Author’s response to reviews

Title: Global research trends in microbiome-gut-brain axis during 2009-2018: a bibliometric and visualized study

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Author’s response to reviews:

Dear editor

Editor-in-Chief

Hope this finds you well

Re: Revised Manuscript Submission (Manuscript ID: BMGE-D-19-00412))

We would like to thank you and all the reviewers for your time and insightful and qualified comments after reviewing our manuscript titled “Global research trends in microbiome-gut-brain axis during 2008-2017: a bibliometric and visualized study”.

We wish to thank editor and reviewers for their time in commenting on the manuscript, which we believe has strengthened the paper.

Our responses to the comments are yellow—highlighted in the revised manuscript. We carefully addressed all the comments of the reviewers.

We look forward to your and the reviewers’ comments on the manuscript and hope that the manuscript is given favorable consideration for publication in BMC Gastroenterology.

Yours sincerely

Sa’ed Zyoud
Reviewer reports:

Sofia Cussotto (Reviewer 1):

Here the authors analyse the trends on microbiome research over the last 10 years. The review is well written, and the authors address an aspect of particular relevance, as the microbiome-brain research is currently facing a period of "hype". I have no major concerns but I suggest some minor comments that the authors may consider in order to improve the manuscript.

Response: We would like to say our appreciation to you for the thorough reading of the manuscript and for the professional comments and constructive recommendations, which help to improve the quality of this manuscript.

1. Page 3, line 3: please cite direct evidence of the statement instead of ref 1-5
Response: we cited this statement with direct evidence (Page 3 Line 4)

2. Page 4, lines 5 and 10: Please cite primary research papers instead of reviews (ref 30 and 23)
Response: we cited this statement with primary research papers instead of reviews (Page 4 Line 4, and Page 4 Line 9)

3. Page 4, line 10: when discussing bifidobacteria increasing resilience in humans, there are also other papers that show the difficulties of translating preclinical findings into humans (e.g. doi: 10.1016/j.bbi.2016.11.018). I think it would be important to stress this point and cite some examples of human research where probiotics failed to improve stress.
Response: we added new statement with reference as you recommended (Page 4 Line 9)

4. Page 5, line 7: what does "has the largest one" mean? Is it referred to the quality standard? Not clear. Please rephrase
Response: we clarified this statement (Page 5 Line 4)
5. Page 10, line 2: capital "A"
Response: we corrected it

6. Table 3: the separation across lines is not clear, I found it difficult to understand which author was linked to which paper. If possible, make it more clear
Response: we clarified it as you recommended (Table 3)

7. Figure 3: why Ireland, UK and Spain are listed in table 1 but are not found on this map? Spain could be missing because of the low number of publications, but Ireland and UK are amongst the most productive countries according to table 1
Response: we changed the setup and frame of the figure to be clearer (Figure 3)

8. Legend of Figure 3 and 4: There is no indication of colour-codes. I suppose they are coloured according to the 4 sub-topics? It would be better to specify this in the figure legends.
Response: We specified the color-codes at the legend of the figures to be clearer (Page 19 Line 19 and 25)

9. Figure 3: is there a specific reason why yellow and blue are not present in figure 3? If yes, please explain in figure legend.
Response: There is no a specific reason why some colors appear in certain figure and disappear in others. Each figure is independent of the others (they do not affect each other).

Cas Swarte (Reviewer 2):
Response: We would like to say our appreciation to you for the thorough reading of the manuscript and for the professional comments and constructive recommendations, which help to improve the quality of this manuscript.
1. Why did the authors choose for the Scopus database? I would strongly advice to extend the research to databases such as Pubmed and Psychinfo to get a true overview of the global activity of MGBA research. For example 'microbiome' in Pubmed results in 56195 hits whereas the authors report 24369 hits on scopus regarding 'microbiome'. Furthermore, why is the year 2018 not included in the analysis?

Response: Thank you for your nice comment, we have taken this into account in revising our manuscript and we added in methods the advances of Scopus over other databases (Page 5 Line 5). Furthermore, in our first draft, we focused only on gut microbiome during the last decade but in your search on PubMed you searched on microbiome without any restriction. In the last version we corrected it to be clearer and expanded our search to include 2018 and to include all publications related to microbiome (Page 6 Line 10).

2. Regarding figure 1: Figure 1 is biased because the authors included both no. of articles regarding gut microbiota and microbiota gut brain axis (MGBA) in one figure. It can be interpreted from this graph that the work in MGBA surpasses the work on gut microbiota alone because the red line crosses the blue line. I would advise the authors to include two separate figures.

Response: we separated Figure 1 to A and B

3. Regarding figure 2: No legend is included in the figure but only in the results section. Furthermore, cluster 1 regards "gut microbiota in animal models". Are these animal models regarding MGBA or only gut microbiota? It is unclear to the reader how the "cluster analysis" was performed. Furthermore, could the authors include an order of magnitude for the diameter.

Response: We think it is an important issue which we did not put enough attention to it. In the last version, we clarified this point in details (Page 5 Line 18), and we clarified it at the legend of the figure 2 to be clearer

4. Regarding figure 3: There are dots in the plot without a country code attached. Furthermore, could the authors include an order of magnitude for the diameter.

Response: We changed the setup and frame of the figure to be clearer (Figure 3) and we clarified it at the legend of the figure 3 (page 20 Line 17). Sometimes, it difficult to label all the items in a map without having labels that overlap each other.
5. Regarding figure 4: There are dots in the plot without an author attached. Furthermore, could the authors include an order of magnitude for the diameter.

We changed the setup and frame of the figure to be clearer (Figure 4) and we clarified it at the legend of the figure 4 (page 20 Line 23). Sometimes, it difficult to label all the items in a map without having labels that overlap each other.

6. "There were statistically significant strong positive correlations 16 (r = 0.991, p <0.001) between the number of publications related to MGBA and the 17 number of publications related to microbiome in all fields over time." It is unclear to the reader how MGBA research is correlated to "publications related microbiome in all fields". Furthermore, the authors conclude through this correlation that "research output related to MGBA have followed the general progress in scientific research production related to the microbiome field". What is the general progress in scientific research that the authors describe here? And why does MGBA follows this progress?

Response: Thank you for this suggestion. We modified it as you suggested (Page 6 Line 18 and Page 9 Line 1).

7. "Research output related to MGBA most often originated from the United States. This finding was similar to other bibliometric studies in different fields." Ref. 29 is about "glyphosate intoxication" not about MGBA. Therefore, this conclusion is invalid.

Response: We corrected it as you suggested (Page 9 Line 3)

8. "In 2013 the USA launched a special research project on gut microbiota-brain 12 axis [86]." Why did this review led to "gradually become the focus of neuroscience".

Response: We clarified it as you suggested (Page 9 Line 13)

9. "A bibliometric analysis applies quantitative methods" do the authors mean qualitative?

Response: We modified it (Page 10 Line 20)

10. "Despite these limitations, we still consider that the result of this bibliometric analysis a is the first one and is sufficient to represent the accurate situation of microbiota-gut-brain..."
axis publications at global level" I think the approach is not accurate because only the Scopus was included.

Response: We modified it to be more accurate (Page 10 Line 20)