Possible Association between SORL1 and Alzheimer Disease?

Reanalysing the Data of Shibata et al.

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Shibata et al. \cite{1} reported that the variants in neuronal sortilin-related receptor (SORL1) were not associated with Alzheimer disease (AD) in a Japanese cohort comprising 180 cases and 130 age-matched controls. The authors performed a genotypic association analysis using 7 single nucleotide polymorphisms (SNPs) that were previously reported to be statistically significant by Rogaeva et al. \cite{2} and subsequently by others \cite{3–5}. The authors reported no association with AD. However, Shibata et al. \cite{1} did observe a weak association ($p = 0.05$) for SNP 8 (rs668387) when restricted to APOE ε4 noncarriers.

We conducted an allelic association analysis of the same data, which shows that 2 SNPs (8 and 24) were significantly associated with AD with $p$ values less than 0.05. Specifically, when all subjects were examined, SNP 24 (rs2282649) and SNP 8 (rs668387) were significant ($p < 0.05$). However, using a model restricted to elderly APOE ε4 noncarriers, the association became somewhat stronger (SNP 8, $p = 0.0163$; SNP 24, $p = 0.0375$). More importantly, the associated variants in the study by Shibata et al. \cite{1} were identical to those in the study by Rogaeva et al. \cite{2}. For SNP 24, the T allele was associated with AD in Caucasians as well as in Japanese people. For SNP 8, the C allele was associated with AD in Caribbean Hispanics, Caucasians, Israeli Arabs, and Japanese people.

In contrast to the original conclusions, this study does support the association between variants in SORL1 and AD in a Japanese population. Although the findings are only marginally significant given the small sample size, this study continues to support the association in both the 3’ and 5’ regions of SORL1.

References


