Author’s response to reviews

Title: Spider phobia is associated with decreased left amygdala volume: a cross-sectional study

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Version: 6 Date: 17 January 2013

Author’s response to reviews: see over
Bern, January 14th, 2013

Dear Editors,

Thank you very much for considering our manuscript for publication in BMC Psychiatry. We also thank the reviewers for their very constructive and helpful comments. The new data are included in the paper and also all other points of the reviewers have been addressed. Please find below the precise manner in which we have dealt with each of the reviewer’s comments.

We hope that you find the revised version of the manuscript acceptable for publication in BMC Psychiatry.

Sincerely,

Melanie Fisler

Reviewer 1

We thank Reviewer 1 for the constructive and helpful comments. As requested from Cindy Eckart the following changes were made:

General
1. Rationale: As the introduction and discussion section seemed to long, we shortened it, in order to reduce complexity and to provide a clearer rationale.

2. Diagnosis / SPQ: Because this data has been collected within a larger project (which included also an image task where pictures of spiders were presented), we excluded those patients who could not keep still when facing pictures of spiders. We did this in order to prevent large motion artifacts. Thus, the mean symptom severity in patients relatively near by the cut-off point of the questionnaire. We included this explanation in the methods section. Primar diagnosis was based on the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV). Specifically, we used a computer-based structured clinical interview (DIA-X) which is based on the Composite International Diagnostic Interview (CIDI). The German version of the Spider Phobia Questionnaire (SPQ) was further used to assess fear of spiders in the patient and control group. In this measurement patients showed significantly more spider phobic symptoms compared to control subjects (SP MEAN = 21.44 / Control MEAN = 6.1).

3. Trait-Anxiety: We mentioned in the limitations section, that STAI-state and trait should be measured in both groups. The Spielberger STAI-state was used before and after the MR-scan.
Due to the image task containing spider pictures we hypothesized that spider phobic patients 
show higher state-anxiety before the MR-scan due to anticipatory anxiety – but the groups 
should not differ anymore after the MR-scan. Based on the existing literature we did not 
hypothesize any difference in trait-anxiety between patients with spider phobia compared to 
control subjects.

Statistics:
1. Left / right hemisphere: We apologize for mistakes in the description of the statistical test. 
Because we were interested on two outcome measures (left/right amygdala) with one 
predictor, we chose a multivariate ANCOVA analysis which is the method of choice for two 
continuous outcome variables and one categorical predictor variable (as we had no repeated 
measure within subjects). Therefore, separate F-values are reported. We additionally added 
the statistical parameters for the covariates.

2. Regression: There were separate regressions computed for the covariates, this was added in 
the statistics session. The expression “decrease of left amygdala volume” is misleading. It is 
meant that the patient group has smaller left amygdala (mean). I changed this expression in 
both the statistics section and the abstract.

3. SPQ and Amygdala: A third figure is added, showing the relation between left/right amygdala 
and SPQ score.

4. Trend duration of illness: We agree with the reviewer that this nearly trend is really marginal, 
so we cropped it.

Minor Essential Revisions:
1. Luteal phase: This data actually has been collected within a larger project, focusing on the 
effects of cortisol on brain functions. Because the menstrual cycle has an influence on 
cortisol levels all female participants were tested in the luteal phase. Nevertheless, there’s a 
study providing evidence that the amygdala underlies volume changes in female over their 
menstrual cycle. Both explanations were added into the manuscript.

2. Questionnaires: More information about the questionnaires is provided.

3. ANOVA STAI-state: The statistical comparison was calculated by t-tests. We agree that a 2x2 
ANOVA is more suitable for this comparison, therefore we substituted these results with the 
parameters of the ANOVA analysis.

Minor issues not for publications: are all set

Reviewer 2

We thank reviewer 2 for the supportive and constructive comments and made the following changes:

1. Questionnaires: The procedure is justified by the following references: As explained above, 
diagnosis was based on the Diagnostic and Statistical Manual of Mental Disorders, fourth 
edition (DSM-IV). Specifically, we used a computer-based structured clinical interview (DIA-X) 
which is based on the Composite International Diagnostic Interview (CIDI). The German 
version of the Spider Phobia Questionnaire (SPQ) was further used to assess fear of spiders in 
the patient and control group and to show that the two samples differ regarding spider
phobic symptoms. SKID-II questionnaire was only assessed for the patient group. SCL-90-R was used as short screening to exclude Axis-I disorders in the control subjects. We analyzed FEE results only among patients, because we wanted to exclude disgust sensitivity as a potential confounder that could explain the smaller amygdala in patients. We changed it now, so that the result of the whole group is provided. The different assessments are added to the limitations section.

2. ANCOVA: There was a mistake in the explanation; we did a MANCOVA with left and right amygdala volume as outcome measures and group as predictor. This is now corrected. Furthermore, the assumption of homogeneity of variances is now mentioned.