Reviewer’s report

Title: Risk variants of the \( \alpha \)-synuclein locus and REM sleep behavior disorder in Parkinson's disease: a genetic association study

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Reviewer: Taku Hatano

Reviewer’s report:

This manuscript by Bjornara KA et al. investigated the risk variants of SNCA locus in PD with or without RBD. The authors found that the risk variant rs3756063 C/G of SNCA was associated with PD with RBD. These findings were replicated by using the data from PPMI. In addition, their and PPMI data was combined and investigated by meta-analysis. Previous reports suggested that although idiopathic RBD is strong risk for developing PD, the clinical phenotypes and risk factors of iRBD showed slightly different from those of PD. Therefore, I am interested in this paper. I have, however, some issues with both the authors approach and discussion:

1. RBD questionnaire usually is not able to predict RBD precisely. Therefore, the authors should discuss this point as the limitation of this paper.

2. In abstract, the authors described the "Indirectly, it also supports the hypothesis of RBD as relevant marker for a distinct subtype of the disorder." However, it remains unclear whether one point questionnaire can reveal the RBD in PD patients. Iranzo and Tolosa reported "there is a group of PD patients and bed partners who report that the frequency and intensity of their RBD symptoms (nightmares and vigorous behaviors) decrease with time and can even disappear" (Ref; Rapid eye movement sleep behavior disorder in Parkinson's disease. In Non-Motor Symptoms of Parkinson's disease. 2nd edition. Oxford, 2014). Therefore, in this study, the authors might not be able to divide from the PD with REM to PD without REM. The authors should discuss this point.

3. In this study, the participants were not confirmed the pathological diagnosis. Therefore, non-RBD group might include non-synucleopathy parkinsonism, such as progressive supranuclear palsy. The authors should interpret the data cautiously.

4. In table 2, the authors should state the 95% confidentiel intervals.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.
Yes

Are the conclusions drawn adequately supported by the data shown?
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No

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