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Polymorphisms of homocysteine metabolism are associated with intracranial aneurysms.

[Semmler A](#), [Linnebank M](#), [Krex D](#), [Götz A](#), [Moskau S](#), [Ziegler A](#), [Simon M](#).

Department of Neurology, University of Bonn, Bonn, Germany.

BACKGROUND: Impaired homocysteine metabolism is associated with a number of vasculopathies including extracranial aneurysms. We analyzed the possible association of nine genetic variants of homocysteine metabolism with the occurrence of intracranial aneurysms. **METHODS:** Caucasian patients (n = 255) treated at two German hospitals for intracranial aneurysms and local controls (n = 348) were genotyped for the following polymorphisms: methionine synthase (MTR) c.2756A-->G, methylenetetrahydrofolate reductase (MTHFR) c.677C-->T, MTHFR c.1298A-->C, cystathionine beta-synthase (CBS) c.844_855ins68, CBS c.833T-->C, dihydrofolate reductase (DHFR) c.594 + 59del19bp, glutathione S-transferase Omega-1 (GSTO1) c.428C-->A, reduced folate carrier 1 (RFC1) c.80G-->A and transcobalamin 2 (Tc2) c.776C-->G. **RESULTS:** The G-allele of the missense polymorphism Tc2 c.777C-->G was found to be underrepresented in patients, suggesting that this variant may protect from the formation of cerebral aneurysms [odds ratio per two risk alleles (OR) 0.48; 95% confidence interval (CI) 0.30-0.77; p = 0.002]. We obtained borderline results for the G-allele of RFC1 c.80G-->A (OR 1.64; 95% CI 1.01-2.65; p = 0.051) and the insertion allele of DHFR c.594 + 59del19bp (OR 1.61; 95% CI 1.00-2.60; p = 0.059), which were found to be overrepresented in patients. **CONCLUSION:** Polymorphisms of homocysteine metabolism are possible risk factors for the formation of intracranial aneurysms. Copyright 2008 S. Karger AG, Basel.

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