Author's response to reviews

Title: Brainstem infarcts predict REM sleep behavior disorder in acute ischemic stroke

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Dr Taoufic Alsaadi
Associate Editors
BMC Neurology

Dear Dr Alsaadi,

Ms. Ref. No.: 6907260871188400

We wish to submit the revision of our manuscript entitled “Brainstem infarcts and REM sleep behavior disorder in stroke.” We thank our reviewers for the constructive comments. We have revised the manuscript according to the recommendations. All changes are typed with **bold** in the revised manuscript for easy inspection.

**Reply to Referee No. 1**

We thank the reviewer for the careful reading of our manuscript and the useful comments. We have revised the text according to the comments and recommendations as detailed below. The changes are indicated with **bold** in the revised manuscript.

#1. There are two major concerns for the current version of the manuscript:

1. It is well known that RBD can be caused by vascular diseases as well as other lesions in brainstem. Clinically, not all the brainstem infarct occurred RBD. The presence of RBD depends on the damaged region associated with the hypothesized REM sleep
related structures and networks in brainstem. In Table 1, authors should summarize more precise infarct regions in brainstem of the RBD patients.

Authors’ reply: The following regions have been added to Table 1: pontine base, pontine tegmentum, coeruleus/subcoeruleus region and laterodorsal tegmental nuclei. Pontine base infarcts was significant in the univariate analysis but not in the subsequent logistic regression (page 7, para 3; Table 1, 3).

#2. Video-PSG is considered as criterion for diagnosis of RBD. The RBDQ may be a practical and easy means assessing RBD. However, v-PSG should be performed and compared with the RBDQ results in this study.

Authors’ reply: We agree that ideally PSG should be performed. Unfortunately, at the time of the study we did not have access to PSG facilities. This has been added as a limitation to the revised text (page 9, para 1).
Reply to Referee No. 2.

We thank the reviewer for the thorough reading of our manuscript and the helpful comments. We have revised the text according to the comments and recommendations as detailed below. The changes are indicated with **bold** in the revised manuscript.

#1. Figure 1 does not seem to convey the procedure to select participants. In the last three lines of Participants section, the patients who showed no acute infarct or more than one acute infarct in MRI is defined as the 8th group of the exclusion criteria. Why were they assessed at 3-month poststroke in Figure 1?

**Authors’ reply:** *These participants were assessed as the reading of MRI was performed only after the rest of the assessment had been completed. This point has been clarified in the statistical analysis section (page 6, para 4).*

#2. In Table 1, if the authors really excluded the patients with no acute or more than one acute infarct, the total number of patients who were classified by the location of acute infarcts (i.e. Frontal, Temporal, Parietal,) should match either 13 (patients with RBD) or 106 (patients without RBD). However, when calculated from the last 12 lines in Table 1, they are 19 (for RBD) and 137 (for Non-RBD). Considering the above two incoherent points, I wonder whether there may be any missing explanation in the Method.

**Authors’ reply:** *The total number of infarcts in individual locations was larger than the number of patients because if an infarct involved more than one location, e.g. basal*
ganglia and subcortical region, then it was counted twice, one for the basal ganglia and one for the subcortical white matter. The method of counting has been clarified in the revised text (page 6, para 3).

#3. Another problem is that the usage of 13-item RBDQ (RBDQ-HK) in a prospective study. As this questionnaire items include both lifetime items and recent 1-year frequency (Did it happen in the recent 1-year?) ones. As the evaluation of RBD by using this questionnaire was performed 3 months after the acute ischemic stroke events, eventually some patients who had already had RBD BEFORE the events may have been included. Therefore, at least, the authors should mention this drawback about using RBDQ-HK, and, if possible, they approach RBD patients (the number is 13, so seems to be not too difficult) to check when the onset of RBD symptoms. According to this procedure, methodology section should be rewritten, but if the onset was really AFTER the stroke events in the majority of the patients with brainstem lesions, this information would strengthen this paper.

Authors’ reply: We accept this critical remark. The fact that the RBDQ could not differentiate the onset of RBD before or after stroke has been added as a limitation to the revised text (page 9, para 1).

Thank you for your attention.
Yours sincerely,

Dr Wai-Kwong Tang