Brain Takes Multiple Hits from Low B12 Levels

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• Note that previous studies have suggested that poor vitamin B12 status may be a risk factor for brain atrophy and possibly cognitive impairment.

• Note that in this study, concentrations of vitamin B12–related markers (methylmalonate, cystathionine, homocysteine) were associated with global cognitive function and with total brain volume.

Review

Low levels of vitamin B12 may contribute to cognitive problems for older adults in more than one way, according to a cross-sectional study.

Markers of B12 insufficiency all predicted lower global cognitive scores over nearly five years of follow-up, Christine C. Tangney, PhD, of Rush University Medical Center in Chicago, and colleagues found.

The mediating factors appeared to be white matter lesions and cerebral infarcts in association with the nonspecific marker homocysteine and brain atrophy for the vitamin B12-specific marker methylmalonic acid (MMA).

"Vitamin B12 status may affect the brain through multiple mechanisms," the group wrote in the Sept. 27 issue of Neurology.

The Institute of Medicine already recommends B12 supplements for seniors, co-author Martha Clare Morris, ScD, director of nutrition at Rush University Medical Center, noted in an interview with MedPage Today.

"Insufficient vitamin B12 is very common in older people," she explained. "The older we get we have a decreased ability to absorb vitamin B12 from our diet. ... Medications can also impair absorption."

But middle age adults may be another important population for screening and possible supplementation, Morris suggested.

Although her group's observational study couldn't say whether boosting B12 would prevent or reverse cognitive effects, a prior randomized trial demonstrated that high-dose B complex supplements could slow down brain atrophy in older adults.
In that study, dubbed VITACOG, supplements did a better job of holding cognitive declines at bay than placebo among those with high homocysteine levels.

"So at least from this one clinical trial it appears that [supplementation] may have some benefit," Morris argued.

Her group dug deeper into their Chicago Health and Aging Project (CHAP), measuring vitamin B12-related markers in relation to brain MRI and neuropsychological test results 4.6 years later in 121 residents of Chicago's South Side, ages 65 and older.

After adjustment for age, sex, education, race, and serum creatinine levels to control for renal function problems that could have an impact on homocysteine, all of the B12-related markers affected global cognitive scores.

The estimated effect from each 1 µmol/L higher concentration of a marker ranged from 0.001 to 0.03 standardized units of lower global cognitive score for MMA ($P=0.02$) and homocysteine ($P=0.04$).

Higher levels of individual markers were related to lower performance on various cognitive domains:

- For homocysteine, trends for perceptual organization and speed
- For cystathionine and 2-methylcitric acid, significant impacts on episodic memory and poor semantic memory
- For MMA, significantly worse episodic memory and perceptual speed

Each of the markers also predicted decreased total brain volume at higher levels.

Homocysteine also correlated with white matter hyperintensity volume at 0.103-units more of this cerebrovascular risk marker per µmol/L ($P=0.009$).

This impact on white matter hyperintensity volume appeared to partly explain homocysteine's effect on global cognitive function.

Cerebral infarcts also appeared to be playing a role as adjustment for the two factors equally attenuated the association between homocysteine and global cognitive score down to a $P=0.08$ level of significance.

Total brain volume, though, appeared to be mediating the other B12 insufficiency markers' effects on global cognition, as adjustment for brain size attenuated away the links with MMA, cystathionine, and 2-methylcitric acid.

Notably, no measures on MRI or cognitive testing linked directly to serum B12 levels.

Although clinical screening typically relies on serum B12, Morris warned that this may not give a full picture of whether the effects of insufficiency are accumulating.

"You might be in the normal range, say in the low normal range, of vitamin B12 in your blood but still have evidence of insufficient vitamin B12 based on these biomarkers," she told MedPage Today.
The researchers cautioned that lack of serial MRI and measurements prevented any conclusions on whether poor vitamin B12 status speeds up brain atrophy and demyelination.

Another limitation was the lack of data on serum folate and vitamin B6, they added.

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Morris reported receiving research support from the U.S. Department of Health and Human Services, the National Institute on Aging, the Abbott Fund, and the Sprague Institute.

Coauthors reported sitting on scientific advisory boards for Pfizer; consulting for Pain Therapeutics, Bayer Schering Pharma, and Avanir Pharmaceuticals; and serving on a data safety monitoring committee for Eli Lilly.

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**Source reference:**


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