Author’s response to reviews

Title: THE CYTOKINE PROFILE OF WOMEN WITH SEVERE ANXIETY AND DEPRESSION DURING PREGNANCY

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Version: 2 Date: 16 Jan 2019

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Response to reviewers’ comments

Technical Comments:

1. On the title page, please include the email addresses for all authors. The corresponding author should still be indicated. Please also ensure these email addresses match the email addresses provided in the editorial manager system.
This information has been included in the revised version of our manuscript.

2. For all abbreviations used in the text, these should be defined in the text at first use, and a list of abbreviations should be provided after the Conclusions in the main manuscript.

As shown, abbreviations have been included in the manuscript, a list of them has been provided after Conclusions.

3. Please add the heading "Consent to publish" to the Declarations section. If your manuscript does not contain data from any individual person, please state “Not applicable” in this section.

We have added “Consent to publish”. It was Not applicable.

4. Please include 'Funding' under the Declarations. Under the heading "Funding", please declare the role of the funding body in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

The role of funding was included.

Reviewer reports:

Michele Okun (Reviewer 1): I very much like the topic, but the revisions are not sufficient.

In the abstract, an updated statistical method is not there.

The updated statistical analysis was included in the Abstract.

It is stated twice that women signed informed consent.

This information was corrected.

In response to the 2nd reviewer, it does not appear that more advanced statistical analyses were performed even though they stated they did in the response. Correlations are not sufficient to answer the hypotheses.
As shown, in the amended version of our manuscript, we performed the following statistical analysis: Unpaired t-test with Welch corrections and pos hoc Tukey test, which are described in methods and in the result sections. As required by the other reviewer, we constructed a model using the group as independent variable, instead of correlating variables among the distinct divided groups.

Did the authors examine women only in the third trimester as it is known that cytokines differ greatly between 2nd and 3rd trimesters? Since the average was 36 weeks, this might be something to consider.

As you mention, cytokine profile significantly changes between the 2nd and 3rd trimesters. As shown the cytokine profile was assayed during the third trimester of pregnancy (27-41 gwk), albeit few participants (n=4) with 20-26 gwk were included in the study, their cytokine profile did not differ from that displayed by participants recruited in the third trimester of pregnancy.

The methods and results are still not clearly written. It is improved from the initial submission.

We have checked and modified the Methods and Results sections in the present version of the manuscript.

So the ratio of pro- to anti appears to be important. It is not clear if the authors looked at the ratio. If PI cytokines go up and AI cytokines go up then one can speculate that there is not risk as the ratio has not changed.

The ratio PI/AI cytokines is very relevant. We analyzed it as suggested, and the data obtained have been included in the body of the manuscript, as described in results and discussion sections.

Linnea Karlsson (Reviewer 2): The authors have thoroughly revised the paper according to reviewer's suggestions. The manuscript has clearly benefited from the revisions. I especially appreciate the Figures including also the control group and the inclusion of more clearly defined hypotheses vs. the first draft.

After the revisions, however, the English language seems to need assistance and I suggest language editing, but this is maybe ultimately for the Editor/Journal to decide.

English was reviewed again, and several modifications were made throughout the text.
One additional minor issue is that I do not understand why the groups are labeled as the column titles in Table 1 - they should be presented in lines but not additionally in the columns?

As depicted in the amended version of the manuscript, Table 1 has been corrected, as suggested.