Introduction: CR1 gene polymorphism rs3818361 was recently reported to increase the risk of Alzheimer’s disease (AD).

Aims: To evaluate a CR1 gene marker with the most consistent association to AD (rs3818361) as genetic modifying factor for AD risk in a sample of Spanish population.

Methods: To conduct this research we studied 2470 Spanish individuals. Specifically, 1140 sporadic AD patients diagnosed as possible or probable AD in accordance with NINCDS-ADRDA criteria, 1209 controls with unknown cognitive status from the general population, and 121 neuropsychological healthy elderly controls (NHEC) screened for the absence of cognitive impairment including neurological examination, neuroimagin and neuropsychological test battery. In addition, parts of data used in the preparation of this article were obtained from the Alzheimer’s Disease Neuroimaging Initiative (ADNI) database, NCBI DbGAP and AlzGene database. The CR1 gene polymorphism rs3818361 was genotyped in a LightCycler 480 instrument (Roche Diagnostics, Switzerland). Meta-analyses were conducted using Episheet.

Results: We have performed an independent replication study of this genetic variant in 2470 individuals from Spain. By applying an allelic model, we observed a trend towards association between this marker and AD (LOAD) susceptibility in our case-control study (OR=1.114 [0.958-1.296], p=0.16). Meta-analysis of available studies (n=31,771 individuals), including previous studies and public GWAS resources (ADNI, TGEN and GenADA) strongly supports the effect of rs3818361 (OR=1.180 [1.113-1.252], p< 2.99E-8) and suggests the existence of between study heterogeneity (p< 0.05).

Conclusions: We conclude that the CR1 gene may contribute to AD risk although its effect size could be smaller than previously estimated.