Author's response to reviews

Title: Major depressive disorder in Parkinson's disease: a cross-sectional study from Sri Lanka

Authors:

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The Editor
BMC Psychiatry

Dear Sir or Madam:

MS: 8624478231320808 - Major depressive disorder in Parkinson's disease: a cross-sectional study from Sri Lanka

I have detailed below the response to reviewers. The changes in the manuscript are highlighted in red.

Thank you

Varuni de Silva
Corresponding author

Reviewer's report

Title: Major depressive disorder in Parkinson's disease: a cross-sectional study in Sri Lanka
Version: 1 Date: 30 June 2014
Reviewer 1: Oliver Riedel
Reviewer's report:

Review

„Major depressive disorder in Parkinson’s disease: a cross-sectional study in Sri Lanka“ (Ketharanathan et al., submitted to BMC Psychiatry)

Summary

The authors present data on the frequency of depression in PD patients, obtained from a sample of 104 PD outpatients in Sri Lanka. All patients were
assessed with established, structured interviews considering the DSM-IV TR criteria for depression as well as screened for depression with the MADRS. The authors found a mean prevalence of depression of 37.5% with higher rates in patients with progressed PD, functional impairment and concomitant diabetes.

General impression

This is a well written paper, addressing an important topic in the area of research. In addition to the brevity and clarity of the manuscript, the clear strength of the underlying study must be seen in the use of a semi-structured interview using the DSM-IV criteria for depression.

Major compulsory revisions

Comment 1

A flaw of the presented work is the lack of cognitive measures such as the MMSE or other appropriate measures, i.e. we do not have any information on whether the patients also suffered from cognitive impairment. This, however, would have been essential as cognitive impairment is a frequent complication in PD and might have limited the validity of the interviews for depression. Some of the data suggest that such a bias might have occurred. For example, the authors found an association between level of education and depression (high level – low rates of depression). This is quite an unusual finding. However, what we do observe in such studies and populations regularly is that there is a link between high educational levels and low rates of cognitive impairment/dementia (which, in turn, is positively associated with increased rates of depression).

Authors: We thank the reviewer for the review and the comments.

We acknowledge the potential influence of cognitive impairment on the presentation and assessment of depression and agree on the importance of cognitive assessment. Cognitive assessment was not carried out majorly due to the practical difficulty of administering the scales to a motor disabled patient population especially in a busy clinic of a tertiary hospital where available time for assessment is limited. Though a priori we aimed to identify patients who had any difficulty in participating in an interview and exclude, in practice we did not encounter anyone having significant cognitive difficulty which could be detectable during the assessment process. The reason may be patients with serious difficulties (either due to PD per se or cognitive impairment) are less likely to attend the clinic for practical reasons and more likely to be represented by their carers who come to collect the medication. However this may not exclude patients with mild cognitive impairment who could appear preserved. Depression and dementia can masquerade as each other in older population. The question related to our study would likely to be whether dementia/ cognitive impairment acted as a confounder in identifying true depression and elevated the depression prevalence rate. We have acknowledged this issue as a potential confounder in the limitations section.

We agree about the negative correlation between educational level and risk of dementia. At the same time past studies on depression in both PD and general population commonly identified lower levels of education as a risk factor for
depression (Pankratz et al, Clinical correlates of depressive symptoms in familial Parkinson’s disease, 2008; Aziz, R. What are the causes of late-life depression?, 2013; Kessler, C. The epidemiology of depression across cultures, 2013). Our study results are in keeping with this evidence.

Comment 2.

The second limitation relates to the presentation of the MADRS. First, the cut-off for depression is not mentioned here. The authors only state that any score equal or less than 20 should be regarded as “mild depression” – but what is the lower cut-off for mild depression? Second, I am not sure whether the presented cutoffs are appropriate for the population under study since Leentjens et al. (2000) have published a validation study on PD patients. Taking the higher overlaps between depressive and PD symptoms into account, they suggested a cut-off 13/14 as indicator for major depression. This cut-off has been widely used since then and should at least be introduced (if not replace) in addition to the cut-offs that have been used by the authors.

Authors: In our study MADRS was used only for severity rating of depression and not used for screening or diagnosis of depression (which was done by DSM IV TR criteria). We mentioned this in the Methods section as: ‘MADRS scores were utilized primarily for severity rating of depression. The MADRS cut-off scores used to rate severity were: #20 mild depression, 21-34 moderate depression, and above 34 severe depression [14]’. Therefore we did not need to consider MADRS cut-off for diagnosis. The severity rating was done only for patients diagnosed with depression by DSM criteria (n=39). During the assessment phase, however, we applied the scale to all subjects to get a mean score for the population.

We thank the reviewer for directing us to Leentjens, 2000 paper. This is an important paper we accessed while writing this article. This paper is aimed at defining diagnostic cut-offs from MADRS for depression and no cut-offs for severity rating were mentioned. Therefore we couldn’t utilise the information from this paper in our initial draft. Now as per the reviewer’s suggestion in Comment 6 we are including a 2*2 table of diagnosis of depression by DSM IV TR and MADRS to reflect the diagnostic sensitivity and specificity of MADRS where we are discussing the diagnostic cut-offs from the Leentjens 2000 paper.

Minor essential issues

Comment 3.

In the results section (manuscript page 9) the authors refer to two publications, regarding the link between ropinirole and depressive symptoms in PD. This should be transferred to the discussion section, since references should not be placed in the results.

Authors: We thank the referee for pointing out this issue. We transferred the relevant part to the Discussion.

Comment 4

In the discussion section (manuscript page 11, last paragraph), the authors state
that “Prevalence of depression was higher in Hoehn&Yahr stages III, IV and above.” This is in fact wrong, since the authors found the highest rates in patients at stage III, while the rates in stages IV/V were similar to those at stage I/II. Thus the authors should reword this sentence accordingly and also add a critical discussion of this finding (as in fact, a more “linear” relationship between both variables would have been expected here).

Authors: As can be seen in Table 2, the rate of depression in stage I/II, III, and IV/V are 8.3, 49.1 and 40% respectively, so depression rates were higher in III and above, compared to I/II. It is the number of patients in stage I/II and IV/V similar. Depression rate is highest in stage III with some decline thereafter. The discussion is now expanded to explain this more clearly, as suggested by the reviewer.

Comment 5
Typo in same paragraph: “maybe” instead of “may be”.
Authors: We have corrected it.

Discretionary Revisions
Comment 6.
Although the sample this is rather small for this, the paper might also profit from some additional results illustrating the sensitivities and specificities of the MADRS as compared to the depression diagnosis according to DSM-IV criteria (a simple small fourfold table would be sufficient).
Authors: We appreciate the reviewer’s suggestion.

We have included the table in the Results section and added description.

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:
I have no competing interests.

Reviewer’s report
Title: Major depressive disorder in Parkinson's disease: a cross-sectional study in Sri Lanka
Version: 1 Date: 14 July 2014
Reviewer 2: Jitse P. van Dijk
Reviewer's report:
BMC Psychiatry
'Major depressive disorder in Parkinson's disease: a cross-sectional study in Sri Lanka'
Tharini Ketharanathan, Raveen Hanwella, Rajiv Weerasundera and Varuni A de Silva
Major Compulsory Revisions
Comment 1
Title
The title seems ok to me, although I prefer to have some result in the title.
Authors: We appreciate the reviewer’s effort in taking time to review and providing valuable suggestions.
We thank for the suggestion about title. However, as the study has more than one objective and inclusion of results will lengthen the title, for the sake of simplicity and space we opted to keep this title.
Comment 2
Abstract
2a) The Abstract is too long, especially the part before the Aim.
Authors: We acknowledge this problem. We reduced the background section; tightened the methods, removing the statistical analyses, and made the abstract concise.
2b) Furthermore the Abstract accurately conveys what has been found.
Authors: We appreciate reviewer’s comment.
Comment 3
Research question-
The Research Question as posed by the authors in the Abstract is well defined; in the Introduction this RQ is lacking fully. It is unclear what the authors want to explore.
Authors: we acknowledge that the research question has not been explicitly stated in the Introduction. We have now included it at the end of the section.
Comment 4
Methods
Sample
4a) I do not understand the sentence: … premier, tertiary care hospital in Colombo … Please clarify (more hospitals? One hospital? Why then premier? Similar question for … of National Hospital of Sri Lanka …)
Authors: We agree that the different descriptions could complicate the understanding. The study was held in the largest public hospital in Sri Lanka which offers tertiary care and best facilities; hence it is termed the premier hospital in the country. The name of the hospital is National Hospital of Sri Lanka and it is located in Colombo (the capital). We have made some changes to the sentence to make it clear.
Measures
4b) How was the Montgomery-Asberg Depression Rating Scale translated into
the local language? Please go into this.
Authors: We did not translate the Montgomery-Asberg Depression Rating Scale to local language as it is an interviewer rated scale with ratings done through a clinical interview.

Statistical analyses
4c) This para is appropriate and well described.
Authors: We thank the reviewer for the comment.

Comment 5
Data
5a) In my opinion it is not necessary to repeat in the text what is already in the table, especially Table 1. On the other hand data should not be mentioned in the text without having them mentioned in the table without mentioning ‘(data not shown)’ in the text.
Authors: We thank the reviewer for pointing out. We have removed the repetitions in the text concerning both table 1 & 2. Further we added ‘data not shown’ to results mentioned only in the text.
5b) This also means that the text of the Results section can be condensed
Authors: We condensed the Results section considerably by removing the repetition of tables in text and reducing parts of results.
5c) Please indicate where Table 1 and Table 2 should be placed in the text. Before Table 1 only text which is related to Table 1; before Table 2 only text related to Table 2. Please restructure the Results section.
Authors: We appreciate the suggestion. We restructured the results section so for e.g. all text related to table 1 to come before the table, and also indicated where to insert tables.

Comment 6
Discussion and conclusions
6a) For the reader: please repeat the aim of the study in the very first line of the Discussion and then please give the condensed answers.
Authors: We thank the reviewer for going through the discussion in detail and the suggestions.
We restated the aims at the start of the discussion and summarised the major findings.
6b) Please discuss more in depth how it is possible that what you state in the Introduction (there is a difference between Western countries and Asia) appears not to be true.
Authors: We have now included this near the end of the discussion section before strengths and limitations.
6c) Perhaps condense the discussion (as it is too long), and where possible relate to Western-Asian differences.
Authors: We acknowledge this issue. Parts of the discussion have been removed to condense the section. In the section we have included more discussion on the similarities and differences of the present study with the past studies in western population.

Strengths and Limitations

6d) Please add a separate heading, and start this para with the study’s strengths. What you did not do, but what should be done is not a Limitation, but an Implication (for further research). What should be mentioned in the limitations is the way of sampling, the way of collecting information, and potential confounders. A para on Implications discussing the finding’s relevance for practice and policy and the recommendations for future research should follow the para on Strengths and Limitations.

Authors: We thank the reviewer for the suggestion. We added a strengths and limitations section, included strengths and made some changes in the limitation to reflect sampling and other methodological issues and confounders. Below the limitations we added a paragraph discussing implication and recommendation for practice and future research.

Writing

The English should be checked by a native speaker.

Authors: The language has been checked and corrected.

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, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.