Abstract view

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Functional polymorphisms in folate metabolism genes influence the risk of meningioma and glioma.

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Folate metabolism plays an important role in carcinogenesis. To test the hypothesis that polymorphic variation in the folate metabolism genes 5,10-methylenetetrahydrofolate reductase (MTHFR), methionine synthase (MTRR), and methionine synthase reductase (MTR) influences the risk of primary brain tumors, we genotyped 1,005 glioma cases, 631 meningioma cases, and 1,101 controls for the MTHFR C677A and A1298C, MTRR A66G, and MTR A2756G variants. MTHFR C677T-A1298C diplotypes were associated with risk of meningioma (P = 0.002) and glioma (P = 0.02); risks were increased with genotypes associated with reduced MTHFR activity. The highest risk of meningioma was associated with heterozygosity for both MTHFR variants [odds ratio (OR), 2.11; 95% confidence interval (95% CI), 1.42-3.12]. The corresponding OR for glioma was 1.23 (95% CI, 0.91-1.66). A significant association between risk of meningioma and homozygosity for MTRR 66G was also observed (OR, 1.41; 95% CI, 1.02-1.94). **Our findings provide support for the role of folate metabolism in the development of primary brain tumors. In particular, genotypes associated with increased 5,10-methylenetetrahydrofolate levels are associated with elevated risk.**