Reviewer’s report

Title: Prenatal Risk Factors for Tourette Syndrome: A Systematic Review

Version: 1 Date: 23 July 2013

Reviewer: Carol Mathews

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Major Revisions

This manuscript aims to synthesize the existing literature on the role of pre- and peri-natal risk factors in the development and expression of Tourette Syndrome. In general, it is nicely written and comprehensive. In general, there is a need for more data on this topic, and a synthesis of the existing literature could be of benefit to the field. The examination of a variety of potential risk factors is a strength, as is the examination of both TS vs controls and associated aspects of the TS phenotype as outcome variables.

However, the paper lacks cohesion, partly due to the wide variety in types and quality of the papers included in the review. It would be much stronger if the authors created a format for summarizing the evidence, perhaps on the basis of p-values and odds ratios. For example, one way to do it would be to combine the outcomes (TS vs control, increased severity, and increased comorbidity rate) for each risk factor, score the evidence for each study on a zero to four plus scale, and create a sum score for each risk factor (e.g., maternal age in relation to risk of TS, increased tic severity, or increased risk of comorbidity, might be a 0, while maternal prenatal smoking might be a 2 on that scale, when all evidence across studies is summed). While this is fairly subjective, it does give a perspective on what the overall evidence suggests, which is a service to the reader. This has been done in other systematic reviews, often drug trial comparisons with different meds, so there is some precedent.

Minor Revisions

In the Methods section, the authors don’t state the criteria for inclusion for full-text review—this should be included, perhaps in the supplement.

In the Results section, page 8, last paragraph, there seems to be a mix of TS/control data and comorbidity data, which is in contrast to the layout of the rest of the paper. The tables are well formatted as is, with the caveat above about trying to quantify the strength of the evidence for each study. Perhaps the text could be combined to discuss overall risk for each factor.

Page 9, last sentence in the combined prenatal and perinatal period needs references.

The Discussion should be tightened up. In some cases, it reiterates what is presented in the Results rather than synthesizing them.
Tables: In all the tables, limit to one or two decimal places. The findings are not precise enough to warrant more, and make the results hard to read. Similarly, could put the SE in parenthses in order to focus attention on the means.

In Table 1, the comparison of TS+ADHD to TS alone should not be included. That either belongs in Table 2, or the comparison should be TS+ADHD to ADHD alone.

Table 2 shows something similar to what is recommended and is generally much easier to read than Table 1, with a direction of association (although no strength of association) a p value, etc.

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.