

Format for ANSWERING REVIEWERS



Dear Editor,

Please find enclosed the edited manuscript in word format (file name: 15353-Review.doc).

Title: Therapeutic targets and delivery challenges for Alzheimer's disease

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Name of Journal: *World Journal of Pharmacology*

ESPS Manuscript NO: 15353

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated.

2 Revision has been made according to the suggestions of the reviewer:

Reviewer 1:

Article needs revision as follows:

- 1) The article seems too long and redundant in some parts: the sections should be divided in available treatments and prospective therapies, or, alternatively, linked to the pathologic mechanisms, as reported in tables.

Response: The manuscript is revised as suggested by the reviewer and the changes are indicated in the manuscript.

- 2) The environmental factors are just mentioned in "4.3 Mitochondrial Dysfunction Cascade Hypothesis": a discussion on them should be expanded.

Response: The Mitochondrial Dysfunction Cascade Hypothesis is elaborated as suggested by the reviewer

- 3) The figures 4-8 should be better connected to figure 3.

Response: The Figure 3 is modified as suggested by the reviewer (It kindly be noted that earlier figure 3 is now figure 2 in the revised manuscript).

- 4) The English language should be ameliorated

Response: The manuscript language and grammar is modified and improved as suggested by the reviewer.

Reviewer 2:

- 1) Many of the paragraphs in the manuscript read as a collection of related facts without a clear and coherent theme. This leaves the reader with information, but without a clear context in which to understand that information. I think many readers will find this material hard to follow in part because it is often not clear why individual paragraphs are included and what the take away message of that paragraph should be. This is a consistent issue throughout the manuscript. Related to item 1 above; Paragraphs often are not focused on a single main point. Instead, many paragraphs lump tangentially related information together into a single paragraph. This style may leave readers confused about the main points the authors intend to highlight. I suggest the authors

only include the material that is most directly related to the points they want the reader to understand.

Response: Various sections in the manuscript are rearranged and the relevant data is added so as to make the manuscript more informative and clear. Changes are indicated in the manuscript.

- 2) Although neuroanatomy does not appear to be the primary focus of this review, the authors do include a limited amount of information about neuroanatomy associated with AD. Unfortunately, the neuroanatomical description is quite vague, does not connect AD symptoms to neuroanatomy well, and leaves the reader feeling like this is an area the authors are somewhat less comfortable/familiar with. This material is largely limited to a few sentences on page 7. This certainly seems like relevant information, but I believe a stronger connection between symptoms (eg memory dysfunction) and brain regions (eg hippocampus) is warranted.

Response: The section 2 of the review is revised and elaborated so as to give better connection between symptoms and affected brain regions (neuroanatomy).

- 3) Figure captions are little more than titles for figures. I believe the captions would be improved by including a more thorough description of the figure so that readers better understand the message they depict.

Response: As suggested by reviewer, the figure captions are modified and elaborated to give thorough description of figures.

- 4) Citations: The manuscript needs significant work in regard to citations. 1) There are paragraphs that do not include citations at all; 2) There are sentences that describe prior work that are not cited; 3) the sole citation for some paragraphs is a prior review paper. I would encourage these authors to cite and sentences that are based on prior work and focus more on the original research rather than prior review papers.

Response: As suggested by reviewer, the references are added at relevant points in the manuscript.

- 5) There are a number of spelling, grammar, punctuation issues throughout the manuscript that interfere with the ease of reading this material.

Response: The manuscript language and grammar is modified and improved as suggested by reviewer.

- 6) A relatively minor issue is that the authors seem to be fond of the use of "viz". As a reader, I found it to be overused and distracting. I certainly think its limited use is appropriate, but would suggest the authors consider alternative wording as well.

Response: As suggested by reviewer, the necessary changes are amended in the manuscript.

3 References and typesetting were corrected.

Thank you again for publishing our manuscript in the *World Journal of Pharmacology*.