Author's response to reviews

Title: The prevalence of psychosis in epilepsy: a systematic review and meta-analysis

Authors:

Maurice J Clancy (mauriceclancy@rcsi.ie)
Mary C Clarke (maryclarke@rcsi.ie)
Dearbhla Connor (dearbhlaconnor@rcsi.ie)
David R Cotter (drcotter@rcsi.ie)
Mary Cannon (marycannon@rcsi.ie)

Version: 2 Date: 3 December 2013

Author's response to reviews: see over
Dear Editor,

Thanks you for reviewing our manuscript. We were pleased to read the very positive reviews.

We have addressed the comments of the reviewers in the order in which they were made by the reviewers.

Furthermore, we have amended the manuscript to take account of these comments and these changes are highlighted for ease of reviewing.

Please see below our responses.

Reviewer 1:

We thank the reviewer for his generous comments. The reviewer suggested that we acknowledge, within the abstract, the fact that most of the key studies were based in specialist centres. We agree that this is important and have amended the abstract accordingly.

Reviewer 2:

We thank the reviewer for her positive comments.

The reviewer made some specific suggestions which are copied below and then responded to;

1. ‘It would be helpful for the readers to have a little more explanation of the meta-analysis process and how the studies are weighted’

Response: We have added a brief text to expand on this issue as requested.
The text now reads; ‘Pooled estimates of the prevalence of psychosis in epilepsy patients were calculated using a random effects meta-analysis. *This allows a more robust and true estimate of effect size and one that is weighted by the sample size of individual studies*’ [This last sentence in *italics* is new added text]. Please see page 5, last paragraph, lines 2 and 3.

2. ‘Likewise in the tables it would be helpful if the ‘n’ for each study was included’;
   
   **Response:** This has been done as requested.

3. ‘Some commentary on the prevalence rates and time periods would be useful’;
   
   **Response** We thank the reviewer for this suggestion – we have now outlined in the results what type of studies the prevalence rates were taken from. We have also clarified the time periods in the studies over which the prevalence rates were calculated.

   The new text read as follows; *‘With regard to the prevalence rates, forty-eight studies were cross sectional studies, 9 were cohort and 1 was case control. The time periods over which the prevalence rates were calculated were as follows: 27 studies were for an unknown time period, 7 studies were lifetime prevalence studies, 21 studies were for more than 1 year, and 3 studies were less than 1 year.’*

   Please see page 7, first paragraph, lines 3 to 8.

4. ‘With regard to the results I am unclear if all possible studies have been included. My study was not included..and it is possible that other studies were not included artificially increasing the prevalence rates’;
   
   **Response** We appreciate the reviewer’s comments. However we are confident that our literature search was exhaustive and indeed we did identify and include the work of Adams. However, in estimating the prevalence of psychosis in temporal lobe epilepsy, we only included studies in which it was possible to calculate psychosis rates from a ‘pure’ TLE sample. Adams 2008 was not included in calculating this estimate as it was impossible to calculate rates of psychosis in TLE alone from her paper. However the data from Adams 2008 was included in the overall prevalence rate of psychosis in epilepsy. We did not contact authors personally to access data as this would not have been possible on a consistent basis as in a lot of cases the contact details were not current (although we do appreciate her generous offer). Twenty two of the studies were conducted before 2000 and did not have email contact details.
We have amended the text slightly to clarify this issue. The text now reads; ‘17 studies had TLE patients only, in 26 studies the authors did not differentiate whether patients had TLE or not and in 15 studies there was a mixture of patients with TLE and other forms of epilepsy but unfortunately it was not possible to extract the non TLE or TLE sample from each other. Therefore for the TLE prevalence sample, we only used studies where all the patients had TLE.’ Please see page 8 first paragraph lines 3 to 7.

5. ‘I would like some additional discussion regarding the rates of TLE in specific studies and some commentary on whether this implies that psychosis is more common in TLE....my feeling is that it is unlikely to be and that the higher numbers reflects statistical anomalies rather than true differences’;

Response: We have added to the text to expand on this issue.

The new text read as follows; ‘TLE is the most common of the anatomically defined syndromes accounting for around 60% of all patients with localisation related epilepsies [23]. It is the most common type of epilepsy in adults who experience seizures poorly controlled by anticonvulsant medication. Our results found a slighter higher rate of psychosis in TLE as compared to all epilepsies (7% v 5.6%). There has been some debate in the past whether there is a higher rate of schizophrenia-like-psychosis in patients with TLE compared to generalized epilepsies. In the original study by Slater et al, the high rates of psychosis may have been in part due to somewhat imprecise clinical diagnostic data as the terms schizophrenia and psychosis were relatively loosely defined by today’s standards [4]. There is also the possibility of an ascertainment bias as the study drew its subjects from tertiary centres in two major London hospitals. More recently, Stevens has argued that the proportion of TLE in epilepsy-psychosis patients is similar to the proportion rate of generalized epilepsy patients with epilepsy psychosis which is estimated to be about 60% [48-50]. Furthermore, in the large epidemiological study by Qin et al, patients with localization related epilepsy were only slightly over-represented among those who were psychotic and this difference fell short of statistical significance [29]. Several studies have failed to confirm the commonly held view that there is a specific association between temporal lobe epilepsy and psychopathology which is in contrast to commonly accepted clinical practice[51-53].’

Please see page 11, second paragraph, first 16 lines and page 12, first paragraph lines 1 to 4.

6. ‘it is clear from the rates of PIP that some may be missed. I think it is important to acknowledge that they may all be over or underrepresented depending on the availability of psychiatric assessment....’;
Response We appreciate the reviewer’s comments and have amended the text on the discussion on post-ictal psychosis.

The new text now reads as follows; ‘However, postictal psychosis may be over or under represented depending on the availability of psychiatric assessment, the frequency of review and potentially the knowledge base of the treating neurologist and neuropsychiatry teams.’ Please see page paragraph 11, lines 7 to 10.

Yours sincerely,

Maurice Clancy,

David Cotter