



November 19 2015

Attention:

Dr Fang-Fang Ji,
Science Editor, Editorial Office
World Journal of Psychiatry
Baishideng Publishing Group Inc
E-mail: f.f.ji@wjgnet.com

Dear Dr. Fang-Fang Ji,

We thank-you and the reviewers for your reading and suggestions for improvements to the paper:

Manuscript NO.: 21340

Column: Systematic Review

Title: White matter alterations in Anorexia Nervosa. A systematic review of Diffusion Tensor Imaging studies

Authors: Beatriz Martin Monzon, Phillipa Hay, Nasim Foroughi and Stephen Touyz

In this letter we first address each of the points raised by the reviewers.

RE: Introduction 1. Paragraph1 line3 “In addition to genetic, neuroendocrinologic and metabolic pathways, findings have also argued in favour of structural abnormalities.” The authors could give more information of this sentence.

We have edited this sentence to be more informative and added a sentence: These include genetic, neuroendocrinologic and metabolic pathways. Furthermore, studies of the brain structure in this mental disorder have identified structural abnormalities.

RE: 2. “brain gray matter (GM) and white matter (WM) might underlie altered brain function and behavior”. The authors should mention why they focus on the WM not GM.

We have extended this paragraph to explain why we focus on WM as it is more novel and in need of study:

The mechanisms addressing brain alterations remains unclear, but brain gray matter (GM) and white matter (WM) might underlie altered brain function and behaviour[9]. Both fibres are part of the Central Nervous System (CNS) which co-ordinates basic activities of the human body. The GM is related to processing and cognition whilst the WM co-ordinates different brain regions. The first studies found differences in the GM



of AN compared to healthy people and other eating disorders. However, the peculiar architecture of WM and the limited availability of imaging methods to study the WM delayed its investigation. Now, new advances in imaging procedures such as Diffusion Tensor Imaging (DTI) allow the study of the structure of WM and its implication in the pathology of AN.

RE: 3. Paragraph5, line 7, “nnutritional”?

Thank-you, we corrected to **nutritional**

RE: Method 3.1. Search strategy 1. Could the authors explain why they use this three steps strategy? Is there any reason that they include an additional search in the Spanish language not other language? And why not include other database such as EMBASE, Elsevier Science Direct, Web of Science, Google Scholar or Cochrane Library?

Reply: The main interest of the study was to identify all the studies of eating disorders in which the WM was analysed with DTI. We expanded the search to consider other languages, in this case Spanish, because it is the second most widely spoken language worldwide, there is a notable source of scientific research from Spanish speaking countries of the Americas and the first author is fluent in the language thus there was no need for translations for which we had no funding. Ideally we would have had no language restriction and have added this as a limitation. As research and imaging methods in AN is continuously evolving, we decided to do a third search after first drafts of the manuscript to see if new knowledge had been reported and ensure the review is as up to date as possible

We amended the third paragraph on page 8 to explain this:

In order to update the search, on April 28th 2015 we conducted a third data search on SCOPUS, Pubmed, Lilacs and CSIC electronic databases. We used the terms previously described.

We have added a paragraph in the discussion page 17 to clarify limitations of our method:

Finally, this review was limited in that only four databases were used and two of which were English language databases. However these two were the most relevant databases to the topic, and one, Scopus, is a composite of papers from many sources including several other databases such as MEDLINE and EMBASE. Insufficient funding for translations also precluded sourcing literature published in languages excepting those which the authors were fluent in.



RE: Results 4.2. Quality assessment 1. Paragraph2, line7, line10 ,“This was clearly described in one study, partially in two studies and not provided in three studies.”, which repeated.

Amended to: This was clearly described in one, partially in two and not provided in three studies.

RE: Discussion 1. Paragraph6, line2,“Alterations of the posterior thalamic radiations are of special interest, as they project to the occipital, the temporal and the parietal cortex, being connected to cortical regions involved in the processing of the body image.”

Please make this sentence clearer.

Amended to: Alterations of the posterior thalamic radiations are of special interest because they are connected with the occipital, temporal and parietal lobes which are all involved with the cortical processing of body image perception.

RE: 2. The authors should arrange the manuscript according to the format of the journal. Some subtitles are in different font, eg. (4. Results, 5. DISCUSSION, Summary of findings, CONCLUSION)

Fonts are all amended.

Specific edits have been made:

1. The Abstract has been rewritten to accord with journal word counts.
2. We have added the comments section.

RE Please update the manuscript according to the Guidelines and Requirements for Manuscript Revision-Systematic Reviews. You can find the Guidelines and Requirements for Manuscript Revision-Systematic Reviews, which includes the detailed writing requirements for the Title, Running Title, Authorship, Abstract, Keywords, Core Tip, Academic Rules and Norms, Tables and Illustrations, Comments and References, as an attachment.

We have attended to these.

RE Please provide an Audio Core Tip. We have prepared an audio core tip and it is attached as a ‘wav’ file.

RE Please subject the manuscript to *CrossCheck* analysis and the final title to Google Scholar search, and store screenshot images of the results. These are attached.



RE Please provide the files related to academic rules and norms. We have included the biostatistics statement, conflict-of-interest statement, and data sharing statement.

RE. Please revise the language of your manuscript. For manuscripts submitted by Non-Native Speakers of English, the authors are required to provide a language editing certificate, which will serve to verify that the language of the manuscript has reached Grade A.

The first author is a non-Native speaker but the corresponding and senior authors are all Native-speakers of English and have further read and edited the manuscript according to standard English. Thus we have not sought a language editing certificate as we did not wish to delay resubmission.

RE. Please sign the Copyright Assignment form. The Copyright Assignment form is attached.

The following are attached

- 1 21340-Revised manuscript
- 2 21340-Answering reviewers
- 3 21340-Copyright assignment
- 4 21340-Audio core tip
- 5 21340-Biostatistics statement
- 6 21340-Conflict-of-interest statement
- 7 21340-Data sharing statement
- 8 21340-Google Scholar
- 9 21340-CrossCheck

Best regards,

Professor Phillipa Hay

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