Author's response to reviews

Title: Actigraphy as a diagnostic aid for REM sleep behavior disorder in Parkinson's disease

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Author's response to reviews: see over
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Dear Dr. Bhidayasiri,

Thank you for the review of our manuscript “Actigraphy as a diagnostic aid for REM sleep behavior disorder in Parkinson’s disease”, and granting us the opportunity to submit a revised version.

Reviewer 2 posed a number of minor essential comments, which we have all addressed. The comment of reviewer 1 was in fact a very useful suggestion, which can be answered with the data we obtained.

We have thoroughly revised the manuscript according to the issues raised. A point-by-point answer has been included. In addition, as requested, we revised the manuscript with respect to language.

We feel that the paper has been substantially improved by the reviewers’ comments, and hope that it is now acceptable for publication in BMC Neurology.

With kind regards, also on behalf of the other authors,

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Comments of reviewer 1:
The authors studied the value of actigraphy as a diagnostic aid for RBD. Even though interesting, the results of the study did not compare the diagnostic value of interviews vs actigraphy so that it is hard to know whether there is any additional value of actigraphy as a screening tool over interview. Furthermore, disorders such obstructive sleep apnea, confusional arousals and nocturnal hallucinations which can be misdiagnosed by interviews were not included in the study. Therefore, the additional value of actigraphy in making a specific diagnosis over interviews is not studied.

- This is a very useful suggestion, which can be answered with the data we obtained. We have now added additional analyses regarding this issue. We have now provided actigraphy outcomes in those patients where the clinical interview was incongruent with the final RBD diagnosis after PSG, showing the additional value of actigraphy. In addition, we listed additional sleep diagnoses in these patients.

Comments of review 2:
Minor essential revisions:
Please explain what was done statistically to adjustment for age, disease duration and LED. It appears that the RBD positive group are older, have longer disease duration, higher LED and higher disease stage and each of these has the potential to contribute to higher amounts of sleep wake disturbance.

- We have now added additional detail regarding this issue to the methods and results sections of the paper, as well as to the discussion.

The Hoehn and Yahr scores for those participants RBD positive do not appear normally distributed. A non-parametric statistical test is advised. An alternative would be to include the UPDRS as a measure of progression of disease.

- We have redone the analysis on H&Y stage using a Mann-Witney U test.

The RBDSQ (Stiasny-Kolster et al 2007 Movement Disorders) does not require a mandatory bed partner. Please correct this statement in the introduction.

- This has been corrected.

The PLM index is much higher in the RBD positive group but yet is not statistically different possibly due to the large difference in variance. This needs to be discussed as a limitation, as PLM are an alternative cause for sleep-wake disturbance.

- This issue has been added to the discussion.
The epoch length was specified by Naismith et al as 30 seconds. The manuscript referred to an earlier study referenced by methodology (Naismith et al 2010 Journal of Geriatric Psychiatry & Neurology). Please include this value.

- This has been added.

“Although a correlation was found between number of bouts classified as wake and actual wake time \(r = .31, p = .39\)”. Is the p value correct?

- Thank you for pointing out this error, the p value was .039. This has been corrected.

More discussion is need in regards to alternative explanations for the results in view of the RBD positive and negative groups not matched for age, disease duration, medication, stage, PLMs.

- We have discussed this in more detail in the revised manuscript.

More discussion is needed regarding the limitations of actigraphy in Parkinson’s disease cohorts. Issues such as on/off fluctuations, dyskinesia, and tremor can all reduce the accuracy of actigraphy and must be included as discussion/limitation points.

- These points have all been added to the discussion.

Discretional revisions:

Given the recent consensus statement for the International REM Sleep Behaviour Disorder Group (IRBD-SG) has suggested strict criteria to quantify RWA, this brings in to question previous studies that did not measure RWA using one of the methods suggested in the IRBD-SG consensus statement. The RBD questionnaire validation studies fall into this category and thus there validity compared to this new standard must be established. Given the comprehensive diagnostic strategy you have fulfilled to satisfy RBD positive status, I don’t think your results can be compared to studies validating questionnaires using the ICSD-2 or AASM without complying with the IRBD-SG consensus statement criteria for RBD. Please add this as a discussion point.

- This is indeed an interesting issue. However, we feel that this (ongoing) discussion may be a bit too detailed for a paper aimed at movement disorders neurologists (not necessarily sleep specialists). Moreover, we do not directly compare our results to the previous questionnaire studies directly.
Do the wake bouts during PSG correlate with the wake bouts from actigraphy? If so this would add further validity to the use of actigraphy.

- This would be an interesting analysis. However, this would require a near perfect time synchronization between the actigraphy and the PSG recording, which we could not achieve in our setup.

Consider including the correlation between REM without atonia scores measured as a continuous variable and the wake scores measured from actigraphy. This would answer the question if more severe REM without atonia contributes to more severe sleep-wake disturbance.

- See our previous answers; although interesting, we cannot answer this question with our measurements.

Your results suggest actigraphy may be useful to identify RBD and thus may be a strategy to identify RBD patients in at risk groups to see who will transition to a neurodegenerative disorder. Please consider adding this discussion point with reference to recent publications supporting this.

- As the prevalence of ‘idiopathic’ RBD is very low, we do not recommend to use actigraphy as a screening tool in this population at this point. This has now been clarified detailed in the discussion.

Consider including the breakdown of different medication groups between RBD positive and negative in addition to the levodopa dose equivalent. Groups could include unmedicated, Levodopa mono therapy, dopamine agonist mono therapy, Levodopa plus adjuvant. This would give a better idea of the different medication regimes potentially contributing to sleep disturbance.

- We have now added this information to the results.