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Symptom severity moderates the outcome of attention bias modification for depression: An exploratory study

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ABSTRACT

A recent meta-analysis has questioned the relevance of attention bias modification (ABM) for depression outcomes. However, there might be patient characteristics not yet accounted for, that are relevant to the outcome. In the context of personalized treatment, the lack of moderator studies have limited the potential for matching ABM-treatment to individual patient characteristics. Subjects ($N = 301$) were randomly assigned 1:1 to receive either active or placebo Attention Bias Modification (ABM) twice daily for 14 days in a double-blind design (placebo $n = 148$; ABM $n = 153$). The outcome was change in symptoms based on the Hamilton Depression Rating Scale (HDRS). Moderator variables were self-reported depression (Beck Depression Inventory-II; BDI-II), anxiety (Beck Anxiety Inventory; BAI) and attentional bias (AB) assessed at baseline. This trial was registered with ClinicalTrials.gov, number NCT02658682. Only BAI (p for interaction = .01, Bootstrap 95% *CI* [0.046, 0.337]) moderated the effects of ABM on change in clinician rated depressive symptoms. Interactions were significant for BAI scores ≥8. The relative effect of the intervention increased with the highest symptom load. ABM was not effective in patients with the lowest symptom load. Future research should validate this finding and continue investigating moderators of the ABM-intervention to further enhance personalization of treatment to individual symptom characteristics.

1. Introduction

Attention bias modification (ABM) is a promising low-cost intervention for alleviating depression symptoms in clinical groups (Beevers et al., 2015; Jonassen et al., 2019; MacLeod and Mathews, 2012), as a mechanism-focused supplement to regular treatments (Blackwell, 2020). ABM-procedures aim at modifying a negative attentional bias through computerized interventions. Studies have found that this type of intervention, specifically targeting one of the casual neuropsychological contributors to the development and maintenance of depression (Chan et al., 2007; Hayward et al., 2005; MacLeod et al., 2002), leads to small, but statistically significant changes in depression symptoms (Beard et al., 2012; Hallion and Ruscio, 2011). However, more studies are needed before ABM becomes a useful treatment option for depression (Beevers et al., 2015).

Depression is associated with high comorbidity, and patients fulfilling the criteria for major depressive disorder often fulfill the criteria for anxiety disorders (Kessler et al., 1997). The etiological heterogeneity in depression might influence how well the intervention targets the patient's problems and whether the intervention is successful at alleviating depressive symptoms. This perspective is in line with the Lancet commission, advocating for personalization of treatment through

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optimizing "the most efficient and favorable response treatment based on individual's unique characteristics (…)" (Holmes et al., 2018, p. 103). Therefore, to focus on patient characteristics is central when investigating the efficiency of treatment. This suggests that we need to look for potential moderators of the ABM effect to pinpoint who will benefit the most from the intervention. Research shows that symptom severity is one of the most reliable predictors of depression course trajectories (Dinga et al., 2018). Hence, self-reported symptom severity could be such a characteristic, supported by studies suggesting that a comprehensive assessment of depression should include both clinician rating, as well as self-report measures, for predicting treatment outcome (Uher et al., 2012).

At current, there are no available moderator studies of patient characteristics in relation to the ABM intervention for depressive symptoms aimed at answering these questions. Primarily, studies of moderators have revolved around varying intervention characteristics moderating bias change, like type of stimuli, number of sessions, and stimuli placement (Beard et al., 2012). A review and meta-analysis of studies suggested that higher symptom level at baseline was associated with greater attentional bias change, but the research data at that time was too scarce to assess the effect of ABM on subjective symptom experiences (Beard et al., 2012). Another meta-analysis including various cognitive bias modification procedures, found that clinical status failed to moderate the effect of ABM on anxiety and depression symptoms (Hallion and Ruscio, 2011). However, this study did not aim to differentiate the effect of symptom severity within clinical groups. Baert and collegues (2010), on the other hand, found in two separate experiments that ABM led to reduction in depressive symptoms among a group of dysphoric students with moderate to severe symptoms of depression, while there was an increase in symptoms among in- and outpatients fulfilling the criteria for major depressive disorder. Their findings indicate that severity of depressive symptoms might moderate the outcome of ABM. However, they did not conduct a moderator analysis as such.

Drawing on studies from related fields of research, a meta-analysis on the effect of antidepressants showed that depression severity moderated treatment response (Fournier et al., 2010). They found that the magnitude of benefit was found to increase with depression severity. Considering that change in attentional bias has been suggested to be the corresponding neuropsychological mechanism for both antidepressant treatment and ABM (Godlewska and Harmer, 2020), this provide indication that symptom severity also might be of relevance to the treatment outcome after ABM. Moreover, research suggests that the primary effect of antidepressants are due to improvement in anxiety, which in longer term could be beneficial for reducing depressive symptoms (Duffy et al., 2019). This could potentially indicate that anxiety might influence the treatment effect of ABM.

The scarcity of available data has been a recurrent limitation to this field of research, and Fodor and collegues (2020) have, after conducting a network analysis of meta-analysis, called for more large-scale studies to reach conclusions regarding the effect of ABM on depression symptoms. In their analysis, including 85 trials, 65 ($n = 3897$) on anxiety and 20 ($n = 1116$) on depression, they found consistent, but small benefits for anxiety, however, insufficient evidence precluded conclusions for depression. Furthermore, the analysis indicated that there were large variances between trials, suggesting that there might exist subgroups that profit from ABM. In 2019, Jonassen and colleagues conducted the largest-to-date clinical trial on the effect of ABM on depression symptoms ($N = 321$). In a group of remitted depressed patient with residual symptoms, they found that two weeks of ABM compared to a placebo condition led to a statistically significant change in clinician-rated depression symptoms. A follow-up network analysis based on the same sample suggested that anxiety might play a central role in explaining the ABM-effect (Kraft et al., 2019). Thus, anxiety symptoms might be a promising candidate for moderating depression treatment outcome, as anxiety is one of the strongest predictors of depression relapse (Buckmann et al., 2018). Hence, if concurrent anxiety symptoms moderates the effect of ABM, this could inform treatment options for patients with comorbid disorders, which have been a patient group with less favorable treatment outcomes (Coplan et al., 2015).

Thus, in this study, with the aspirations of personalized treatment in mind (Holmes et al., 2018), we reanalyzed data from Jonassen et al. (2019), and examined whether self-reported symptom levels of anxiety and depression moderate the outcome from this computerized ABM intervention. Available evidence suggest that depressed individuals show heightened AB for negative information (Peckham et al., 2010) and that greater AB is associated with worsening over time (Disner et al., 2017). Therefore, we also examine whether baseline AB moderate treatment response to ABM.

The lack of moderator studies and conflicting findings (e.g. Baert et al., 2010) within this field of research makes it difficult to formulate a specific hypothesis regarding the potential role of symptom severity and AB as moderators. Hence, this study is exploratory, aiming at identifying whether severity of self-reported anxiety and depression symptoms and AB, all of which are associated with worsening of depression symptoms over time, moderate the outcome of ABM.

2. Methods

This is a reanalysis of data from a large-scale double-blind randomized clinical trial of ABM targeting depressive symptoms in patients with remitted depression (Jonassen et al., 2019). The moderators of this current paper (symptom severity measures and AB) were not specified when registering the trial, and is therefore considered exploratory.

2.1. Participants

The sample consists of 301 subjects aged 18–72. See Jonassen et al. (2019) for further details. All were formally diagnosed with the Mini international neuropsychiatric interview (M.I.N.I.; Sheehan et al., 2006) prior to inclusion, and all fulfilled the criteria for current or remitted Major depressive disorder (MDD) and have had more than one previous episode. The fact that 37 subjects with current MDD were included is a violation of the protocol, but since the study adhered to an intention-to-treat criterion they were included in the analysis.

In the sample, 84 subjects had ongoing anxiety disorders; PTSD (9), social phobia (31), agoraphobia (23), generalized anxiety disorder (18), panic disorder (26), and obsessive compulsive disorder (17). The numbers add up to more than 84, because some had more than one anxiety diagnosis (one anxiety disorder = 54; two anxiety disorders = 18; more than two anxiety disorders = 10). Seven subjects had missing data on comorbid anxiety disorder (2 in the placebo condition and 5 in the active ABM condition).

2.2. Randomization and masking

Between January 2015 and October 2016, subjects were included in the study An independent lab technician randomized the subjects according to a randomization list in a 1:1 ratio and programmed the laptops to deliver either ABM or placebo treatment, thereby ensuring that allocation was concealed from all both participants and researchers involved in screening and evaluation. Assignment to intervention condition was revealed only after the end of the data collection period in October 2016, making sure that the study was conducted in a double-blind manner.

2.3. Clinical scales

2.3.1. Hamilton Depression Rating Scale (HDRS)

This 21-item questionnaire is used by health professional in relation to a clinical interview with patients already being identified as suffering from depression. Its psychometric properties are good (Bagby et al., 2004). The HDRS is widely used in clinical trials assessing the

effectiveness of antidepressant medication. To ensure consistent rating criteria there were bi-weekly supervision meetings.

2.3.2. Beck Depression Inventory – II (BDI-II)

BDI-II is a self-report questionnaire assessing 21 groups of depressive symptoms and attitudes on a 4-point Likert scale, ranging from 0 to 3 (Beck et al., 1988b). The questionnaire is among the most used scale for assessing depression in clinical research. Cronbach's alpha of .917 suggests excellent reliability.

2.3.3. Beck Anxiety Inventory (BAI)

BAI is a 21-item self-report measure assessing severity of anxiety symptoms on a 4-point Likert scale ranging from zero ("not at all") to three ("severe"). The scale is developed to reliably discriminate anxiety from depression (Beck et al., 1988a). Cronbach's alpha of .918 suggests excellent reliability.

2.4. Attention bias modification procedure

The computerized ABM intervention was based on a dot-probe task, similar to the one used in the study by Browning and collegues (2012).

Stimuli were pairs of pictures showing different facial expressions; negative (anger, fear), positive (happy) and neutral. They were randomly presented vertically on the computer screen for either 500 ms or 1000 ms. In a total of 96 trials, the stimuli were presented in pairs, either positive - negative, positive - neutral, or negative -neutral. After stimuli presentation, one or two dots appeared, either in the upper or the lower location, and subjects were required to quickly and accurately indicate the number of presented dots by means of response buttons.

In the active condition, the dots were presented in the location of the picture presenting the most positive/least negative facial expression in 87% of the trials, whereas the dots appeared in the location of the most negative/least positive facial expression in only 13% of the trials. In the placebo condition, the dots appeared equally often in both the location of the most positive and most negative facial expression.

The intention behind the procedure, unbeknownst to the subjects, is to reinforce an attentional preference for more positive/less negative information, and thereby induce a shift in attentional bias from more negative information towards more positive information.

The subjects conducted 28 training sessions at home (twice daily for fourteen days) on study laptops provided by the research group.

2.5. Measurement of attentional bias (AB)

The AB assessment task was identical to a single session of the placebo-training task, but used novel face stimuli. AB was calculated as the difference in reaction time in milliseconds between trials in which the probe replaced the relatively more negative face vs. the more positive face ([(SUM (more positive face in upper screen position - locus of probe in lower screen position, more positive face in lower screen position, locus of probe upper screen position) – SUM (more positive face in upper screen position - locus of probe in upper screen position, more positive face in lower screen position-locus of probe in lower screen position)]/2). Hence, a more positive score reflects a greater bias towards the more positive stimuli.

2.6. Outcome

The main outcomes of the trial were changes in self-reported (BDI-II) and clinician-rated depression symptoms (HDRS). For this paper, significant interaction terms, indicative of a moderator effect of depression severity, anxiety severity, and attentional bias, on clinician-rated depression symptoms, respectively, are of interest.

2.7. Ethical considerations

The study was conducted in accordance with the Helsinki Declaration and the ethical principles for Nordic Psychologists, as issued by the Norwegian Psychological Association. The study was approved by the Regional committees for medical and health research ethics. All subjects gave their informed consent before taking part in the study.

2.8. Statistical analysis

All data were analyzed using SPSS 27.0 (IBM).

Differences in demographics and sample characteristics were investigated with Mann-Whitney *U* test for continuous variables and Pearson Chi-square test for dichotomous variables. Spearman's rho correlation was used for investigating relation between clinical and cognitive symptom variables.

To investigate the moderator role of depression symptoms, anxiety symptoms, and attentional bias, we conducted three different moderator analyses, all with clinician-rated depression (HDRS) as outcome. The assumptions for testing moderator effects, are the same as for OLS analysis. Outliers were investigated through Mahalanobis distance, Cook's distance, and Centered leverage distance, and deemed outlier if positive for two out of three of this indices. When change in HDRS was the outcome variable, this led to the exclusion of 11 cases on the BDI-II analysis, 21 cases in the BAI analysis, and 6 cases in the AB analysis. After exclusion of outliers, the data fulfilled the assumptions of normality of residuals, linearity, homogeneity, and homoscedasticity for all analysis.

Using the Process macro in SPSS (Hayes, 2017), which applies a linear regression model to the data, we tested whether the relationship between the focal predictor (ABM) and the outcome (change in HDRS from pre to post intervention) depends on the moderators (clinical and cognitive symptom severity). Hence, both main effects (ABM and symptom severity) and interaction effect were included in the model. However, to prevent suppressor effects, both symptom severity measures were not included in the same model, i.e. BDI-II was not included in the regression model of BAI as moderator, and vice versa. Main effects were included to prevent inflation of the interaction term. ABM was classified as 0 (placebo) and 1 (active). HDRS scores (pre intervention) was added as covariate, since higher scores has greater potential for change than lower scores. If the interaction terms (ABM x symptom to severity) were significant, additional follow-up analyses were conducted to facilitate interpretation of the results. Follow-up analyses consisted of estimating (probing) the effect of ABM on HDRS change at certain levels of symptom severity. Following recommendations by Hayes (2017), probing was conducted at 16th, 50th, and 84th percentiles (guaranteeing that the probed symptom levels were within the range of the data). The Johnson-Neyman technique, implemented in the Process macro (Hayes, 2017), was used to identify ranges of values of the moderator for which the interaction effect was significant. Non-parametric bootstrapping ($N = 5000$) was conducted to ensure robust estimates of the interaction effect.

The conceptual and statistical model of the moderator analyses is shown in Fig. 1.

3. Results

3.1. Demographics

Sample characteristics are summarized in Table 1. Correlation among clinical and cognitive symptom measures are presented in Table 2.

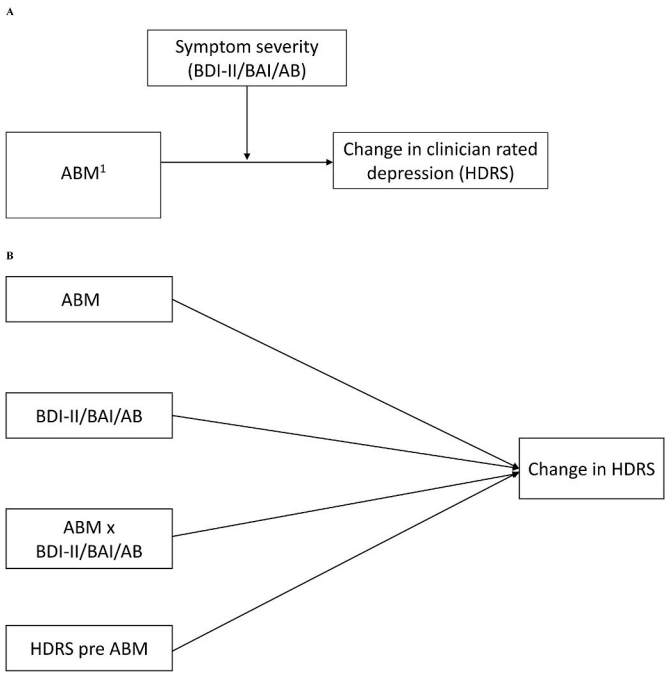

Fig. 1. Moderator model.
AB = attentional bias, ABM = Attention Bias Modification, BAI = Beck Anxiety Inventory, BDI-II = Beck Depression Inventory-II, HDRS = Hamilton Depression Rating Scale. [1] 0 = placebo, 1 = active.
*Note.***A** The conceptual relation between moderator (BDI-II/BAI/AB), predictor (ABM) and outcome (change in HDRS). **B** The statistical model of moderation with HDRS pre ABM as covariate.

Table 1
Demographic and Sample Characteristics (means (SD) or frequency).

	Placebo ($n = 148$)	ABM ($n = 153$)	p
Sex (females)	103	109	.75
Age	41.5 (13.6)	40.2 (12.7)	.40
Education level (ISCED)	5.9 (1.2)	6.0 (1.0)	.88
Current SSRI *(n)*	43	38	.49
HDRS pre ABM	8.3 (5.1)	9.3 (6.0)	.21
HDRS post ABM	8.7 (5.6)	8.4 (6.0)	.43
AB pre ABM *(ms)*	−1.2 (28.0)	−0.9 (28.2)	.95
Subjective symptoms at baseline:			
BDI-II	13.5 (9.7)	15.1 (10.6)	.23
BAI	9.1 (7.5)	9.7 (9.6)	.71
Current comorbid anxiety disorder *(n)*	41	43	.85
Compliance (%)[a]	80.0 (21.5)	83.4 (15.0)	.12

Note. AB = Attentional Bias, ABM = Attention Bias Modification, BAI = Beck Anxiety Inventory, BDI-II = Beck Depression Inventory-II, HDRS = Hamilton Depression Rating Scale, ISCED = International Standard Classification of Education, SSRI = Selective Serotonin Reuptake Inhibitors.
[a] Missing data for 7 subjects (2 in the placebo group and 5 in the ABM group).

Table 2
Correlations between symptom measures.

	1.	2.	3.	4.	5.
1. BDI-II	-				
2. BAI	.67**				
3. HDRS pre	.65**	.55**	–		
4. HDRS post	.60**	.52**	.64**	–	
5. AB	.03	.07	-.01	.08	–

Note. ** Correlation is significant at the 0.01 level.
AB = Attentional Bias, ABM = Attention Bias Modification, BAI = Beck Anxiety Inventory, BDI-II = Beck Depression Inventory-II, HDRS = Hamilton Depression Rating Scale.

3.2. Moderation analysis

3.2.1. Change in clinician rated depression

Coefficients from the moderator analyses are presented in Table 3.

Regarding the relationship between ABM condition and change in HDRS, BDI-II was not a significant moderator, F (4, 284) = 17.953, $p <$ .001, MSE = 16.473. R^2-change = 0.003, F (1, 284) = 1.136, p = .29. Bootstrapping 95% confidence interval for the coefficient of the interaction term was (−0.047, 0.157).

BAI was a significant moderator between ABM condition and change in HDRS, F (4, 274) = 17.991, $p <$ .001, MSE = 15.689. R^2change = 0.019, F (1, 294) = 6.684, p = .010, Bootstrapping 95% confidence interval for the coefficient of the interaction term was (0.046, 0.337). The difference in the slopes of the two regression lines (placebo vs. ABM) represents the interaction effect described in Table 3. The two regression lines converged at the lower end of the range of severity scores and the magnitude of the difference between the treatments increased with increasing anxiety severity prior to ABM-training. (See Fig. 2 for graphical display of the interaction). According to the Johnson-Neyman technique, the interaction was significant for scores of 8 and above. Follow-up analyses showed that the effect of the active ABM condition, compared to the placebo condition, was only present at the highest symptom level. At the highest symptom level, there is a difference of 1.85 HDRS points between the placebo condition and the active ABM condition. (See Table 4).

AB was not a significant moderator between ABM condition and change in HDRS, F (4, 290) = 13.544, $p <$ .001, MSE = 18.781. R^2change = 0.008, F (1, 290) = 2.636, p = .106, Bootstrapping 95% confidence interval for the coefficient of the interaction term was (−0.068, 0.007).

4. Discussion

Previous studies show that the effect of ABM on clinician rated depressive symptoms is small (Beard et al., 2012; Hallion and Ruscio, 2011). However, given the heterogeneity of depression it is pertinent to investigate whether patient characteristics moderate the outcome of the intervention. In this paper, we investigated moderators of ABM using data from the largest RCT study on ABM and depression symptoms conducted to date (Jonassen et al., 2019). Results showed that self-reported anxiety symptoms, but not depressive symptoms nor attentional bias, moderated the outcome of the ABM. Specifically, subjects whom had more profound anxiety symptoms prior to treatment demonstrated relatively better effect of the intervention. This study serves as in important first step in identifying characteristics that will promote personalization of ABM-training for depression symptoms.

The findings are in line with previously published studies from our group on the same sample, showing that ABM leads to symptom network changes involving reduced centrality of anxiety symptoms and negative thinking (Kraft et al., 2019). On the other hand, our results contradict the study of Baert et al. (2010), who found improvements after ABM in

Table 3
Moderation analysis of BAI on the effect of ABM.

			95% Confidence Interval			
	b	SE	Lower	Upper	t	p
Constant	−1.16	.61	−2.36	.05	−1.89	.059
ABM[a]	-.63	.75	−2.12	.85	-.84	.402
BAI	-.34	.06	-.45	-.22	−5.78	<.001
ABM x BAI	.19	.07	.05	.34	2.59	.010
HDRS pre ABM	.42	.06	.31	.54	7.46	<.001

Note. b – unstandardized coefficients. ABM = Attention Bias Modification, BAI = Beck Anxiety Inventory, HDRS = Hamilton Depression Rating Scale.
*p < .05, **p < .001.
[a] 0 = placebo, 1 = active.

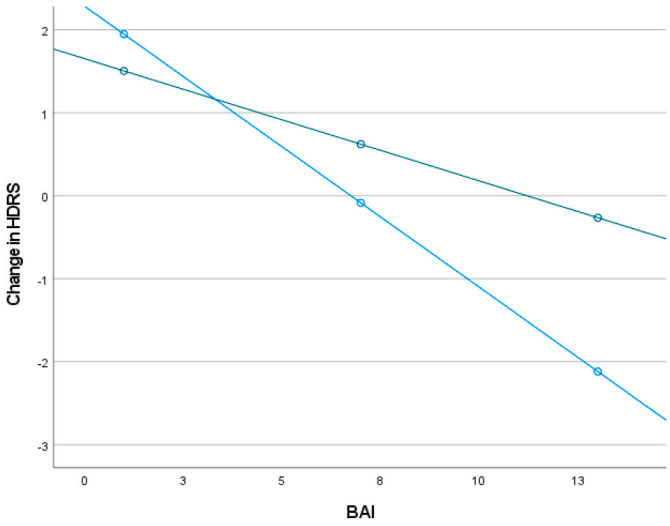

Fig. 2. BAI score as moderator for the effect of ABM with HDRS pre ABM as covariate = 8.78. Blue lines represent placebo, while the green line represents the active ABM condition. According to the Johnson-Neyman procedure, the interaction is significant at BAI score 8. Markers are placed at 15th, 50th, and 85th percentile. N = 279. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table 4
Conditional effect of ABM on change in HDRS at different values of the moderator.

			95% Confidence Interval			
Moderator level	*b*	SE	Lower	Upper	t	*p*
16th percentile = 1	-.44	.70	−1.82	.93	-.63	.52
50th percentile = 7	.71	.48	-.24	1.65	1.47	.14
86th percentile = 13	1.85	.61	.66	3.05	3.05	.003

Note. Post hoc probing of simple slopes at different values of BAI. *b* = unstandardized coefficients of the interaction term at different levels of the moderator. ABM = Attention Bias Modification, BAI = Beck Anxiety Inventory, HDRS = Hamilton Depression Rating Scale.

subjects with less severe depression symptoms, but worsening in patients with more severe depression symptoms. This could maybe be due to our sample had relatively mild depression symptoms, as the treatment context was secondary prevention. Hence, our sample could actually be more similar to the dysphoric sample in Baert's study than initially suggested. Moreover, only some subjects in our sample ($N = 27$) displayed severe symptoms (BDI-II score > 29), and of these 18 experienced a current episode of MDD. Future studies needs to clarify the role of ABM on full range symptom severity.

Also, both our sample and the dysphoric sample in the study of Beart and colleagues (2010) had high levels of concurrent anxiety symptoms. While our study used pictures of fearful or angry faces, the latter used sadness-related verbal stimuli for ABM. This might imply that improvement in depression symptomatology might be target in to different ways; either through alleviating mechanisms more relevant for anxiety (e.g., reduced threat monitoring) than depression, or vice versa. Attention bias towards threat is considered to play a causal role in the etiology and maintenance of anxiety disorders. This is manifested in threat monitoring where the individual automatically scans the environment for potential dangers. ABM paradigms applying threat related stimuli, like fearful and angry faces, can then decrease this tendency. Given that improvements in depression symptoms was driven by reduced anxiety mechanisms, this paradigm may have been suited to the current sample experiencing high levels of comorbid anxiety. This is in line with previous studies showing that the effect of ABM has been more convincing for anxiety symptoms compared to depression symptoms (MacLeod and Mathews, 2012).

While most subjects at inclusion had recovered from their depressive episode, about one-third fulfilled the diagnostic criteria for one or more ongoing anxiety disorders. When considering accepted cut-off values for the BAI (Beck et al., 1988a), the interaction was still significant at levels within the minimal range for anxiety. This suggests that ABM for depression may be particularly well suited for persons with concurrent anxiety and depression symptoms, and could therefore hold important promise as a transdiagnostic treatment option.

Our results speak to findings on antidepressant treatment effects and the neuropsychological explanation for this effect. Regarding symptom severity, a meta-analysis has shown that only patients with severe symptoms have substantial benefit of antidepressants (Fournier et al., 2010). For patients with mild to moderate symptoms, however, the benefit was found to be minimal or nonexistent. Given that the proposed neuropsychological mechanism of both antidepressants and ABM involves reduced negative attentional bias (Godlewska and Harmer, 2020), it might be the case that these interventions require a certain symptom load for negative attentional bias to be amendable. Meaning that ABM in the present study only targeted the underlying mechanism in patients with higher symptom loads. On the other hand, AB did not moderate the outcome of ABM. This could be due to questionable validity of measures of AB, which have been widely discussed in the literature (e.g. Van Bockstaele et al., 2020). It could also relate to lack of power in the statistical analysis due to insufficient sample size for detecting the small effect sizes of the moderator effect.

An alternative explanation is that patients whom have higher symptom levels also have greater potential for reductions. However, we did statistically control for symptom level pre intervention in our analysis. Still, if there is a floor effect, there is no opportunity for improvement to occur, possibly reflecting a general principle rather than being a finding specific to ABM. At the same time, using an alternative measure more sensitive to subclinical symptoms, for example measures used in epidemiological studies (e.g., CES-D; Radloff, 1977), could possibly have provided us with greater statistical power to detect moderator effects at lower symptom levels.

The placebo condition is closely matched to the active condition, the specific factor (i.e, bias modification), compared to the common factors associated with the two conditions (e.g., structured activity, attentional training, etc.). Hence, this mechanistic approach for comparison could have masked some of the applied benefits of the ABM-intervention, as many of the characteristics of the active condition also applies to the placebo condition. Future studies should consider including other control conditions for facilitating the translation of this intervention into clinical practice (Blackwell, 2020; Blackwell et al., 2017).

This particular ABM-intervention, including threat stimuli, rather than sad stimuli, including both short (500 ms) and long (1000 ms) stimuli durations, may have made this intervention particularly well suited for patients with depression, reporting even marginal symptoms of anxiety. Potentially, ABM might be such a supplement to treatment, as patients with comorbid disorders have generally had worse treatment outcome (Coplan et al., 2015). The fact that anxiety symptoms moderated the outcome of the ABM-intervention suggests that the intervention may hold important promise as a transdiagnostic treatment option, possibly increasing the effect of other psychotherapeutic treatment options by targeting rapid implicit emotional reactions, compared to the slowly deployed emotional responses targeted by CBT (e.g., White et al., 2017). This study serves as an important first step in identifying characteristic that will promote personalization of ABM-training for depressive symptoms.

4.1. Strengths and limitations

Our findings are in line with a previously published study on the same sample, highlighting the importance of anxiety symptoms for

ABM-treatment (Kraft et al., 2019). In the study by Kraft et al. (2019), this was found by conducting a network analysis on the symptoms derived from single items of the HRDS. The present study supports this finding by employing psychometrically rigid and well-known subjective symptom scales. This could imply that patients themselves can initiate ABM when experiencing a certain level of symptoms. However, we did not stratify randomization based on moderator variables, which would have ensured equal distribution of symptom scores across conditions. At the time this study was conducted, the role of symptoms severity as moderator of the ABM-effect was not yet known. Therefore, to stratify randomization based on these characteristics was not yet called for. The simple randomization procedure indicated that there were no statistically significant differences in subjective anxiety and depression between the two intervention groups. Future studies should consider using stratified randomization procedures to increase precision in estimating moderator effects, and conduct power analyses in advance for identifying the required sample sizes of detecting these effects. Also, symptom constellations might be more relevant for personalization of treatment than symptom severity as such. Lowered mood and lack of interest/anhedonia are two main clinical dimensions in depression, and the latter might in particular be relevant in the context of personalizing ABM treatment.

In this paper, we have investigated whether symptom severity measures may moderate clinical outcomes of ABM-treatment. For the sake of understanding the mechanisms of ABM, future studies could investigate moderators of change in attentional bias following treatment. This might be done by investigating the psychometric properties and conditional benefit from ABM by use of trained machine learning and clustering analysis that personalize the intervention based on symptom severity and AB evolution over the training period.

5. Conclusion

Severity of anxiety symptoms, but not depression symptoms nor attentional bias, moderated the outcome of ABM. This study serves as an important first step in personalizing ABM for patients with depression and indicates that only patients with higher levels anxiety symptoms benefit from ABM compared to placebo.

Contributors

NIL designed the study and acted as principal investigator. RJ, TCS, VØH and CJH, co-designed the study. BK, RJ, and EH collected the data. RB did the statistical analysis in collaboration with BK, who also verified the underlying data, and wrote the first draft with input from NIL, BK, MEBA and HS. All authors critically read the manuscript and contributed academically to the data interpretations and writing. All authors approved the final version of the manuscript before submission.

Declaration of competing interest

The authors reports no related conflicts of interest.

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