Reviewer's report

Title: Association of TPH-1 and TPH-2 genes with suicidal behavior: A systematic review and meta-analysis

Version: 6  Date: 3 May 2014

Reviewer: Zainab Samaan

Reviewer's report:

General comments and essential revisions

1. Grammatical and sentence structure revision. Consider revising the following:
   a. Abstract: “The study provided evidence that A218C/A779C TPH-1 variants may be a risk factor to manifest for SB at the clinical level” (Page 2; Paragraph 3, Line 17).
   b. Introduction: “Suicidal behavior has become a public health issue worldwide” (Page 4, Paragraph 1, Line 1). Suicidal behavior isn't a new public health issue. We suggest to place this introductory statement in context and describe if the trends are increasing or stable.
   c. Discussion: “In addition, we performed a sub-analysis…” (Page 14, Paragraph 1, Line 4), “We also conducted a sub-analysis…” (Page 14, Paragraph 2, Line 22). Should be sub-group analysis.

2. In addition, some statements need clarification: “TPH-1 gene variants showed a significant difference” (Abstract, Page 2, Paragraph 2, Line 14). Did you mean significant association? In which direction?

3. References also need to be added in some areas. For example:
   a. Introduction: “Even though there are previous meta-analyses…” (Page 5, Paragraph 2, Line 21). These meta-analyses should be cited.
   b. Discussion: “Various published studies show the search for possible genetic markers…. ” (Page 13, Paragraph 2, Line 11). Please cite these published studies.

4. A clear definition of SB and a description of how SB was defined among included studies should be addressed, preferably in the Introduction. What specific symptoms are required for a diagnosis? Over what time period? Were any specific assessments used for diagnosis (i.e. SCID, M.I.N.I., etc.)?

5. The Methods section does not mention the use of fixed effects models however they are found in your results and tables. This should be indicated in the methods, as well as an explanation of why both random and fixed effects models were employed.
6. Justification for excluding the studies by Yoon & Kim, Zhou, and Zupanc based on heterogeneity needs to be decided a priori and described in the Methods so that the analysis is not results driven.

7. Has the concept of the “virtual” control group been used in previous studies? If so, please cite them.

8. Please clarify the association found between A218C and A779C variants (TPH-1) in the Results section (i.e. positive or negative). Include the corresponding OR, CI, and p-values for all results reported.

Discretionary revisions

1. Consider adding a table to outline the exact search strategy that was used in each electronic database.

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, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests