Observational Study

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Genetic effect of *MTHFR* C677T, A1298C, and A1793G polymorphisms on the age at onset, plasma homocysteine, and white matter lesions in Alzheimer's disease in the Chinese population

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Abstract

Background: Three polymorphisms in the *Methylenetetrahydrofolate reductase (MTHFR)* gene (C677T, A1298C, and A1793G) were reported associated with AD. However, their genotype distributions and associations with age at onset (AAO), homocysteine, and white matter lesions (WML) were unclear in the Chinese AD population.

Method: We determined the presence of C677T, A1298C, and A1793G polymorphisms in the *MTHFR* gene using Sanger sequencing in a Chinese cohort comprising 721 AD patients (318 early-onset AD patients (EOAD) and 403 late-onset AD patients (LOAD)) and 365 elderly controls. Additionally, the homocysteine level and WML were evaluated in 121 AD patients.

Results: The frequency of allele T of C677T polymorphism was significantly higher in AD patients than in controls ($P = 0.040$), while no statistical difference was observed in A1298C and A1793G ($P > 0.05$). Besides, genotype distributions of C677T and A1298C polymorphisms statistically varied between AD patients and controls ($P = 0.021$, $P = 0.012$). Moreover, the AAO was significantly lower in CT/TT (C677T) genotypes carriers ($P = 0.042$) and higher in AC/CC (A1298C) and AG/GG (A1793G) genotypes carriers ($P = 0.034$, $P = 0.009$) in patients with LOAD. We also found that patients with CT/TT (C677T) genotypes were prone to present an increased homocysteine level ($P = 0.036$) and higher Fazekas

score (*P* = 0.024). In comparison, patients with AG/GG genotypes (A1793G) had a significantly lower Fazekas score (*P* = 0.013).

Conclusions: The genotype distributions of C677T and A1298C polymorphisms are associated with AD in the Chinese population. Moreover, AD patients with C677T polymorphism are prone to present an earlier onset, higher homocysteine level, and more severe WML.

Keywords: Alzheimer's disease; Chinese; MTHFR; homocysteine; white matter lesions.

Conflict of interest statement

CONFLICTS OF INTEREST: The authors declare no conflicts of interest.