

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors:

In this review article, the authors analyze the possible link between CD and ataxia, evaluating autoantibodies that could be used as a diagnostic biomarker. But, do the data really support role of CD in different neurological disorders?

- We appreciate your insightful feedback on our review article exploring the potential link between celiac disease (CD) and ataxia, particularly in evaluating autoantibodies as diagnostic biomarkers. In response to your valuable comments, we have made several improvements to enhance the clarity and accuracy of the manuscript.

However, there are a few issues of concern in this study. First, we should define the terms. In the title, the authors used the term gluten enteropathy, and in text in many places the term gluten sensitivity. Ingestion of gluten is associated with several clinical disorders, collectively referred to as gluten-related disorders. Shortly, that is a wheat allergy, CD and non-celiac gluten sensitivity. All of these types are gluten sensitivity, but not all of them is CD. The term gluten enteropathy refers only to CD.

- We acknowledge your concern regarding the terminology discrepancy between "gluten enteropathy" and "gluten sensitivity." To address this, we have carefully revised the manuscript to ensure consistency in using the appropriate term, "gluten-related disorders," encompassing wheat allergy, CD, and non-celiac gluten sensitivity. Our first intention was to mention the other disorders from the spectre, fully aware of the fact that only gluten enteropathy is an autoimmune disease.

Second, several studies are showing the fallacy of relying on antibody tests. Serologic tests, particularly the IgA EMA and the IgA tTGA, have become a relatively sensitive and specific way to initially detect CD. Many studies demonstrate a specificity of IgA tTGA greater than 95% and a sensitivity in the range of 90% to 96%. The EMA has a slightly lower and variable sensitivity but an excellent specificity (99.6%). Many individuals without CD express AGA IgG antibody (sensitivity of AGA IgA among adults ranges between 0.65 and 1.0 and the specificity between 0.71 and 0.97). The AGA IgG is similar in sensitivity to the AGA IgA, but the specificity is much lower, approximately 0.5. Because of the variable and generally inferior accuracy of the AGA, the use of AGA IgA and AGA IgG tests is no longer recommended for identifying individuals with CD (ESPGHAN, NASPGHAN, AGA Institute, NIH). False positive antigliadin antibody tests have been recorded in individuals with a variety of other gastrointestinal disorders, including esophagitis, gastritis, gastroenteritis, inflammatory bowel disease, cystic fibrosis and cow's milk protein intolerance.

- We agree completely with the reviewer's point and thank for the great suggestion. We have thoroughly revised the sections discussing serologic tests, incorporating a more nuanced understanding of their limitations and emphasizing the fallibility of relying solely on antibody tests for CD diagnosis. A comprehensive overview of the specificity and sensitivity of various

antibody tests has been provided, addressing concerns about false positives in certain conditions – at the end of the manuscript, called Limitations.

Finally, serologic tests may have false positive results (usually low antibody titers) in patients with other immune or inflammatory conditions such as many neurological disorders. AGA Institute recommended testing for CD in persons with peripheral neuropathy, cerebellar ataxia, and recurrent migraine, but confirmation of the diagnosis of CD requires an intestinal biopsy in all cases.

- Based on your input, we have incorporated the latest recommendations from authoritative bodies like ESPGHAN, NASPGHAN, AGA Institute, and NIH. Emphasis has been placed on the necessity of intestinal biopsy for confirming CD diagnosis, particularly in individuals with peripheral neuropathy, cerebellar ataxia, and recurrent migraine.
- These revisions aim to address the concerns raised and enhance the overall accuracy and clarity of the manuscript. We appreciate the opportunity to improve our work based on your constructive comments.