

June 29, 2021

To: Rajesh R Tampi, MD

Editor-in-chief, World Journal of Psychiatry

Dear Professor Tampi,

On June 15, we received the peer-review report on our manuscript entitled "Mood, suicide, and the renin-angiotensin system" (Number ID: 03885497). We are now resubmitting the paper, after addressing the issues raised by the reviewers (please see below). We thank you, the reviewers, and the editorial office for the comments and the attention dispensed to our manuscript.

Sincerely,

Marsal Sanches, MD, PhD

Antonio L. Teixeira, MD, PhD

In response to reviewer 1:

Please, consider a different title for the manuscript, for example "Exploring the association between Renin-Angiotensin System and mood disorders/ suicide risk" Also, you should update your references.

We thank the reviewer for these comments. The title of the manuscript was changed slightly, following the reviewer's suggestion. We also added/replaced some of the references with more updated ones, as recommended. Some of the older references, however, could not be updated, as they contained original data that were critical for the present review.

In response to reviewer 2:

This mini-review provides a comprehensive description of the researchers' findings of the renin-angiotensin-aldosterone system in mood and suicide. It is a good review article. Based on the current research, the relationship between RAS and suicide cannot be determined. The biomarkers of depression and suicide are a hot spot in the current study. This review provides researchers with a clue.

We thank the reviewer for their thoughtful comments and nice words.

In response to reviewer 3:

The mood disorders section deals only with depression. Mania does not appear. Schizophrenia should not be included in this section. The suicide section is superficial and lacks analysis.

We thank the reviewer for these comments. We updated the mood disorders section and added one paragraph containing information about the possible involvement of RAS in mania (Page 5, last paragraph). Please notice that the evidence in that regards is much scunter than the one related to RAS and depression. The schizophrenia mention was included in that section just for purposes of illustrating the role of the RAS in other neuropsychiatric conditions, in addition to mood disorders. Nevertheless, following the reviewer's suggestion, we removed that mention from the mood disorders section. As for the suicide section, we respect the reviewer's comment. Given the nature of the present paper (mini-review) we did not go into too much deepness in terms of critically analyzing the available evidence and specifically stated that such analysis would be addressed in the discussion section. We agree a deeper analysis of the presented would be of interest but it would be out of the scope of the present work.