Contribution of the MTHFR gene to the causal pathway for depression, anxiety and cognitive impairment in later life.

Abstract:
Homocysteine (Hcy) is harmful to neurons and blood vessels, including the cerebral microvasculature. It is possible that such effects contribute to the cascade of events that leads to cognitive decline, dementia, and depression in later life. Hcy is produced during the metabolism of the essential amino-acid methionine, which also involves a methyl group transfer derived from folate and choline metabolism. Its plasma level can be influenced by factors such as age, vitamin deficiency, renal function, and a common mutation in the methylenetetrahydrofolate reductase (MTHFR) gene, where cytosine is replaced by thymidine (C-->T) at nucleotide position 677. Subjects with the TT genotype have higher homocysteine levels and may be particularly prone to experiencing depression as a result of high plasma Hcy and dysfunction of methylation metabolic pathways critical to the synthesis of noradrenaline and serotonin. We designed the present study to investigate whether older women with the TT genotype would have higher depression and lower cognitive scores than women with CT and CC genotypes. A total of 240 community-dwelling women aged 70 years or over volunteered to take part in the study - 29 carried the TT genotype, 113 the CT and 98 the CC genotype. The Beck Depression Inventory (BDI) score for subjects with the TT genotype was statistically
similar to the other groups (P = 0.609). Plasma Hcy showed a modest and significant correlation with BDI scores (r = 0.21) that was independent from age, B12 and folate levels. There was no association between beck anxiety inventory (BAI) scores and MTHFR genotype or homocysteine levels. The cognitive assessment of participants included measures of verbal memory, memory for faces, verbal fluency, visuo-spatial abilities and the cognitive section of the Cambridge Examination For Mental Disorders Of The Elderly (CAMCOG)-MTHFR genotype had no clear association with cognitive scores. These results indicate that, in isolation, the MTHFR C677T gene variation does not play an important role in the modulation of mood and cognitive performance in later life.