Author’s response to reviews

Title: The Prevalence of Obstructive Sleep Apnea in Mild Cognitive Impairment: A Systematic Review

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Dr. Samuel Harris

Editor-in-Chief
BMC Neurology

Dear Drs. Harris, Abushouk and Correa,

Thank you very much for reviewing our paper and providing excellent comments. We have responded to the comments below accordingly and hope that our paper will be accepted for publication after these changes. Thanks again.

Sincerely,
Abdelrahman Ibrahim Abushouk (Reviewer 1):

1- I understand the author's inability to conduct a meta-analysis due to the significant heterogeneity both in the used diagnostic methods and outcomes; however, the way they presented their data with a prevalence rate ranging between 11% and 70% does not really give much information to the reader. This work should only be described as preliminary to guide future work.

Thank you for your comment. We agree with your statement. In the MCI population, we reported the prevalence rate in a range format (11-70%) to highlight the reported variations of the prevalence of OSA due to differing study methodology and patient characteristics. In the manuscript, we did indicate that our data has various limitations and future work is needed to reliably estimate the prevalence of OSA in MCI (limitation and conclusion section of the discussion; pages 15-16).

2- Another limitation that should be added to the discussion is that the majority of included studies were cross-sectional study that are prone to multiple confounders and the chicken-egg dilemma.

Thank you for your comment. We have added this to our limitation (page 16, lines 5-7).

3- Did you apply any restrictions (filters) to your search?

We conducted a comprehensive search of 10 databases. The main filters/restrictions we used in our search involved an adult (>18 years) population with sleep disorder and cognitive impairment, selecting for studies in English. Hence, we had over 11,000 studies. We aimed to have a high sensitivity in our search strategy. Upon the screening process, we excluded studies with a mixed population with neurodegenerative disorders and defined sleep disorders other than OSA. These are indicated in the methodology (pages 6-7, lines 20-22)

4- "When relevant, study authors were contacted for clarification and provision of additional information for the systematic review". Did you get any response?

We contacted three study authors. Dlugaj et al were contacted for the sample size of their control population. We used this to calculate the odds ratio (Table 3). Similarly, Osorio et al were contacted to obtain data specific to outcome and exposure, as their study also included information on patients with Alzheimer’s disease. This information was used to calculate the odds ratio (Table 3). Finally, in our search we identified another study for inclusion in our review (Wilson et al. 2014. Screening for Sleep Apnea in Mild Cognitive Impairment: The Utility of the
Multivariate Apnea Prediction Index). The authors of this study unfortunately did not provide us with the relevant data on prevalence of OSA in MCI or the odds of OSA in MCI vs. controls.

5- You specify in the methods how OSA was diagnosed, but you do not do the same for MCI.

Thank you for your comment. The MCI diagnostic method is specified in the result section of page 9 under the subheading MCI criteria.

Diogo Correa (Reviewer 2):

1- The methods are well explained. The authors explained the inclusion and exclusion criteria adequately. However, the main limitation of the review is the small number of articles included in the final analysis (only 5). With so few adequate studies on the theme, would it be possible to make a systematic review on the subject?

Thank you for your comment. To answer this particular question whether five articles can be used to do a systematic review, we found no specific criteria on the number of studies required for a systematic review. The purpose of this review is not necessarily the data it provides but the missing gap it highlights in our proposed research question. This is an important preliminary work to guide future studies on this topic.

2- Results: The review included only cross-section studies, then a temporal relationship between the OSA and MCI could not be defined. Although the authors mentioned this in the results, this should be said in the limitation paragraph.

Thank you for your comment. We have added this to our limitation (page 16, lines 5-7).

3- In the discussion section, the authors should add some possible pathophysiological explanations about the correlation between OSA and MCI.

Thank you for your comment. We have added a paragraph on possible pathological mechanisms of OSA and MCI on page 15, lines 3-17.