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BACKGROUND: Apolipoprotein E (APOE) promoter polymorphisms have long been linked to Alzheimer disease (AD) susceptibility, although the established data remains controversial.

OBJECTIVE AND METHODS: Using meta-analysis, our study aimed to clarify the nature of the genetic risks contributed by the three polymorphisms for developing AD. Medline, Embase, and Alzgene search identified 40 studies with 9,662 cases and 9,696 controls.

RESULTS: Both -491A/T polymorphism (AA vs AT + TT: OR = 1.49, 95% CI=1.29-1.72) and -219T/G polymorphism (TT vs TG + GG: OR=1.30, 95% CI=1.10-1.55) showed a significant association with AD susceptibility; however, significant association was not identified in the analysis for -427T/C polymorphism (TT vs TC + CC: OR =1.03, 95% CI= 0.82-1.30). Among the APOE epsilon 4 carriers, the -491A homozygotes were at higher risk to develop AD compared with the -491T carriers (OR=1.42, 95% CI =1.15-1.76). For subjects carrying the -491AA genotype, the presence of the APOE epsilon4 allele increased the risk of AD 4.37-fold (95% CI=3.43-5.56). Subgroup analysis restricted to the late-onset or the Caucasian individuals revealed a similar association as that identified without restriction regarding -491A/T polymorphism.

CONCLUSION: Our results confirm a significant but modest association between APOE promoter -491A/T and -219T/G polymorphisms and AD susceptibility.

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