Author's response to reviews

**Title:** Internet-delivered attention training in individuals with social anxiety disorder - a double blind randomized controlled trial

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Thomas Ehring  
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Internet-delivered attention training in individuals with social anxiety disorder - a double blind randomized controlled trial

[Response to Reviewers]

Dear Dr. Ehring,

Attached please find an explanation of our responses with the places in the document where the changes have been made indicated. These refer to the version we have submitted with all changes indicated in track changes. In addition we have made a few minor changes to the wording not in direct response to the reviewer comments to improve readability. Also, we have added a statement on competing interests stating that one of the authors is involved in a company that sells CBM paradigms. We agree that the requested changes have improved the clarity and overall quality of the publication.

We thank you in advance for your consideration of this revised manuscript for publication in BMC Psychiatry.

Best regards,

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Reviewer 1

Minor essential revision

1. In the section, "Change in Attention Bias (p.10), the authors report a measure of attention bias and they write that they followed the procedure of the Amir et al. study. However, Amir et al. included an independent measure of attention bias at pre- and post assessment (a modified version of the Posner paradigm). As far as I understand it, the authors in this study did not include such an independent measure. Instead, they estimated the attention bias from performance data in the training/treatment sessions. I do not understand how the attention bias can be estimated this way because in the treatment condition the probe was always presented at the location of the neutral face. Thus, as far as I understand it, there is no way to measure a possible attention bias away from threat (since the probe never appeared in the position of the disgust face). This should be clarified, or this section should be dropped.

Response:

We used a measure of bias reported by Amir, Taylor, & Donohue (2011) where bias was calculated by subtracting response latencies of trials where the probe preplaced a neutral face of a disgust-neutral face pair from trial where both faces were neutral. This bias has also been used by other investigator to index disengagement (Koster et al 2006).


Discretionary revision

2. p.3: "The idea behind the treatment is the notion that cognitive biases cause pathological anxiety and that a treatment that targets the subcortical processes might be an effective treatment." Please check if "subcortical" is the right term here ("cortical" processes may also be involved; in short, I would not refer to brain structures here)

Response:

We agree with the comment and have deleted the sentence. (Lines 61-63)
Reviewer 2

Minor essential revisions

1) Method section, Treatment and Placebo paragraph: Some information regarding the training is missing. It is explained that participants receive 160 trials in each session and 128 of those trials contained a neutral and disgust face with the probe appearing at the location of the neutral face. Please explain what happens in the remaining 32 trials.

Response:
The remaining 32 are “neutral-neutral”. To clarify this we had added the following: “The remaining 32 trials were neutral-neutral with the probe randomly presented at the top/bottom”. (Lines 160-161)

2) Are the same faces used in every session, or do they receive new faces every session?

Response:
We have added the following text: “There are a total of 8 persons showing 2 different facial expressions; 4 male and 4 female showing disgust or neutral”. (Lines 155-156)

3) Results section: Second sentence; please describe in more detail the conducted statistical analysis (a 2 (Group) x 8 (Time) Repeated Measures ANOVA?)

Response:
We have changed the sentence to the following in order to make it clearer: “We submitted the participants’ performance on the Attention Task during each session to a 2 × 8 (Group [treatment, control] × Time [session 1-8]) analysis of variance (ANOVA).” (Lines 230-232)

4) Change in Attention bias paragraph; please explain how the attentional bias score was calculated.

Response:
We used a measure of bias reported by Amir, Taylor, and Donohue (2011) where bias was calculated by subtracting response latencies of trials where the probe preplaced a neutral face of a disgust-neutral face pair from trial where both faces were neutral. This bias has also been used by other investigator to index disengagement (Koster 2006).


We have added the following sentence: Change in attention bias was subsequently calculated by subtracting response latencies of trials where the probe preplaced a neutral face of a disgust-neutral face
pair from trial where both faces were neutral. This bias has also been used by other investigator to index disengagement [43, 44](Lines 224-227)

5) Change in Attention bias paragraph; a correlation was calculated between the post-training bias score and change in LSAS-SR scores, however it seems that a correlation between change in attention bias and change in LSAS-SR scores would be more informative and more consistent with your hypothesis.

Response:
Following this reviewers suggestion, we calculated a correlation between session 1 bias score and change in LSAS. We added the following text: “This correlation was only significant in the active group (r = 0.32, p < 0.05 active ; r = -0.14, p = 0.37 placebo group.” (Lines 238-240)

Discretionary Revisions
6) Procedure and Design: I wondered how written informed consent was obtained, as data was collected via Internet.

Response:
Written informed consent was collected via surface mail. The text was altered as follows: “The study protocol was approved by the regional ethics committee, and written informed consent was obtained from all participants by surface mail.” (Line 172)
Reviewer 3

Major Compulsory Revisions

Several substantial points of improvement to the manuscript: -

1) The authors should conduct and report one or more post hoc analyses in addition to the intent to treat main analysis. This is an accepted addition that can provide more illuminating information for future studies, around factors that may improve chances of later success. As a minimum they should look at a) the dose-response relationship – do those receiving most training trials improve most? (clearly there is considerable information on exact number of trials received as well as sessions) - and
b) predictors of success – eg starting attentional bias, or some proxy for it and perhaps other individual differences (eg continuous measures of severity). Although both are mentioned in the text, they should be examined quantitatively.

Response:

a) We agree that the suggested additional analysis could potentially reveal important information. Unfortunately, the dataset does not permit such an analysis. Given that almost all (74 of the 79) participants completed all 8 training sessions, there is not enough variance in amount of training to make inferences. Out of a maximum 8 training sessions the mean number was 7.8. The range of the minority that did not complete all training sessions was 3-6 in total.

We have added the following sentence: “Most participants (74 of 79) completed all 8 training session for a mean of 7.8.” (Line 195)

b) We have added the text given in reply to Reviewer 2, Comment 5):
“\textit{This correlation was only significant in the active group (r = 0.32, p < 0.05 active ; r = -0.14, p = 0.37 placebo group.}” (Lines 238-240)

2) More information should be contained in the introduction regarding the cognitive mechanistic rationale behind CBM (attention) and reference made to the large body of experimental manipulation studies that have led to it, and before that the decades of experimental work examining the naturally occurring prevalence of attentional biases. Demonstrating this linkage between basic research and their translational application is contextually important and of benefit to both domains of research.

Response:

We have added the following text with references: “\textit{There is an extensive literature on the link between attention and anxiety} [1] \textit{and this link appears to be causal} [4, 45].” (Lines 51-52)

3) The analysis of change in attention bias (p10) is helpful and important, however the authors should also add results and discussion of correlations involving outcome measures and a) change in bias (ie pre to post bias scores or some proxy for it) and b) starting bias (see first point, above). Just looking at post-intervention bias leaves a lot unexamined.

Response:

We have added the text given in reply to Reviewer 2, Comment 5):
“\textit{This correlation was only significant in the active group (r = 0.32, p < 0.05 active ; r = -0.14, p = 0.37 placebo group.}” (Lines 238-240)
4) Consider the implications of the fact that the intervention (and those before it) only train attention away from negativity. Consider added benefits - in terms of efficacy - of additionally training attention towards positivity. Rather than training what is essentially avoidance, would it be an improvement to train active selection of positive mood-supporting information? This much-discussed point has received little coverage in the literature, but deserves it.

Response:

We agree and have added the following sentence to the discussion supported by this publication: “It should be noted that the intervention employed only trains attention away from negativity. There could be added benefits of instead of training what is essentially avoidance, to also or instead train active selection of positive mood-supporting information [42].” (Lines 296-299)


Minor Essential Revisions

5) Paragraph 2 page 3 line 5 refers to “subcortical processes” giving a misleading impression - there is no clear evidence that CBM is targeting subcortical processes. The fMRI attentional training study of Harmer and colleagues that the authors may be thinking of has many flaws, in the opinion of some. This reference to neural substrates should simply be removed.

Response:

This issue was also made by Reviewer #1 (comment 2) and we have deleted the sentence.

6) P13, 5 lines from bottom –the reference to disengagement should be removed since to date it is far from clear whether this effect replicates in clinical disorders. If the authors strongly disagree then strong evidence should be cited – ie reports of disengagement effects in clinical (not subclinical) samples. It is my understanding that there is only 1 such study at present together with unpublished replication failures. The point is not necessary for the present paper.

Response:

We agree and have deleted the sentence. (Lines 299-300)

7) P14 last line. Rather than ‘to be altered’ which implies the authors are problematically concluding on the null hypothesis (rather than simply reporting their data), they might say ‘further investigation’.

Response:

We have changed the sentence accordingly: “We conclude that attention bias modification may need to be further investigated before dissemination for the Internet.” (Line 304)

8) P12 line 4 – trails -> trials

Response:

We have made the correction. (Line 258)
9) P9 – please explain what a ‘first order autoregressive covariance structure’ is and what benefit it conveys for the analysis. How does it handle missing data and why is that better than other methods?

Response:

We have added the following: “The first-order autoregressive covariance structure has the property that observations on the same subject that are closer in time are more highly correlated than measurements at times that are farther apart.” (Lines 189-191)

10) P8 – by whom was the follow up conducted?

Response:

We have added the following sentence (as the last in the “procedure and design” heading) to clarify that the follow-up was done online by the respective participant:

“Finally, to check if the effects were stable over time a follow-up was conducted 4 months after the post-treatment assessment, conducted online by the respective participant.” (Line 180)

11) P3 last line criteria of -> criteria for

Response:

The word has been changed. (Line 72)

12) In line with good practice in psychiatric journals, always report absolute Ns alongside %s

Response:

The only place where we have not reported the absolute numbers is in the following, where it would not add clarity but only more numbers since the total numbers are given:

“The CGI-I rating at post-treatment (n = 79) showed the following non-significant results for the treatment group vs. placebo group: very much improved (5.0% vs. 2.6%), much improved (2.5% vs. 20.5%), small improvement (32.5% vs. 35.9%), unchanged (57.5% vs. 38.5%) and small deterioration (2.5% vs. 2.6%) (chi-2(4, N=79) = 7.5; p = .112).”

13) P3 para 2 – it is an overstatement that ABM is a computerised ‘treatment’ – it is arguably not established as such. Add a qualifier such as ‘potential’ or ‘putative’.

Response:

The sentence has been changed accordingly and now reads as follows: “Attention bias modification is a potentially effective computerized treatment that most often has been delivered in a laboratory setting with subclinical samples” (Line 59)

Acknowledgement

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