

Peer Review File

Article information: <https://dx.doi.org/10.21037/tp-24-182>

Reviewer A

The manuscript does not meet the criteria of scientific rigor. For example, the use of the term "epidemiological research" in the first paragraph of the introduction implies that this kind of research will determine "cause" of disease. Epidemiological research investigates factors associated with the development of disease NOT causation. There are multiple causes for every disease. Causation deals with underlying mechanisms of disease. One underlying mechanism of autism is the bio-accumulation of heavy metals in blood and brain cells. This bio-accumulation occurs via different mechanisms, one of which is zinc deficiency which is a common condition found in children with autism. Dietary heavy metals also impact gut biota and create another dietary mechanism for the development of autism.

The writers did not do a thorough literature review as they missed many important articles. In a literature review manuscript, the key words for the search engines are normally provided to the reader.

Response: Thank you for your comment. we improved our manuscript according to reviewer comment. also, the manuscript was revised by A native English Speaker to improve its language.

This manuscript did not follow the standard protocol for conducting a literature review. The reader has no clue as to how the literature review was done. The authors also wrote many ideas and provided no references to support the ideas.

Response: We have made considerable improvements to our review to ensure consistency in our ideas.

Several paragraphs talk about a few different ideas and then only one reference is provided for the ideas.

We improved this issue in our manuscript.

In a literature review, one main idea is supported by several references. Several sentences begin with "According to [ref number], children with ASD....." Normally, the sentence would be written with the name of the lead author and the reference number would be provided at the end of the sentence. ("According to Dufault et al, total blood mercury levels may be influenced by dietary intake of highly processed foods [1]."

Thank you for your comment. This issue has been addressed throughout the manuscript. We have highlighted the corrections in yellow.

Reviewer B

Summary:

This review pertains to gut, nutrition, and autism spectrum disorders (ASD). It discusses a range of topics: gastrointestinal symptoms and feeding disorders, nutritional deficiencies in ASD, the gut-brain-gut axis, gut microbiome, dietary interventions in ASD and related brain disorders, such as Ketogenic diet, probiotics supplementation, Specific carbohydrate diet, Vitamin A, C, B vitamins, and Camel milk.

Response. We appreciate your time and efforts in revision our manuscript. The manuscript has been revised by native English speaker.

Comments:

1. This review discusses an important and interesting topic: nutrition, gut, and ASD. Due to so many different contents, the review is diffuse, and unfocused. The authors may want to center around some key topics and trim others.

Response: thank you for your comment, and your time in improving our manuscript. We improved our manuscript according to your recommendations.

2. Title: the title did not seem to capture the review content well. Suggested title:” Brain-gut-brain axis, nutrition, and autism spectrum disorders.”

Response The title has been changed according to reviewer suggestion.

3. Abstract can be further improved to better capture the key contents of the review.

Response: the abstract has been improved.

4. Lines 72-76: “According to [14], ASD-affected youngsters imply that there are biological, metabolic, and dietary connections to the disorder. To assess these characteristics' reliability and accuracy as indicators of ASD, a case-control research approach is necessary because they seem like major possible anomalies. Additionally, [15] stated that everyone is required to eat well because it is one of our fundamental biological necessities”.

Two issues with this paragraph:

a. The authors should not use reference numbers to refer to studies in the text.

Response: improved.

b. It is unclear why case-control study is necessary? Other study designs such as prospective birth cohort study or clinical trial could be even more powerful.

Response: We are sorry for this inconvenience issue. This issue has been deleted.

5. Fig. 1. Nutritional control of metabolism in children with ASD. The quality of Fig 1 needs to be improved. Some words were buried partially.

Response: Thank you for your observation. We reedited all figures to be clearer and more understanding.

6. Line 327 “Different types of treats for metabolic status in ASD”. Please change to “Different types of treatment for metabolic status in ASD.”

Response: corrected.

7. Line 693-694: “Nevertheless, because there aren't enough blind studies, control groups, or high expectations, the efficacy of these therapies is frequently uneven”. Authors should use standard terminology, such as “randomized controlled clinical trial.”

Response: corrected.

8. The flow of the review is not well-organized, the contents often jumped around, not logically connected between paragraphs. The English sentences can be improved to improve readability.

Response: thank you for your comment. the manuscript has been revised by A native English Speaker