Reviewer's report

Title: Nitrosamine exposure exacerbates high fat diet-mediated neurodegeneration

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Reviewer: Cheng Juei-Tang

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The authors assumed that peripheral exposure to nitrosamines that are widely present in the environment, amplifies the deleterious effects of high fat intake in promoting type 2 diabetes mellitus (T2DM) and neurodegeneration relating to Alzheimer’s disease (AD). Thus, they injected N-nitrosodiethylamine (NDEA) into Long Evans rat pups that were fed with high fat (60%; HFD) or low fat (5%; LFD) chow for 6 weeks. They found that exposures to nitrosamines, together with chronic high fat intake promote T2DM and neurodegeneration in animal. It seems interesting and helpful in the understanding of nitrosamine and insulin resistance (IR). However, some of the points as follows shall be concerned.

1. Lipids both cholesterol and triglyceride were reduced in Vehicle + HFD group as compared to Vehicle + LFD group. Why? Please give a suitable reason.

2. What is the level of plasma insulin? It is important to make sure the formation of IR. The data in cerebellum (Table 3) provided the mRNA level only.

3. The protein level and activity of enzyme will support the reliable data. But authors showed the gene expression (mRNA level) through qRT-PCR determination only.

4. Morphologic data showing neurodegeneration of brain and changes of behavior in these animals will be more reliable for formation of AD.

5. The background for treatment of NDEA at this applied dose and the duration of 6 weeks shall be indicated.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.