

Review of: "Somatostatin and the pathophysiology of Alzheimer's disease"

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Potential competing interests: No potential competing interests to declare.

Thank you for inviting me to review the manuscript entitled "Somatostatin and the pathophysiology of Alzheimer's disease". I found the review really interesting and constructive, with a well done description of the molecular mechanisms involved in this proposed model for AD pathophysiology. However, I would suggest some revisions, that according to me could help to improve the paper:

- After reproducing figure 1 from Hama and Saido (2005), the author says that the model has been recently updated. I would suggest to remake the figure 1, including both the old and the updated version of the model, adding more details about how SST could be or not protective. In this way, the model expansion following in the sequent chapters would be easier to understand.
- Please consider to add an abbreviations list.
- Please check typos (rendersthes, alsofrom...)
- In chapter 3 I would suggest to reduce a little bit the description of APOE4 gene function. In this way, according to me it would be easier to point out the connection between APOE4 and SST dysfunction and improve the understanding of SST involvement in AD.
- To make the whole molecular model clearer, I would suggest to add another image resuming all the aspects of the molecular theory.
- In the cognition model, there is a continuous iteration between animal models and AD patients (especially in the chapter 4.3). I would suggest to divide the part in which the author speaks about animal models from the clinical evidence part. In this way, it would be easier for the readers to understand the clinical implications of what is observed at the molecular level. Moreover, according to me part 4 could be a little bit reduced, and there would be the need to enhance in a deeper way the connection between SST dysfunction, the animal models of cognition disruption and the consequent clinical AD evidence.
- In part 4.3 and 4.4 I would suggest to remove the literal citation of other authors manuscripts.
- It would be really interesting to add at the end of the review a discussion part, in which the author resume the whole model, both biological and cognitive, and point out possible therapies or the advantages that this model would add in the development of future interventions.

