Reviewer's report

Title: Space-time clustering of childhood central nervous system tumours in Yorkshire, UK

Version: 1 Date: 29 October 2011

Reviewer: Faith G Davis

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Major

General Comments;

1. This appears to be a competently conducted space-time clustering analysis for brain tumors where the hypothesis of an infectious etiology is an open and important question. Unfortunately the background and discussion have been limited to an extremely narrow subset of the literature on this topic and the authors leave the readers to do the work of setting these results in the context of what is known. The analysis is very specific and not something most readers will be familiar with, so while they have described data and methods they have not tied the methods back to the hypothesis well, given the logic involved in the analytic decision, nor have they addressed the strengths and limitations of the different methods used well. In the end I wondered why these results, which are regional and therefore more limited in sample size for the tumor subsets, should be considered stronger than the two earlier analyses of larger national GB data. That point needs to be addressed more clearly throughout.

Specific Comments

Methods

2. Para 2 – was the case review conducted by a single neuropathologist or a panel of neuropathologists? How were discrepancies resolved?

Discussion

3. Para 1. In the abstract and results you say you saw an association with PNETS which is inconsistent with this paragraph and do not mention any result with all brain tumours. The Tables do not support evidence for all CNS tumours although you do indicate this in the text with a different statistic – for which the exact interpretation is unclear in the methods. Clarify and make consistent throughout.

Minor Essential

Background

4. This section is limited to studies of space-time clustering – omits seasonality
studies and case-control studies that have looked at infectious disease hypothesis. This is a very narrow lens through which to evaluate these results and is appropriate only if hypothesis 1 is changed.

Prior Hypothesis

5. The specific statement about infections does not belong in the hypotheses as you cannot directly test that. Here "environment" can be used in its broadest sense as you have geographic data

Methods

6. Some discussion of why you repeated analysis between case pairs, then using a case-control approach and the relative merits would be helpful in the methods section.

Results

7. Para 4 – there is no rationale for the analysis of time periods given to help the reader follow why you are doing this. It was not a part of the hypothesis. You allude to it in the discussion but that should be moved up.

Discretionary

Statistical Methods

8. It would be helpful to have these methods tied to the hypotheses. While you cite Birch and colleagues a brief interpretation of these interactions would be appropriate for readers of this journal

9. Page 14. Why would you get different results using the Knox method and the Kulldorff scan statistic? Is one more robust that the other? I sense from the methods they may ask slightly different questions but that doesn’t seem to follow into the results section.


The results of pairs of cases with one male and with one female are identical and does not need to be repeated.

11. Page 17 – top – this discussion about transient agents seems appropriate – doesn’t overstate the link to infectious processes.

12. The paper needs to be written so that the reader understands what each statistic is telling them with respect to the hypothesis, how these regional data are adding to the already existing national and related literature on the topic and how the results fit within the larger body of literature on infectious agents (should they wish to keep this as their hypothesis)

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

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare I have no competing interests.