Identifying novel genetic variants for brain amyloid deposition: A genome-wide association study in the Korean population

Abstract

Background: Genome-wide association studies (GWAS) have identified a number of genetic variants for Alzheimer's disease (AD). However, most GWAS were conducted in individuals of European ancestry, and non-European populations are still underrepresented in genetic discovery efforts. Here, we performed GWAS to identify single nucleotide polymorphisms (SNPs) associated with amyloid β (Aβ) positivity using a large sample of Korean population.

Methods: 1,474 participants of Korean ancestry were recruited from multicenters in South Korea. Discovery dataset consisted of 1,190 participants (383 with cognitively unimpaired [CU], 330 with amnestic mild cognitive impairment [aMCI], and 477 with AD dementia [ADD]) and replication dataset consisted of 284 participants (46 with CU, 167 with aMCI, and 71 with ADD). GWAS was conducted to identify SNPs associated with Aβ positivity (measured by amyloid positron emission tomography). Aβ prediction models were developed using the identified SNPs. Furthermore, bioinformatics analysis was conducted for the identified SNPs.

Results: In addition to *APOE*, we identified nine SNPs on chromosome 7, which were associated with a decreased risk of Aβ positivity at a genome-wide suggestive level. Of these nine SNPs, four novel SNPs (rs73375428, rs2903923, rs3828947, and rs11983537) were associated with a decreased risk of Aβ positivity ($p < 0.05$) in the replication dataset. In a meta-analysis, two SNPs (rs7337542 and rs2903923) reached a genome-wide significant level ($p < 5.0\times10^{-8}$). Prediction performance for Aβ positivity increased when rs73375428 were incorporated (area under curve=0.75; 95% CI =0.74-0.76) in addition to clinical factors and *APOE* genotype. Cis-eQTL analysis demonstrated that the rs73375428 was associated with decreased expression levels of *FGL2* in the brain.

Conclusion: The novel genetic variants associated with *FGL2* decreased risk of Aβ positivity in the Korean population. This finding may provide a candidate therapeutic target for AD, highlighting the importance of genetic studies in diverse populations.

참고문헌

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