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Appraisal-based cognitive bias modification in patients with posttraumatic stress disorder: a randomised clinical trial

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ABSTRACT

Background: Negative appraisals of the trauma and its sequela play a crucial role in the development and maintenance of Posttraumatic Stress Disorder (PTSD). Experimental studies have shown promise in reducing negative appraisal through Cognitive Bias Modification (CBM) training.

Objective: To determine whether an online CBM training designed to modify dysfunctional appraisals is successful in reducing appraisal bias in PTSD patients.

Method: In this double-blinded 2-arm randomised clinical trial, 107 patients with PTSD were randomly allocated to active (n = 49) or control online CBM training (n = 57). Training comprised the completion of four sessions of online CBM training within one week. Change in bias, as measured by a scenario task and questionnaire (i.e. PostTraumatic Cognition Inventory), was the primary outcome. Secondary outcome included change in PTSD symptoms. Assessments took place prior to training, during training sessions, post-training and at 1- and 6-month follow-up.

Results: Intent-to-treat analysis indicated that there was no interaction effect of condition by time. Regardless of training condition, participants showed a small to moderate decline in appraisal bias and PTSD symptoms from pre- to post-training. In both conditions, bias change during training sessions was related to decline in PTSD symptomatology following training. No moderators of outcome were found.

Conclusions: There was no evidence that active training was more effective than control training in reducing dysfunctional appraisals. In both conditions, participants showed a decline in dysfunctional appraisals and PTSD symptoms following training. Importantly, bias reduction during training was related to PTSD symptom decline following training. Explanations and future research directions are discussed.

HIGHLIGHTS
- Negative appraisals of the trauma and its sequela play a crucial role in PTSD.
- Online CBM training designed to modify dysfunctional appraisals is successful in reducing appraisal bias in PTSD patients.
- There was no evidence that active training was more effective than control training in reducing dysfunctional appraisals.
- Bias reduction during training was related to PTSD symptom decline following training.

KEYWORDS
- Cognitive bias modification;
- appraisal bias;
- posttraumatic stress disorder;
- randomised clinical trial;
- trauma-related cognitions

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Supplemental data for this article can be accessed here.

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1. Introduction

Information processing theories posit that biased cognitive processes play a cardinal role in the onset and maintenance of emotional disorders (Mathews & MacLeod, 2005). Similarly, theoretical frameworks of posttraumatic stress disorder (PTSD) have emphasized the importance of cognitive factors with respect to the development and maintenance of PTSD (Ehlers & Clark, 2000; Foa, Ehlers, Clark, Tolin, & Orsillo, 1999). In DSM-5 (American Psychiatric Association, 2013), persistent negative beliefs about oneself or the world are included as one of the diagnostic criteria of PTSD.

Indeed, a broad range of empirical studies has demonstrated biased interpretation and appraisals in those suffering from PTSD (see for review Woud, Vervoord, & Krans, 2017). Interpretation bias refers to the tendency to interpret ambiguous information in a negative and danger-congruent manner. Relatedly, appraisal bias refers to the tendency to value the trauma and its sequelae in an excessively negative manner. Studies assessing biased interpretation and appraisals through experimental paradigms demonstrated that PTSD patients have a tendency to interpret ambiguous stimuli (for example, ambiguous sentence stems or video-clips with ambiguous outcome) in a dysfunctional manner (Amir, Coles, & Foa, 2002; Elwood, Williams, Olatunji, & Lohr, 2007; Kimble, Batterink, Marks, Ross, & Fleming, 2012; Kimble et al., 2002). Likewise, studies assessing explicit biased appraisals (by means of the Posttraumatic Cognition Inventory (PTCI); Foa et al., 1999), have shown that dysfunctional appraisals are linked to PTSD symptoms. To illustrate, prospective studies showed that dysfunctional appraisals about the self before trauma-exposure were predictive of later PTSD symptom development (Bryant & Guthrie, 2005, 2007). Similarly, dysfunctional appraisals immediately after trauma-exposure were found to be predictive of the onset and maintenance of PTSD symptoms (Dunmore, Clark, & Ehlers, 2001; Ehring, Ehlers, & Glucksman, 2008). Moreover, reductions in dysfunctional appraisals have been shown to predict PTSD symptom improvement during trauma-focused treatment (Kleim et al., 2013; McLean, Yeh, Rosenfield, & Foa, 2015; Zalta et al., 2014). Together, these studies suggest that dysfunctional interpretation and appraisal bias plays a central role in PTSD, and that modification of this bias may reduce PTSD pathology. Trauma-focused treatments, such as prolonged exposure or cognitive processing therapy, reduce these dysfunctional appraisals (Kumpula et al., 2017; McLean et al., 2015; Schumm, Dickstein, Walter, Owens, & Chard, 2015; Zalta et al., 2014). However, a substantial proportion of patients remains symptomatic after trauma-focused treatment (Carpenter et al., 2018; Loerinc et al., 2015), and dysfunctional appraisals only partly diminish over treatment (Kleim et al., 2013). Investigating novel interventions that target dysfunctional appraisals in PTSD might serve as additions to currently available treatment strategies or identify specific subgroups of patients that are responsive to these cognitive interventions, working towards more personalized treatment indications.

Cognitive Bias Modification (CBM, see Koster, Fox, & MacLeod, 2009; Woud & Becker, 2014 for review) originates from experimental psychopathology research and...
aims at directly changing dysfunctional cognitive processes via computerized tasks. Originally, CBM studies aimed to test the idea that biased cognitive processes were causally linked to symptoms of psychopathology, and that modification of such biases leads to symptom elevation. In later studies, the clinical utility of CBM was tested. Thus far, there are a couple of studies demonstrating the impact of CBM on appraisal bias in analogue trauma samples, with promising results (Schartau, Dalgleish, & Dunn, 2009; Woud et al., 2018, 2018; Woud, Holmes, Postma, Dalgleish, & Mackintosh, 2012; Woud et al., 2018). In these studies, participants were exposed to a stressful situation (e.g. aversive video-clips) or they recalled a negative autobiographical memory. Next, they completed one or more computerized CBM training sessions. In these CBM sessions, participants were trained to appraise ambiguous, trauma-relevant information in a positive or negative manner. Importantly, Woud et al. (2012) showed that those who received computerized positive appraisal training reported lower levels of dysfunctional appraisals and PTSD symptoms such as intrusions in the week following training, as compared to those who received negative training. Related to these CBM studies, a study in refugees high in PTSD symptoms examined the effect of a non-computerized appraisal training, wherein participants were explicitly instructed to reappraise the meaning of trauma-related images. Results demonstrated that appraisal training led to lower trauma-related intrusions than emotion suppression training (Nickerson et al., 2017). Together, these studies indicate that training aimed at reducing dysfunctional appraisal might decrease PTSD pathology, and support testing the efficacy of an appraisal-based CBM training in a clinical population.

The aim of the current study was to investigate the efficacy of a brief CBM intervention designed to decrease dysfunctional appraisal in a large treatment-seeking PTSD sample. Based on the positive experimental and preclinical findings, we expected CBM training to be more effective than control training in reducing dysfunctional appraisals, both on a measures of idiosyncratic and functional appraisals, both on a measures of idiosyncratic and functional appraisal might decrease PTSD pathology, and related psychopathology. Thirdly, we expected bias reduction during training to predict symptom improvement following training. Last, we explored whether clinical relevant baseline patient characteristics (e.g. trauma exposure, comorbidity, self-esteem) moderated the outcome.

2. Methods

2.1. Participants

Participants (N = 107) were primarily patients of a large Dutch mental health-care organization (with four different sites: Nijmegen, Arnhem, Tiel, Ede/Veenendaal), and were either in treatment or on the waiting list for treatment of their PTSD. They were recruited during their first interview, by their therapist or via advertisement in waiting areas. Four participants learned via advertisements of the study at other locations and contacted the research team for participation. Participants were enrolled between May 2014 and September 2016, with final follow-ups completed in April 2017. Inclusion criteria were (I) between 18 and 70 years of age; (II) current PTSD DSM-IV diagnosis confirmed by a structured diagnostic interview (see Measures); (III) history of interpersonal violence; (IV) self-reported PTSD symptoms of at least moderate severity (i.e. PSS-SR score ≥20); (V) internet access and desktop computer. The inclusion criterion of history of interpersonal violence was chosen to reduce heterogeneity within the sample. Moreover, we expected that dysfunctional appraisals would be most severe in those suffering from PTSD following interpersonal violence. Exclusion criteria were (1) (current or past) psychosis or delusional disorders; (2) acute suicidal tendency; (3) mental retardation; (4) substance abuse or dependence; (5) insufficient ability to speak and write Dutch. Written informed consent was obtained from all participants. An a-priori power analysis indicated that 51 subjects per condition were needed to have 80% power for detecting a medium-sized effect (i.e. Cohen’s $f = 0.31$). As such, we aimed for 102 training completers. The study protocol was approved by the medical ethics committee of the Radboud Medical Center and pre-registered at www.trialregister.nl (TRIAL NL4269).

Of the 107 eligible participants randomly assigned in double-blind fashion to the training conditions, 104 participants completed all training sessions, and 100 completed all training sessions and the post-training assessment. See Figure 1 for a flow-chart of all study participants.

The sample characteristics are presented in Table 1. The majority of the patients (81.3%) were female and the sample’s mean (SD) age was 38.8 (11.3) years. For the majority of participants (n = 84, 78.5%) the traumatic event underlying PTSD comprised sexual violence either during childhood, adulthood or both. More than half of the participants (58.9%), who were equally distributed across the two groups, were taking psychotropic medication: 34 participants benzodiazepines, 46 participants antidepressants, 22 antipsychotics and six participants used other psychotropic drugs (e.g. antiepileptic drugs). In addition to the PTSD diagnosis, diagnostic interviews (M.I.N.I.; Sheehan et al., 1998) revealed that 78.5% (n = 84) had comorbid depressive disorder. Despite randomisation there were significant between group differences regarding age and trauma-type. That is, the active group was significantly older than the control group, and reported less exposure to trauma during childhood.
(both sexual and physical trauma) and less violence/physical assault in adulthood. No significant group differences were found for any outcome measure at baseline, gender, education, psychotropic medication use, and comorbid depressive disorder.

A minority of the participants (n = 34; 31.8%) reported to have received treatment for their PTSD during the active phase of the study (i.e. during the training week or in the week before the post-training assessment). Of these 34 participants, 27 received trauma-focused treatment for their PTSD (either EMDR or Prolonged Exposure). The number of participants being in trauma-focused treatment did not differ between training conditions (Yes vs. No, χ² = 0.07, p = .788).

**Figure 1.** Progress of participants in the study.
Table 1. Baseline characteristics of study participants (N = 107).

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Total sample</th>
<th>Active</th>
<th>Control</th>
<th>t or χ², p</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 107</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at time training, mean years (SD)</td>
<td>38.79 (11.25)</td>
<td>41.29 (11.22)</td>
<td>36.69 (10.93)</td>
<td>2.14, .035</td>
</tr>
<tr>
<td>Gender (female), n (%)</td>
<td>87 (81.3)</td>
<td>39 (79.6)</td>
<td>48 (82.8)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Education, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>24 (22.4)</td>
<td>12 (24.5)</td>
<td>12 (20.7)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Middle</td>
<td>46 (43.0)</td>
<td>18 (36.7)</td>
<td>28 (48.3)</td>
<td>n.s.</td>
</tr>
<tr>
<td>High</td>
<td>37 (34.6)</td>
<td>19 (38.8)</td>
<td>18 (31.0)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Married/Cohabiting, n (%)</td>
<td>49 (47.7)</td>
<td>25 (51.0)</td>
<td>24 (41.4)</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

| Trauma history | | | | |
| Childhood (16 ≤ y), n (%) | | | | |
| Sexual abuse | 60 (56.1) | 21 (42.9) | 39 (67.2) | 6.41, .011 |
| Physical abuse | 55 (51.4) | 19 (38.8) | 36 (62.1) | 5.77, .016 |
| Emotional abuse | 83 (77.6) | 34 (69.4) | 49 (84.5) | n.s. |
| Number of reported trauma’s during childhood, mean (SD) | 4.34 (2.82) | 3.61 (2.30) | 4.95 (3.08) | −2.50, .014 |
| Adult, n (%) | | | | |
| Sexual assault and rape | 78 (72.9) | 32 (65.3) | 46 (79.3) | n.s. |
| Domestic violence/physical assault | 74 (69.2) | 29 (59.2) | 45 (77.6) | 4.22, .040 |
| Number of reported trauma’s during adulthood, mean (SD) | 4.78 (2.83) | 4.65 (2.78) | 4.88 (2.88) | n.s. |
| Comorbid depressive disorder, n (%) | 84 (78.5) | 41 (83.7) | 43 (74.1) | n.s. |
| Receiving psychotropic medication, n (%) | 63 (58.9) | 28 (58.3) | 35 (60.3) | n.s. |

N = sample size, SD = standard deviation, t = t-statistic, χ² = chi kwadraat, p = p-value, n.s. = non-significant.

2.2. Measures

The DSM-IV axis-I diagnoses of PTSD and depressive disorder were established with the Mini-International Neuropsychiatric Interview (M.I.N.I.; Sheehan et al., 1998) a valid and reliable structured interview to assess axis-I psychiatric diagnoses.

2.2.1. Posttraumatic cognitions

The Post Traumatic Cognition Inventory (PTCI; Foa et al., 1999) is a self-report measure, consisting of 33 statements that reflect appraisals surrounding distressing or traumatic experiences (e.g. ‘I can’t trust that I will do the right thing’). It contains three subscales: negative cognitions about Self (21 items), negative cognitions about the World (7 items) and Self-Blame (5 items). Each item is rated using a 7-point Likert scale ranging from 1 ‘totally disagree’ to 7 ‘totally agree’. Internal consistency is high for both the original (α = .97; Foa et al., 1999) and Dutch version (α = .94; van Emmerik, Schoorl, Emmelkamp, & Kamphuis, 2006; current study α = .92). The PTCI was assessed pre-training, post-training and at both follow-up assessments.

2.2.2. PTSD symptom severity

The severity of PTSD symptoms was assessed with the Posttraumatic Stress Symptom Scale, Self-Report (PSS-SR) (Foa, Riggs, Dancu, & Rothbaum, 1993), a 17-item questionnaire with which patients rate the frequency of PTSD symptoms. Reliability analyses showed a high internal consistency (α = .91; Foa et al., 1993). The Dutch version also shows good internal consistency (Mol et al., 2005; current study α = .82). The PSS-SR was administered pre-training, post-training and at both follow-up assessments.

2.2.3. Depressive symptom severity

Depressive symptoms were assessed with the Beck Depression Inventory (BDI-II). The BDI (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961) is a 21-item self-report questionnaire assessing the severity of depressive symptoms, with scores ranging from 0 to 3. Psychometric qualities are good (Beck, Steer, & Garbin, 1988, current study α = .86). The BDI was administered pre-training, post-training and at both follow-up assessments.

2.2.4. Self-esteem

Self-esteem was assessed with the Rosenberg Self Esteem Scale (RSES; Rosenberg, 1965). The RSES is a 10-item self-report questionnaire assessing global self-esteem, with total scores ranging from 0 to 30. Psychometric qualities are good (Franck, De Raedt, Barbez, & Rosseel, 2008, current study α = .86). The RSES was administered pre-training.

2.2.5. Scenario task

To assess appraisal styles, participants were asked to complete 10 ambiguous open-ended trauma-related scenarios that could be appraised in a dysfunctional manner (see also Hertel, Brozovich, Joormann, & Gotlib, 2008; Woud et al., 2018). Each scenario was composed of one or two sentences and ended abruptly, thereby providing the opportunity for a participant created continuation, based on the participant’s first interpretation of the open-ended cognition. For example: You never know what the future will bring. I believe the future ... To ensure that the scenarios targeted typical trauma-related cognitions, themes of the PTCI were used as the basis for the scenarios (see also Woud et al., 2018). Each scenario reflected one of the three PTCI domains (self-blame;
The PTCI self-subscale was used to develop two types of scenarios, namely scenarios related to self (i.e. changes in personality or emotions since the trauma; self) or scenarios related to PTSD symptoms (i.e. appraisal of trauma-related thoughts; self-symptom). The distinction in the self-subscale was motivated by our interest in assessing appraisal with respect to general, negative appraisals about oneself (e.g. ‘I am weak’) and appraisals specific to PTSD symptoms (e.g. ‘Having nightmares means I am going mad’). In line with the PTCI, more scenarios were developed with respect to cognitions about the self (48 self and 24 self-symptom scenarios), than with respect to self-blame (24 scenarios) and cognitions about the world (24 scenarios). Participants completed the scenario task at baseline, prior and immediately after each training session, at post-training and at both follow-up assessments. We developed 120 unique scenarios, distributed over 12 blocks containing 10 scenarios each, such that at each time point the participant completed different scenarios. The order of blocks was randomised, thus each participant completed all 120 scenarios over the 12 assessments, but in random order. Within each block, the same proportion of sentences reflecting the different PTCI domains was ensured (i.e. 4 self, 2 self-symptom, 2 self-blame and 2 world), and the order of the scenarios was randomised.

The raw data from the 10 scenarios was converted into an ‘Appraisal Index’, that is the degree to which ambiguous scenarios had been completed in a dysfunctional way. Raters scored I) whether participants made an appraisal; II) and if so, whether appraisals were dysfunctional (Yes = 1 vs. No = 0). Appraisals were scored as dysfunctional if the participant’s continuation reflected a dysfunctional appraisal of the self (i.e. the participant valued the own personality as bad or weak), present PTSD symptoms (i.e. the participant interpreted PTSD symptoms as a sign of weakness), or self-blame (i.e. the participant valued his or her actions during the traumatic event as wrong), and the world (i.e. other people and the world were perceived as dangerous), and; III) the valence of the given appraisals on a 7-point Likert scale (−3 very negative to +3 very positive). The Appraisal Index (score between 0 and 1) reflects the proportion dysfunctional appraisals of all appraisals made. The valence score represents the mean valence of the appraisals. The data (N = 12,050 scenarios in total) were sorted by scenario and anonymized, such that raters scored the same scenario in succession and were unaware of the participant who completed the scenario and the time point of completion (i.e. completely blinded). Eight raters scored each a proportion of the scenarios, and for all scenarios there was an overlap between raters, such that each scenario was rated twice. Next, the raters that scored the same scenarios discussed the ratings and gave a consensus rating. Disagreement between raters was solved by discussion with one of the senior authors. Agreement between raters was good (level of agreement prior to discussion of scoring: appraisal: yes vs. no: 97.4%; dysfunctional: yes vs. no: 86.7%). For all analyses, the consensus scores were used. Most completions were rated as appraisals (95.6%, n = 11,524), and approximately half of these appraisals were rated as dysfunctional (55.0%, n = 6334). Notably, the correlation between the Appraisal Index and the valence score was very high (r = −.93). As such, the valence score was deemed redundant, and we only used the Appraisal Index in our statistical analyses.

2.3. CBM training
The CBM training was adapted from the training developed by Woud et al. (2012), which proved to effectively induce positive versus negative appraisal styles following analogue trauma (i.e. highly stressful films). In the current study, participants completed four training sessions within one week time. Each training session comprised processing a series of 40 reappraisal-related scripted vignettes that appeared to participants as a sentence completion task. Each vignette reflected one of the domains of the PTCI (self-blame: 28 vignettes; self: 72 vignettes; self-symptoms 32 vignettes; world: 28 vignettes), and comprised two short sentences, with the second sentence including a to-be-completed word fragment. The meaning of the vignette remained ambiguous until the word fragment was resolved. The participant’s task was to complete the word fragment by typing in the first missing letter. In the active training, the meaning of the sentence became positive upon completion of the word fragment, whereas in the control training the meaning of the sentence remained neutral. For example, You never know what the future will bring was followed by I believe the future holds g-d things for me in the active CBM condition, whereas it was followed by I believe the future holds d-f-f-r-n things for me in the control condition.

The trial order was as follows. The first sentence of each vignette was displayed on the computer screen (for 2000 ms; in black). Next, the second sentence containing the to-be-completed word fragment was presented. Participants were then instructed to type the first missing letter of the word fragment. If correct, the completed correct word appeared on the screen (for 1000 ms; in green). If participants gave an incorrect answer the to-be-completed word fragment was presented again (in red), until the participant gave the correct response.

In total, 160 vignettes were presented throughout the training in four blocks, one block of 40 vignettes...
per training session. Vignettes were randomised to each block, with the condition that each block contained the same number of vignettes reflecting a certain PTCI subscale (i.e. per block: self-blame: 7 vignettes; self: 18 vignettes; self-symptoms 8 vignettes; world: 7 vignettes). The order of the blocks was fixed; the order of the vignettes within each training session was randomised. During each training session, a short break was provided after 10 vignettes. Almost all CBM training sessions (97.4%, n = 410) were completed within 15-minutes time (median = 6).

### 2.4. Randomisation

Participants were randomly allocated to one of the training conditions before the first training session. Randomisation was stratified by treatment site (Nijmegen, Arnhem, Tiel, Ede/Veenendaal) and PTCI baseline score (low vs. high; cut-off PTCI baseline 133). Assignment to condition was randomised for each stratum in blocks of six, by using a computer software program generating the random sequence. The randomisation scheme was programmed in the online platform. Everyone involved in the study (i.e. researchers, participants, and assessors) were blind to the training condition until all follow-up assessments were completed.

### 2.5. Procedure

After informed consent, participants took part in a baseline assessment wherein they completed a structured interview (MINI), questionnaires (including PSS-SR, BDI, PTCI), and computer tasks (scenario task, word sentence association paradigm (WSAP^2)). All questionnaires, computer tasks and training sessions were provided on a secured website and accessible through a personalized ID and access token. At the end of the baseline assessment, participants were familiarized with the training program and received written instructions to be able to complete the training sessions at home. Upon completion of the baseline assessment and when meeting all inclusion criteria, participants received an email containing a link that gave access to the first training session. Randomisation of study participants occurred at the beginning of the first training session. Participants were encouraged to complete all four training sessions within one week. Upon completion of a prior session they received an email containing the access link to the following session. To promote compliance, all training sessions were scheduled at the baseline assessment, and participants received reminders when they lagged behind planning. One week following the last training session participants came to the treatment facility for the post-training assessment. This assessment was done onsite to promote contact with the research team, with the idea to enhance retention and to provide room for participants to provide feedback on the training program and study procedure. Follow-up assessments (one and six months post training) were completed via the secured website.

### 2.6. Statistical analysis

Differences between the training conditions on frequency variables were analysed using chi-square. To compare differences between conditions on other variables independent sample t-tests were performed. Continuous outcome variables (Appraisal Index; PTCI; PSS-SR; BDI-II) were analysed by specifying linear grow models with random intercept and random slope using mixed models procedure. Time was entered as a continuous variable, i.e. the absolute day of assessment. To fit linear regression lines we used the square root of the day. Group was entered as a fixed factor. Estimated marginal means (EMM) were computed for the square root of the day at 0 (pre-training), 4 (post-training), 6 (one month FU) and 14 (six-month FU). Within-group effect sizes were computed as the difference between the EMM pre and EMM post divided by square root of the model estimate of the variance of the measure at pre-training, i.e. the variance of the intercept. Between-group effect size was computed from the EMM tests using Viechtbauer’s (2007) equation (28) for between groups d and equation (34) for within group d CIs.

To investigate whether change in bias during training influenced training effects as measured with the PSS-SR (see also Lazarov, Pine, & Bar-Haim, 2017), we modelled the four pre-session appraisal scores in a linear grow model with random intercept and random slope. These modelled scores represent the individual bias change, and they were entered as time-varying person level covariate within the same analytic framework as our main analysis. Specifically, bias change main effect, the two-way interaction term of bias change × condition and bias change × time, and a three-way interaction term of bias change × condition × time were included in the model.

To determine whether baseline patient characteristics predicted differential outcome (as measured with the PSS-SR), we examined the effect of possible predictive variables (i.e. trauma exposure, baseline severity of PTSD symptoms, trauma-related cognitions, and depressive symptoms, and self-esteem) using the same model as our main analyses and the predictor as time-invariant person-level covariate. The predictor was included as a main effect, two-way interaction with time or condition, and three-way interaction with time by condition. All analyses were conducted using SPSS (IBM) version 25.
3. Results

3.1. Primary measures

Intent-to-treat mixed model analysis revealed no significant effect of condition nor a significant interaction of condition and time on change in bias (Appraisal Index: \(F(1, 86) = 0.01, p = .944\); PTCI: \(F(1, 79) = 0.33, p = .567\); see Table 2). Specifically, we found no differences between conditions at post-training (Appraisal Index: \(F(1, 101) = 0.08, p = .774\); PTCI: \(F(1, 114) = 1.29, p = .259\)). For the overall-mixed model, there was a main effect of time for both the Appraisal Index (\(F(1, 86) = 91.93, p < .001\)) and the PTCI (\(F(1, 79) = 46.54, p < .001\)). Within-groups effect sizes for pre to post training change for the Appraisal Index and PTCI, respectively, were \(d = 0.38, 95\% CI [0.07, 0.69]\) and \(d = 0.30, [0.08, .52]\) in the active condition, and \(d = 0.37, [0.08, .66]\) and \(d = 0.25, [0.05, .45]\) in the control condition. The between-groups effect size for change from baseline to post-training assessment was \(d = 0.05, [-.15, .25]\) for the Appraisal Index and \(d = 0.18, [-.02, .38]\) for the PTCI.

Importantly, our findings were not affected by whether participants received concurrent trauma-focused treatment. That is, receiving trauma-focused treatment (yes vs. no) did not interact with time, group, nor time \(\times\) group interaction terms on both Appraisal Index and PTCI scores (all \(p\)-values >.10).

3.2. Secondary outcome

3.2.1. PTSD and depressive symptoms

Intent-to-treat mixed model analysis revealed a main effect of time on PSS-SR scores across time (\(F(1, 81) = 105.44, p < .001\)). Neither a significant effect of condition (\(F(1, 113) = 0.50, p = .464\)) nor a significant interaction between condition and time was found (\(F(1, 81) = 0.14, p = .707\)). Specifically, there was no significant difference between groups in PSS-SR scores at the post-training assessment (\(F(1, 111) = 0.35, p = .555\)). Similar results were obtained with the BDI-II scores as dependent variable. Again, self-reported depressive symptoms declined over time (\(F(1, 80) = 33.75, p < .001\)), with no evidence of a condition effect (\(F(1, 109) = 0.55, p = .462\)) or a condition by time effect (\(F(1, 80) = 1.53, p = .219\)). Within-groups effect sizes for pre- to post-change for the PSS-SR and BDI, respectively, were \(d = 0.43, 95\% CI [0.21, .65]\) and \(d = 0.23, [-.01, .47]\) in the active condition, and \(d = 0.46, [0.25, .67]\) and \(d = 0.15, [-.07, .37]\) in the control condition. The between-groups effect size for change from baseline to post-training assessment was \(d = 0.14, [-.06, .34]\) for the PSS-SR and \(d = 0.14, [-.06, .34]\) for the BDI-II.

Again, receiving concurrent trauma-focused treatment did not interact with time, group, time \(\times\) group interaction for predicting outcome on the PSS-SR or BDI-II (all \(p\)-values >.10).

3.3. Potential predictors of outcome

3.3.1. Bias change across training sessions as a predictor of outcome

Mixed-model analyses revealed a main effect of bias change during training (as assessed with the Appraisal Index), on PSS-SR scores (\(F(1, 206) = 52.10, p < .001\)), as well as an interaction effect of bias change \(\times\) time on PSS-SR scores (\(F(1, 226) = 30.86, p < .001\)). That is, those who showed more bias reduction on the Appraisal Index during training reported lower PSS-SR scores and demonstrated a sharper decline in PSS-SR scores over time. Again, no three-way interaction effect of condition \(\times\) time \(\times\) bias change was found (\(F(1, 239) = 0.67, p = .415\)).

3.3.2. Baseline patient characteristics as predictors of outcome

None of our potential moderators (i.e. PTSD baseline severity (low vs. high); PTCI baseline severity (low vs. high); comorbid depressive disorder (yes vs. no); trauma exposure (low vs. high); and self-esteem (RSES baseline low vs. high)) showed to moderate training effects. That is, independent mixed model analyses with Appraisal Index and PTCI scores as dependent variables showed no significant three-way interaction of time by condition by variable of interest (all \(p\)-values >.05).

3.4. Satisfaction and blindness

At the post-training assessment, participants were asked to evaluate their training experiences on a 10-point scale ranging from very negative (0) to very positive (10). There were no statistically significant

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<table>
<thead>
<tr>
<th>Outcome</th>
<th>Pre M (SE)</th>
<th>Post M (SE)</th>
<th>1 MFU M (SE)</th>
<th>6 MFU M (SE)</th>
<th>Pre M (SE)</th>
<th>Post M (SE)</th>
<th>1 MFU M (SE)</th>
<th>6 MFU M (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appraisal index</td>
<td>0.62 (0.03)</td>
<td>0.55 (0.03)</td>
<td>0.51 (0.03)</td>
<td>0.35 (0.04)</td>
<td>0.64 (0.03)</td>
<td>0.56 (0.03)</td>
<td>0.52 (0.03)</td>
<td>0.36 (0.04)</td>
</tr>
<tr>
<td>PTCI</td>
<td>147.91 (4.32)</td>
<td>139.82 (4.35)</td>
<td>135.77 (4.59)</td>
<td>119.59 (6.58)</td>
<td>153.33 (3.96)</td>
<td>146.50 (3.97)</td>
<td>143.08 (4.16)</td>
<td>129.42 (5.82)</td>
</tr>
<tr>
<td>PSS-SR</td>
<td>30.53 (1.11)</td>
<td>27.62 (1.10)</td>
<td>26.17 (1.17)</td>
<td>20.35 (1.71)</td>
<td>31.63 (1.02)</td>
<td>28.50 (1.01)</td>
<td>26.94 (1.06)</td>
<td>20.68 (1.51)</td>
</tr>
<tr>
<td>BDI</td>
<td>31.93 (1.56)</td>
<td>29.65 (1.53)</td>
<td>28.52 (1.57)</td>
<td>23.97 (2.04)</td>
<td>33.49 (1.43)</td>
<td>32.02 (1.40)</td>
<td>31.28 (1.42)</td>
<td>28.53 (1.80)</td>
</tr>
</tbody>
</table>

Abbreviations: MFU = Month Follow-up; M = mean; SE = standard error; PTCI = Posttraumatic Cognition Inventory; PSS-SR = Posttraumatic Symptom Scale – Self-report; BDI = Beck Depression Inventory.
differences between the two conditions in how positively participants evaluated the training program (active: \( M = 6.84, SD = 1.98 \) vs. control: \( M = 6.88, SD = 1.99; p > .05 \)). Similarly, participants rated how stressful the training had been on a 10-point scale from not stressful at all (0) to extremely stressful (10). Again, there were no between-group differences in how stressful the training was experienced (active: \( M = 5.47, SD = 2.38 \) vs. control: \( M = 5.30, SD = 2.70; p > .05 \)). At the post-training assessment, all participants were furthermore asked whether they believed to have received the active or control training. There were no statistical differences between the two training conditions (active vs. control) in the percentages of participants believing to have received the active training (64.4% vs. 58.2%, \( \chi^2_1 = .41, p = .523 \)).

4. Discussion

The aim of this study was to investigate whether a CBM-intervention aimed at reducing negative interpretation, and appraisal bias was successful at modifying this bias in a large sample of patients suffering from chronic PTSD. We expected that, in comparison to the control training, the active training would lead to a greater reduction in interpretation and appraisal bias and lower PTSD symptoms at the post-training assessment. Our findings did not support this hypothesis. Regardless of training condition, participants had lower bias and PTSD symptoms at the post-training and follow-up assessments. Moreover, in both conditions, bias change across training sessions was related to change in PTSD symptoms over time. Thus, independent of condition, participants had less dysfunctional appraisals following training and modification of negative appraisals over training sessions appeared to influence PTSD pathology. We explored moderators of training effects, but found no indications that training effects were moderated by baseline patient characteristics.

As our study is the first to study the efficacy of a CBM intervention aimed at the reduction of negative interpretation and appraisal bias in a sample of treatment-seeking PTSD patients, we can only compare our results to those obtained in CBM appraisal studies in trauma analogue samples (Woud et al., 2018, 2018, 2012; Woud, Postma, Holmes, & Mackintosh, 2013). Our null-finding is in contrast with the positive findings of this earlier work. However, it should be noted that in these studies the effects of a positive (active) CBM training were compared to a negative (control) training, i.e. a training wherein participants were trained to appraise scenarios in a negative manner. These studies showed that CBM training resulted in training-congruent appraisals, thus those who were trained positively made more positive appraisals as compared to those who were trained to negatively appraise ambiguous scenario’s (Woud et al., 2018, 2012, 2013, 2018). The comparison to a negative control condition makes it difficult to draw conclusions on whether the positive active training really reduced bias. Another explanation for our findings might be the control training we developed as comparator. To test the clinical efficacy of the CBM training, we wanted to develop a neutral training without the active ingredient. However, as PTSD patients are characterized by negative interpretation and appraisals (Ehlers & Clark, 2000; Foa et al., 1999; Woud et al., 2017), in hindsight, our control training might not have been neutral, but rather a light version of the positive training. For instance, a participant in the control condition would complete sentences resulting in appraisals as ‘people are diverse’ or ‘my personality is multifaceted’. Granted that participants were marked by high dysfunctional appraisals at baseline, the control training was rather a milder positive than a neutral training. In that way, our finding that dysfunctional appraisals reduced in both conditions can be explained as an indication that both training conditions induced training-congruent appraisals. That said, we had expected that the active training would lead to more positive appraisals than the control training, and interpretations of the effect of merely time should be made with caution. Future experimental work should compare the efficacy of a negative, neutral, and positive training in changing interpretation and appraisal bias in trauma analogue samples (Blackwell, Woud, & MacLeod, 2017). In clinical studies, including other control conditions, such as non-appraisal-related tasks (i.e. peripheral vision task, see Woud et al., 2018), will shed more light on the mechanisms and effects of CBM trainings targeted at dysfunctional appraisals in PTSD.

The within-groups pre-to-post effect sizes for bias change and PTSD symptom change were in the small to moderate range (Cohen’s \( d = 0.25 \) to 0.46). Again, interpretation of these time-effects is difficult. But, given the high patient retention, good acceptability, and low investment in time and effort (<2 hours in total over 7 days), even these small effect sizes might be relevant. If any, it supports further investigations of CBM appraisal training in PTSD patients.

Given the fact that we found change in both conditions, but no differential effects between conditions, an alternative explanation for our finding is that the appraisal bias and PTSD symptoms changed merely as a result of the passage of time. Although unlikely given the fact that many patients suffered from PTSD symptoms for a long period of time, and that the training and post-training assessment were completed within two weeks, we cannot exclude this possibility. As such, the lack of a no intervention
wait-list control group should be considered a major limitation of the current study. Comparison to a wait list group would have allowed us to examine whether any training was more efficacious than no training in reducing appraisal bias and PTSD symptoms. Moreover, demand effects might explain our results (Cristea, Kok, & Cuijpers, 2015). The fact that participants were actively involved in a study to reduce negative appraisal, and invested time and effort in the training sessions might have resulted in a lower report of bias and symptoms at the post-training assessments.

The findings of our predictor analyses indicate that the degree of bias change during training was related to PTSD decline following training. This finding stands in line with earlier work showing that change in appraisal precedes PTSD symptom decline (McLean et al., 2015) and the idea that biases are causally related to psychopathology (Mathews & MacLeod, 2005). Recently, it has been proposed that CBM interventions can only be expected to be efficacious when the bias under study is effectively modified during the training (Grafton et al., 2017). Indeed, our findings suggest that those who show a reduction in bias while training show a more favourable outcome. Notably, we found no interaction between bias change across training sessions and training condition, and thus cannot fully establish whether indeed the proposed mechanism of bias modification led to bias change across training sessions, and not an alternative mechanism, such as exposure to trauma-related stimuli (Mathews & MacLeod, 2005). None of the patient characteristics at baseline proved to be related with training effects.

Our study has a number of limitations. First, as said earlier, the lack of a waiting list control condition should be considered a major limitation. Second, participants completed the training sessions at home. While this limited the burden for participants and may have contributed to the high participant retention, we do not know how participants (i.e. with what level of attention or in which state) completed the training sessions. A meta-analysis on CBM efficacy showed higher effect sizes for trainings exclusively delivered in the laboratory than those with a home-based component (Grafton et al., 2017), but the driving mechanism of this finding has to be determined. Third, about one-third of participants received concurrent psychotherapeutic treatment between pre- and post-assessment. Last, while retention during training sessions and post-training assessment was high, we did loose participants to the follow-up assessments (1 month FU = 22.4%; 6 Month FU = 32.7%).

Strengths of the current study include the inclusion of a clinical representative sample, allowing us to make conclusions on the feasibility of this CBM intervention for those suffering from PTSD in routine clinical care, the large sample size, and the low level of attrition during training (3.8% drop-out, in comparison: in a study on attentional bias modification (ABM) in a comparable sample the drop-out was 15.7% (Schoorl, Putman, & Van Der Does, 2013)).

To conclude, the findings of this study do not support superior effects of positive CBM appraisal as compared to control training in a sample of treatment-seeking PTSD patients. Irrespective of training condition, change in appraisal bias over training sessions predicted change in PTSD symptoms at post-training and follow-up. Thus, while we found evidence that a reduction in negative appraisal bias was related to a decline in PTSD symptoms, we found no evidence that active training was more effective than control training in reducing bias. Experimental work has shown promise for CBM training targeting dysfunctional appraisal in trauma-analogue studies. This is the first clinical study examining the efficacy of this CBM training in PTSD patients, and our findings did not confirm our hypotheses. However, in line with theory, we found that a reduction in dysfunctional appraisals was related to a decrease in PTSD symptoms. In future studies on appraisal-based CBM, researchers should consider controlling concurrent treatment and including a waitlist and/or other (non-appraisal-related) control condition.

**Notes**

1. At the start of this study, only participants who were on the waiting list for PTSD treatment were considered eligible for participation. However, to secure inclusion and after approval of the medical ethics committee, we removed this criterion. As such, all PTSD patients, irrespective of whether they were on the waiting list or in treatment for their PTSD treatment were eligible for participation. Note, that participants still had to fulfill all inclusion criteria (i.e. satisfy DSM-IV PTSD criteria and self-reported PTSD symptoms of at least moderate severity).

2. The WSAP is a measure of interpretation bias, which was included as a secondary outcome measure. However, given the length of our manuscript, we chose to report the outcome of the WSAP data in a supplementary file. Please see this file for a full description of the instrument, procedure and findings.

3. The results of the intent-to-treat analyses are presented in the main text. The findings of the per protocol analyses were comparable to those presented here, and are reported in a supplementary file.

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Data availability statement

The data that support the findings of this study are available from the corresponding author, [RK], upon reasonable request.

Disclosure statement

No potential conflict of interest was reported by the authors.

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