Negative results

Replication analysis of SNPs on 9p21.2 and 19p13.3 with amyotrophic lateral sclerosis in East Asians

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Abstract

We performed a replication study of the 2 genetic variants, rs2814707 on 9p21.2 and rs12608932 on 19p13.3 that are recently reported to be most significantly associated with sporadic amyotrophic lateral sclerosis (ALS) in Caucasians. Both rs12608932 and rs2814707 showed no evidence of association in Japanese and Chinese (rs12608932, combined \textit{p} = 0.58, odds ratio [OR] = 1.03, 95% confidence interval [CI] 0.93–1.13; rs2814707, combined \textit{p} = 0.88, OR = 1.10, 95% CI 0.93–1.30). The association of these loci with susceptibility to sporadic ALS is considered negative in East Asians.

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Recently, van Es et al. (2009) identified 2 loci significantly associated with sporadic amyotrophic lateral sclerosis (ALS) in Caucasians. The genome-wide level association was identified on 3 single nucleotide polymorphisms (SNPs), in the order of significance, rs12608932 on chromosome 19p13.3 and rs2814707 and rs3849942 on chromosome 9p21.2. In this study, we checked replication of the association of the 2 loci in Japanese (1179 cases and 1645 controls) and Chinese (684 cases and 830 controls) cohorts by examining the most significantly associated SNPs (rs12608932 and rs2814707) in the previous study (van Es et al., 2009). Detailed materials and methods are described in Supplementary data.
The allele frequency of rs12608932 was different between Caucasians and East Asians (Supplementary Table 1). The association in Japanese did not reach statistical significance by a logistic regression analysis ($p = 0.67$, odds ratio [OR] = 1.02, 95% confidence interval [CI] 0.91–1.16). Similarly, no association of rs12608932 with sporadic ALS was detected in Chinese ($p = 0.73$, OR = 1.02, 95% CI 0.88–1.20). We then calculated combined $p$ value for the Japanese and Chinese studies by an inverse variance method and observed no association in the East Asians ($p = 0.58$, OR = 1.03, 95% CI 0.93–1.13).

We found that rs2814707 was not associated with susceptibility to sporadic ALS in Japanese and Chinese (Supplementary Table 1). The meta-analysis showed that there was no evidence for the association between rs2814707 and risk of sporadic ALS in East Asians ($p = 0.88$, OR = 1.10, 95% CI 0.93–1.30). However, because the power of the study was less than 80%, this negative association may be due to lack of power that resulted from the limited sample size and/or low risk allele frequency in East Asians. The association between rs2814707 and sporadic ALS in East Asians requires confirmation in further replication studies.

Appendix A. Supplementary data


Reference