

Abstract

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Homocysteine and folate as risk factors for dementia and Alzheimer disease.

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BACKGROUND: In cross-sectional studies, elevated plasma total homocysteine (tHcy) concentrations have been associated with cognitive impairment and dementia. Incidence studies of this issue are few and have produced conflicting results.

OBJECTIVE: We investigated the relation between high plasma tHcy concentrations and risk of dementia and Alzheimer disease (AD) in an elderly population.

DESIGN: A dementia-free cohort of 816 subjects (434 women and 382 men; mean age: 74 y) from an Italian population-based study constituted our study sample. The relation of baseline plasma tHcy to the risk of newly diagnosed dementia and AD on follow-up was examined. A proportional hazards regression model was used to adjust for age, sex, education, apolipoprotein E genotype, vascular risk factors, and serum concentrations of folate and vitamin B-12.

RESULTS: Over an average follow-up of 4 y, dementia developed in 112 subjects, including 70 who received a diagnosis of AD. In the subjects with hyperhomocysteinemia (plasma tHcy > 15 micromol/L), the hazard ratio for dementia was 2.08 (95% CI: 1.31, 3.30; P = 0.002). The corresponding hazard ratio for AD was 2.11 (95% CI: 1.19, 3.76; P = 0.011). Independently of hyperhomocysteinemia and other confounders, **low folate concentrations (< or = 11.8 nmol/L) were also associated with an increased risk of both dementia (1.87; 95% CI: 1.21, 2.89; P = 0.005) and AD (1.98; 95% CI: 1.15, 3.40; P = 0.014)**, whereas the association was not significant for vitamin B-12.

CONCLUSIONS: **Elevated plasma tHcy concentrations and low serum folate concentrations are independent predictors of the development of dementia and AD.**

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