

Article information: <https://dx.doi.org/10.21037/amj-22-74>

Reviewer Comments

Comment 1: First, the abstract needs some revisions. Because the Mendelian randomization is used to ascertain the causal relationship between exposure and health outcome, the authors need to have comments on the uncertain causal relationship in clinical practice in the background and explain why Mendelian randomization is suitable to answer this research question. The sentence “The exact relationship between omega-6 fatty acids and ADHD is still unknown” is not informative and accurate. The methods need to describe the databases used including the diagnosis of ADHD and experimental methods of the SNPs, as well as the sample representativeness in the databases. The results need to report the findings from sensitivity analyses based on weighted median mode, MR-Egger, simple mode and other methods. The conclusion needs to have comments on the limitations of this study to explain other possible reasons for the negative findings.

Reply

Dear reviewer,

Many thanks for reviewing our paper. We are grateful to your thoughtful comments that helped to improve the overall quality of our work. In the revised version, we have marked all changes as much as possible accordingly

Changes in text : we also removed that line (The exact relationship between omega-6 fatty acids and ADHD is still unknown) .At same time information have been addressed ,according to reviewer comments (line 56-69 page #2)

At same time changes have also been made in conclusion part (81-85 line page #2).

Comment 2: Second, in the introduction of the main text, the authors need to have a brief review on known factors associated with ADHD, in particular environmental factors including the intake of omega 6 fatty acid. It is also necessary to review all available studies on omega 6 fatty acid-ADHD relationships and analyze the potential reasons for the clinical controversy to indicate the clinical needs for this Mendelian randomization study.

Reply:

We really appreciate precious directions given by reviewer, so according to above comments we made following changes

Changes in text:

We add some brief lines and references on known factors associated with ADHD,enviromental

factors including the intake of omega 6 fatty acid and also find possible studies on omega 6. Some changes and studies have been added (line 106-108,114-116,124-129,133-135 page 3-4)

Comment 3: Finally, the authors need to analyze the potential unique contribution of omega 6 fatty acid to the risk of ADHD if the contribution is small, the current study should have negative findings. Third, in the methodology of the main text, the authors need to describe the datasets used in detail, including sample representativeness, sampling, measurements of omega 6 fatty acid and SNPs, and diagnosis of ADHD. In the analyses, please repeat the analyses according to subtypes of ADHD, Attention deficit, hyperactivity, and mixed subtype. Fourth, in the discussion, an extensive discussion on the possible reasons for the negative findings is needed.

Reply:

We really appreciate precious directions given by reviewer, so according to above comments we made following changes

Changes in text :

Changes have been made in methodology sections (149-156 page #4), we also discuss how patients were diagnosed with ADHD, Patients with ADHD were found in the national Psychiatric Central Research Register and diagnosed by psychiatrists in a psychiatric hospital using the ICD10 code. We also add Assumption of 2-sample Mendelian randomization where we discuss 3 assumptions of MR base in methodology(line 173-192, page # 5). At the same time we also add a portion in the discussion section where we discuss about the possible reasons for the negative findings and limitations of this study (line 257-268 page #7).