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Preventing Alzheimer's disease-related gray matter atrophy by B-vitamin treatment.

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Abstract

Is it possible to prevent atrophy of key brain regions related to cognitive decline and Alzheimer's disease (AD)? **One approach is to modify nongenetic risk factors, for instance by lowering elevated plasma homocysteine using B vitamins**. In an initial, randomized controlled study on elderly subjects with increased dementia risk (mild cognitive impairment according to 2004 Petersen criteria), **we showed that high-dose B-vitamin treatment (folic acid 0.8 mg, vitamin B6 20 mg, vitamin B12 0.5 mg) slowed shrinkage of the whole brain volume over 2 y**. Here, we go further by demonstrating that **B-vitamin treatment reduces, by as much as seven fold, the cerebral atrophy in those gray matter (GM) regions specifically vulnerable to the AD process, including the medial temporal lobe**. In the placebo group, higher homocysteine levels at baseline are associated with faster GM atrophy, but this deleterious effect is largely prevented by B-vitamin treatment. **We additionally show that the beneficial effect of B vitamins is confined to participants with high homocysteine (above the median, 11 μmol/L) and that, in these participants, a causal Bayesian network analysis indicates the following chain of events: B vitamins lower homocysteine, which directly leads to a decrease in GM atrophy, thereby slowing cognitive decline**. Our results show that **B-vitamin supplementation can slow the atrophy of specific brain regions that are a key component of the AD process and that are associated with cognitive decline**. Further B-vitamin supplementation trials focusing on elderly subjets with high homocysteine levels are warranted to see if progression to dementia can be prevented.