

Abstract

PLoS One. 2010 Sep 8;5(9):e12244.

Homocysteine-lowering by B vitamins slows the rate of accelerated brain atrophy in mild cognitive impairment: a randomized controlled trial.

Smith AD, Smith SM, de Jager CA, Whitbread P, Johnston C, Agacinski G, Oulhaj A, Bradley KM, Jacoby R, Refsum H.

Oxford Project to Investigate Memory and Ageing, University of Oxford, Oxford, United Kingdom.

BACKGROUND: An increased rate of brain atrophy is often observed in older subjects, in particular those who suffer from cognitive decline. Homocysteine is a risk factor for brain atrophy, cognitive impairment and dementia. Plasma concentrations of homocysteine can be lowered by dietary administration of B vitamins.

OBJECTIVE: To determine whether supplementation with B vitamins that lower levels of plasma total homocysteine can slow the rate of brain atrophy in subjects with mild cognitive impairment in a randomised controlled trial (VITACOG, ISRCTN 94410159).

METHODS AND FINDINGS: Single-center, randomized, double-blind controlled trial of high-dose folic acid, vitamins B(6) and B(12) in 271 individuals (of 646 screened) over 70 y old with mild cognitive impairment. A subset (187) volunteered to have cranial MRI scans at the start and finish of the study. Participants were randomly assigned to two groups of equal size, one treated with folic acid (0.8 mg/d), vitamin B(12) (0.5 mg/d) and vitamin B(6) (20 mg/d), the other with placebo; treatment was for 24 months. The main outcome measure was the change in the rate of atrophy of the whole brain assessed by serial volumetric MRI scans.

RESULTS: A total of 168 participants (85 in active treatment group; 83 receiving placebo) completed the MRI section of the trial. The mean rate of brain atrophy per year was 0.76% [95% CI, 0.63-0.90] in the active treatment group and 1.08% [0.94-1.22] in the placebo group ($P = 0.001$). The treatment response was related to baseline homocysteine levels: the rate of atrophy in participants with homocysteine $>13 \mu\text{mol/L}$ was 53% lower in the active treatment group ($P = 0.001$). A greater rate of atrophy was associated with a lower final cognitive test scores. There was no difference in serious adverse events according to treatment category.

CONCLUSIONS AND SIGNIFICANCE: The accelerated rate of brain atrophy in elderly with mild cognitive impairment can be slowed by treatment with homocysteine-lowering B vitamins. Sixteen percent of those over 70 y old have mild cognitive impairment and half of these develop Alzheimer's disease. Since accelerated brain atrophy is a characteristic of subjects with mild cognitive impairment who convert to Alzheimer's disease, trials are needed to see if the same treatment will delay the development of Alzheimer's disease.

TRIAL REGISTRATION: Controlled-Trials.com ISRCTN94410159.

PMID: 20838622

FREE FULL TEXT

