No association of *GRIA1* polymorphisms with schizophrenia in the Chinese Han population

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Schizophrenia is a polygenic and psychiatric disorder prevalent worldwide with high heritability. The largest genome-wide association study of schizophrenia has shown a genomic locus upstream of the *GRIA1* gene as genome-wide significant (Ripke *et al.*, 2013). Magri *et al.* (2006) reported that *GRIA1* might be a susceptible gene to schizophrenia in the Italian population. However, this original research failed to be replicated in the German population (Leon *et al.*, 2011) or in the Korean population (Crisafulli *et al.*, 2012). The aim of this study was therefore to investigate whether single nucleotide polymorphisms (SNPs) in *GRIA1* were associated with schizophrenia in the Chinese Han population.

For this case–control study, we recruited 1034 (409 women and 625 men, age: 45.06 ± 12.88, onset age: 25.98 ± 9.65) unrelated schizophrenic patients and 1034 (446 women and 588 men, age: 34.06 ± 10.00) healthy controls of Chinese Han origin. All the schizophrenic patients were diagnosed on the basis of *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. (DSM-IV) criteria. Clinical interviews were carried out by two board-certified psychiatrists. Each individual or their legal guardian fully understood the procedure and signed informed consents. This study was approved by the Ethics Committee of the Human Genetic Center in Shanghai. Genomic DNA was acquired from participants' peripheral blood using the standard phenol–chloroform method. We used SHEsis (*http://analysis.bio-x.cn/myAnalysis.php*) (Shi and He, 2005) to analyze allelic and genotypic distributions, Hardy–Weinberg equilibrium, and pairwise linkage disequilibrium.

Five SNPs (rs472792, rs3828595, rs478962, rs12658202, and rs812389) of *GRIA1* were genotyped successfully using the MassARRAY Analyzer 4 platform (Sequenom, San Diego, California, USA). The results showed that the observed genotypic distributions were all in Hardy–Weinberg equilibrium ($P > 0.05$). The genotypes for the *GRIA1* polymorphisms in patients and controls were distributed as follows: rs472792 GG 19 : 17, GT 234 : 248, TT 778 : 767; rs3828595 GG 782 : 799, GT 233 : 218, TT 18 : 15; rs478962 CC 737 : 731, CT 254 : 272, TT 26 : 23; rs12658202 AA 79 : 59, AC 380 : 371, CC 572 : 597; and rs812389 AA 649 : 651, AG 333 : 336, GG 42 : 33. However, there were no significant discrepancies in alleles or genotype frequency distributions between cases and control participants ($P > 0.05$). We also calculated D' and r^2 for all combinations of the five SNPs (data not shown). Strong linkage disequilibrium was found between rs472792 and rs3828595. Haplotype analysis was also carried out using SHEsis (data was not shown). Haplotypes under 3% frequency were excluded. However, no significant association was found between this block and schizophrenia.

In conclusion, our present findings do not support the association of *GRIA1* SNPs with schizophrenia in the Chinese Han population. Taking the limitation of incomplete SNP coverage into account, further researches need to be performed with larger sample sizes with more coverage in other ethnic groups.

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Conflicts of interests

There are no conflicts of interest.

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