Manuscript NO.: 65062

Title: Neural stem cell therapy for brain disease

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We would like to thank all the reviewers for their explicit review and constructive comments.

We have made all the changes as suggested, and incorporated them in the revised manuscript.

Listed below are our point-by-point responses to their comments.

Response to Comments of Reviewer #1:

Critique #1: This review discusses Neural stem cell therapy for various brain diseases, which is

interesting. However, there are some concerns need to be addressed before publication, as below: 1.

Please double check whether the singular and/or plurality is correct in the manuscript. Some should be

"were", but not "was".

Response: Thank you for your advice. We have checked and corrected the singular/plural errors.

Critique #2: 2. The sentence, such as "Previous studies have suggested that repair and regeneration after

the central nervous system (CNS) may be very challenging due to the following reasons" is puzzling.

Please check and revise carefully.

Response: We have checked and rewritten the puzzling sentences.

Critique #3: 3. In the part of Introduction, the authors mentioned cellular therapy. It would be better to

make it clear what they mean about "cellular therapy".

Response: We are sorry we did not identify this part clearly. Cellular therapy is just same as cell therapy. This term is used for NSCs cells transplantation, as cells are used for treating neurodegenerative disorders. We have now redescribed cellular therapy in the part of Introduction.

<u>Critique #4</u>: 4. In the end of Introduction, it would be better to add a summary and illustrate the purpose and significance of the review article.

Response: We have added a summary illustrating the purpose and significance of this review at the end of introduction.

<u>Critique #5</u>: 5. Some words is misspelling, such as "injuty". The authors are strongly encouraged to check the spelling and grammar throughout the manuscript.

Response: We have checked the spelling and grammar throughout the manuscript.

<u>Critique #6</u>: 6. It would be gratifying to see the figure to summarize and illustrate NSC therapy for each type of brain disease to make people better understand.

Response: We have added figures to summarize and illustrate NSC therapy for each type of brain disease as suggested.

Response to Comments of Reviewer #2:

Critique #1: This article has variety of big topics including traumatic brain injury, hypoxic-ischemic brain injury, Alzheimer disease and Parkinson disease. And the weight is not distributed very evenly.

Most of the author's focus is on traumatic brain injury and hypoxic-ischemic brain injury. You should add more content to the other two topics (Alzheimer disease and Parkinson disease), or reduce the content of the brain injuries.

Response: We have modified the article as suggested, and added more content to Alzheimer disease and Parkinson disease, and balanced the weight of the articles with regards to other two diseases.

Critique #2: Suggest adding more citations of this journal.

Response: We have added the citations of the World Journal of Stem Cells articles.

<u>Critique #3</u>: Some of the contents listed in the table did not appear in the text of this manuscript. It is recommended that this needs to be explained clearly.

Response: We have included the Table's details in the text.

Response to Comments of Reviewer #3:

Critique #1: The authors provide a review about neural stem cell therapy in brain disease. Unfortunately, this review does not provide any new insights or a good overview about the current status, problems or future perspectives. While covering e.g. NSC related aspect in Alzheimer, Hypoxic or Parkinson disease the details remain more or less superficial. General and very important aspects which are major problems for translation of NSC therapies to the clinic such as the definition, generation and quality control of NSCs are completely missing. Table I provides an overview of listed NSC based trials. However, the informational value is limited since e.g. details about the cells and the trial aims are missing.

Response: Thank you for the constructive criticism. We have changed the overall structure of review article, by including the details of neural stem cell generation methods, and the recent findings using neural stem cells. We have replaced the table with two fresh tables, in which the suggested missing information has been mentioned.

Scientific editor suggested to keep the self-citations less than 10%. We keep around 8% self-citations in this article and remove all other improper citations.