Reviewer's report

Title: Case-control and family-based association studies of candidate genes in autistic disorder and its endophenotypes: TPH2 and GLO1

Version: 1 Date: 6 December 2006

Reviewer: Sabine M Klauck

Reviewer's report:

General

The authors describe allelic screening of SNPs in the TPH2 and GLO1 gene in two different samples of autistic patients to replicate previously published positive association findings. The present findings do not support association of the two genes with autism in the sample under study. The protective effect of allele A419 of GLO1 in unaffected siblings is discussed.

-----------------------------------------------------------------------------------

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

From the allelic distribution of the study here it seems obvious that the A419 allele of GLO1 may exert a protective effect towards the autism phenotype. On the other hand, the findings of Junaid et al point towards the A419 allele as predisposing factor for autism with the additional possibility of decreased glyoxalase I enzymatic activity. This is contradictory and not mentioned in the discussion. Possible explanations for this discrepancy should be discussed more clearly besides the second last sentence in the Discussion part.

-----------------------------------------------------------------------------------

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

1. The number of unaffected siblings is missing in the Abstract.
2. Methods, Subjects: The number of siblings from simplex and multiplex families is missing.
3. Results, TPH2: In Table 2 it is not clear how many Italian and U.S. complete trios each have been included from the total set of 261 for each of the SNPs (N=168, N= 166). In addition, table 5 data are not outlined in this part of the manuscript.
4. Results, GLO1: Authors differentiate Italian and U.S. patients for the case-control data but not for the TDT and FBAT analysis, respectively.
5. Discussion, page 12: The frequency of the controls from this study is written mistakenly wrong. It should read "(0.4400 vs. 0.5439)."
6. References: Ref. 22, the given web address is apparently wrong. Please correct appropriately.
7. Table 4: It is confusing to read “patients” and “controls” above the columns with the allele frequency in the part CASE-CONTROL. This is chromosome numbers.

-----------------------------------------------------------------------------------

Discretionary Revisions (which the author can choose to ignore)

1. Methods, Subjects: A brief outline of the instruments used for diagnosis of the patients would be preferable despite this has been outlined in reference [8].
2. Methods, Markers and genotyping: What is the percentage of the other polymorphism in the PCR fragment for GLO1 SNP genotyping?

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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

Quality of written English: Acceptable

Statistical review: No
Declaration of competing interests:

I declare that I have no competing interests.