

PEER-REVIEW REPORT

Name of journal: World Journal of Psychiatry

Manuscript NO: 34110

Title: Biobehavioral assessment of the anxiety disorders: Current progress and future directions

Reviewer's code: 03672830

Reviewer's country: United States

Science editor: Fang-Fang Ji

Date sent for review: 2017-03-29

Date reviewed: 2017-04-14

| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|--|---|--|--|
| <input type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing | Google Search: | <input type="checkbox"/> Accept |
| <input checked="" type="checkbox"/> Grade B: Very good | <input checked="" type="checkbox"/> Grade B: Minor language polishing | <input type="checkbox"/> The same title | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C: Good | | <input type="checkbox"/> Duplicate publication | |
| <input type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> Plagiarism | <input type="checkbox"/> Rejection |
| <input type="checkbox"/> Grade E: Poor | | <input checked="" type="checkbox"/> No | <input checked="" type="checkbox"/> Minor revision |
| | <input type="checkbox"/> Grade D: Rejected | BPG Search: | <input type="checkbox"/> Major revision |
| | | <input type="checkbox"/> The same title | |
| | | <input type="checkbox"/> Duplicate publication | |
| | | <input type="checkbox"/> Plagiarism | |
| | | <input checked="" type="checkbox"/> No | |

COMMENTS TO AUTHORS

There are key challenges in the current categorical and subjective approach to diagnosing and assessing psychiatric disorders. From the angle of anxiety disorders, Abbott and colleagues dissected the roots of these challenges and proposed biobehavioral measurements as promising solutions. They focused on two types of biobehavioral measurements, eye tracking and electrocardiogram. For each measurement, they went in depth to introduce the methodology and state-of-the-art devices and provided differential analyses of clinical findings for specific types of anxiety disorders. The discussions, analyses, and citations support the authors' view that "Eye-tracking devices are uniquely capable of providing data that can be used to differentially diagnose anxiety disorders from both other commonly comorbid and misdiagnosed disorders. Both eye-tracking and electrocardiogram devices are able to provide change-sensitive assessment information." In the discussion section of the paper, the authors described a vignette where a boy receives higher quality diagnosis and

treatment involving biobehavioral measurements and invited the field to embrace these measurements as resources for research, to further validate and standardize the methodology, and to develop powerful and user-friendly data-processing software. Overall, the article is insightful, informative and inspiring. The reviewer would like to suggest the following minor revisions: 1. Page 9, the second paragraph that begins with the sentence "In addition to these general issues". This paragraph appears to serve multiple purposes in the writing: transitioning from the general issues of DSM-5 to anxiety disorders, summarizing and re-emphasizing the general issues, and proposing solutions. The language and its organization in this paragraph do not bear all these purposes sufficiently. Please consider making the paragraph more fluid in the context of neighboring paragraphs. 2. Page 10, the first paragraph, the sentence "Despite their greatly decreased cost, these tools are so sensitive that they can clearly identify unique symptoms of anxiety disorders salient to accurate differential diagnoses that previous methods of assessment could not detect [34]". The reviewer understand that here the sensitivity of the tools are very promising, but considering that the statement is part of the introduction, it feels a bit like jumping to conclusions. 3. Page 10, the second paragraph, toward the end of it, "... the available literature on these two biobehavioral measures will be discussed". This statement appears to be redundant with earlier portions the paragraph. 4. Page 11, toward the bottom of the page, "Post-traumatic stress disorder requires a person experience a traumatic event, experience intrusive dreams, memories, dissociative, distressing, and/or physiological reactions and hyperarousal long after experiencing the traumatic event". Please double-check the grammar. 5. The reviewer did not have prior experience himself specifying prices of medical devices in a review article, although he understands that the pricing information was meant to show affordability. Please check with the editor if this is an accepted practice for the journal. 6. Page 15, the second paragraph, the term "negative feedback". An alternative term coming to the reviewer's mind is "reinforcing feedback". The reviewer is a neuroscientist doing drug discovery research. In his own work, "negative feedback" means signaling to oppose the current trajectory of things. If negative feedback is the right psychological term to use in this case, please keep it. 7. Two suggestions on the section discussing eye-tracking research: a. It will be nice to see a table listing characteristics of eye tracking data associated with different types of anxiety. b. It will also be nice to use a figure to recap a few interesting examples of original eye-tracking studies. Such a figure might be a powerful way to demonstrate how eye-tracking data meets the expectation of a dimensional approach to diagnosis and clinical assessment. 8. Page 24, the second paragraph, "In summary all anxiety disorders exhibit..." Does this summary reflect the incongruent findings in PD and lack of research in OCD as discussed earlier? 9. Page 24, the third and fourth paragraphs. The two paragraphs do not seem to transition very well from the earlier paragraphs. It

seems to the reviewer that the purpose of these two paragraphs is to provide specific examples in which HRV is used as a biomarker (or endpoint) in clinical trials assessing cognitive behavioral therapies. Is so, some adjustments in the wording may help integrate these examples into the discussion. 10. Page 26, statements "To do so, large scale studies with diverse populations comprised of clinical and healthy participants are needed. This requires funding and cooperative research relationships on a large scale. To this end, we exhort institutions to secure grants and other funding for this imperative research." As complementary efforts, pharmaceutical and digital therapeutic companies should be encouraged to file IND clinical plans describing biobehavioral measures as endpoints. If not primary points, secondary endpoints from multiple trials should also be informative. It might also be nice to have a brief discussion on whether FDA and EMA are encouraging biobehavioral measures in clinical trials for anxiety disorders.

PEER-REVIEW REPORT

Name of journal: World Journal of Psychiatry

Manuscript NO: 34110

Title: Biobehavioral assessment of the anxiety disorders: Current progress and future directions

Reviewer's code: 02445209

Reviewer's country: Czech

Science editor: Fang-Fang Ji

Date sent for review: 2017-04-14

Date reviewed: 2017-04-25

| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|--|--|--|---|
| <input checked="" type="checkbox"/> Grade A: Excellent | <input checked="" type="checkbox"/> Grade A: Priority publishing | Google Search: | <input type="checkbox"/> Accept |
| <input type="checkbox"/> Grade B: Very good | <input type="checkbox"/> Grade B: Minor language polishing | <input type="checkbox"/> The same title | <input checked="" type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C: Good | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> Duplicate publication | <input type="checkbox"/> Rejection |
| <input type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade D: Rejected | <input checked="" type="checkbox"/> No | <input type="checkbox"/> Minor revision |
| <input type="checkbox"/> Grade E: Poor | | BPG Search: | <input type="checkbox"/> Major revision |
| | | <input type="checkbox"/> The same title | |
| | | <input type="checkbox"/> Duplicate publication | |
| | | <input type="checkbox"/> Plagiarism | |
| | | <input checked="" type="checkbox"/> No | |

COMMENTS TO AUTHORS

Dear Authors, I do not have any negative comment on your manuscript, I like it. It may shift our understanding of anxiety disorders and their biomarkers further. The reviewer

PEER-REVIEW REPORT

Name of journal: World Journal of Psychiatry

Manuscript NO: 34110

Title: Biobehavioral assessment of the anxiety disorders: Current progress and future directions

Reviewer's code: 02445374

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| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|---|--|--|--|
| <input type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing | Google Search: | <input checked="" type="checkbox"/> [Y] Accept |
| <input checked="" type="checkbox"/> [Y] Grade B: Very good | <input checked="" type="checkbox"/> [Y] Grade B: Minor language polishing | <input type="checkbox"/> The same title | <input type="checkbox"/> [] High priority for publication |
| <input type="checkbox"/> Grade C: Good | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> Duplicate publication | <input type="checkbox"/> [] Rejection |
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| <input type="checkbox"/> Grade E: Poor | | BPG Search: | <input type="checkbox"/> [] Major revision |
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| | | <input type="checkbox"/> Duplicate publication | |
| | | <input type="checkbox"/> Plagiarism | |
| | | <input checked="" type="checkbox"/> [Y] No | |

COMMENTS TO AUTHORS

Excellent review of eye-tracking and electrocardiogram data and their use in diagnosing anxiety disorders.

PEER-REVIEW REPORT

Name of journal: World Journal of Psychiatry

Manuscript NO: 34110

Title: Biobehavioral assessment of the anxiety disorders: Current progress and future directions

Reviewer's code: 02445261

Reviewer's country: Italy

Science editor: Fang-Fang Ji

Date sent for review: 2017-04-14

Date reviewed: 2017-04-26

| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|---|---|--|--|
| <input type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing | Google Search: | <input type="checkbox"/> Accept |
| <input type="checkbox"/> Grade B: Very good | <input checked="" type="checkbox"/> Grade B: Minor language polishing | <input type="checkbox"/> The same title | <input type="checkbox"/> High priority for publication |
| <input checked="" type="checkbox"/> Grade C: Good | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> Duplicate publication | <input type="checkbox"/> Rejection |
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| | | <input type="checkbox"/> Duplicate publication | |
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| | | <input checked="" type="checkbox"/> No | |

COMMENTS TO AUTHORS

This is, in summary, an interesting review paper aimed to summarize the current state of the art about recent technological advances that may enable practitioners to use objective, biobehavioral measures of Anxiety Disorders assessment. The authors stated that eye-tracking devices are uniquely capable of providing data that can be used to differentially diagnose anxiety disorders from both other commonly comorbid and misdiagnosed disorders. They also added that both eye-tracking and electrocardiogram devices are able to provide change-sensitive assessment information. In addition, it has been reported that the use of these biobehavioral devices would supply an objective, dimensional component to the current categorical diagnostic assessment system. The authors concluded that this area of research could revolutionize diagnostic and ongoing assessment practices together with bringing the field of diagnosis out of the 20th century. The authors may find as follows my main comments/suggestions. First, throughout the Introduction section, the authors expressed many correct and critical

beliefs/assumptions regarding our currently available classification systems but they arrived in my opinion too late to propose the inclusion of one/more standardized biobehavioral methods of assessment. While the proposed background is coherent and logically proposed, the key solution of the mentioned problems has been expressed really too late. Overall, i suggest to reduce the whole length of this section and delete the redundant statements. Conversely, when the biobehavioral approach has been mentioned, here more details/suggestions may be added for the general readership. Moreover, within the “anxiety and related disorders” section, the authors could also present the issue of “specifiers” that introduced in DSM-5 some at risk dimensions related to the common categorical entities and may be useful in order to help clinicians to more appropriately manage the enhanced severity of some disorders subtypes. In addition, what the authors believe regarding nonadherence to treatment in patients with anxiety disorders? Nonadherence to treatment may affect motivation and the level of physical activity and is predictive of negative outcomes such as high rates of recurrence/relapse, hospitalization, functional impairment and suicide. The identification of the most relevant predictors of nonadherence in the clinical practice may provide clinicians with a guide to recognize subjects at risk for nonadherence. In order to address this issue, i suggest to cite and discuss the systematic review of Pompili and colleagues which has been published on Expert Rev Neurother in 2013. Furthermore, i believe that some topics such as the overlap between anxiety disorders and attention-deficit/hyperactivity disorder (ADHD) may be redundant and could be deleted by the main text. The authors should insert a specific rationale regarding the description of this comorbidity; alternatively, the topic needs to be removed. Similarly, when the authors stated that some of the deficits experienced by ADHD sufferers can be seen using eye-tracking methods. The mentioned sentence may be deleted by the mentioned manuscript. Importantly, when they also referred to the existence of some physiological markers such as pupil dilation, eye-movements, and fixations concerning eye-tracking technology, they should cite and discuss the biomarker nature of these biological indicators. Here, one or more citations are needed to support the proposed assumption. Similarly, when the authors mentioned the rapid breathing, suppressed digestive processing, pupil dilation, endorphin release, heart palpitations, and reflex acceleration regarding the involvement of the autonomic nervous system in the anxiety related disorders. Notably, the most relevant shortcomings/limitations related to the use of eye tracking to assess/diagnose the different types of anxiety disorders need to be extensively reported throughout the main text. Also, some statements such as: “the future of psychotherapy should rely on the interaction between basic science, technological advancements, and clinical practice” are too vague and need to be more deeply developed. How, specifically, the authors believe to the interaction between basic science, technological advancements, and clinical practice for psychotherapy? Finally,



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what is the take-home message of this manuscript? Here, some conclusive remarks need to be more clearly and extensively elucidated by the authors.

PEER-REVIEW REPORT

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| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|--------------------------|---|---------------------------|-------------------------------------|
| [Y] Grade A: Excellent | [Y] Grade A: Priority publishing | Google Search: | [] Accept |
| [] Grade B: Very good | [] Grade B: Minor language polishing | [] The same title | [Y] High priority for publication |
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| [] Grade D: Fair | [] Grade D: Rejected | [Y] No | [] Minor revision |
| [] Grade E: Poor | | BPG Search: | [] Major revision |
| | | [] The same title | |
| | | [] Duplicate publication | |
| | | [] Plagiarism | |
| | | [Y] No | |

COMMENTS TO AUTHORS

The article "Biobehavioral Assessment of the Anxiety Disorders: Current progress and future directions" I can recommend for a publication in WJP. The article is novel, informative and well structured.