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The Effects of Modifying Dysfunctional Appraisals in Posttraumatic Stress Disorder Using a Form of Cognitive Bias Modification: Results of a Randomized Controlled Trial in an Inpatient Setting

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Keywords

Posttraumatic stress disorder · Dysfunctional appraisals · Cognitive bias modification · Cortisol · Intrusive memories

Abstract

Introduction: Dysfunctional appraisals about traumatic events and their sequelae are a key mechanism in posttraumatic stress disorder (PTSD). Experimental studies have shown that a computerized cognitive training, cognitive bias modification for appraisals (CBM-APP), can modify dysfunctional appraisals and reduce analogue trauma symptoms amongst healthy and subclinical volunteers. ***Objective:*** We aimed to test whether CBM-APP could reduce dysfunctional appraisals related to trauma reactions in PTSD patients, and whether this would lead to improvements in PTSD symptoms. ***Methods:*** We compared CBM-APP to sham training in a parallel-arm proof-of-principle double-blind randomized controlled trial amongst 80 PTSD patients admitted to an inpatient clinic. Both arms comprised a training schedule of 8 sessions over a 2-week period and were completed as an adjunct to the standard treatment programme. ***Results:*** In intention-to-treat analyses, participants receiving CBM-APP showed a greater reduction in dysfunctional appraisals on a scenario task from pre- to posttraining (primary outcome) assessments, compared to those receiving sham training (d = 1.30, 95% CI 0.82–1.80), with between-group differences also found on the Posttraumatic Cognitions Inventory (PTCI; d = 0.85, 95% CI 0.39–1.32) and the PTSD Checklist for DSM-5 (PCL-5; d = 0.68, 95% CI 0.23–1.14), but not for long-term cortisol concentrations (d = 0.25, 95% CI –0.28 to 0.78). Reductions in dysfunctional appraisals assessed via the scenario task correlated with reductions on the PTCI, PCL-5, and hair cortisol concentrations from pre- to

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posttraining time points. ***Conclusions:*** Results support dysfunctional appraisals as a modifiable cognitive mechanism, and that their proximal modification transfers to downstream PTSD symptoms. These findings could open new avenues for improving present therapeutic approaches.

Introduction

The importance of dysfunctional appraisals in posttraumatic stress disorder (PTSD) is acknowledged by their inclusion in the most recent diagnostic criteria [1]. Accordingly, dysfunctional appraisals are increasingly regarded as a core component of PTSD [2, 3], and thus a crucial target both for treatments such as cognitive therapy [4] and cognitive processing therapy [5–7], and for experimental work seeking to understand the underlying mechanisms [8–10]. A key assumption of cognitive behavioural theories of PTSD is that the way in which an individual appraises a traumatic event and their own reactions to it plays a central role in the disorder's development and maintenance [4, 11–13]. That is, dysfunctional appraisals of both trauma symptoms and reactions to the trauma may exacerbate the disorder, leading to increases in symptoms such as intrusive memories. There is a substantial body of research providing convergent evidence that dysfunctional appraisals are correlated with and predictive of PTSD severity, even after controlling for initial symptom levels [14–18]. Further, in the context of cognitive behaviour therapy (CBT) for PTSD, changes in dysfunctional appraisals have been found to predict symptom reduction, and not vice versa [19].

Critically, direct evidence for a potential *causal* influence of appraisals has come primarily from our experimental work on analogue trauma. Using experimental designs, individuals were trained to adopt a benign (adaptive) versus dysfunctional appraisal style by means of computerized cognitive training paradigms developed within the framework of cognitive bias modification (CBM) techniques [20, 21]. This appraisal-focused approach was based on the original CBM interpretation training paradigm [22], but with one critical change: rather than focusing on ambiguous *stimuli*, the target was the modification of the participants' *own beliefs*/*appraisal*s about their trauma symptoms and reactions to the event. The general hypothesis for our lab-based studies was that the training would not only influence proximal appraisals, but would have downstream effects (i.e., far transfer) to symptoms associated with PTSD. Using distressing film clips (i.e., the trauma film paradigm [23]), we found that inducing a dysfunctional versus benign appraisal style leads to corresponding differences in analogue trauma symptoms, such as fewer intrusive memories and lower levels of intrusion distress [8, 9]. The next critical step was to use distressing, autobiographical events, that is, moving to a subclinical sample in the context of trauma. Here, results were similar (e.g., less intrusion distress), further supporting dysfunctional appraisals being an important mechanism [10].

To conclude, there is systematic evidence highlighting the role of dysfunctional appraisals as a correlate, predictor, and potential causal factor for trauma-relevant symptoms [24]. However, the next critical step is to work with patients with PTSD [25], that is, to bridge the experimental work manipulating appraisals in the context of analogue trauma with clinical research highlighting appraisals as a key treatment target. Translation of experimental psychopathology research into clinical settings provides the opportunity to test key assumptions about the mechanisms underlying disorders and their treatments, which in turn allows development of more efficient mechanism-focused interventions [26, 27]. Further, if the CBM-APP procedure could modify dysfunctional appraisals within a clinical sample of PTSD patients, and this in turn leads to PTSD symptom reduction, not only would this provide evidence supporting a causal role of appraisals, but would also significantly extend previous research testing appraisals as a correlate and predictor of PTSD symptoms.

Apart from cognitive dysfunctions, PTSD is also characterized by neuroendocrinological dysregulations [28, 29]. The glucocorticoid hormone cortisol, which is the major end product of the hypothalamic-pituitary-adrenal axis regulating the body's response to stress [30–32], has received much attention in the context of PTSD [e.g., 33, 34]. Since cortisol secretion is highly volatile due to, for example, circadian and ultradian rhythmicity [33, 35], recent studies have started to focus on hair cortisol concentrations (HCC), which serve as a valid and reliable indicator of cumulative cortisol levels reflecting long-term retrospective stress exposure [34]. In fact, growing evidence highlights the utility of this relatively novel tool to elucidate knowledge on the links between trauma exposure, cortisol dysregulation, and PTSD [35, 36]. For example, lower HCC were related to the experience of multiple events, as well as an increased severity of intrusions [37] and childhood adversity [38]. However, the extent to which dysfunctional appraisals may contribute to long-term cortisol changes reflected in hair is unclear, and experimentally manipulating such appraisals within a clinical sample provides an opportunity to investigate this.

The present study examined whether it is possible to modify dysfunctional appraisals about trauma and associated reactions using CBM-APP in a clinical sample of PTSD patients and whether manipulating such appraisals has downstream effects on symptoms of PTSD and other outcomes such as HCC. We therefore carried out a randomized controlled trial (RCT), recruiting participants from a specialist inpatient clinic for PTSD [39]. Participants completed 8 sessions of CBM-APP or a sham training control condition, the Peripheral Vision Task (PVT), over a 2-week period as an adjunct to their inpatient treatment. The PVT had previously been used as a control condition in depression research [40], and we used it as a psychological "attention placebo" [41, 42] or "non-specific factors component" [43] condition, controlling for non-specific aspects of the intervention (e.g., cognitive engagement in a task requiring concentration) but containing none of its putative "active ingredients" (e.g., training functional appraisals). We included follow-up assessments up to 3 months after discharge to investigate longevity of training effects.

The study's primary aim was to test whether CBM-APP, compared to the control condition, could successfully reduce dysfunctional appraisals, operationalized via a scenario-based approach assessing idiosyncratic, trauma-relevant appraisals [44]. A secondary aim was to test whether the effects of CBM-APP on appraisals would generalize to another measure of dysfunctional appraisals, the Posttraumatic Cognitions Inventory (PTCI) [17]. We also sought to examine downstream effects of whether modifying dysfunctional appraisals would lead to reductions in symptoms of PTSD (e.g., assessed via the PTSD Checklist for DSM-5 (PCL-5) [45, 46]). We further aimed to test whether the effects of CBM-APP would generalize to a long-term biological stress marker, hair cortisol. Exploratory correlational and mediation analyses were conducted to better understand associated mechanisms underlying the training effects. Finally, we also collected data about acceptability of the CBM-APP and control training.

Materials and Methods

Design, Power Analyses, and Study Setting

The study was a randomized controlled superiority trial with 2 parallel arms, comparing Cognitive Bias Modification for Appraisals (CBM-APP) to a sham training control condition, the PVT. The trial was prospectively registered (clinicaltrials.gov identifier NCT02687555), and a protocol paper was published [39]. Ethical approval was provided by the ethics committee for the Faculty of Psychology, Ruhr-Universität Bochum (approval No.: 204), and the ethics committee for the Faculty of Medicine, Ruhr-Universität Bochum (approval No.: 15-5477). All participants provided written and informed consent.

A total sample size of $n = 80$ (i.e., $n = 40$ per condition) was determined via an a priori power analysis: we aimed to have 80% power to detect a between-group effect of $d = 0.70$ on our primary outcome at $p < 0.05$, allowing for up to 15% attrition. This was informed by a prior meta-analysis [47], which reported a between-group effect size of $g = 0.81$ for the effect of CBM on dysfunctional interpretations. We took a more conservative estimate of the effect of our training on dysfunctional appraisals of $d = 0.70$. Recruitment stopped when the target sample size was reached.

The study was conducted in the inpatient ward of the Department of Psychosomatic Medicine and Psychotherapy, LWL-University Clinic of Ruhr-Universität Bochum, Germany. This clinic has a specialist inpatient unit providing multimodal treatment for PTSD. Treatment lasts about 8 weeks, and each week includes 1 session of individual CBT, 3 sessions of trauma group therapy, 2 sessions of trauma stabilization group therapy, 2 sessions of kinesitherapy, 2 sessions of art therapy, physiotherapy, clinical rounds, and daily short sessions with a nurse. All patients received this same standard inpatient treatment programme. Patients started CBM-APP or the PVT approximately 2 weeks after admission to the clinic, at which point their standard therapeutic interventions had already begun.

Eligibility Criteria

Eligible participants were those aged 18–60 years, male or female, fluent in German, motivated and willing to take part in the study, and with a primary diagnosis of PTSD according to the criteria of both the International Classification of Diseases (ICD-10 F43.1) and the DSM-5. PTSD diagnosis was confirmed via a structured clinical interview, the Clinician Administered PTSD Scale for DSM-5 (CAPS-5) [48, 49]. Exclusion criteria as reported in the protocol paper [39] were experiencing active suicidal thoughts or intentions, substance abuse/substance dependence currently or in the past 6 months, a past or present psychotic disorder, learning disability/intellectual impairment and red-green colour blindness or non-corrected vision impairment (required since the control condition, the PVT, required participants to discriminate coloured stimuli).

Interventions

Cognitive Bias Modification-Appraisal

The CBM-APP was a computerized training procedure targeting dysfunctional appraisals about trauma and associated reactions, adapted from previous laboratory-based studies [8–10]. Whereas previous studies had used the PTCI Self subscale [17] to generate training sentences, the present study used all scales, that is, Self, World, Self-Blame, in order to train a heterogeneous set of functional appraisals. The Self subscale was used to produce 2 types of sentences [44], that is, sentences describing appraisals to the Self and related to the evaluation of specific symptoms. However, in line with previous studies, roughly two thirds of the training sentences targeted appraisals of the Self (see online suppl. material [see www.karger.com/doi/10.1159/000514166 for all online suppl. material] for more detailed information and example scenarios). During training, participants were instructed to read the sentence and then to proceed via pressing the spacebar. Next, a

word fragment appeared on the screen, and it was the participants' task to complete it by pressing its first missing letter. All word fragments were positive, and completing them thus resolved the sentence's ambiguity in a functional/positive manner. The training only continued to the next sentence if a correct response was entered. To ensure the sentences' contents were processed adequately, several sentences were followed by a short comprehension question using a yes/no answering format. To facilitate participants' engagement, the training sentences were designed to gradually become more positive over the course of the intervention. Each training session included 66 trauma-related sentences and 15 neutral non-trauma-related fillers and lasted for approximately 20 min. For further details, see the online supplementary material.

Peripheral Vision Task

The PVT was adapted from a previous study [40]. During the PVT, participants were presented with 15 small grey circles arranged in a large circle on the computer screen. A fixation cross was presented in the center of this larger circle, and participants were instructed to keep their eyes on the fixation cross while also paying attention to the small circles. At the beginning of each trial, one of the outer 15 circles was highlighted with a white frame to indicate the starting position of the trial. Afterwards, participants heard several beeps, with number of beeps differing randomly per trial (ranging from 1 to 9 beeps). Participants were instructed to shift their peripheral vision one small circle further every time they heard a beep. A trial ended via presentation of a higher pitched beep. Simultaneously, the small circles turned from grey to a variety of different colours, and participants were asked to indicate the colour of the circle on which their attention had ended. After each trial, participants were provided with feedback as to whether or not their answer was correct. The difficulty of the PVT was designed to be adaptive to the participants' performance. That is, after 4 consecutive correct answers, 1 additional small circle appeared, and the circles became smaller in size. Conversely, after 4 consecutive errors, one small circle disappeared, and the size of the circles increased. Each training session included 96 trials and, matching the CBM-APP training, lasted approximately 20 min. For further details, see the online supplementary material.

Measurements

Measurement Schedule

Assessments took place at the following time points: baseline, midintervention (approx. 1 week after baseline), after the intervention (approx. 2 weeks after baseline), end of inpatient admission (approx. 6 weeks after baseline), 6 weeks after discharge, and 3 months after discharge [see 39, for a more detailed overview]. Assessments were conducted at the LWL clinic except for the post-discharge measures, which the patients completed from home and returned by post.

Primary Outcome

Dysfunctional Appraisals Assessed via a Scenario Task

The primary outcome was dysfunctional appraisals at postintervention assessment relative to the pretraining one as measured by a scenario task [44]; for a similar approach, see de Kleine et al. [50]. Participants were given a paper and pencil booklet containing 10 ambiguous, open-ended, trauma-related scenarios, based on items of the PTCI, and 4 ambiguous non-trauma-related filler scenarios (see online suppl. material for examples). Participants were instructed to complete each scenario by writing down the first spontaneous ending that came to mind. Each booklet yielded a dysfunctional appraisal score operationalized as the total number of endings classed as dysfunctional appraisals divided by the total number of codable endings (as in Woud et al. [44]). As such, higher scores indicate a higher proportion of dysfunctional appraisals (see online suppl. material for more details about the coders' training and coding rules). Endings provided by participants were rated by 2 external coders not otherwise involved in the data analyses and blind to participant condition. Raters first coded whether the ending was an appraisal and second whether or not this appraisal was dysfunctional (both using a yes = 1 vs. no = 0 format). Raters first coded all scenario endings independently, and then met to discuss their coding and generate a final consensus score (where 1 = dysfunctional appraisal, 0 = not a dysfunctional appraisal) used in analyses[1]. Disagreements were resolved via discussion with the first author (M.L.W.). There was 96.82% agreement between the 2 raters for dysfunctionality, Cohen's $\kappa = 0.94$ (95% CI 0.92–0.96). The split-half reliability of the consensus score was low at the pretraining time point: split-half reliability = 0.39 (95% CI 0.12–0.58) and good at the posttraining one: split-half reliability = 0.87 (95% CI 0.80–0.91).

Secondary Outcomes

Dysfunctional Appraisals over the Course of the Study

The scenario task was also used at midtraining, at the end of admission, at 6-week and at 3-month follow-ups. Similar to the CBM-APP training, the scenarios were designed to gradually become more positively interpretable over the course of the study.

Posttraumatic Cognitions (PTCI)

To test for generalization effects to another measure of dysfunctional appraisals, the German translation of the PTCI was used [17, 51]. The PTCI consists of 33 trauma-related appraisals for which participants are instructed to rate their level of agreement in relation to the previous week on a 7-point scale ranging from 1 (totally disagree) to 7 (totally agree). The PTCI includes 3 subscales: appraisals related to the Self, the World, and Self-Blame. Previous studies reported excellent reliability for the full scale [17] and Cronbach's α in our sample was 0.80 (95% CI 0.73–0.86) at the pretraining and $\alpha = 0.95$ (95% CI 0.94–0.97) at the posttraining assessments. The PTCI was administered at pretraining, midtraining, posttraining, at the end of admission, as well as at 6-week and 3-month follow-ups.

[1] We followed the scoring procedure developed in our preliminary validation study [44] which was completed while this trial was ongoing. However, we note that our protocol only indicated a 1 = dysfunctional appraisal versus 0 = not a dysfunctional appraisal (there termed trauma-relevant interpretation vs. non-trauma-relevant interpretation, respectively) coding scheme and did not specify the 2-part process (i.e., coding first as an appraisal, then dysfunctional or not) used to arrive at this coding. Further, the protocol reported that a sum score rather than proportion score would be calculated. Given the small number of uncodable endings (14 in total across all endings provided by all participants across all time points), use of a proportion versus a sum score would make no meaningful difference to the results. Hence, we chose to use the scoring presented in the validation study, which we would see as preferable and the standard to be used in future.

Symptoms of PTSD (PCL-5)

Symptoms of PTSD were assessed via the German translation of the PTSD checklist for DSM-5 (PCL-5) [45, 46]. The PCL-5 is a 20-item checklist assessing PTSD symptoms in accordance with the DSM-5 criteria. The scale consists of 4 subscales, reflecting the 4 symptom clusters in DSM-5, that is, re-experiencing, avoidance, negative cognitions and mood, and hyperarousal. Each item represents a PTSD symptom, and participants are instructed to rate how strongly they experienced each symptom during the previous week, using a 5-point Likert scale ranging from 0 (not at all) to 4 (strongly). Previous studies reported good psychometric properties of the German translation [46] and Cronbach's α in our sample was 0.76 (95% CI 0.69–0.84) at pretraining and α = 0.85 (95% CI 0.80–0.90) at posttraining assessments. The PCL-5 was administered at pretraining, midtraining, posttraining, at the end of admission, as well as at 6-week and 3-month follow-ups. For reliability indices of further time points of assessment, see the online supplementary material.

Hair Cortisol Concentrations

HCC were determined in the first scalp-near 3-cm hair segment following the published liquid chromatography tandem mass spectrometry protocol [52]. Assuming a hair growth rate of 1 cm per month [53], these hair segments reflect integrated cortisol levels over the 3-month period prior to hair sampling. Hair sampling took place at baseline, at the end of admission, and at the 3-month follow-up (for more details see the online suppl. material).

Details of further secondary outcomes and other measures can be found in the online supplementary material.

Other Measures

Credibility/Expectancy Questionnaire

The Credibility/Expectancy Questionnaire (CEQ) [54, 55] comprises 3 questions asking participants' views of the credibility of an intervention, and 3 questions asking to what extent they expect their symptoms to improve (answered on a 10-point rating scale ranging from 1 "not at all" to 9 "very strongly"/10-point scale ranging from 0 to 100%). The CEQ was administered at the first training session after randomization, after the task had been explained to the participants, and before the first training session started.

Feedback Questionnaire

Participants were asked to provide feedback on the study and the intervention they had received using a questionnaire that was sent via post, together with the 3-month follow-up material. Participants were asked to rate how satisfied they were with the training, whether they would recommend it to a friend, whether they would try it again, and whether they felt that it had a positive impact on (i) their mood, (ii) their thoughts, and (iii) their behaviour, using a 9-point Likert scale ranging from 1 to 9, with higher values indicating a more positive evaluation of the training (see online suppl. material for additional questions).

Adverse Events

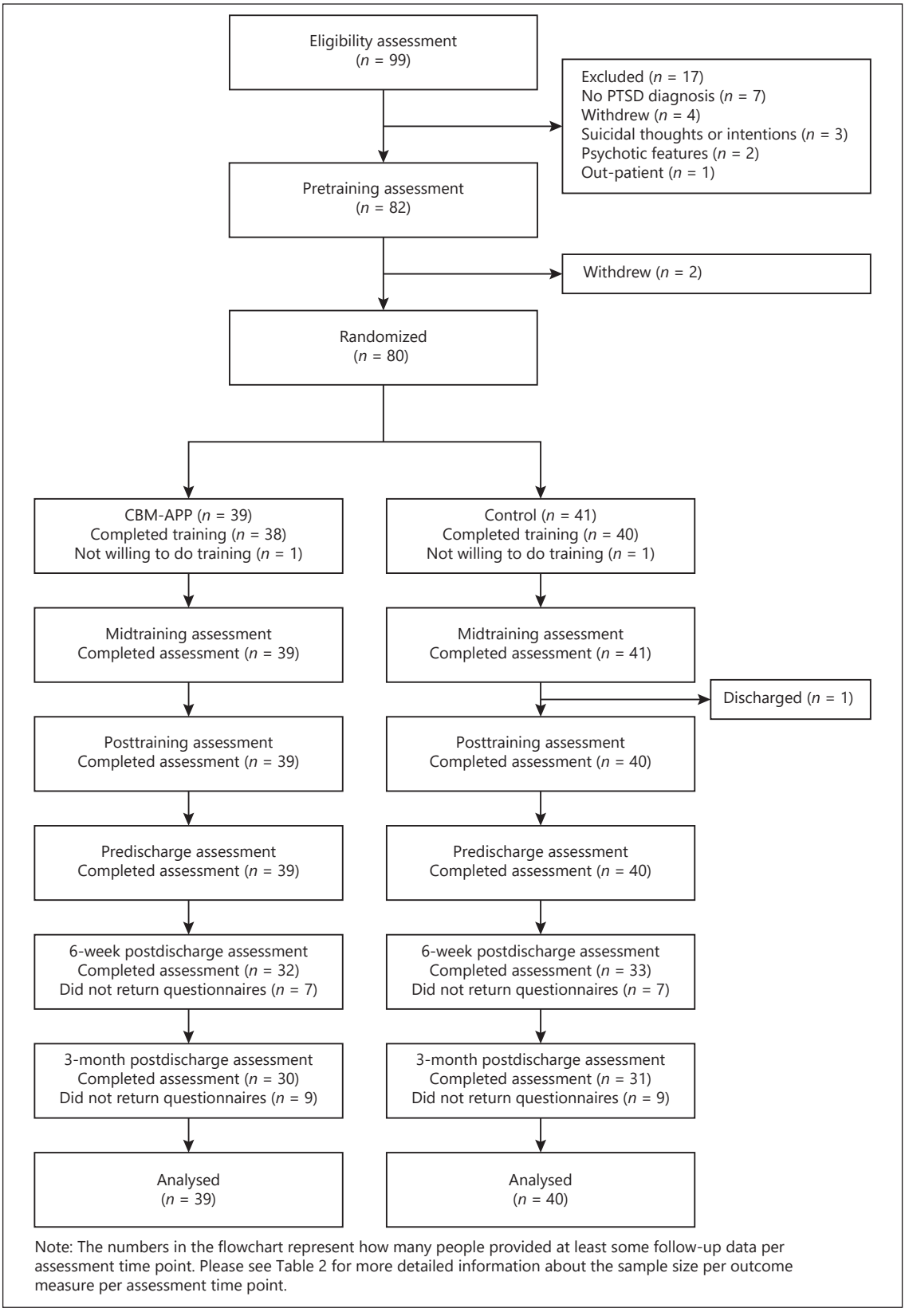
Adverse events were recorded by trial researchers using an adverse event checklist. During and after trial completion, the relationship to the study intervention was rated by the trial management group (M.L.W., H.K., J.C.C., and S.E.B.) from "unrelated" to "definitely related" for each recorded adverse event. Adverse events were predefined as suicidal ideation (indicated by BDI-II item 9 score of ≥2 or score ≥2 on the suicide ideation item on the intrusion questionnaire; see the online suppl. material), self-harm (indicated by a score ≥2 on the self-harm item on the intrusion questionnaire, confirmed by clinical assessment), worsening of PTSD symptoms (i.e., reliable deterioration [42], indicated by a significant increase in the PCL-5 score from baseline to the end of admission assessment using a "reliable change index" [56]), discontinuing inpatient treatment against medical advice, study termination due to negative effects on recovery, and/or readmission to the inpatient unit during the follow-up period of the study.

Randomization and Blinding

Participants were randomly allocated to CBM-APP or PVT in a 1:1 ratio, with randomization stratified by total scores on the PTCI [17], using 2 strata derived from data obtained during piloting of study procedures in the study setting (<165 vs. ≥165). The allocation sequence was generated by a researcher not involved in the study using a true randomization process (https://www.random.org). The study was double-blind (participants and outcome assessors). Lapses of blinding were recorded in a study log. To facilitate participant blinding (i.e., as to whether they were in an "active" or "sham" training condition), the study information did not specifically mention training appraisals but rather explained the study in terms of training concentration, using either words (CBM-APP) or visual patterns (PVT; for more details of randomization and blinding, see the online suppl. material).

Statistical Analyses

The primary analysis was conducted as intention to treat, including all participants randomized to a condition (with the exception of cortisol data, see below); secondary analyses were conducted as both intention to treat and per protocol. The per-protocol sample was defined as participants who provided complete outcome data for the relevant measure and who completed at least 4 out of the 8 training sessions. Efficacy analyses were conducted using mixed models, which were fitted across all time points using the R package "nlme" [57], using maximum likelihood estimation and an AR1 covariance structure. Between-group contrasts (change from baseline) at each time point were derived from the mixed models. Effect sizes were estimated as a form of Cohen's *d*, dividing estimated mean differences derived from the mixed models by observed SD. For between-group effect sizes, the SD of the relevant change score (from baseline) was used, and for within-group effect sizes the pooled SD of scores at baseline and the relevant time point were used. The Hedges' *g* correction for sample size was applied, and 95% CIs were calculated using the R package "MBESS" [58]. Cohen's κ and reliability indices for the scenario task and all questionnaire measures were computed using the R package "psych" [59]. For the analyses of the HCC, log transformations were applied to reduce skewness. Participants using glucocorticoid-containing medications over the course of the study, which would confound interpretation of their cortisol data [60], were excluded from these analyses (n = 3 CBM-APP group, n = 2 in the control group), as were data points with outlying values of >3 SD from the mean (before training: n = 1 in CBM-APP group; before discharge: n = 2 in the CBM-APP group). We note that although such exclusions are standard in cortisol analyses, they had not been prespecified in our written protocol. In exploratory anal-



Note: The numbers in the flowchart represent how many people provided at least some follow-up data per assessment time point. Please see Table 2 for more detailed information about the sample size per outcome measure per assessment time point.

Fig. 1. Flowchart of the 2 groups.

Table 1. Descriptive statistics of the study sample and clinical and training characteristics

	CBM	Control
Sociodemographic measures		
Gender female, *n* (%)	36 (92.3)	34 (82.9)
Mean age (SD), years	42.41 (12.42)	39.05 (12.45)
Marital status, *n* (%)		
Single	16 (41)	15 (36.6)
Married/civil partnership	14 (35.9)	15 (36.6)
Not living with partner	1 (2.6)	4 (9.8)
Divorced/revoked civil partnership	8 (20.5)	7 (17.1)
Children, *n* (%)	17 (43.6)	20 (48.8)
Migration background, *n* (%)	6 (15.4)	4 (9.8)
Native German speaker, *n* (%)	35 (89.7)	38 (92.7)
Education level, *n* (%)		
Low	8 (20.51)	9 (21.95)
Middle	22 (56.41)	28 (68.29)
High	7 (17.95)	2 (4.88)
Missing	2 (5.13)	2 (4.88)
Employment, *n* (%)		
Student	2 (5.13)	4 (9.76)
Employed	35 (89.74)	34 (82.93)
Not employed	2 (5.13)	3 (7.32)
Index trauma CAPS-5		
Experienced, *n* (%)		
Sexual violence	20 (51.28)	25 (60.98)
Non-sexual violence	8 (20.51)	8 (19.51)
Life-threatening accident	3 (7.69)	1 (2.44)
War	1 (2.56)	–
Captivity	1 (2.56)	–
Witnessed, *n* (%)		
Sexual violence	1 (2.56)	–
Non-sexual violence	1 (2.56)	2 (4.88)
Sudden death	2 (5.13)	2 (4.88)
Learned about, *n* (%)		
Murder	–	1 (2.44)
Missing values, *n* (%)	2 (5.1)	2 (4.88)
Mean CAPS-5 trauma severity score (SD)	2.74 (0.55)	2.78 (0.57)
Mean LEC-5 (SD)	7.49 (2.90)	7.07 (3.07)
Clinical characteristics		
Mean length of inpatient stay (SD), days	48.21 (9.34)	47.61 (10.38)
Comorbidities, *n* (%)		
Major depression	37 (94.87)	40 (97.56)
Eating disorders	8 (20.51)	6 (19.51)
Anxiety disorders	2 (5.13)	6 (14.63)
Borderline personality	6 (15.38)	4 (9.76)
Pain or conversion disorder	3 (7.69)	9 (21.95)
Substance dependence/abuse	4 (10.26)	1 (2.44)
Other	8 (20.51)	6 (14.63)
Mean number of comorbidities (SD)	1.69 (0.86)	1.72 (0.92)
Medication at eligibility, *n* (%)	34 (87.2)	37 (90.2)
Antidepressants	28 (71.8)	35 (83.4)
Neuroleptics	3 (7.7)	2 (4.9)
Sedatives/sleep medication	16 (41.0)	14 (34.1)
Opioids	4 (10.3)	2 (4.9)
Other psychotropics	9 (23.1)	4 (9.8)
Non-psychotropics	23 (59.0)	25 (61.0)

Table 1 (continued)

	CBM	Control
Baseline characteristics		
Mean BDI-II (SD)	35.69 (7.19)	34.83 (10.15)
Mean BAI (SD)	32.15 (12.98)	31.60 (8.50)
Mean scenario task (SD)	0.80 (0.15)	0.78 (0.14)
Mean PTCI (SD)	162.82 (29.13)	163.12 (32.48)
Mean PCL-5 (SD)	54.25 (9.43)	55.82 (9.66)
Training characteristics		
Mean total number of training sessions (SD)	7.54 (1.19)	7.44 (1.16)
Mean credibility (SD)	0.65 (2.68)	–0.62 (2.44)
Mean expectancy (SD)	0.45 (2.60)	–0.47 (2.31)
Mean days since first training session (SD)		
Posttraining assessment	10.24 (0.50)	10.03 (0.81)
Predischarge	30.74 (7.53)	30.46 (7.42)
6 weeks after discharge	79.03 (9.60)	77.69 (10.14)
3 months after discharge	126.90 (16.22)	120.29 (10.54)

CAPS-5, Clinician-Administered PTSD Scale for DSM-5; LEC-5, Life Event Checklist for DSM-5; BDI-II, Beck Depression Inventory-II; BAI, Beck Anxiety Inventory; PTCI, Posttraumatic Cognition Questionnaire; PCL-5, PTSD Checklist for DSM-5.

yses, we examined correlations between baseline and change (from pre- to posttraining assessments) scores on the scenario task and other measures, and conducted several mediation analyses. Correlations, descriptive statistics, and mediation analyses were calculated in SPSS (version 25) [61], with mediation examined via the PROCESS macro (version 3.5 [62]; 5,000 bootstrap samples). All statistical tests were 2-tailed using a significance value of $p < 0.05$. Anonymized outcome data and analysis scripts for the efficacy analyses are available at: https://osf.io/jvstf/.

Results

Participants were recruited and tested between March 10, 2016, and May 23, 2019. Recruitment stopped at 80 participants, which was the planned sample size. Attrition was comparable between the 2 conditions (Fig. 1), as were baseline characteristics (Table 1). There was no difference between the groups in number of training sessions completed, $t(78) = 0.38$, $p = 0.71$, or the timing of the assessments (in terms of days since baseline). However, participants in the CBM-APP group scored higher on the credibility scale of the CEQ than the control group, $t(78) = 2.23$, $p = 0.03$, but not on the expectancy scale, $t(78) = 1.68$, $p = 0.10$.[2]

Primary Outcome

There was a significantly greater reduction in dysfunctional appraisals, as measured using the scenario task, from pre- to posttraining assessments in the CBM-APP group compared to the control group, $t(352) = 6.42$, $p < 0.001$, $d = 1.30$ (95% CI 0.82–1.80). This was reflected by a large, statistically significant reduction in dysfunctional appraisals within the CBM-APP group, $t(352) = 10.32$, $p < 0.001$, $d = 1.71$ (95% CI 1.17–2.30), but no change within the control group, $t(352) = 1.34$, $p = 0.18$, $d = 0.28$ (95% CI –0.11 to 0.67; see Table 2 and Fig. 2 for more details).

Secondary Outcomes before to after Training

In the *PTCI,* participants in the CBM-APP group showed a significantly greater reduction in dysfunctional appraisals assessed compared to those in the control group from pre- to posttraining time points (see Table 2 and Fig. 2 for details).

In the *PCL-5,* investigating possible transfer to PTSD symptoms, the same pattern was found, that is, greater reductions in scores from pre- to posttraining time points for the CBM-APP compared to the control group (see Table 2 and Fig. 2 for details).

[2] Sensitivity analyses investigating the relationship between credibility scores and outcomes indicated that this between-group difference was unlikely to have any influence on the results of our analyses; see online supplementary material for details.

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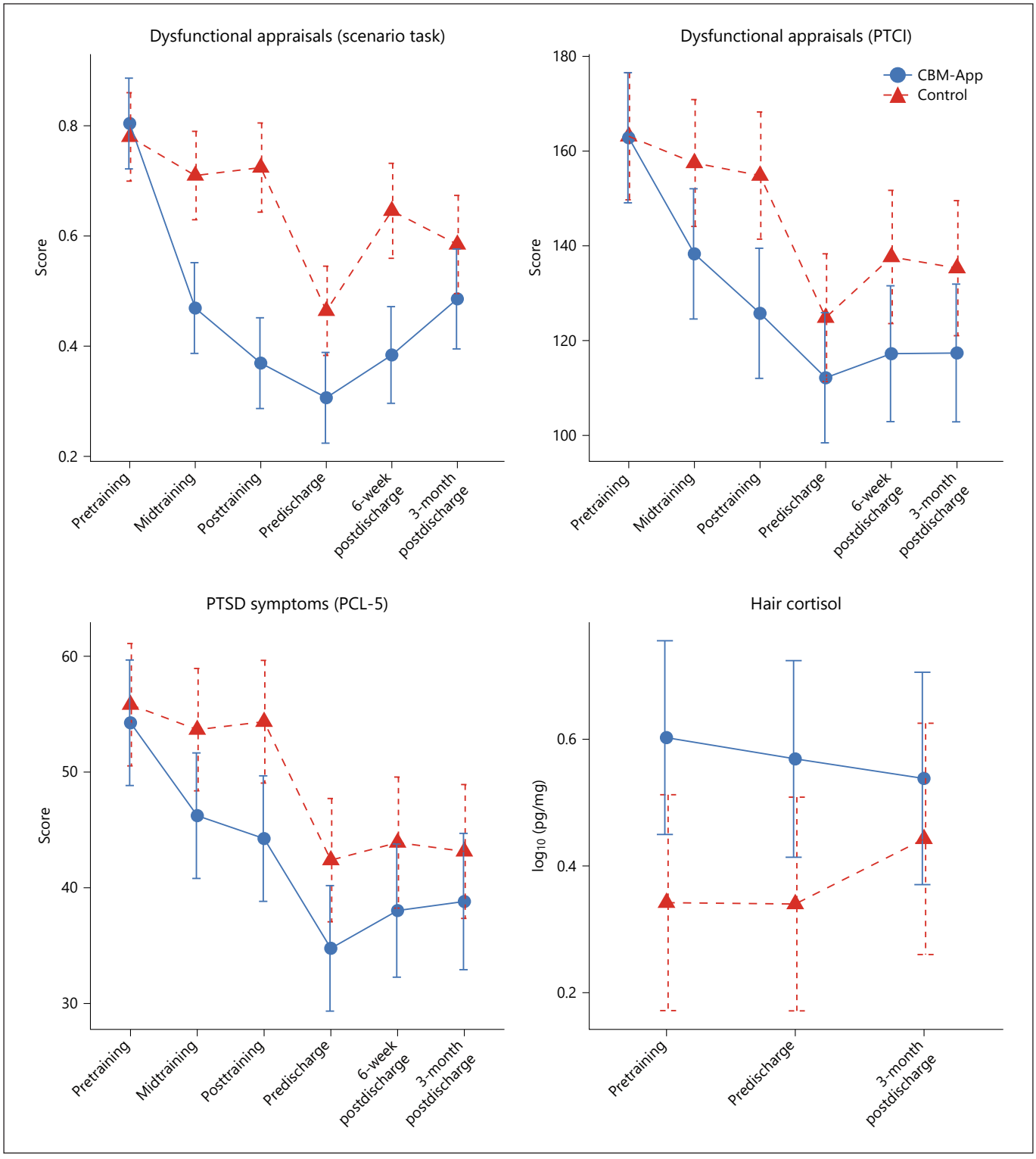
Table 2. Intention-to-treat outcomes for the scenario task, PTCI, PCL-5, and hair cortisol data

	Pretraining	Midtraining	Posttraining	Predischarge	6 weeks after discharge	3 months after discharge
Dysfunctional appraisals (scenario task)						
CBM-APP	*n* = 39	*n* = 39	*n* = 39	*n* = 39	*n* = 32	*n* = 29
Mean (SD)	0.80 (0.16)	0.47 (0.32)	0.37 (0.32)	0.31 (0.24)	0.39 (0.28)	0.50 (0.28)
Within-group *d* (95% CI)		1.30*** (0.83 to 1.81)	1.71*** (1.17 to 2.30)	2.41*** (1.79 to 3.11)	1.80*** (1.18 to 2.49)	1.37*** (0.84 to 1.97)
Control	*n* = 41	*n* = 41	*n* = 40	*n* = 40	*n* = 33	*n* = 30
Mean (SD)	0.78 (0.14)	0.71 (0.21)	0.72 (0.24)	0.46 (0.27)	0.64 (0.31)	0.56 (0.31)
Within-group *d* (95% CI)		0.39 (0.05 to 0.74)	0.28 (–0.11 to 0.67)	1.44*** (0.96 to 1.97)	0.55** (0.11 to 1.00)	0.79*** (0.33 to 1.28)
Between-group *d* (95% CI)		1.01*** (0.55 to 1.49)	1.30*** (0.82 to 1.80)	0.72** (0.27 to 1.18)	0.94*** (0.43 to 1.46)	0.44 (–0.07 to 0.96)
Dysfunctional appraisals (PTCI)						
CBM-APP	*n* = 39	*n* = 39	*n* = 39	*n* = 39	*n* = 32	*n* = 30
Mean (SD)	162.82 (29.13)	138.31 (36.77)	125.76 (42.69)	112.15 (45.65)	117.09 (41.11)	118.63 (46.89)
Within-group *d* (95% CI)		0.72*** (0.41 to 1.06)	0.99*** (0.60 to 1.42)	1.30*** (0.88 to 1.76)	1.25*** (0.77 to 1.77)	1.13*** (0.69 to 1.63)
Control	*n* = 41	*n* = 41	*n* = 40	*n* = 40	*n* = 33	*n* = 31
Mean (SD)	163.12 (32.48)	157.49 (35.96)	154.45 (43.86)	124.65 (47.82)	137.09 (48.39)	132.26 (52.57)
Within-group *d* (95% CI)		0.16 (0.00 to 0.32)	0.21 (–0.01 to 0.43)	0.92*** (0.58 to 1.28)	0.60*** (0.26 to 0.97)	0.62*** (0.24 to 1.02)
Between-group *d* (95% CI)		0.77*** (0.32 to 1.23)	0.85*** (0.39 to 1.32)	0.32 (–0.13 to 0.76)	0.50* (0.01 to 1.00)	0.41* (–0.09 to 0.92)
PTSD symptoms (PCL-5)						
CBM-APP	*n* = 39	*n* = 39	*n* = 39	*n* = 39	*n* = 32	*n* = 30
Mean (SD)	54.25 (9.43)	46.23 (13.33)	44.25 (14.92)	34.77 (19.90)	38.18 (19.65)	38.77 (20.92)
Within-group *d* (95% CI)		0.68*** (0.31 to 1.07)	0.79*** (0.41 to 1.19)	1.23*** (0.79 to 1.70)	1.03*** (0.50 to 1.59)	0.93*** (0.42 to 1.47)
Control	*n* = 41	*n* = 41	*n* = 40	*n* = 40	*n* = 33	*n* = 31
Mean (SD)	55.82 (9.66)	53.66 (12.36)	54.23 (13.34)	42.28 (19.62)	44.42 (16.96)	42.57 (20.37)
Within-group *d* (95% CI)		0.19 (–0.04 to 0.43)	0.12 (–0.16 to 0.41)	0.85*** (0.44 to 1.29)	0.84*** (0.43 to 1.28)	0.78*** (0.33 to 1.25)
Between-group *d* (95% CI)		0.55** (0.10 to 1.00)	0.68** (0.23 to 1.14)	0.33 (–0.12 to 0.77)	0.23 (–0.25 to 0.72)	0.14 (–0.36 to 0.64)
Hair cortisol (log_{10} pg/mg)						
CBM-APP	*n* = 32			*n* = 30		*n* = 23
Mean (SD)	0.59 (0.47)			0.59 (0.47)		0.59 (0.48)
Within-group *d* (95% CI)				0.07 (–0.12 to 0.27)		0.10 (–0.25 to 0.45)
Control	*n* = 25			*n* = 26		*n* = 19
Mean (SD)	0.31 (0.44)			0.34 (0.34)		0.43 (0.43)
Within-group *d* (95% CI)				–0.07 (–0.31 to 0.17)		–0.17 (–0.79 to 0.43)
Between-group *d* (95% CI)				0.25 (–0.28 to 0.78)		0.25 (–0.35 to 0.87)

Observed means and standard deviations are presented, alongside the number of participants providing data at each time point. Effect sizes (*d*) are calculated as change from baseline using estimated means from the mixed model analysis and include the correction for sample size (often termed "Hedges' *g*"; see Methods section for details). Statistical significance of the between- or within-group comparisons for change from baseline from the mixed model analyses is indicated by the asterisks next to the corresponding effect size, where: * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.



Color version available online

Fig. 2. Outcome measurements.

Hair Cortisol Concentration

For the HCC analyses, the body mass index (BMI) was included as a covariate since the BMI could potentially confound interpretation of the cortisol data [35]. There was no effect of CBM-APP training on HCC, neither from pretraining to predischarge nor from pretraining to 3-month postdischarge time points (see Table 2 and Fig. 2 for details). As the inclusion of the BMI as a covariate was post hoc based on the large variance in the BMI data, we carried out further sensitivity analyses to assess the impact of its inclusion. Running the analyses without this covariate, or using an alternative method for reducing the potential impact of the BMI (excluding participants with BMI >40; $n = 6$ in the CBM-APP group, $n = 6$ in the control group), led to the same pattern of results.

Additional Assessment Points for Primary and Secondary Outcomes

Compared to participants in the control group, participants in the CBM-APP group showed significantly greater reductions in dysfunctional appraisals assessed via the scenario task from baseline up to the follow-up at 6 weeks after discharge, but the between-group difference was no longer statistically significant at the final follow-up at 3 months after discharge. Participants in the CBM-APP group showed significantly greater reductions on the PTCI compared to participants in the control group across all follow-up assessment points (apart from before discharge, that is, the last assessment in the clinic). For the PCL-5, between-group differences were no longer statistically significant at the predischarge follow-up and following assessments (see Table 2 and Fig. 2 for details, and online suppl. material for other secondary outcomes and questionnaire subscales).

Feedback Questionnaire

Participants' ratings for satisfaction with the training, whether they would recommend it to a friend, and whether they would be motivated to try it again in future were around or just above the middle of the 9-point scales and did not differ between conditions (satisfaction: CBM-APP: mean = 6.40, SD = 1.96; control: mean = 5.81, SD = 1.45; $t(59) = 1.35$, $p = 0.18$; recommend to a friend: CBM-APP: mean = 5.63, SD = 2.53; control: mean = 4.87, SD = 2.46, $t(59) = 1.19$, $p = 0.24$; would try again: CBM-APP: mean = 6.57, SD = 2.40; control: mean = 5.71, SD = 2.34, $t(59) = 1.41$, $p = 0.16$). Compared to those in the control group, participants in the CBM-APP group felt that the training had had more of a positive impact on their mood (CBM-APP: mean = 5.33, SD = 2.68; control: mean = 4.13, SD = 1.91; $t(59) = 2.02$, $p = 0.047$), thoughts (CBM-APP: mean = 5.87, SD = 2.45; control: mean = 4.17, SD = 2.18; $t(58) = 2.84$, $p = 0.006$), and behaviour (CBM-APP: mean = 4.97, SD = 2.31; control: mean = 3.87, SD = 1.91; $t(58) = 2.01$, $p = 0.049$).

Adverse Events

No serious adverse events were recorded. According to our predefined criteria, 2 adverse events related to suicidal ideation were recorded (one in each condition), and 4 adverse events related to worsening of symptoms (on the PCL-5) were recorded (3 in the CBM-APP group, 1 in the control group). The number of these adverse events did not differ between the 2 groups, $\chi^2(1, n = 80) = 0.62$, $p = 0.43$. Two of these (worsening of symptoms in the CBM-APP group) were judged as possibly related to the study, in that the patients reported the training as distressing (triggering memories of their traumatic event). While several patients answered "yes" to the self-harm question, on further questioning or discussion with the responsible clinician, none of these responses were judged to reflect an adverse event (e.g., long-standing superficial scratching).

Correlational and Mediation Analyses

At baseline, there was a significant and moderate correlation between dysfunctional appraisals assessed via the scenario task and scores on both the PTCI and PCL-5, showing the stronger participants' dysfunctional appraisals on the scenario task, the stronger participants' dysfunctional appraisals on the PTCI and the higher participants' symptom levels on the PCL-5 (Table 3). There were strong correlations between change scores (pre- to posttraining), in that a stronger reduction in dysfunctional appraisals assessed via the scenario task was associated with a stronger reduction in dysfunctional appraisals on the PTCI, symptom levels assessed via the PCL-5, and HCC.

We carried out exploratory mediation analyses to test the hypothesis that the differential impact of CBM-APP versus PVT on symptoms of PTSD would be mediated by the induced reduction in dysfunctional appraisals. First, we examined whether the relationship between group allocation and change in symptoms of PTSD, on the PCL-5, from pre- to posttraining assessments was mediated by change in dysfunctional appraisals, on the scenario task, from pre- to midtraining assessments. This midtraining time point for change on the scenario task was taken as an assessment of change in the hypothesized mediator prior to the change in symptoms (i.e., temporal sequence

Table 3. Correlations at baseline and between change scores of the scenario task, PTCI, PCL-5, and hair cortisol concentration

	Pretraining			Change from pre- to posttraining		
	PTCI	PCL-5	cortisol	PTCI	PCL-5	cortisol[a]
Scenario task	0.48***	0.38***	0.10	0.60***	0.51***	0.32*
PTCI	–	0.61***	0.02	–	0.67***	0.16
PCL-5	–	–	−0.02	–	–	0.24

For pretraining correlations, $n = 80$ except for those with cortisol ($n = 57$). For change score correlations, $n = 79$ except for those with cortisol ($n = 55$). * $p < 0.05$; *** $p < 0.001$ (uncorrected p values; correcting for the number of correlations at each time point, for example, via Bonferroni or Bonferroni-Holm procedures, would result in the correlation currently marked * no longer being statistically significant). PTCI, Posttraumatic Cognitions Inventory; PCL-5, PTSD Checklist for DSM-5. [a] Cortisol measured at predischarge rather than posttraining time point.

of mediator and outcome [63], although we realize that most change in symptoms had already occurred by this time point). We assessed mediation using the PROCESS macro (version 3.5 [62]; 5,000 bootstrap samples), with group as predictor, change in PCL-5 from pre- to posttraining time point as outcome, and change in score on the scenario task from pre- to midtraining time point as mediator. In the full model, there was no significant direct effect of group on PCL-5 change, $B = -4.83$ (95% CI −10.81 to 1.14), SE = 3.00, $p = 0.11$, but an indirect effect via the mediator, $B = -3.78$ (95% CI −7.78 to −0.83], SE = 1.77, consistent with the hypothesized mediation. We further investigated mediation of change on the PCL-5 from pretraining to the final study follow-up via change in score on the scenario task from pre- to posttraining assessment. This found a similar result, with no significant direct effect of group on PCL-5 change, $B = 7.64$ (95% CI −3.53 to 18.80), SE = 5.58, $p = 0.18$, but an indirect effect via the mediator, $B = -11.82$ (95% CI −19.82 to −5.13), SE = 3.78. An equivalent pattern of results was found using change on the PTCI instead of change on the scenario task as the index of change in dysfunctional appraisals (see online suppl. material for details).

Discussion

The RCT's primary aim was to test whether CBM-APP can modify dysfunctional appraisals in a clinical sample of PTSD, and whether this, in turn, would have downstream effects on symptoms associated with PTSD (i.e., far transfer). Results supported our hypotheses: there was a greater reduction in dysfunctional appraisals, as assessed both by a scenario completion task (primary outcome) and the PTCI, in the CBM-APP compared to the control group. This was accompanied by a greater reduction in PTSD symptoms in the CBM-APP compared to the control group. The relatively greater reduction in dysfunctional appraisals in the CBM-APP group was maintained up to 6 weeks (scenario task) and 3 months (PTCI) after discharge. Exploratory mediation analyses suggested that changes in dysfunctional appraisals were a mechanism underlying reductions in PTSD symptoms observed. Effects of CBM-APP did not generalize to a biological stress marker, hair cortisol, and between-group differences in reductions in PTSD symptoms were not maintained beyond the posttraining assessment. Overall, results provide proof-of-principle for CBM-APP as a potential means to reduce dysfunctional appraisals amongst patients with PTSD and that this has a downstream impact on PTSD symptoms, at least in the short term. Importantly, CBM-APP was still beneficial over the control training despite participants in both groups receiving treatment. Our results thus provide a valuable extension of previous experimental work in healthy and subclinical samples in the context of PTSD [8, 9, 22, 64–66], as well as other clinically relevant areas such as depression [67, 68] and social anxiety [69].

Although our results are in line with the broader literature, such as recent meta-analyses of the efficacy of reappraisal interventions on subjective stress reactivity [70] and CBM interventions targeting interpretive biases on anxiety [71], they need to be reconciled with the most comparable study to date. In a recent RCT, the Changing Interpretations in PTSD study (ChIP [50]), patients with PTSD on a waiting list for therapy completed either a 4-session CBM-APP training scheduled over 1 week, or a sham training control. Although participants in both

conditions displayed reductions in dysfunctional appraisals and PTSD symptoms, the 2 groups did not differ on these outcomes. One reason proposed by the authors for this lack of between-group differences was the control condition chosen, which closely resembled the active CBM-APP condition: participants were also presented with open-ended, ambiguous scenarios and a to-be-completed word fragment, but these word fragments were neutral rather than positive. While the expectation was that this would not induce changes in appraisal style, exposure to trauma-relevant ambiguity with provision of non-dysfunctional resolutions may in fact be sufficient to induce changes, as participants' expectations of a dysfunctional resolution would still be violated. However, the use of a different control condition cannot in itself explain the different results between the present RCT and the ChIP study: even at our midtraining assessment, which maps on to the ChIP's posttraining assessment (1 week after baseline and 4 sessions completed), the changes observed in appraisals and PTSD symptoms in the current RCT appear considerably larger than those of the ChIP study. In fact, the within-group effect size for change in dysfunctional appraisals in our control group (d = 0.39) at midtraining is similar to that found for their active CBM-APP group (d = 0.38) after training. As such, the present CBM-APP seems more able to induce changes in dysfunctional appraisals than that of the ChIP study. A plausible explanation may lie in the different study settings and administration mode (inpatients completing the training with a researcher present vs. people on a waiting list completing it online from home). When the CBM is completed in parallel to other psychotherapeutic interventions, there could be potentially mutually beneficial interactions between the CBM and psychotherapy if similar processes (e.g., in this case, dysfunctional appraisals) are targeted in each. Further, although online administration of CBM paradigms is attractive from the perspective of accessibility, the controlled environment of lab- or clinic-based implementation may be preferable for establishing first proof of principle in clinical populations.

The efficacy of CBM-APP in reducing dysfunctional appraisals and symptoms of PTSD (at least at the posttraining time point) in the current study also indicates potential clinical utility, albeit with a number of caveats. Of course, dysfunctional appraisals are already a key target for evidence-based interventions [4, 7], but appraisal-focused adjuncts may be beneficial. Interestingly, sudden gains in trauma-focused CBT have been linked to lower levels of dysfunctional appraisals in the preceding session [72], and potentially CBM-APP could provide a route to potentiate such an effect. However, before clinical recommendations could be made the results of the current study would clearly require replication in appropriately powered samples, with a symptom measure, ideally clinician-administered, as the primary outcome, and prespecified criteria defined for treatment success [43]. The lack of statistically significant between-group differences on PTSD symptoms after the posttraining assessment in the current study, corresponding to small between-group effect sizes, leaves open the possibility that such a future trial would not find longer-term effects on symptom outcomes either. However, even a short-term effect of an adjunctive intervention on symptoms can in itself be clinically valuable if it represents accelerated symptom reduction. Further, the proof of principle for the putative mechanism established in the current study provides a promising foundation for further investigating the potential clinical applications of CBM-APP as an adjunctive intervention, for example, via larger studies powered to find longer-term effects on clinical outcomes.

The proof of principle provided by our results also provides a basis for future work to refine and improve the effects of CBM-APP in clinical applications. The specific implementation of the training used in the current RCT was guided by previous research, but it would be surprising if this "first guess" was the optimal way to implement the training for best clinical outcomes. We have made some initial investigations into means for improving the effects of CBM-APP via enhancing associative learning through sleep [73] or *d*-cycloserine [74], albeit without clear-cut success. Other potential routes forward could involve focusing on more specific aspects of PTSD and trauma-relevant appraisals, for example, as has been done for appraisals related to the "event centrality" of the traumatic event [75]. In evaluating the potential promise for CBM-APP as a treatment adjunct it would also be important to put this in the context of other potential adjunctive interventions. However, a recent systematic review for treatment adjuncts to psychotherapy for PTSD [76] concluded that at present there is no strong evidence base in this area and thus it is difficult to find a suitable benchmark for comparison. There are a number of approaches emerging from experimental psychopathology research that could provide alternative or potentially complementary treatment adjuncts for PTSD, such as CBM approaches targeting attentional processes [77], or investigations of the potential of different tasks taxing visuospatial working memory to reduce vividness [78] or intrusion frequency [25, 79–82] in relation to trauma memories. However, these are also at relatively early stages of clinical

translation, and whether these or other approaches provide the best methods for improving PTSD treatment outcomes remains an open question.

An important consideration in investigating potential new interventions is their acceptability to patients and possible negative effects [42], which have historically often been neglected in psychological therapy research [83, 84]. Our adherence data suggest a high level of acceptability, and ratings of satisfaction and willingness to try the training again were on average in the upper half of the scale. Although the overall pattern of feedback was rather mixed (see online suppl. material), negative training effects referred to short-term discomfort, for example, being reminded of the trauma. Given that almost all effective treatments for PTSD involve the experience of distress, this does not necessarily reflect anything unusual. Further, this questionnaire was returned via post, leaving no opportunity to clarify the patients' feedback. Similarly, it is unsurprising that we detected some adverse events (6 in total) given the study population and context. However, the fact that the threshold for one of the adverse event categories, reliable symptom deterioration, was only calculated after study completion, precluded us from being able to investigate possible relationships between this and the study procedures. These results therefore highlight the importance of monitoring adverse events, including procedures to disambiguate the information collected in a timely manner, for example, via structured measures [85].

The present results need to be interpreted within the context of several limitations. While our primary outcome (dysfunctional appraisals measured via a scenario task) was chosen as most closely reflecting the mechanism being targeted in the training, in line with the proof-of-principle early-phase nature of our RCT, the only previous applications of such a task in a PTSD context are the cross-sectional study in a non-clinical sample [44] and the ChIP study [50]. Hence, there is not an extensive literature validating the task as a measure of PTSD-relevant appraisals or as sensitive to treatment effects. Second, from a mechanism perspective, the fact that patients in our study were also receiving treatment as usual means that strictly speaking we were not observing a pure effect of CBM-APP, but rather its combined effect with other treatment elements. However, it is very encouraging that CBM-APP could still show benefits over the control condition. Third, while our choice of control condition may have controlled for non-specific effects of a cognitive training intervention, it does not allow isolation of the specific active ingredients of CBM-APP. For example, taken together with the results of the ChIP study [50], the possibility remains that simple exposure to ambiguous appraisal-related stimuli may lead to reductions in dysfunctional appraisals and symptoms, in the absence of any training contingency to resolve these positively. Finally, the trial was powered to find immediate effects of the training, that is, from pre- to posttraining assessments, on the target mechanism of interest, that is, change in dysfunctional appraisals, and did not include a greater range of clinical outcome measures such as interview-based assessments. The fact that mid- and posttraining measures were administered directly after a training session may have inflated between-group differences at these time points. Overall, larger studies would be needed in future to test potential longer-term effects of CBM-APP on clinical outcomes.

To conclude, the present preregistered, double-blind study found that dysfunctional PTSD-relevant appraisals could be modified in an inpatient sample using a computerized appraisal training (CBM-APP). Further, reductions in dysfunctional appraisals were accompanied by reductions in PTSD symptoms. While the results should be regarded as proof of principle, they open a number of avenues for future research to unravel the mechanisms underlying PTSD and its treatment, and to develop and test adjunctive computerized interventions to improve treatment outcomes.

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Statement of Ethics

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee of both the Faculty of Psychology and the Faculty of Medicine at the first author's university (Ruhr-Universität Bochum) (ethical approval No. Faculty of Psychology: 204;

ethical approval No. of the Faculty of Medicine: 15-5477) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. All participants provided written informed consent. The original full trial protocol (German) is available from the first author on request.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

M.L.W. conceived the study and acquired funding. M.L.W., S.E.B., J.C.C., J.M., E.A.H., S.S.-S., S.H., and H.K. contributed to the study design. M.L.W., S.E.B., F.W., L.S., and S.S.-S. were involved in the data preparation and analyses and wrote the first draft of the paper. All authors contributed to refinement of the paper and approved it.

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