the association is causal, supplementation with B vitamins may be effective for prevention of brain damage due to increased levels of total homocysteine. Adequately timed and powered randomized clinical trials are needed to determine efficient treatment guidelines."

The research was [published online](#) April 27 in *JAMA Psychiatry*.

Homocysteine and Brain Tissue Loss

The researchers examined data on 501 participants aged 60 years and older from the Swedish National Study on Aging and Care, in Kungsholmen. All participants were free of dementia at baseline. Of these, 299 underwent repeated structural brain MRI between 2001 and 2009.

At baseline and at each follow-up, participants underwent a thorough clinical examination, an interview, and assessment. Data on sociodemographic characteristics, medical history, drug use, and cognitive function were collected.

Venous blood samples were collected at baseline, from which circulating levels of vitamin B12, red blood cell folate, and sulfur amino acids were determined. These were correlated with changes in brain tissue volumes and total white matter hyperintensity (WMH) over 6 years.

Between baseline and the 6-year follow-up, the mean total brain tissue (TBT) volume decreased from 74.3% to 71.6% of the total cranial volume ($P < .001$), whereas the mean WMH volume increased from 0.0004% to 0.0007% ($P < .001$).

Multadjusted linear mixed model analysis revealed that increased baseline levels of vitamin B12 and holotranscobalamin (the biologically active fraction of B12) were associated with a decreased rate of TBT volume loss, at respective beta values of 0.048 ($P < .001$) and 0.040 ($P = .002$) for each standard deviation increase.

Furthermore, the researchers found that each standard deviation increase in total homocysteine levels was linked to more rapid rates of TBT volume loss, at a beta value of -0.035 ($P = .02$).

Increases in total homocysteine levels were also associated with increases in the progression of WMH in individuals with a systolic blood pressure >140 mmHg, at 0.000019 per standard deviation increase ($P = .047$).

The results suggested that there was no association between markers of brain aging and levels of red blood folate and other sulfur amino acids.

Modest Effect

Commenting on the findings for *Medscape Medical News*, E. Sherwood Brown, MD, PhD, professor of psychiatry and director of the Psychoneuroendocrine Research Program at the University of Texas Southwestern Medical Center, Dallas, described the study as "interesting," with the "main plus" being the large sample size.

Dr Brown noted that although similar studies have been published, "the longitudinal aspect of looking at the vitamin levels as a

predictor of later changes is somewhat novel...and might offer some insights into ways to maybe prevent cognitive decline or decline in brain volume or even dementia."

Dr Brown emphasized that although the researchers took into account a range of variables related to vitamin B12 and homocysteine, "it's very hard to know whether it's the levels of them per se or whether they're somehow a marker for some other lifestyle health factors that are really the culprit here, and that's certainly a legitimate limitation."

In future studies, Dr Brown would like to see cognitive data along with the brain structural data to identify clinical correlates for the findings, as well as multiple measures of the vitamin and homocysteine levels.

"I think the other cautionary note to throw in there is, even though the relationships were highly significant...the effect you're seeing is always pretty modest. I think you'd have to put all this in the context of one of probably many factors that might influence the degree of brain aging over time," he concluded.

B12 Trial Warranted

Dr Hooshmand agreed with Dr Brown that it would have been valuable to have multiple vitamin B12 and homocysteine assessments for the current analysis.

"It is ideal if we have brain measures three times over 6 years, but the better situation is also to have vitamin B12 three times over 6 years," he said, adding that the team plans on taking multiple vitamin measurements in future studies.

Nevertheless, he believes that the finding of an association between vitamin B12 levels and brain volume loss suggests that a randomized controlled trial of vitamin B12 supplementation is warranted to determine whether it could prevent brain aging.

"But not everyone will benefit from supplementation," Dr Hooshmand told *Medscape Medical News*. "Those who have low levels of these vitamins, those who have clinical signs of vitamin B12 deficiency...those are the people who will benefit from receiving the supplements."

He also pointed to the single-center, randomized [VITACOG study](#), in which 271 individuals older than 70 years who had mild cognitive impairment received supplementation with high-dose folic acid and vitamins B6 and B12.

"They lost less brain compared to people who had normal homocysteine and normal vitamin levels, meaning that those with high levels of homocysteine or with clinical or biochemical vitamin deficiency can benefit from supplementation," said Dr Hooshmand.

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