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Association of methylenetetrahydrofolate reductase (MTHFR) gene C677T polymorphism with autism: evidence of genetic susceptibility

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Abstract

Autism (MIM 209850) is a heterogeneous neurodevelopmental disease that manifests within the first 3 years of life. Numerous articles reported that dysfunctional folate-methionine pathway enzymes may play an important role in the pathophysiology of autism. Methylenetetrahydrofolate reductase (MTHFR) is a critical enzyme of this pathway and MTHFR C677T polymorphism reported as risk factor for autism in several case control studies. However, controversial reports were also published. Hence the present meta-analysis was designed to investigate the relationship of the MTHFR C677T polymorphism with the risk of autism. Electronic databases were searched for case control studies with following search terms - 'MTHFR', 'C677T', in combination with 'Autism'. Pooled OR with its corresponding 95 % CI was calculated and used as association measure to investigate the association between MTHFR C677T polymorphism and risk of autism. Total of thirteen studies were found suitable for the inclusion in the present meta-analysis, which comprises 1978 cases and 7257 controls. Meta-analysis using all four genetic models showed significant association between C677T polymorphism and autism (ORTvs.C = 1.48; 95 % CI: 1.18-1.86; P = 0.0007; ORTT + CT vs. CC = 1.70, 95 % CI = 0.96-2.9, p = 0.05; ORTT vs. CC = 1.84, 95 % CI = 1.12-3.02, p = 0.02; ORCT vs.CC = 1.60, 95 % CI = 1.2-2.1, p = 0.003; ORTT vs.CT+CC = 1.5, 95 % CI = 1.02-2.2, p = 0.03). In total 13 studies, 9 studies were from Caucasian population and 4 studies were from Asian population. The association between C677T polymorphism and autism was significant in Caucasian (ORTvs.C = 1.43; 95 % CI = 1.1-1.87; p = 0.009) and Asian population (ORTvs.C = 1.68; 95 % CI = 1.02-2.77; p = 0.04) using allele contrast model. In conclusion, present meta-analysis strongly suggested a significant association of the MTHFR C677T polymorphism with autism.

Keywords: Autism; C677T polymorphism; Homocysteine; MTHFR; Meta-analysis; Methylation.