

ROUND 1

Dear reviewers and editorial board of World Journal of Psychiatry

We have carefully reviewed the comments of the reviewers and have made a sincere attempt to address all issues. The revised manuscript has been extensively revised to address all concerns. We appreciate the reviewers and the editors for their valuable inputs.

Sincerely yours,

Yan Ma and Shuo Zhang.

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Major revision

Specific Comments to Authors: This is a thorough review of psychosis in Parkinson's disease. I see two issues: 1. When citing the literature, please distinguish treated from not treated PD patients since it is usually thought that Rx with DA agonists is the cause of PD psychosis. 2. The English needs a fair amount of improvement, in some sections more than in others. Please correct grammar, spelling, sentence construction and use of capital letters

Response: Thank you for the valuable suggestions. The revised manuscript has been extensively edited and proofread to address all language-related issues.

Most of the studies included in this review were observational studies, which were not able to distinguish treated from non-treated PD patients. The results of antiparkinsonian medications (not only DA agonists) on PD psychosis originate from observational studies with long-term follow-up. In most observational studies, treatment with DA agonists as a confounding factor was controlled for in the analysis. In the subsections 4.6 (Antiparkinsonian medications) and 5 (Treatment and Management), we have discussed the effect of antiparkinsonian medications on PD psychosis. Moreover, we have acknowledged the following limitations in the Conclusion section:

“Unfortunately, most of the studies included in this review were observational studies that did not distinguish between and non-treated PD patients, since treatment with DA agonists is considered as a potential cause of PD psychosis. A follow-up prospective study to investigate whether antiparkinsonian medications have a significant impact on the development and progression of PD psychosis in a cohort of patients receiving different kinds and doses of antiparkinsonian medications should be conducted in future.”

Please see the content in the conclusion section.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Major revision

Specific Comments to Authors: Development of Parkinson's disease (PD) psychosis may involve dysfunctional imbalance of neurotransmitters, structural and network changes, genetic profiles, and cognitive impairments. The therapeutic approaches for PD psychosis include reducing or ceasing the use of d dopaminergic drug, antipsychotics, cholinesterase inhibitors, and non-pharmacological interventions. Emerging research based on new biomarkers and genetic factors may facilitate a tailoring therapeutic strategy. The article is timely and important. This reviewer has some comments: 1. More comprehensive review is suggested; for example, while compounds based upon traditional theories have been limited in efficacy, more novel compounds based upon other theories deserve more studies. Here is one of the examples: there has been a clinical trial which indicates that activation of N-methyl-D-aspartate receptor glycine site temporally ameliorates neuropsychiatric symptoms of PD with dementia. 2. Extensive English editing is suggested too. Here is one of the examples: "Similarly, a cross-sectional study involving 805 PD patients showed that the use of DR agonists were associated with impulse control disorders (mainly pathological gambling and hypersexuality) [64]."

Response: Many thanks for valuable suggestions. We have revised and added the clinical trials and mechanism of action of NMDAR agonists (sarcosine) on PD psychosis. Please see the subsection 5.4 (Other antipsychotics and N-methyl-D-aspartate receptors agonists). The revised parts are indicated in the conclusion section.

108 Frouni I, Belliveau S, Maddaford S, Nuara SG, Gourdon JC, Huot P. Effect of the glycine transporter 1 inhibitor ALX-5407 on dyskinesia, psychosis-like behaviours and parkinsonism in the MPTP-lesioned marmoset. *Eur J Pharmacol* 2021; 910: 174452 [PMID: 34480885 DOI: 10.1016/j.ejphar.2021.174452]

109 Tsai CH, Huang HC, Liu BL, Li CI, Lu MK, Chen X, Tsai MC, Yang YW, Lane HY. Activation of N-methyl-D-aspartate receptor glycine site temporally ameliorates neuropsychiatric symptoms of Parkinson's disease with dementia. *Psychiatry Clin Neurosci* 2014; 68(9): 692-700 [PMID: 24612097 DOI: 10.1111/pcn.12175]

The revised manuscript has been extensively edited and proofread to address all language-related issues.

Reviewer #3:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: Thanks for recommending me as a reviewer. In this opinion review, authors summarized and analyzed the identification, screening, epidemiology, mechanisms, risk factors and therapeutic strategy of PD psychosis identified from current clinical evidence. PD psychosis tended to have negative influence on patients' quality of life and increase the burden of family caregiving. Screening and

identification in early stage of disease is crucial for establishing tailored therapeutic strategies and predicting the long-term outcome. This review paper is well written. If you complete minor corrections, the quality of your research will be further improved. If the authors describe the conclusion section more clearly, it can help readers understand it.

Response: Many thanks for valuable suggestions. We have revised the conclusion section for better clarity. Please see the content in the conclusion section.

ROUND 2

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This is a very good review but requires further careful English editing.

Response: I have revised the manuscript according to the reviewer's comments(second round) and the language company (Medjaden) made some tweaks to further improve.