Editor-in-Chief
World Journal of Diabetes
December 2022

Dear Editor in Chief,

Resubmission of a manuscript entitled: "Diabetes and Cognitive Decline: Challenges and Future Direction

I have enclosed a resubmission of manuscript entitled "Diabetes and Cognitive Decline: Challenges and Future Direction" to be considered for acceptance and publication in your journal.

2. This study reviews the consequences of prolonging hyperglycemia on brain function which is cognitive decline. This review discusses the current factors and pathophysiology and also the animal models used for diabetes-induced cognitive decline research.

Should you have any inquiries, please do not hesitate to contact me.

Thank you.

Best regards,

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Reviewer 1	Changes
I would like to bring to the notice of the authors that the mini-review lacks any figures to explain the mechanism they have explained. It is necessary to have atleast one or two figures in this mini-review which will attract readers.	Figures has been added in the text to explain the mechanism.
Reviewer 2	
1. Are there controversies in this field? What are the most recent and important achievements in the field? In my opinion, answers to these questions should be emphasized. Perhaps, in some cases, novelty of the recent achievements should be highlighted by indicating the year of publication in the text of the manuscript.	The role of insulin in the brain, particularly the hippocampal region, has been demonstrated to be critical for functional and structural changes in the brain for cognitive processes. Understanding the molecular mechanisms of insulin on brain plasticity is critical for identifying the mechanisms that regulate neural plasticity in health and metabolic disease, such as diabetes-induced cognitive decline, as well as neurodegenerative disease, particularly AD.
The results and discussion section is very weak and no emphasis is given on the discussion of the results like why certain effects are coming in to existence and what could be the possible reason behind them?	Has been improved in the text.
Conclusion: not properly written	Has been improved in the text.
Results and conclusion: The section devoted to the explanation of the results suffers from the same problems revealed so far. Your storyline in the results section (and conclusion) is hard to follow. Moreover, the conclusions reached are really far from what one can infer from the empirical results	Has been improved in the text.
The discussion should be rather organized around arguments avoiding simply describing details without providing much meaning. A real discussion should also link the findings of the study to theory and/or literature.	Has been improved in the text.
Spacing, punctuation marks, grammar, and spelling errors should be reviewed thoroughly. I found so many typos throughout the manuscript	Already check by proofreading service.
English is modest. Therefore, the authors need to improve their writing style. In	Already check by proofreading service.

addition, the whole manuscript needs to be checked by native English speakers.	

Round 2

Point to point answer to opinion.

Reviewer 2	Changes
Results and conclusion: The section devoted to the explanation of the results suffers from the same problems revealed so far. Your storyline in the results section (and conclusion) is hard to follow. Moreover, the conclusions reached are really far from what one can infer from the empirical results	The results section discusses about the proposed molecular mechanism for diabetes-induced cognitive decline. It is can derived from fluctuation in glycemic status (hyperglycemia and hypoglycaemia) that led to macrovascular and microvascular dysfunction in blood vessel. An increase in the AGE product during diabetes, trigger the cerebral insulin resistance in the brain especially in the hippocampus with became worst with occurrence of neuroinflammation in this site. It will following mitochondrial dysfunction with can activates the apoptotic pathway. This cycle with repeating as vicious cycle and became worst during prolong diabetes. This situation also influences by the drugs used in the treatment of diabetes that has been discussed in the text. Furthermore, diabetic autonomic dysfunction also can be linked to cognitive decline, but the mechanism is still unknown. As conclusion, the pathophysiology of diabetes-induced cognitive decline is still an elusive. The pathophysiology of diabetes-induced cognitive decline had a similar mechanism to AD, which is development of brain insulin resistance especially in hippocampus region that affected

	their neuroplasticity during cognitive processing. It still needs further investigation and the creation of reliable animal model to fully understand how diabetes causes cognitive decline and its comparable to the mechanism of AD. All of this argument has been added in the text.