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Fang-Fang Ji,  
Science Editor  
Editorial Office  
Baishideng Publishing Group Inc

Dear Fang-Fang Ji,

We would like to thank the reviewers for their comments on our manuscript entitled “The glutamate transporters, EAAT1 and EAAT2, are potentially important in the pathophysiology and treatment of psychiatric illnesses” which have led to a revised version of the manuscript. We will address the comments by the reviewers in a systematic fashion:

**Reviewer #1**

Comment: Interesting work addressing a very important topic in the intersection of basic sciences and clinical research.

Response: We thank the reviewer for their appreciation of our review.

## **Reviewer #2**

Comment: The main feature and merit of this well done and well written review is that of considering the solely on the Na<sup>+</sup>- dependent EAAT family. Literature search was complete and appropriate. The introduction section should be shortened and focused mainly on psychiatric disorders. In the section "EAATs in psychiatric illness" I would suggest authors to add data regarding OCD, for this disorder papers regarding the consequence of excessive release of glutamate into the synapse and glutamate-mediated neuronal degeneration are available.

Response: We thank the reviewer for their assessment of our manuscript.

- We have simplified sections of the introduction.
- We agree that data regarding OCD would be beneficial to the scope of the manuscript, and have added a paragraph discussing EAATs in association with this disorder to our manuscript.

## **Reviewer #3**

Comment: This was on the whole a well written review, but I had some concerns about its content and organization. • Firstly, there have been several recent reviews on the subject e.g. - Takahashi et al. Glutamate transporter EAAT2: regulation, function, and potential as a therapeutic target for neurological and psychiatric disease. *Cell. Mol. Life Sci.* (2015) 72: 3489. <https://doi.org/10.1007/s00018-015-1937-8> - O'Donovan et al. The role of glutamate transporters in the pathophysiology of neuropsychiatric disorders. *npj Schizophrenia* (2017) 3:32 ; doi:10.1038/s41537-017-0037-1 The authors of the current review need to ensure that their review has something new to add. • Secondly, I found that a relatively greater proportion of the review was devoted to basic sciences aspects of the topic and comparatively less devoted to the clinical implications among psychiatric disorders. Some of the molecular and genetic aspects appeared too complicated to me. I wonder whether a

review on glutamate transporters in the pathophysiology and treatment of psychiatric illnesses requires to go to this depth to discuss neurobiological aspects, or whether this part can be shortened and simplified. • Finally, the authors have covered the role of glutamate transporters in schizophrenia and mood disorders, but (somewhat inexplicably) left out a host of other psychiatric disorders where abnormalities of glutamate transporters may be involved, such as anxiety disorders including OCD and PTSD, neurodevelopmental disorders such as autism and ADHD, neurodegenerative disorders such as dementia, substance use and chronic pain disorders. The authors may want to cover these, at least briefly.

Response: We thank the reviewer for their assessment of our manuscript.

- With regards to the papers mentioned: We presume that the reviewers comments are made with regard to the sections on EAAT2, as neither paper mentioned covers EAAT1 in great detail; Takahashi *et al.* includes only a very brief mention of schizophrenia, and no reference to bipolar disorder (or OCD and PTSD); O'Donovan *et al.* similarly do not cover bipolar disorder (or OCD and PTSD). Our manuscript is unique in that it discusses the potential role of EAAT1 and EAAT2 in affective disorders.
- We have simplified sections of the introduction. We feel however that a thorough discussion of the biology behind EAAT1 and EAAT2 is necessary in order to fully understand how their regulation is affected in psychiatric illness.
- With regard to the disorders covered in our manuscript: Our intent was to focus the scope of the manuscript on schizophrenia and affective disorders – we understand that the title of the manuscript may have been misleading and have adjusted it accordingly to clearly state this intent. Furthermore, we have added paragraphs detailing any currently known associations between EAAT1, EAAT2, OCD and/or PTSD. We do however feel that neurodevelopmental disorders such as autism and ADHD, as well as

neurodegenerative disorders such as dementia, substance abuse and chronic pain are outside the intended scope of our manuscript. We have included references for further reading on these topics under “EAATs in psychiatric illness”

Our original manuscript now titled “The glutamate transporters, EAAT1 and EAAT2, are potentially important in the pathophysiology and treatment of schizophrenia and affective disorders” has been revised to address the comments raised by the three reviewers and therefore we hope that the version of the manuscript we now submit is suitable for publication in The World Journal of Psychiatry.

We look forward to hearing from you.

Sincerely,

A handwritten signature in black ink, appearing to read 'G. Parkin', written in a cursive style.

**Georgia M Parkin**

(On behalf of the authors)