Reviewer's report

Title: No Association Between the Sigma Receptor Type 1 Gene and Schizophrenia, Results of Analysis and Meta-analysis

Version: 2 Date: 16 September 2003

Reviewer: George Kirov

Reviewer's report:

This is now the third study from Japan examining the role of the sigma1 receptor in schizophrenia using a case-control design. The previous two studies showed some marginally significant results and replication was clearly needed. The present study uses an adequate sample size (198 cases/206 controls). The authors also screened the gene again and did not find other polymorphisms. The results of the present study are clearly negative. When all the three studies were put together, the differences between cases and controls did not reach significance. These results more or less exclude a contribution of the tested polymorphism to schizophrenia, at least in the Japanese population. Researchers in the field will find this useful to know, in order to avoid duplication of the work.

I have a few suggestions to the authors, in order to make the paper clearer. In the Background Section they should mention the numbers of patients/controls tested in the previous studies, as this information appears only in the tables. In the Results Section the authors state that the power of the study was 1.0 to detect significant allelic association. This is quite impossible, especially as the previous effect size was so small. The authors have clearly used the wrong parameters when calculating the power and should repeat the calculations /seek advice on that matter. They should also state what statistical method/programme was used for power calculation in the Methods Section. Alternatively, they can drop all the discussion on power, as a knowledgeable reader will have a good idea what the power of 200 cases/200 controls could provide. In any case this does not affect the conclusions of the study.

For the legend to Table 1 the authors should add that the C allele at A61C corresponds to the T allele at -241-240 reported in previous studies. The authors need to correct a number of style errors. Here are a few examples:

Page 2: "role of receptors in etiology" should read "role of receptors in the etiology"
Page 3, line 3: "it has been defined" should read "they have been defined"
Last sentence of the Background needs improving
Page 4, Methods: "each 4 exon" should read "each of the four exons of the gene"
Page 5, Results: "SIGMAR1 does not associated" should read "SIGMAR1 is not associated"
In the Authors contributions: "all authors recruited DNA samples" should read "all authors recruited subjects"
Table 1: as there are only 2 catatonic patients, they should not be presented in the table.
Table 2 typo: "Contro" instead of "Control"

a) Discretionary Revisions (which the author can choose to ignore)
In the Background Section the authors should mention the numbers of patients/controls tested in the previous studies, as this information appears only in the tables.

b) Minor Compulsory Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. In the Results Section the authors state that the power of the study was 1.0 to detect significant allelic association. This is quite impossible, especially as the previous effect size was so small. The authors have clearly used the wrong parameters when calculating the power and should repeat the calculations /seek advice on that matter. They should also state what statistical method/programme was used for power calculation in the Methods Section. Alternatively, they can drop all the discussion on power, as a knowledgeable reader will have a good idea what the power of 200 cases/200 controls could provide. In any case this does not affect the conclusions of the study.
2. For the legend to Table 1 the authors should add that the C allele at A61C corresponds to the T allele at -241-240 reported in previous studies.
3. The authors need to correct a number of style errors. Here are a few examples:
   - page 2: "role of receptors in etiology" should read "role of receptors in the etiology"
   - Page 3, line 3: "it has been defined" should read "they have been defined"
   - Last sentence of the Background needs improving
   - Page 4, Methods: "each 4 exon" should read "each of the four exons of the gene"
   - Page 5, Results: "SIGMAR1 does not associated" should read "SIGMAR1 is not associated"
   - In the Authors contributions: "all authors recruited DNA samples" should read "all authors recruited subjects"
   - Table 1: as there are only 2 catatonic patients, they should not be presented in the table.

Advice on publication: Accept after minor compulsory revisions

Level of interest: A paper whose findings are important to those with closely related research interests

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