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Research paper

Cognitive bias modification as an add-on treatment in clinical depression: Results from a placebo-controlled, single-blinded randomized control trial

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ABSTRACT

Background: Only 60% of depressed patients respond sufficiently to treatment, so there is a dire need for novel approaches to improve treatment effects. Cognitive Bias Modification (CBM) may be an effective and easily implemented computerized add-on to treatment-as-usual. Therefore, we investigated the effects of a positivity-attention training and a positivity-approach training compared to control trainings.

Methods: In a blinded randomized-controlled design, 139 depressed inpatients received either the CBM Attention Dot-Probe Training (DPT) or the CBM Approach-Avoidance Training (AAT), next to treatment as usual. $N = 121$ finished all four training sessions. Both trainings had an active and a control condition. In both active conditions, patients were trained to preferentially process generally positive pictures over neutral pictures. Depressive symptom severity was assessed before and after CBM, and positivity bias was measured at the start and end of each session.

Results: Clinician-rated depressive symptom severity decreased more in patients who received the active condition of the DPT or the AAT compared to patients in the control conditions. Significant change in positivity bias was found for the DPT (not the AAT), but did not mediate the effect of the training on depressive symptoms.

Conclusions: The results suggest that both types of CBM (i.e., DPT and AAT) may provide a fitting add-on treatment option for clinical depression. The working mechanisms and optimal dose of CBM trainings, plus their possible combination, should be examined in more detail.

1. Introduction

Although treatment options are continuously improving, only approximately 60% of depressed patients respond to pharmacological or psychological treatment (DeRubeis et al., 2005), and most depressed patients will experience multiple depressive episodes (Burcusa & Iacono, 2007; Essau et al., 2010; Pettit et al., 2006). With the related increasing treatment costs, there is a dire need for novel ways to improve depression treatment effectiveness.

The cognitive model of depression (Beck, 2008) indicates a promising target for treatment improvement. The model proposes that cognitive schemata develop based on our experiences. Negative experiences lead to the development of negative schemata, which in turn result in dysfunctional thoughts about the self, the world, and the future. On an automatic level, schemata result in negatively biased information processing and action tendencies, such as preferential attentional processing and automatic approach of negative information (Chen & Bargh, 1999; Gotlib & Joormann, 2010; Heuer et al., 2007; Mathews & MacLeod, 2005). Importantly, the lack of a positive bias is also related to emotional problems (e.g., Joormann & Gotlib, 2007; Liang et al., 2011). Negative automatic biases, as well as the lack of positive biases, contribute to the development and relapse of depression (De Raedt & Koster, 2010; Gotlib & Joormann, 2010; Mathews & MacLeod, 2005). Moreover, there is evidence for cognitive bias as a working mechanism of Cognitive Behavioral Therapy (CBT) and antidepressant medication, as primary depression treatments (e.g., Bowler

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et al., 2012; Harmer et al., 2009; Harmer & Cowen, 2013; Reinecke et al., 2013a; 2013b). Therefore, modifying biases is expected to increase depression treatment effectiveness.

Recently, computerized trainings, called Cognitive Bias Modification or CBM, have been developed on the basis of cognitive theory (Beck, 2008), offering a way to modify automatic processing biases (Hertel & Mathews, 2011). Importantly, CBM can be applied without clinical supervision and is low in costs. CBM is therefore a promising add-on treatment as it is designed to change dysfunctional cognitive strategies at an automatic level, while therapies target these dysfunctional processes in an overt and explicit way.

A meta-analysis of CBM-Attention and CBM-Interpretation concluded that the results of CBM as a mono-treatment for depression were mixed, with limited effects on symptomatology (Cristea et al., 2015). However, a recent reanalysis of the data in this meta-analysis shows overall positive findings of CBM on emotional vulnerability when selecting studies in which bias was successfully modified, indicating target engagement (Grafton et al., 2017; see also commentary by Cristea et al. (2017)). Besides CBM-Attention and CBM-Interpretation, Positive Imagery-Based CBM is another promising treatment option for depression (Blackwell et al., 2015; Williams et al., 2015). Despite its potential as an add-on treatment, CBM has so far not been systematically studied on top of treatment-as-usual (TAU). Moreover, most studies so far (see Cristea et al., 2015) only examined CBM targeting depression-*specific* biases. This might be suboptimal for depressed and dysphoric individuals. In contrast to addictions and anxiety disorders, for which CBM may be more effective (Cristea et al., 2015; Eberl et al., 2013), depression is characterized by a more general bias towards negative information and/or away from positive information (Gotlib & Joormann, 2010). This process seems to be conceptually closely linked to anhedonia - the inability to experience pleasure from activities usually found enjoyable - which is a core symptom of depression (see DSM criteria for major depressive disorder). While specific clusters of stimuli may trigger biased processing, e.g., alcoholic drinks in alcohol addiction (Woud et al., 2014), or threatening faces in social phobia (Bantin et al., 2016), stimuli covering a wide range of generally positive and negative topics may be more powerful in challenging depressotypic biases. In fact, positive biases seem rather general in nature and not restricted to specific content (Broeren & Lester, 2013). Hence, CBM for depression should focus on the processing of diverse categories of positive information instead of content-specific stimuli.

To select the optimal CBM paradigm and evaluate the relevance of CBM for clinical practice as add-on treatment, we need to compare different CBM trainings (i.e., CBM targeting different automatic processes, or modalities) that have been frequently used and found to be effective. We aimed to select two CBM training modalities that train automatic processing biases and lend themselves to the use of the same stimuli, to allow for optimal comparison. CBM-Attention (based on a selective attention task) is one of the most widely used CBM training types. CBM-Attention decreased negative attentional bias as well as depressive symptoms in individuals with varying levels of (residual) depressive symptoms in different studies: A moderately depressed adult sample (Beevers et al., 2015), a remitted depressed sample (Browning et al., 2012), and a mild-to-severely depressed adolescent sample (Yang et al., 2016). However, we need to note that most CBM-Attention studies used disorder-specific stimuli (e.g., sad faces or schemata-related words) and not generally positive stimuli, the latter proposedly being especially salient in depression. CBM-Approach/Avoidance (based on a joystick task) has been developed more recently, and shows promise for depression treatment (Becker et al., 2016,2017; Ferrari et al., 2018). Specifically, recent studies show that modifying approach-avoidance behavior for generally positive stimuli can increase approach of positive materials (Ferrari et al., 2018), and it can decrease emotional reactivity in dysphoric individuals (Becker et al., 2016) as well as symptoms in depressed patients (Becker et al., 2017).

Based on the aforementioned background, we set out to investigate the clinical effectiveness on top of TAU of two frequently used and promising CBM approaches using generally positive stimuli, namely CBM-Attention and CBM-Approach/Avoidance, in a clinically depressed sample. As the CBM-Attention paradigm, we used the frequently employed Dot-Probe Training (DPT) (Amir et al., 2009). The Approach-Avoidance Task (AAT) has mostly been used in CBM-Approach/Avoidance research (e.g., Asnaani et al., 2014). To yield results relevant for daily practice, we created an active and a control condition of both the AAT and DPT trainings. The trainings were administered besides TAU in the clinical setting, and we studied the effects of CBM-Attention and CBM-Approach/Avoidance on depressive symptoms and positivity bias. Offering both interventions in a blinded randomized controlled trial besides TAU directly addresses the critical question as to whether CBM can serve as a potential add-on therapy. Depressive symptom level was assessed using both a self-rated and clinician-rated instrument (see recommendation by Cuijpers et al. (2010). Change in different types of cognitive bias has been related to treatment success with psychological (e.g., study on implicit association bias: Reinecke et al., 2013b) and pharmacological interventions (e.g., studies on attention, appraisal, and memory biases: Harmer et al., 2009; Harmer & Cowen, 2013). Importantly, modification of cognitive bias is the proposed mechanism-of-change in CBM with the type of bias depending on the training technique. It is deemed important to evaluate target engagement in CBM studies (see Grafton et al., 2017), hence the mediating role of change in positivity bias in the effect of CBM-Attention and CBM-Approach/Avoidance on depressive symptoms was also examined.

2. Methods

2.1. Participants

A total of 140 currently depressed inpatients between 18 and 60 years of age were recruited at the Clinic for Psychiatry and Psychotherapy of the LVR-Hospital, Essen, Germany. Three patients did not participate in the baseline depressive symptom meaures. Five patients dropped out during the training (four due to dismissal from the clinic and one patient did not want to continue) and 11 particpiants' data could not be used because of technical problems on one or more training sessions.

Patients were diagnosed using the Structural Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders (SCID, DSM-IV). Patient with a current major depressive disorder diagnosis were included in the study. Psychiatric comorbidity was established in 27 patients (anxiety disorder = 21; history of substance abuse = 3; PTSD = 2; somatoform disorder = 1). Exclusion criteria were: Current psychosis, current substance abuse or dependency, and major neurological or somatic disorders (including haemorrhagic or ischemic insults within the subject's history as well as endocrinologic diseases such as thyroid dysfunction, hypercorticolism or adrenal dysfunction). Patients all received the same psychological inpatient treatment-as-usual, or TAU. Patients received different forms of pharmacological treatment (data of $N = 122$ was available): No medication = 10; antidepressant medication only (SNRIs only = 39; SSRI only = 29; SNDRI only = 3; tricyclic substances only = 2; details missing for one patient) = 74; neuroleptics only = 5; antidepressant mediction with neuroleptics = 14; combination treatment of antidepressants with other substances = 19), with no differences between the four training groups, $\chi^2(21) = 26.74$, $p = 180$.

Patients were recruited 2–3 weeks after intake ($M_{Days} = 16.08$; $SD = 11.96$) when they had settled into a stable treatment regime. The study was approved by the ethical committee of the University Hospital of the University Duisburg-Essen. All participating patients provided written informed consent after the procedure was fully explained. The trial was registered by the German (DRKS) and the WHO International Trials Registry (number DRKS00004896, www.drks.de, www.who.int/ictrp/en/). The actual sample size is higher than the intended *N*. Based

on the initial calculation, we intended to include 4 × 15 subjects. However, when reaching 60 subjects, newer CBM studies were published presenting lower effect sizes (see Cristea et al., 2015; Jones & Sharpe, 2017). To present reliable results, we therefore increased our *N* to 140.

3. Procedure

After inclusion, patients were randomly assigned to the active or the control version of either the CBM Attention Dot-Probe Training (DPT) or the CBM Approach-Avoidance Training (AAT): DPT_{Exp}, DPT_{Ctrl}, AAT_{Exp}, and AAT_{Ctrl}. Blocked randomization was used: Patients were first randomized over the CBM training type (AAT or DPT) and then over the condition type (active or control). An external researcher assigned patients to a condition based on pre-defined randomization lists. In the inpatient clinic and in line with other treatment protocols (e.g., Micco et al., 2014; Wiers et al., 2011), patients were trained on four days spaced out over 14 days, allowing for scheduling flexibility to avoid intervening with TAU. Each session lasted approximately 20 minutes. The patients were blind to whether they were in the active or control condition of the training, but they knew whether they received the AAT or the DPT because the different trainings required different instructions. The HAMD (blinded clinician assessments) and BDI-II were assessed right before the first training session and directly after the last training session (session 4), so always 14 days apart. See Fig. 1 for an overview of the study's procedure.

4. Materials and apparatus

4.1. Dot-Probe Training (DPT)

For the DPT (see Fig. 2 for a sample trial), 100 positive and 100 neutral pictures covering a broad range of content categories (e.g., animals, people, objects; in approximate equal proportions) were selected from the International Affective Picture System (IAPS; Lang et al., 1997). Each trial was initiated automatically and started with a central fixation cross presented for 1000 ms. It was followed by a picture pair consisting of a positive and a neutral picture (one at the top and one at the bottom of the screen) presented for 500 ms. One of the pictures was replaced by a small arrow pointing either to the right or to the left. Patients were asked to merely observe both pictures and then indicate the direction of the arrow by pressing a matching button (right or left) on the keyboard as quickly as possible. Upon a correct response, the following trial started automatically. In case of an incorrect response or no response within 5 s, an error message appeared. Reaction times, as defined by the delay between the appearance of the probe and the button press, were recorded for every trial. Trials in which an arrow replaced the positive picture were considered as depression-incongruent.

Each training session was divided into four parts unknown to patients: Eight practice trials, 40 test trials to assess pre-training bias, 200 training trials, and another 40 test trials to assess post-training bias. In each session, all 200 stimuli were used for training. In total 40 of the 200 were in advance randomly selected for the pre-assessment at the beginning of each session. Another 40 were in advance randomly selected for the post-assessment at the end of each session. The same stimuli were used in each session. For patients in the active DPT condition (i.e., DPT_{Exp}), the probe always replaced the positive pictures and never the neutral pictures during training. For patients in the control condition (i.e., DPT_{Ctrl}) and on the pre- and post-training assessment trials, the probe replaced both positive and neutral pictures with a 50/50 contingency.

5. The Approach-Avoidance Training (AAT)

The stimuli in the AAT (see Fig. 2) were identical to the stimuli used in the DPT. Patients initiated each trial by pressing the "fire button" on the joystick, while the joystick was in the neutral position. A medium-sized picture appeared in the centre of the screen, and patients were instructed to respond as quickly as possible by either pushing or pulling the joystick. The correct response depended on the tilt of the picture (3° to the left or right). Joystick movement was accompanied by a zooming-effect creating a visual connection between the arm movement and the proximity to the picture (i.e., the pictures increased in size upon pulling and decreased in size upon pushing the joystick), thereby creating the impression of pulling or pushing the picture itself. After the joystick reached an angle of approx. 30° in the correct direction, the picture remained on the screen for 50 ms in the modified size and then disappeared, presuming the correct movement was made. The starting size was medium: 260 pixels in height, width varied depending on picture format (landscape vs. portrait). Finishing size was 90 pixels in height for pushing away, and 768 pixels in height for pulling closer.

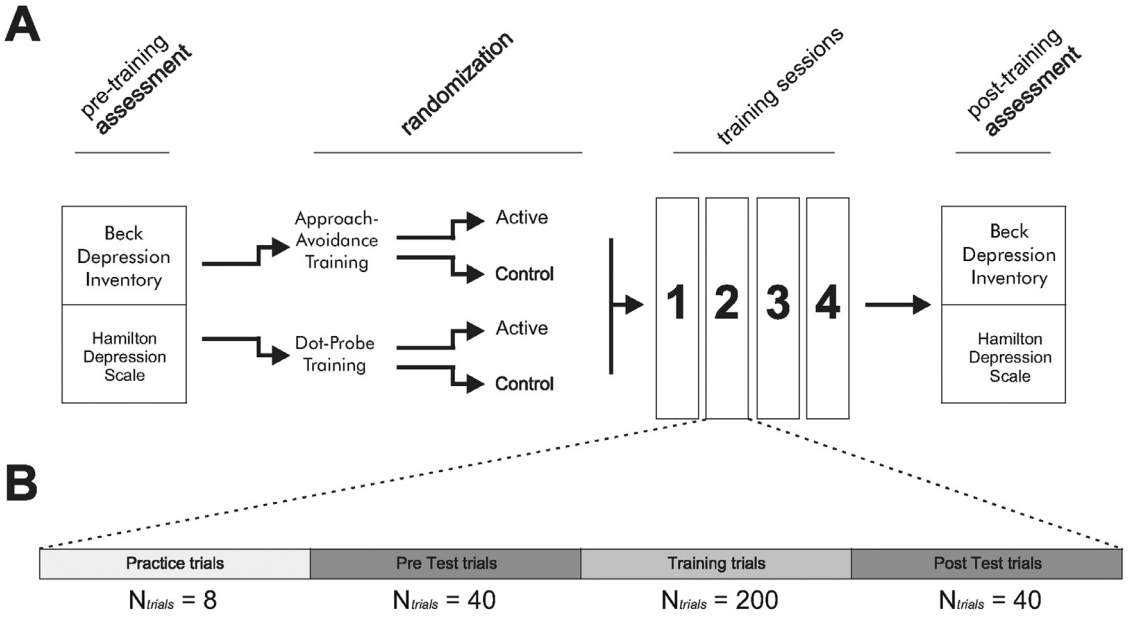

Fig. 1. Experimental timeline. A: General procedure of the experiment. B: Session structure (identical for the DPT and the AAT).

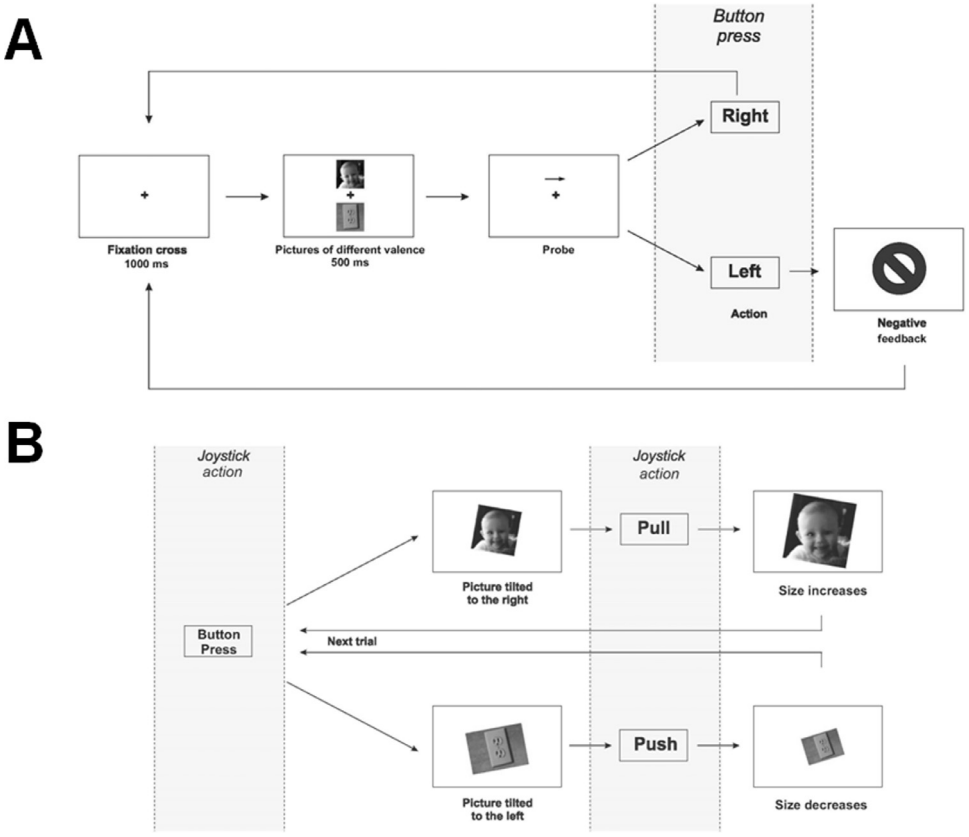

Fig. 2. Overview of training trials. A: A Dot-Probe Training (DPT) trial. Note: In the task, the arrow was smaller and the two pictures were presented further appart than shown in the figure. B: An Aproach-Avoidance Training (AAT) trial.

Thus, the maximum size was such that the largest picture would fill the screen (which had a resolution of 768 × 1024). The duration of growing or shrinking depended on the speed of the joystick movement. Depending on the combination of response direction (pulling vs. pushing) and stimulus valence (positive vs. neutral), trials were considered congruent or incongruent to depressive state. That is, pushing away (i.e., avoiding) positive pictures is considered congruent to depression. Trials on which positive pictures had to be pulled and neutral pictures had to be pushed away were considered depression-incongruent. Throughout each session, no more than three trials of the same type were presented successively. Reaction times - the delay between appearance of the picture and sucessful trial completion–were recorded on each trial.

The session structure was the same as in the DPT: Eight practice trials, 40 pre-training test trials, 200 training trials, and 40 post-training test trials. The 200 training trials consisted of 200 picture pairs such that each of the 200 pictures was used twice (once in the first half, once in the second half, combined with different opposite pictures). Pre- and post-assessment contained 40 different picture pairs each, such that 80 of the 100 positive pictures and 80 of the 100 neutral pictures were used for assessment as well. In the training trials of the active condition (i.e., AAT_{Exp}), all positive pictures had to be pulled closer and all neutral pictures had to be pushed away. In the control condition (i.e., AAT_{Ctrl}), patients pushed and pulled the positive and neutral pictures with a 50/50 contingency (i.e., pushing positive pictures half of the time).

6. Outcome measures

6.1. Primary outcome measure

Clinician-rated level of depressive symptom severity was the primairy outcome measure. The clinician was blind to the patient's training condition. Depressive symptoms were assessed before and after the four training sessions using the Hamilton Depression Scale (HAMD; Hamilton, 1960). The HAMD is a 21-item structured clinical interview, which was conducted by trained clinicians. This observer-rated measurement has been found to have acceptable (Endicott et al., 1981) to high (Baumann, 1976; Hamilton, 1960) reliability. The HAMD is sensitive to change in symptoms, allowing an accurate and precise quantification of changes in depressivity throughout treatment (Miller et al., 1985).

6.2. Secondary outcome measure

Self-rated depressive symptom severity was the secondary outcome measure. This was measured using the Beck Depression Inventory (BDI-II; Beck et al., 1996). The BDI-II is a 21-item questionnaire assessing depressive symptoms conform the DSM-IV criteria. The BDI-II is a reliable and valid instrument (Beck et al., 1996; Osman et al., 1997).

7. Data preparation and statistical analyses

On both the AAT and DPT, reaction time trials in the top and bottom 2% of variance were removed, as well as trials with incorrect responses. A 'positivity bias-score' was computed separately for each training paradigm (AAT, DPT), and within the paradigm per session for both test timepoints (pre-training, post-training), accordingly:

− $AAT_{PosBias}$ = (Mean RT Positive Push + Mean RT Neutral Pull) –(Mean RT Positive Pull + Mean RT Neutral Push).

− $DPT_{PosBias}$ = Mean RT Dot Replacing Neutral Stimuli – Mean RT Dot Replacing Positive Stimuli.

In both tasks, positive scores reflect a positive processing style. For the AAT, a positive score reflects relatively more approach of positive

than neutral pictures. For the DPT, a positive score reflects selective attention to positive relative to neutral pictures.

T-tests and Chi^2 tests were used for group comparisons. Training effects were tested using ANOVAs. Mediation was tested using the PROCESS macro for SPSS (Hayes, 2013). A bootstrapping method was used to assess the indirect effect based on 1000 bootstrapped samples using bias-corrected and accelerated 95% confidence intervals (BCa CI). Note that if zero is not in the interval, then the indirect effect is statistically significant at the 0.05 level.

Because most of the missing data/exclusion was due to technical errors (n = 11) and not drop-out (n = 5), we based the main analyses on the per-protocol (PP) sample: 121 patients who completed all four training sessions: DPT_{Exp} (n = 32), DPT_{Ctrl} (n = 22), AAT_{Exp} (n = 35), and AAT_{Ctrl} (n = 32). This means a 121/137*100 = 88% compliance with the training protocol. Analyses were repeated using an intention-to-treat (ITT) approach including all available data (N = 137). Here, the baseline HAMD scores were carried forward to the post-measure for the patients for whom post-training data were missing, hence assuming no change. Importantly, because the full post-training measures were missing, we could not use the BDI-II post-training scores to replace missing HAMD scores. Post-treatment HAMD scores were missing for 16 patients (11.5%, DPT_{Exp} (n = 5), DPT_{Ctrl} (n = 11). These patients had higher baseline HAMD scores (M = 28.6, SD = 7.3, t(135) = 4.10, p < .001) compared to the patients who finished the training without technical errors (M = 20.9, SD = 7.0). However, the self-rated depressive symptoms (BDI-II scores) did not differ between the ITT and the PP samples, ITT: M = 29.7, SD = 12.3, PP: M = 30.4, SD = 10.5, t(134) = 0.23, p = .817. Note that baseline BDI-II data were missing for one patient in the ITT sample, and that session 2 training data were missing for two patients in the DPT condition (one in the active and one in the control condition).

8. Results

8.1. Group comparisons

The four training groups did not differ in sex distribution, age, educational level, depressive symptom level at baseline, length of current clinical admission, or specification of diagnosis (i.e., first episode or recurrent depression) in the PP sample. See Table 1 for means and group comparisons.

8.2. Change in depressive symptoms

A 2 × 2 × 2 repeated-measures ANOVA with the between-subjects factors training type (AAT vs. DPT) and condition (active vs. control) and the within-subjects factor time (pre-training vs. post-training) was computed for the HAMD and BDI-II total scores separately, in both the PP and the ITT sample. The three-way interaction was significant neither for the HAMD scores, F(1,117) < 1, p = .391, η_p^2 = 0.01, nor for the BDI-II scores of the PP sample, F(1,117) < 1, p = .975, η_p^2 < 0.01, indicating no significantly different effects of training type. However, the interaction between condition and time, regardless of training type, was significant for both the HAMD, F(1,117) = 8.36, p = .005, η_p^2 = 0.07, and the BDI-II, F(1,117) = 6.70, p = .011, η_p^2 = 0.05, revealing a significant effect of active over control training. The same pattern of results was found in the ITT sample: The three-way interaction between training type, condition, and time was significant neither for the HAMD scores, F(1,133) = 0.35, p = .558, η_p^2 < 0.01, nor for the BDI-II scores, F(1,132) = 0.04, p = .842, η_p^2 < 0.01. The interaction between condition and time, regardless of training type, was again significant for the HAMD, F(1,133) = 11.72, p = .001, η_p^2 = 0.08, as well as for the BDI-II scores, F(1,132) = 9.08, p = .003, η_p^2 = 0.06.

Post-hoc tests in the PP sample showed that at baseline, neither self-rated nor clinician-rated depressive symptoms differed between the active and the control conditions, t(119) < 1, p = .732 for the BDI-II, and t(119) = 1.89, p = .062 for the HAMD. Thus, differences after training could not be attributed to a-priori baseline differences. Although the interaction effect was significant, the conditions did not differ on BDI-II scores measured after the training, t(119) = 1.61, p = .110. However, the conditions did differ on the clinician-rated HAMD scores, t(119) = 3.98, p < .001. As Fig. 3 shows, depressive symptoms decreased more in the active conditions than in the control conditions, regardless of training type. The average HAMD score in the experimental conditions decrease approximately 6 points from pre- to post-training going from moderate to mild level of depressive symptoms (from M = 20.2 to M = 14.0, decrease of 31%). The BDI-II score in the experimental conditions decreased approximately 9 points, from severe to moderate depression (from M = 30.1 to M = 21.0, decrease of 30%).

8.3. Change in positivity bias

To examine modification of positivity bias as mechanism-of-change, we compared the positivity bias measured at the start of session 1 to the same bias at the end of session 4. Given that the positivity score represents a different type of bias for the AAT and DPT, the condition (experimental vs. control) by time (pre-session 1 vs. post-session 4) was examined separately per task. Positivity bias changed over time in the DPT, F(1,52) = 11.16, p = .002, η_p^2 = 0.18, but not in the AAT, F(1,65) < 1, p = .328, η_p^2 = 0.02. Because the experimental and control condition of the DPT differed on positivity bias before session 1, t

Table 1
Percentages or means (with Standard Deviations) of demographic and assessment measures, including baseline group comparisons in the per-protocol sample (N = 121).

	Training condition				
	AAT_{Exp}	AAT_{Ctrl}	DPT_{Exp}	DPT_{Ctrl}	F(3, 117) =
Sex, % female	51%	56%	72%	55%	χ^2(3) = 3.29, p = .339
Age, years	38.8 (12.1)	36.9 (11.1)	41.3 (12.3)	38.0 (10.9)	0.78, p = .506
Education, % per level[a]	1: 3% 2: 68% 3: 29%	1: 14% 2: 69% 3: 17%	1: 12% 2: 72% 3: 16%	1: 27% 2: 64% 3: 9%	χ^2(6) = 8.90, p = .179
Baseline HAMD, total score	31.8 (11.2)	31.8 (10.9)	29.3 (10.4)	27.4 (8.6)	1.10, p = .353
Baseline BDI-II, total score	19.4 (5.2)	20.7 (7.6)	20.3 (7.9)	24.5 (6.6)	2.62, p = .054
Length of admission, days	15.4 (12.7)	20.2 (11.8)	15.4 (11.9)	13.6 (11.1)	1.63, p = .187
First episode, %	29%	34%	31%	32%	χ^2(15) = 10.38, p = .795

Note. [a]Educational level represents the maximum finished level: 1 = lower secondary school, 2 = upper secondary school and/or high school, 3 = tertiary school (college/university). Educational level data were missing for seven patients.

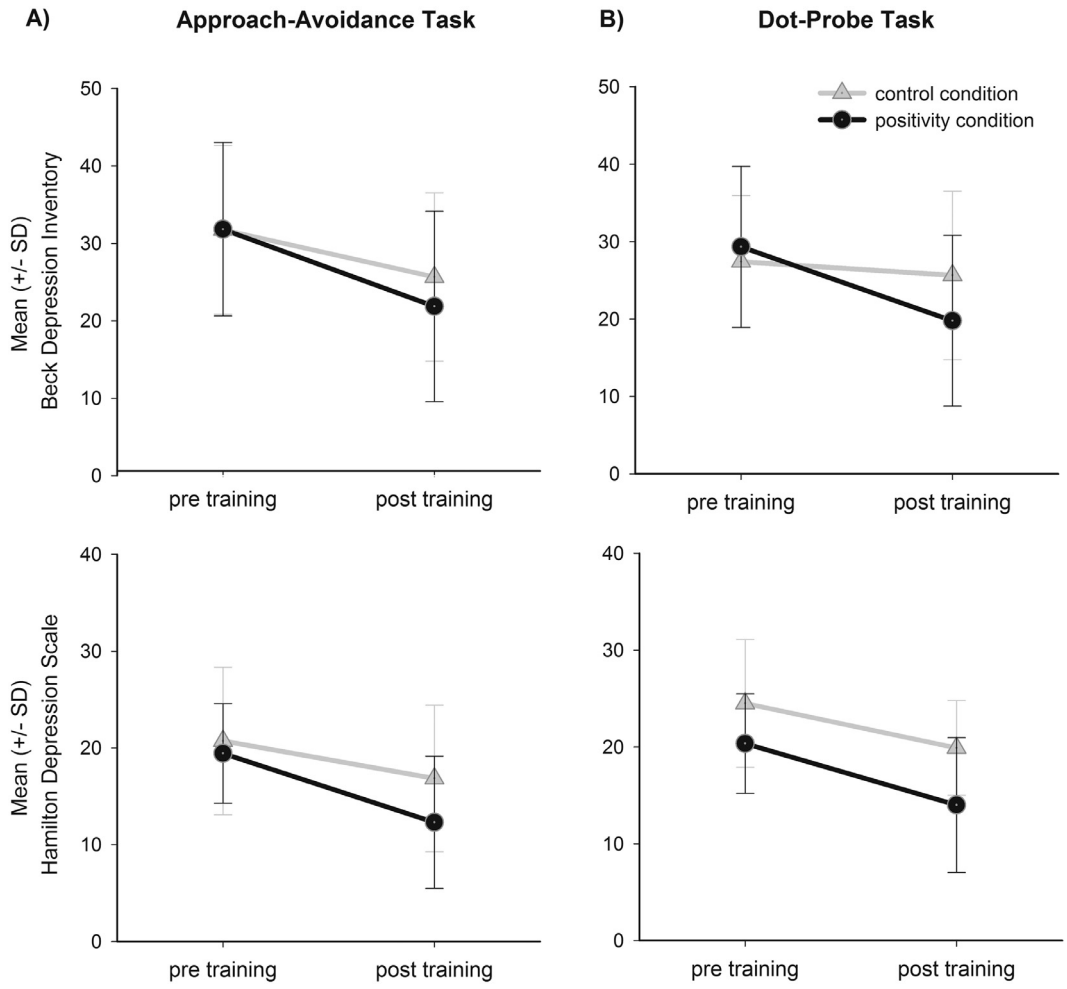

Fig. 3. Mean Beck Depression Inventory (BDI-II; top graphs) and Hamilton Depression Scale (HAMD; bottom graphs) depression severity scores for the active and control conditions for the CBM Approach-Avoidance Training (AAT; A: left) and the CBM Dot-Probe Training (DPT; B: right) assessed pre- and post-training. Error bars represent standard deviations.

(52) = 2.40, p = .02, we compared the conditions at post-session 4 bias correcting for variance in pre-session 1 bias. This yielded a significant effect of DPT condition, $F(1,51) = 4.85$, p = .032, $\eta_p^2 = 0.09$. As can been seen in Table 2, positivity bias decreased in the DPT control condition, $t(22) = 2.14$, p = .044, and increased in the experimental condition, $t(32) = 2.76$, p = .010.

8.4. Mediation analyses

We examined whether the change in bias from pre session 1 to post session 4 mediated the effect of the DPT and the AAT on clinician-rated (HAMD) depressive symptoms after the training, while controlling for depressive symptom level before the training. We first present the results for the AAT. Neither the regression coefficient for the direct effect of condition on change in bias ($a = -63.6$), nor the association between change in bias and depressive symptom level ($b < 0.01$) was significant. Hence, mediation was not possible, which is also represented by the bootstrapped unstandardized indirect effect 95% confidence interval (BCa CI) that ranged from −0.46 to 0.38. The BCa CI includes zero, indicating a nonsignificant indirect effect.

For the DPT, the direct effect of condition on change in bias ($a = 60.3$) as well as on depressive symptoms was significant ($c' = -3.8$). Change in bias was not significantly associated with depressive symptoms ($b < 0.01$). No evidence for mediation was found, as the BCa CI ranged from −0.27, to 2.08, indicating a nonsignificant indirect effect. The standardized indirect effect 'ab' was 0.51. The ratio of the indirect effect (referred to as P_M) to the direct effect was 0.13. The P_M value provides an index of effect size, and in this case it indicates that 13% of the effect of training condition on depression symptoms may operate indirectly through change in positivity bias.

9. Discussion

To the best of our knowledge, this is the first study that investigated and compared the clinical effect and mechanism of change of two types of CBM training. Depression scores improved from pre to post-training in all training conditions, indicating successful treatment-as-usual. Importantly, we could show that depressive symptoms decreased significantly more (approximately 30%) in patients who received the active CBM condition of either the AAT or the DPT than in individuals in the control conditions. Positivity bias increased in the active DPT condition compared to the DPT control condition, whereas no such difference was found for the AAT. Finally and contradictory to our hypothesis, the change in bias from pre-session 1 to post-session 4 did not mediate the effect of the DPT or the AAT training on clinician-rated (HAMD) depressive symptoms.

Notably, our results were strongest for clinician-rated depressive symptoms. Several reasons may account for this. Patients may have biases in describing symptomatology, limited insight into own symptom change, and/or cognitive deficits that compromise self-monitoring of improvement (Corruble et al., 1999; Rush et al., 2006). The differences in results between the BDI-II and the HAMD are supported by the notion

Table 2
Mean (Standard Deviation) positivity bias scores in msec pre and post each of the four sessions, presented separately for the active and the control conditions of the Dot-Probe Training (DPT) and the Approach-Avoidance Training (AAT) in the per-protocol sample ($N = 121$). A higher score represents relatively stronger positive bias; a negative score represent a relative stronger bias towards neutral stimuli. Statistics comparing pre and post positivity bias scores of the active and control condition per task are also presented.

	Training condition				
	AAT_{Exp}		AAT_{Ctrl}		Condition x Time: F (1,65) =
	Pre	Post	Pre	Post	
Session 1	55 (232)	35 (220)	−31 (218)	11 (315)	0.53, $p = .489$
Session 2	−5 (191)	82 (218)	11 (162)	18 (204)	1.79, $p = .185$
Session 3	62 (151)	40 (164)	22 (213)	15 (236)	0.06, $p = .802$
Session 4	50 (127)	19 (174)	−25 (166)	1 (159)	1.19, $p = .279$
	DPT_{Exp}		DPT_{Ctrl}		Condition x Time: F (1,52) =
	Pre	Post	Pre	Post	
Session 1	−11 (48)	10 (57)	20 (53)	−10 (46)	7.91, $p = .007$
Session 2	16 (42)	4 (59)	−10 (54)	12 (61)	2.11, $p = .153$
Session 3	12 (51)	2 (45)	5 (51)	−17 (39)	0.31, $p = .583$
Session 4	18 (57)	28 (67)	4 (43)	−9 (40)	1.64, $p = .206$

that self-rated depressive symptom measures are more conservative and less sensitive to change (Cuijpers et al., 2010). If this is true, the trend change on BDI-II scores might have reached significance when assessed at a later timepoint. Hence, the HAMD may have picked up on symptom change over the training period, whereas changes in BDI-II scores may occur at a later stage.

Change in positivity bias was found for the DPT and not for the AAT. The AAT may work through a different route than expected: Possibly not by changing automatic approach-avoidance of positive information wich was our predicted mechanism of change, but perhaps by targeting general non-emotional avoidance. Indeed, we know that general behavioral avoidance (i.e., of positive, neutral, and negative events) is a symptom of depression, while the evidence for valence-specific approach-avoidance tendencies is mixed. To illustrate, less automatic approach as well as more avoidance of positive stimuli was found in an unselected and a sad dysphoric student sample (Vrijsen et al., 2013; Bartoszek & Winer, 2015, respectively). Also, depressed patients in a study by Seidel et al. (2010) showed automatic avoidance in response to angry faces, whereas no such results were found by others (Derntl et al., 2011; Radke et al., 2014). The AAT may have clinical benefits as add-on treatment, but modification of emotional bias may not be the mechanism of change. Further research is required to examine if AAT in fact modifies bias, or targets a different depression-related process (e.g., general avoidance, anhedonia).

Attentional biases–as modified by the DPT–are valence-specific in depression (Gotlib & Joormann, 2010; Mathews & MacLeod, 2005). However, the current results indicate that the change in positivity bias may not mediate the change in depressive symptoms instigated by the DPT training. So the DPT may change bias (i.e., target engagement), but the effect may not contribute to the subsequent symptom change. This is contrary to the basic idea of attention bias modification (see Grafton et al., 2017): The training changes bias and this brings about symptom change. However, it is important to note that lack of reliability of reaction time measures is a plausible reason for lack of mediation. A new approach to CBM-Attention, using eye-tracking, may offer a more reliable option to assessing and mofifying positivity bias (see e.g., Möbius et al., 2018).

Change in bias has been implicated as the earliest indicator of treatment success, as the patient responds to the reduced impact of negative events, stressors, and cues (Harmer et al., 2009). It is important to monitor bias change during treatment with antidepressant medication or psychological interventions such as CBT. This may be especially valuable for more severely disordered depressed patients who do not respond to the standard treatment protocol. Monitoring bias change can facilitate decision-making as it may indicate whether the treatment is not working, or whether clinical effects are not observed yet but can be expected with a higher dose and/or prolonged treatment. However, the current results can neither substantiate nor refute this proposition. A future CBM add-on study including a long-term follow-up including frequent measures of bias during and after training as well as depressive symptoms may provide the necessary substantiation to this proposition.

Our results suggest that both types of CBM training (i.e., DPT and AAT) may provide a clinically useful add-on treatment option for clinical depression. In contrast to e.g., anxiety and addiction disorders (Bantin et al., 2016; Woud et al., 2014), for depression it may be valuable to select generally positive stimuli instead of disorder-specific stimuli for CBM. This is the case because global cognitive schemata may drive attentional and automatic behavioral processes in schema-related disorders such as depression (Beck & Haigh, 2014). Still it would be interesting and theoretically valuable to study transdiagnostic applicability of Positivity-CBM. Although other disorders such as anxiety disorders are characterized by biases for specific information, this does not mean that positivity trainings cannot yield valuable mechanistic and symptomatic change in disorders other than depression. More specifically, repetitive negative thinking is a transdiagnostic feature of depression and generalized anxiety disorder (Kircanski et al., 2015). This is reflected by the high comorbidity between depression and anxiety. Positivity-CBM counters a general negative thinking style. Hence, its effects on anxiety should be investigated. Moreover, current CBM techniques in addiction train the avoidance of addiction-related stimuli, either as attentional avoidance with the DPT or as behavioral avoidance with the AAT. In both cases, it is not always clear what the opposing to-be-attended-to or to-be-approached stimulus category should be. A broad range of positive stimuli, as in the positivity trainings tested here, might be a promising candidate. This would combine drug-avoidance training with simultaneous positivity-approach training, and possibly amplify the effects. A similar suggestion in the area of anxiety-related attention training was recently offered by Luo et al. (2015) who improved a DPT that trained attention away from snakes or spiders by simultaneously training attention towards positive stimuli.

The study has strengths and limitations. Strengths are that the trial included not one but two different CBM techniques, along with their respective control conditions. In comparison to many other CBM studies, the trial was pre-registrered and is well powered. One limitation is that the study was single-blinded: The clinician was always blind to the patient's training condition when administering the HAMD, but patients knew whether they received the AAT or the DPT because the instructions and set-up differed. This might have introduced a bias as characteristics of the DPT and the AAT (e.g., the joystick, instructions) might have induced differential motivation or believe in the training's effectiveness. However, patients were blind to whether they were in the active or control condition of the training. The majority of missing data was in the DTP control condition. This disbalance was unexpected because randomization was successful, but we cannot rule out that it induced bias. Also important to note and relevant for many CBM studies, is that our measures of bias have low reliability. We currently have no data on the optimal number of training sessions for depressed patients, and whether this differs between CBM modalities. This should be a focus of future systematic research. So far, the current results indicate that four sessions of CBM positivity training can decrease depressive symptoms, but the mechanism of change is unclear at this point. Another next step is to systematically examine which CBM modality is (most) effective in yielding bias change and subsequent depressive

symptom change by comparing training paradigms that target different cognitive and behavioral domains in a clinical setting. For example, CBM-Interpretation may be more effective than CBM-Attention (Cristea et al., 2015) and CBM-Memory is a new approach to CBM (Hertel et al., 2017; Vrijsen et al., 2016; Vrijsen et al., 2018). Importantly, different CBM training modalities are not mutually exclusive. Given that they all address different processes, we should study whether and how they can be combined to yield even better clinical effects.

Author disclosure

None

Contributors

Authors VF, BM, MR and IT designed the study. Authors BM, NS and IT supervised data collection and VF primarily carried out data collection. Author JV did the analyses and drafted the manuscript. All authors contributed to the writing of the manuscript.

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Conflicts of interest

There are no conflicts of interest to report.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2018.06.025.

References

Amir, N., Beard, C., Burns, M., Bomyea, J., 2009. Attention modification program in individuals with generalized anxiety disorder. J. Abnorm. Psychol. 118 (1), 28–33.
Asnaani, A., Rinck, M., Becker, E., Hofmann, S.G., 2014. The effects of approach-avoidance modification on social anxiety disorder: a pilot study. Cognit. Ther. Res. 38 (2), 226–238.
Bantin, T., Stevens, S., Gerlach, A.L., Hermann, C., 2016. What does the facial dot-probe task tell us about attentional processes in social anxiety? A systematic review. J. Behav. Ther. Exp. Psychiatry 50, 40–51.
Bartoszek, G., Winer, E.S., 2015. Spider-fearful individuals hesitantly approach threat, whereas depressed individuals do not persistently approach reward. J. Behav. Ther. Exp. Psychiatry 46, 1–7.
Baumann, U., 1976. Methodische untersuchungen zur hamilton-depression-skala. Arch. Psychiatr. Nervenkr. 222 (4), 359–375.
Beck, A.T., 2008. The evolution of the cognitive model of depression and its neurobiological correlates. Am. J. Psychiatry 165 (8), 969–977.
Beck, A.T., Haigh, E.A., 2014. Advances in cognitive theory and therapy: the generic cognitive model. Annu. Rev. Clin. Psychol. 10, 1–24.
Beck, A.T., Steer, R.A., Brown, G.K., 1996. Manual For Beck Depression Inventory-II. Psychological Corporation, San Antonio, TX.
Becker, E.S., Barth, A., Smits, J.A.J., Beisel, S., Lindenmeyer, J., 2017. A positivity-approach-training in depressed patients. In: Proceedings of the Conference on Anxiety and Depression Association of America (ADAA). San Francisco, USA 6-9 April 2017.
Becker, E.S., Ferentzi, H., Ferrari, G., Möbius, M., Brugman, S., Custers, J., Geurtzen, N., Wouters, J., Rinck, M., 2016. Always approach the bright side of life: a general positivity training reduces stress reactions in vulnerable individuals. Cognit. Ther. Res. 40, 57–71.
Beevers, C.G., Clasen, P.C., Enock, P.M., Schnyer, D.M., 2015. Attention bias modification for major depressive disorder: effects on attention bias, resting state connectivity, and symptom change. J. Abnorm. Psychol. 124 (3), 463–475.
Blackwell, S.E., Browning, M., Mathews, A., Pictet, A., Welch, J., Davies, J., Watson, P., Geddes, J.R., Holmes, E.A., 2015. Positive imagery-based cognitive bias modification as a web-based treatment tool for depressed adults: a randomized controlled trial. Clin. Psychol. Sci. 3 (1), 91–111.
Bowler, J.O., Mackintosh, B., Dunn, B.D., Mathews, A., Dalgleish, T., Hoppitt, L., 2012. A comparison of cognitive bias modification for interpretation and computerized cognitive behavior therapy: Effects on anxiety, depression, attentional control, and interpretive bias. J. Consult. Clin. Psychol. 80 (6), 1021–1033.
Broeren, S., Lester, K.J., 2013. Relevance is in the eye of the beholder: attentional bias to relevant stimuli in children. Emotion 13 (2), 262–269.
Browning, M., Holmes, E.A., Charles, M., Cowen, P.J., Harmer, C.J., 2012. Using attentional bias modification as a cognitive vaccine against depression. Biol. Psychiatry 72 (7), 572–579.
Burcusa, S.L., Iacono, W.G., 2007. Risk for recurrence in depression. Clin. Psychol. Rev. 27 (8), 959–985.
Chen, M., Bargh, J.A., 1999. Consequences of automatic evaluation: immediate behavioral predispositions to approach or avoid the stimulus. Personal. Individ. Differ. 25, 215–224.
Corruble, E., Legrand, J.M., Zvenigorowski, H., Duret, C., Guelfi, J.D., 1999. Concordance between self-report and clinician's assessment of depression. J. Psychiatr. Res. 33 (5), 457–465.
Cristea, I.A., Kok, R.N., Cuijpers, P., 2015. Efficacy of cognitive bias modification interventions in anxiety and depression: meta-analysis. Br. J. Psychiatry 206 (1), 7–16.
Cristea, I.A., Kok, R.N., Cuijpers, P., 2017. Invited commentary on … Confusing procedures with process in cognitive bias modification research. Br. J. Psychiatry 211, 272–273.
Cuijpers, P., Li, J., Hofmann, S.G., Andersson, G., 2010. Self-reported versus clinician-rated symptoms of depression as outcome measures in psychotherapy research on depression: a meta-analysis. Clin. Psychol. Rev. 30 (6), 768–778.
De Raedt, R., Koster, E.H.W., 2010. Understanding vulnerability for depression from a cognitive neuroscience perspective: a reappraisal of attentional factors and a new conceptual framework. Cognit. Affect. Behav. Neurosci. 10 (1), 50–70.
Derntl, B., Seidel, E.M., Eickhoff, S.B., Kellermann, T., Gur, R.C., Schneider, F., Habel, U., 2011. Neural correlates of social approach and withdrawal in patients with major depression. Soc. Neurosci. 6 (5-6), 482–501.
DeRubeis, R.J., Hollon, S.D., Amsterdam, J.D., Shelton, R.C., Young, P.R., Salomon, R.M., O'Reardon, J.P., Lovett, M.L., Gladis, M.M., Brown, L.L., Gallop, R., 2005. Cognitive therapy vs medications in the treatment of moderate to severe depression. Arch. Gen. Psychiatry 62 (4), 409–416.
Eberl, C., Wiers, R.W., Pawelczack, S., Rinck, M., Becker, E.S., Lindenmeyer, J., 2013. Approach bias modification in alcohol dependence: do clinical effects replicate and for whom does it work best? Dev. Cognit. Neurosci. 4, 38–51.
Endicott, J., Cohen, J., Nee, J., Fleiss, J., Sarantakos, S., 1981. Hamilton depression rating scale. Extracted from regular and change versions of the schedule for affective disorders and schizophrenia. Arch. Gen. Psychiatry 38 (1), 98–103.
Essau, C.A., Lewinsohn, P.M., Seeley, J.R., Sasagawa, S., 2010. Gender differences in the developmental course of depression. J. Affect. Disord. 127 (1-3), 185–190.
Ferrari, G.R., Möbius, M., Becker, E.S., Spijker, J., Rinck, M., 2018. Working mechanisms of a general positivity approach-avoidance training: effects on action tendencies as well as on subjective and physiological stress responses. J. Behav. Ther. Exp. Psychiatry 59, 134–141.
Gotlib, I.H., Joormann, J., 2010. Cognition and depression: current status and future directions. Annu. Rev. Clin. Psychol. 6 (1), 285–312.
Grafton, B., MacLeod, C., Rudaizky, D., Holmes, E.A., Salemink, E., Fox, E., Notebaert, L., 2017. Confusing procedures with process when appraising the impact of cognitive bias modification on emotional vulnerability. Br. J. Psychiatry 211 (5), 266–271.
Hamilton, M., 1960. A rating scale for depression. J. Neurol. Neurosurg. Psychiatry 23 (56), 56–63.
Harmer, C.J., Cowen, P.J., 2013. 'It's the way that you look at it'–a cognitive neuropsychological account of SSRI action in depression. Philos. Trans. R. Soc. Lond. B Biol. Sci. 368 (1615), 20120407.
Harmer, C.J., Goodwin, G.M., Cowen, P.J., 2009. Why do antidepressants take so long to work? A cognitive neuropsychological model of antidepressant drug action. Br. J. Psychiatry 195, 102–108.
Hayes, A.F., 2013. Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-based Approach. Guilford Press, New York, NY.
Hertel, P.T., Mathews, A., 2011. Cognitive bias modification: past perspectives, current findings, and future applications. Perspect. Psychol. Sci. 6 (6), 521–536.
Hertel, P.T., Maydon, A., Cottle, J., Vrijsen, J.N., 2017. Cognitive bias modification: retrieval practice to simulate and oppose ruminative memory biases. Clin. Psychol. Sci. 5 (1), 122–130.
Heuer, K., Rinck, M., Becker, E.S., 2007. Avoidance of emotional facial expressions in social anxiety: the approach-avoidance task. Behav. Res. Ther. 45 (12), 2990–3001.
Jones, E.B., Sharpe, L., 2017. Cognitive bias modification: a review of meta-analyses. J. Affect. Disord. 223, 175–183.
Joormann, J., Gotlib, I.C.H., 2007. Selective attention to emotional faces following recovery from depression. J. Abnorm. Psychol. 116 (1), 80–85.
Kircanski, K., Thompson, R.J., Sorenson, J., Sherdell, L., Gotlib, I.C.H., 2015. Rumination and worry in daily life: examining the naturalistic validity of theoretical constructs. Clin. Psychol. Sci. 3 (6), 926–939.
Lang, P.J., Bradley, M.M., Cuthbert, B.N., 1997. International Affective Picture System (IAPS): Technical Manual and Affective Ratings. NIMH Center for the Study of Emotion and Attention, pp. 39–58.
Liang, C.W., Hsu, W.Y., Hung, F.C., Wang, W.T., Lin, C.H., 2011. Absence of a positive bias in social anxiety: the application of a directed forgetting paradigm. J. Behav.

Ther. Exp. Psychiatry 42 (2), 204–210.
Luo, X., Ikani, N., Barth, A., Rengers, L., Becker, E., Rinck, M., 2015. Attention bias modification in specific fears: spiders versus snakes. J. Behav. Ther. Exp. Psychiatry 49, 30–36.
Mathews, A., MacLeod, C., 2005. Cognitive vulnerability to emotional disorders. Annu. Rev. Clin. Psychol. 1 (1), 167–195.
Micco, J.A., Henin, A., Hirshfeld-Becker, D.R., 2014. Efficacy of interpretation bias modification in depressed adolescents and young adults. Cognit. Ther. Res. 38, 89–102.
Miller, I.W., Bishop, S., Norman, W.H., Maddever, H., 1985. The modified hamilton rating scale for depression: reliability and validity. Psychiatry Res. 14 (2), 131–142.
Möbius, M., Ferrari, G.R., van den Bergh, R., Becker, E.S., Rinck, M., 2018. Eye-tracking based attention bias modification (ET-ABM) facilitates disengagement from negative stimuli in dysphoric individuals. Cognit. Ther. Res. 42 (4), 408–420.
Osman, A., Downs, W.R., Barrios, F.X., Kopper, B.A., Gutierrez, P.M., Chiros, C.E., 1997. Factor structure and psychometric characteristics of the beck depression inventory. J. Psychopathol. Behav. Assess. 19 (4), 359–376.
Pettit, J.W., Lewinsohn, P.M., Joiner, T.E., 2006. Propagation of major depressive disorder: relationship between first episode symptoms and recurrence. Psychiatry Res. 141 (3), 271–278.
Radke, S., Güths, F., André, J.A., Müller, B.W., de Bruijn, E.R., 2014. In action or inaction? Social approach-avoidance tendencies in major depression. Psychiatry Res. 219 (3), 513–517.
Reinecke, A., Hoyer, J., Rinck, M., Becker, E.S., 2013a. Cognitive-behavioural therapy reduces unwanted thought intrusions in generalized anxiety disorder. J. Behav. Ther. Exp. Psychiatry. 44 (1), 1–6.
Reinecke, A., Rinck, M., Becker, E.S., Hoyer, J., 2013b. Cognitive-behavior therapy resolves implicit fear associations in generalized anxiety disorder. Behav. Res. Ther. 51 (1), 15–23.
Rush, A.J., Carmody, T.J., Ibrahim, H.M., Trivedi, M.H., Biggs, M.M., Shores-Wilson, K., Crismon, M.L., Toprac, M.G., Kashner, T.M., 2006. Comparison of self-report and clinician ratings on two inventories of depressive symptomatology. Psychiatr. Serv. 57 (6), 829–837.
Seidel, E.M., Habel, U., Finkelmeyer, A., Schneider, F., Gur, R.C., Derntl, B., 2010. Implicit and explicit behavioral tendencies in male and female depression. Psychiatry Res. 177, 124–130.
Vrijsen, J.N., Dainer-Best, J., Witcraft, S.M., Papini, S., Hertel, P., Beevers, C.G., Smits, J.A., 2018. Effect of cognitive bias modification-memory on depressive symptoms and autobiographical memory bias: two independent studies in high-ruminating and dysphoric samples. Cogn. Emot In press.
Vrijsen, J.N., Hertel, P.T., Becker, E.S., 2016. Practicing emotionally biased retrieval affects mood and establishes biased recall a week later. Cognit. Ther. Res. 40 (6), 764–773.
Vrijsen, J.N., van Oostrom, I., Speckens, A., Becker, E.S., Rinck, M., 2013. Approach and avoidance of emotional faces in happy and sad mood. Cognit. Ther. Res. 37 (1), 1–6.
Wiers, R.W., Eberl, C., Rinck, M., Becker, E.S., Lindenmeyer, J., 2011. Retraining automatic action tendencies changes alcoholic patients' approach bias for alcohol and improves treatment outcome. Psych. Sci. 22 (4), 490–497.
Williams, A.D., O'Moore, K., Blackwell, S.E., Smith, J., Holmes, E.A., Andrews, G., 2015). Positive imagery cognitive bias modification (CBM) and internet-based cognitive behavioral therapy (iCBT): a randomized controlled trial. J. Affect. Disord. 178, 131–141 Erratum in: 2016, J. Affect. Disord. 190, 896.
Woud, M.L., Pawelczak, S., Rinck, M., Lindenmeyer, J., Souren, P., Wiers, R.W., Becker, E.S., 2014. Alcohol-related interpretation bias in alcohol-dependent patients. Alcohol. Clin. Exp. Res. 38 (4), 1151–1159.
Yang, W., Zhang, J.X., Ding, Z., Xiao, L., 2016. Attention bias modification treatment for adolescents with major depression: a randomized controlled trial. J. Am. Acad. Child. Adolesc. Psychiatry 55 (3), 208–218 e2.