Reviewer’s report

Title: Schizophrenia susceptibility and NMDA-receptor mediated signalling: an association study involving 47 tagSNPs of DAO, DAOA, PPP3CC, and DTNBP1 genes

Version: 2 Date: 7 August 2012

Reviewer: Daimei Sasayama

Reviewer’s report:

This study showed that polymorphisms of the NMDA-receptor-mediated signaling genes (DAO, DAOA, PPP3CC, and DTNBP1) may have different effects on susceptibility to schizophrenia in men and women. The results may be of interest to those with closely related research areas. However, the sample size was not large enough to achieve sufficient statistical power to detect small effect size, especially when stratified by gender and diagnostic subtypes. Ideally, the positive findings presented in this study should be confirmed using an adequately powered replication sample.

There are several other issues to address.

Minor Essential Revisions

1. In Genotyping of the Methods section, I do not understand what the authors mean by the fourth criterion for the inclusion of the SNPs in the analyses (i.e. including SNPs with “successful genotyping of at least 50% of the SNPs”). Is this a criterion for inclusion of the sample (i.e. including samples with successful genotyping of at least 50% of the SNPs)?

2. In Genotyping of the Methods section, the authors listed SNPs excluded from the analyses. How many of the SNPs were excluded due to low call rates? How many due to deviation from HWE? How many due to low MAF? If sample replicates have not been included in the assay to ensure consistent genotypes, the quality of genotyping can only be assessed by call rates and deviation from HWE. Thus, it is important to state whether these SNPs were excluded due to low quality typing or simply due to low MAF.

3. What algorithm did the authors use to select the tagging SNPs?

4. In Table 1, show the number of male and female samples included in the haplotype analyses.

5. Line 11 of Page 6: Correct this sentence: “A recent convergent functional genomics in schizophrenia has identify top genes among which DTNBP1.”; Line 10 of Page 14: non-GAC should be corrected to non-CAG.

Discretionary Revisions
6. The Supplementary Table showed that none of the examined SNPs were significantly associated with schizophrenia susceptibility. It would be more informative if odds ratio and 95% CI are shown in the table.

7. Is it possible to show the results of the secondary analyses also in a supplementary table?

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.