Name of journal: World Journal of Diabetes

ESPS Manuscript NO: 19395

Response to the Editor

Editor

- *Indication of family name.*
- *Audio core tip*
- *Offer reference No to all cited references (Table 1, Table 2A & Table 2B)*
- *Provide decomposable figures*
- *Add PUBMID ID and DOI to all references.*

According to the valuable suggestions of the Editor, all needful is fixed.

Response to the Reviewers

Reviewer 506250

This review describes in detail on the issues between the Alzheimer disease and diabetes. This review is excellent. I noted only minor points as follows. ***1. In my opinion, the term type 3 diabetes is not yet general. Therefore this term may be omitted at least in abstract (but not in text). 2. In therapeutic opportunities in text, if possible, please add brief comment on the possible effect of DPP4-I on AD.***

- According to the very first valuable suggestion from the first reviewer , term T3D has been omitted from the abstract and mentioned in text with more clarity for the better understanding of the readers.
- As suggested, effects of DPP IV inhibitors on Alzheimer's disease is reported in clinical opportunity with its clinical trial status

Reviewer 00506304

Rajat and Smriti have reviewed how metabolic disturbances in diabetes mellitus and brain insulin resistance/dysfunction are related to Alzheimer's disease. Brain insulin signaling, insulin resistance in the brain and insulin resistance-associated neuronal function/cognitive declines have been discussed. The authors also describe the possible roles of key intracellular mediators, e.g., PI3K, Gsk3-beta, FOXO, and mTOR in diabetes-related brain dysfunction. In general, this review article is informative. ***There are few minor comments as follows. Specific comments 1.***

Page 4: The sentence "Glucose is the only required source of energy for neurons and any disruption in glucose metabolism leads to compromised neuronal functions" should be removed or moved to other section. In the "Diabetes Mellitus" section, diabetic complications (e.g., diabetic nephropathy, neuropathy, etc.) should be briefly mentioned. Brain microvascular complications might also contribute to cognitive decline in diabetic patients. 2. The authors should mention about protein misfolding (i.e., amyloid-beta) and accumulation of misfolded proteins in Alzheimer's disease and diabetes mellitus. 3. Please correct typographical errors (such as Page 4 "obesity y"; Page 11 "brain stem" should be "brainstem").

- As per first valuable suggestion from the second reviewer, the sentence "Glucose is the only required source of energy for neurons and any disruption in glucose metabolism leads to compromised neuronal functions" has been moved to section "Insulin resistance as common metabolic compromise in alzheimer's disease and diabetes".
- Microvascular complications of diabetes have been added to the diabetes mellitus section as per reviewer advice.
- As per advice, protein mis-folding is added under section "Amyloidogenesis: a common pathology of alzheimer's disease and diabetes".
- Typographical error at page no. 4 and 11 have been fixed.

Reviewer 00009616

Nicely written review. My only criticism is that ***the authors themselves did not perform any original work previously. As a result the review fails to give any additional new ideas, what needs to be done next and what studies need to be performed and what results are expected as a result and what alternative hypothesis need to be considered. The absence of these new insights is a major drawback and such insights will come only form those who have also contributed to the topic under discussion. Reviews without such insights can be written by any person familiar with the literature and as a result this review is just a collection of existing facts. There is no new interpretation of the existing data. This seriously hampers in recognising this as a useful review.***

- Keeping in mind the critical appraisal of reviewer, we would like to mention that, our lab is working on diabetic neuropathy since last five years and the work we have published is available at Pubmed. As this is a review article, it is mere a compilation of previous reports.

But looking into common footprints of AD and DM and then prediction of common therapy after keeping every molecular players in mind is a unique approach in this review. Although type 3 diabetes was already mentioned first time in 2005 but we provided a new therapeutic platform to brain diabetes after reviewing all relevant reports. In our new project we are planning our work in this direction as well.