Commentary

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Possible Association between SORL1 and Alzheimer Disease?

Reanalysing the Data of Shibata et al.

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Shibata et al. [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. [2] and subsequently by others [3–5]. The authors reported no association with AD. However, they *did* observe a weak association ($p = 0.05$) for SNP 8 (rs668387) when restricted to APOE $\varepsilon 4$ 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 $\varepsilon 4$ 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. [1] were identical to those in the study by Rogaeva et al. [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

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