Reviewer’s report

Title: Spider phobia is associated with decreased left amygdala volume

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Reviewer: Cindy Eckart

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The manuscript “Spider phobia is associated with decreased left amygdala volume” investigates potential structural alterations in the amygdalae of 20 female subjects suffering from spider phobia in comparison to 20 female controls. In doing so, a significant volume reduction was revealed in the left (but not the right) amygdala of the patient group. Furthermore, the volume of the left amygdala was correlated to the severity of spider phobia symptoms. The manuscript is interesting and well written and provides a comprehensible rationale arguing for structural alterations in the amygdala of spider phobic patients.

Major Compulsory Revisions:

General:

1. The subject of the manuscript (volume changes in the amygdalae of spider phobic patients) is clearly defined (what I would see as a major strength of the paper). However, in light of this clear topic, the introduction to and discussion of the results seems partly too long and detailed – in my opinion, the manuscript would improve substantially if you would shorten these parts to provide a clearer rationale

2. I have no experience with the SPQ; however, you mention that the cut-off for healthy controls was at a score of 21; however, the mean symptom severity in the patient group was just slightly higher (21.55)? Does that mean that symptom severity in the patients was particularly low in this sample? If yes, please discuss this issue shortly in the manuscript

3. In the “comments” you mention that you provided some explanation why the STAI trait was only evaluated in the patient group; however, I was not able to find this section in the manuscript? I apologize if I should have skipped it by accident

Statistics:

1. I was kind of confused concerning the statistical comparison of amygdala volumes: in the method section, you mention that a repeated measurement ANCOVA has been calculated (what would indeed be the most suitable statistical model); however, later you provide separate F-values for the left and right hemisphere? Could you please provide full information about statistical parameters (main effects of group and hemisphere, interaction group x hemisphere and maybe for the covariates as well)?
2. I apologize, but I did not understand your regression models properly: were they corrected for age and BMI? You mention that the decrease of amygdala volume was independent of age and BMI. However, it seems as if separate regression models have been calculated to show this? And what do you mean with ‘decrease of left amygdala’ – has a difference measure, e.g. deviation from the mean, been calculated?
3. Please provide a figure illustrating the association between left/right amygdala volume and the SPQ.
4. The ‘nearly’ statistical trend towards an association between amygdala volume and disease duration is really marginal and might have been the result of the many regression models that have been calculated.

Minor Essential Revisions:

1. Has the data been collected within a larger project (what would e.g. explain the effort of scanning all subjects in the luteal phase of their menstrual cycle)? If yes, a short sentence describing the scope of this project would be valuable.
2. Could you please provide some more information (possible score ranges, clinical cut-offs etc.) describing the questionnaires?
3. How was the statistical comparison of the STAI state (pre vs. post between groups) calculated? With separate t-tests? In my opinion, calculating a 2 x 2 ANOVA (pre/post as within- and group as between-subjects factor) would be the more suitable model.

Minor issues not for publication:

1. On page 8 the date is missing in the reference of Patenaude et al.
2. On page 6 you refer to a “case report of a patient”; this might have been introduced by mistake?
3. Page 9: the abbreviation AMV should be introduced.
4. In figure 2 titles (left/right amygdala) would be helpful.

Level of interest: An article of importance in its field.

Quality of written English: Acceptable.

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.