Author’s response to reviews

Title: Effects of Attentional Bias Modification on Residual Symptoms in depression. A Randomized Controlled Trial.

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Dear Editor

The following rebuttal letter address the remaining point raised from one of the reviewers, and describe exactly what amendments have been made to the manuscript text and where these can be viewed (line, page).

Reviewer comments: I'm afraid my main concern regarding Figure 1 is still not addressed, and I think there's no way to resolve this unless the manuscript is substantially rewritten to tell the story differently.

Response: We apologize that we have not addressed this concern properly. We notice that the reviewers concern is regarding results related to Figure 1., and particularly that the reported effects show a negative change in the placebo group. Here, we argue that a fundamental premise for an RCT is to compare the intervention to whatever happens in the control group. The
primary, and preregistered, outcome shows an effect of the intervention for clinician rated symptoms as shown by the interaction between time (pre-post symptoms) and intervention. We have provided potential explanations and solutions in the discussion section (line 345-351, page 8).

The story is in line with the results, and demonstrates that AB is associated with HDRS change, and a post-hoc combined factor repeated ANOVA shows that this association is driven by the ABM group (line 294-301, page 7), meaning that the a different story that claims that “AB change may be a useful clinical measure since it is sensitive to individual differences in HRSD”, as opposed to ABM as a treatment” is not supported by data. The main findings are now more explicit in the abstract (line 83-85, page 2) and conclusion (line 408-410, page 10).

Specifically, I previously mentioned that results from Figure 1. seems to be driven, in part, by increased HRSD in the control group. Upon a closer look at the Results section (and please correct me if I'm wrong), I think the authors have observed a significant interaction between time and ABM, but no significant post-hoc t-tests in either comparison? This suggests that the interaction is driven by effects from both directions (higher HRSD in control and lower HRSD in ABM), albeit nonsignificant in either way. I think this confusion can be avoided if all statistical comparisons are reported, as opposed to reporting only the significant ones.

Response: The repeated measure ANOVA shows that the changes (from pre-post, which is the time factor) differ between ABM and Placebo (time*intervention in repeated ANOVA) and accounts for both positive and negative changes (variance) within- and between groups. The only other factor in model is the main effect of time. The main effect of time is now added to HRSD analysis (as in BDI-II) and shows no general effect across groups (line 262-264, page 7).

There are no post-hoc t-tests in results, as time is the pre-post factor that interacts with the dichotomous ABM vs. placebo variable. There is therefore also no variable that distinguish e.g. symptom improvement from symptom worsening or combined factors that warrants post-hoc comparisons.

To address this, the authors did the post hoc sensitivity test to put the two groups on the same level. This is fine, but now the authors report a significant difference in HRSD between ABM and placebo (main effect), and no interaction anymore. Again, complete reporting of all statistical comparisons is suggested here. The data here (baseline at 7.5 for ABM and 7.2 for placebo, to 7.3 and 8.1 after two weeks) now really suggest an increase in HRSD in controls, and no effect of ABM.

Response: We apologize for the confusing wording in the sensitivity analysis and have corrected the sentence to: “… also showed a statistical significant difference (time) between ABM and the control condition in blinded clinician-rated symptoms as measured by the HRSD” in accordance with the suggestion from Reviewer 1. in the original reviewer reports. Hence, the statistical approach in the sensitivity analysis is identical to the ones in primary outcomes (line 270-271, page 7).
Since Figure 3 clearly shows that ABM works differently for everyone, and may even backfire for some patients, the key finding from this study for me is that "AB change may be a useful clinical measure since it is sensitive to individual differences in HRSD", as opposed to ABM as a treatment.

Response: We thank the reviewer for the opportunity to make this clearer. The results show that there is an association between AB and HRSD within the ABM group, but not within the placebo group (line 298-301, page 7). As the reviewer noticed, there is substantial variance within groups, and many patients show no change- or symptom worsening in both groups (line 298-301, page 7, and line 381-384, page 9).

We humbly hope that we fully understood the reviewers’ concretisations related to results presented in Figure 1. Complete reporting of all statistical comparisons conducted is now reported in the revised version of the manuscript (line 262-264, page 7).

Finally, we thank the reviewer for the extra comments that we think further clarified important aspects of the study.

Kind Regards

Prof. Nils Inge Landrø & Dr. Rune Jonassen