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Dialectical Behavior Therapy for Posttraumatic Stress Disorder (DBT-PTSD) Compared With Cognitive Processing Therapy (CPT) in Complex Presentations of PTSD in Women Survivors of Childhood Abuse

A Randomized Clinical Trial

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IMPORTANCE Childhood abuse significantly increases the risk of developing posttraumatic stress disorder (PTSD), often accompanied by symptoms of borderline personality disorder (BPD) and other co-occurring mental disorders. Despite the high prevalence, systematic evaluations of evidence-based treatments for PTSD after childhood abuse are sparse.

OBJECTIVE To compare the efficacy of dialectical behavior therapy for PTSD (DBT-PTSD), a new, specifically designed, phase-based treatment program, against that of cognitive processing therapy (CPT), one of the best empirically supported treatments for PTSD.

DESIGN, SETTING, AND PARTICIPANTS From January 2014 to October 2016, women who sought treatment were included in a multicenter randomized clinical trial with blinded outcome assessments at 3 German university outpatient clinics. The participants were prospectively observed for 15 months. Women with childhood abuse–associated PTSD who additionally met 3 or more *DSM-5* criteria for BPD, including affective instability, were included. Data analysis took place from October 2018 to December 2019.

INTERVENTIONS Participants received equal dosages and frequencies of DBT-PTSD or CPT, up to 45 individual sessions within 1 year and 3 additional sessions during the following 3 months.

MAIN OUTCOMES AND MEASURES The predefined primary outcome was the course of the Clinician-Administered PTSD Scale for *DSM-5* (CAPS-5) score from randomization to month 15. Intent-to-treat analyses based on dimensional CAPS-5 scores were complemented by categorical outcome measures assessing symptomatic remission, reliable improvement, and reliable recovery.

RESULTS Of 955 consecutive individuals assessed for eligibility, 193 were randomized (DBT-PTSD, 98; CPT, 95; mean [SD] age, 36.3 [11.1] years) and included in the intent-to-treat analyses. Analysis revealed significantly improved CAPS-5 scores in both groups (effect sizes: DBT-PTSD: *d*, 1.35; CPT: *d*, 0.98) and a small but statistically significant superiority of DBT-PTSD (group difference: 4.82 [95% CI, 0.67-8.96]; $P = .02$; *d*, 0.33). Compared with the CPT group, participants in the DBT-PTSD group were less likely to drop out early (37 [39.0%] vs 25 [25.5%]; $P = .046$) and had higher rates of symptomatic remission (35 [40.7%] vs 52 [58.4%]; $P = .02$), reliable improvement (53 [55.8%] vs 73 [74.5%]; $P = .006$), and reliable recovery (34 [38.6%] vs 52 [57.1%]; $P = .01$).

CONCLUSIONS AND RELEVANCE These findings support the efficacy of DBT-PTSD and CPT in the treatment of women with childhood abuse–associated complex PTSD. Results pertaining to the primary outcomes favored DBT-PTSD. The study shows that even severe childhood abuse–associated PTSD with emotion dysregulation can be treated efficaciously.

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Supplemental content

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The experience of childhood abuse (CA), whether sexual and/or physical, increases the likelihood of mental disorders later in life, particularly posttraumatic stress disorder (PTSD) and borderline personality disorder (BPD).[1-6] Cooccurrence of these 2 disorders is frequent: in epidemiological studies, 15% to 29% of individuals with PTSD also met criteria for BPD, while 17% to 53% of individuals with BPD reported PTSD.[7-10] In clinical samples, BPD-PTSD comorbidity often exceeds 50%.[11-13] Recent studies suggest that the experience of CA in particular results in complex presentations of PTSD, with high cooccurrence of these disorders.[8,14]

A recent meta-regression involving 51 randomized clinical trials found that patients with a history of CA and complex PTSD symptoms responded poorly to psychotherapy for PTSD.[15] This might be because of trauma-associated morphological alterations of the central nervous system,[16,17] increased dissociative features,[18] or severe self-criticism,[19] which might impede neural plasticity, emotional learning, and treatment motivation. The empirical base for a negative outcome of co-occurring BPD on treatment response is sparse. One study that investigated efficacy of cognitive behavioral therapy for survivors of childhood sexual abuse found that all the patients with co-occurring BPD dropped out of the cognitive behavioral therapy arm.[20] Five studies[21-25] documented no significant associations of BPD with treatment outcome; however, 3 of these studies[21-23] had excluded patients with current self-injurious behavior. This exclusion corresponds to the frequent exclusion from PTSD trials of patients with severe psychopathology, such as suicidality, ongoing self-harm, and substance abuse.[26,27]

Conversely, a study[28] showed that dialectical behavior therapy (DBT), one of the currently best-established treatments for BPD, did not significantly improve co-occurring PTSD. An attempt to address this problem has been made by adding prolonged exposure therapy to the standard DBT procedure.[29] However, the dropout rates were high, and the data are limited.

Currently, treatment of CA-associated PTSD mostly relies on established treatments that were developed for survivors of adult-onset trauma. Most treatment guidelines recommend prolonged exposure, cognitive processing therapy (CPT), or trauma-focused cognitive behavioral therapy,[30-32] but there is debate on whether these treatments are sufficient for patients with CA-associated PTSD.[33,34] Some authors favor phase-based treatments, focusing on emotion regulation before addressing traumatic memories,[35-39] while others maintain that standard trauma-focused programs without additional components are sufficient.[40,41] To date, no direct comparison has been carried out between standard PTSD therapies and specifically designed phase-based therapies.

Dialectical behavior therapy for PTSD (DBT-PTSD) is a prototypic phase-based treatment that is designed to meet the needs of survivors of CA with highly complex presentations of PTSD, including features of BPD. The first evaluation of this treatment supported its efficacy under residential treatment conditions.[42,43] The present study aimed at testing the superiority of DBT-PTSD compared with CPT in outpatients. We chose CPT as the comparator treatment because it is a highly efficacious,[41,44-46] non–phase-based, well-established therapy for PTSD that has been shown to be efficacious in treating CA-associated PTSD.[44]

Key Points

Question Is dialectical behavior therapy for posttraumatic stress disorder (DBT-PTSD) superior to cognitive processing therapy (CPT) in reducing the severity of complex presentations of posttraumatic stress disorder associated with childhood abuse?

Findings In this randomized clinical trial, treatments with DBT-PTSD and CPT both created large and significant improvements in PTSD severity, with improvement more pronounced under DBT-PTSD. The proportions achieving symptomatic remission were 58% in DBT-PTSD vs 41% in CPT, a significant difference.

Meaning In this trial, patients with severe childhood abuse–associated complex posttraumatic stress disorder highly improved under both DBT-PTSD and CPT, with DBT-PTSD being superior to CPT.

Methods

Trial Design and Participants

The study was conducted at 3 sites in Germany. Approval was obtained from the applicable ethics committees (Medical Faculty Mannheim at Heidelberg University in Mannheim, Goethe University in Frankfurt, and Humboldt University in Berlin). Before randomization, participants provided written informed consent. Safety and data quality were independently monitored by the Coordination Centre for Clinical Trials, Heidelberg. The study protocol has been published elsewhere[47] and is available in Supplement 2.

Inclusion criteria included female sex and gender identity; an age of 18 to 65 years; a diagnosis of PTSD (according to the *DSM-5*) following sexual or physical abuse before age 18 years; meeting 3 or more BPD criteria, including criterion 6 (affective instability); and availability for 1 year of outpatient treatment. Exclusion criteria included lifetime diagnoses of schizophrenia, bipolar I disorder, mental retardation, or severe psychopathology requiring immediate treatment in a different setting (eg, a body mass index <16.5); life-threatening suicide attempts within the last 2 months; current substance dependence (any usage within the last 2 months); medical conditions contradicting exposure protocol (eg, pregnancy); a highly unstable life situation (eg, homelessness); scheduled residential treatment; and receipt of either CPT or DBT-PTSD treatment during the last year. Patients with ongoing self-harm, suicidality, or high-risk behaviors were not excluded.

Participants were recruited from waiting lists of outpatient clinics in Mannheim, Frankfurt, and Berlin, Germany; through advertisements; and from therapists who had been informed about the study. Recruitment occurred from January 2014 to October 2016. Data analysis took place from October 2018 to December 2019.

Randomization and Masking

Web-based randomization software (http://randomizer.at) was used to assign participants in a 1:1 ratio to DBT-PTSD or CPT. Assessments were conducted by trained and experienced clinicians who were blinded to assignments.

Interventions

Detailed descriptions of the interventions were published elsewhere and are provided in the supplementary material (eAppendix in Supplement 1).[41,42,47,48] Briefly, DBT-PTSD is a multicomponent phase-based program based on the principles, modes, and functions of standard DBT[49] but supplemented by trauma-focused cognitive-behavioral interventions[40,50] and specific techniques from compassion-focused therapy[51] and acceptance and commitment therapy.[52] Cognitive processing therapy is an established trauma-focused cognitive therapy aiming at challenging dysfunctional trauma-associated cognitions and emotions. Treatment, modified for this study, followed a session-by-session protocol. The first 4 sessions aimed at elaborating a case history, the patient's specific problem behaviors, and emergency plans; the next 12 sessions encompassed the original 12 CPT core sessions; and the content of the remainder was derived from the patient's individual stuck-point log.

To achieve structural equality of the arms, both treatments included individual therapy, plus homework and telephone consultation as needed. All patients received up to 45 weekly sessions over a year, followed by a booster phase of 3 monthly sessions. Participants who missed 6 consecutive weekly sessions or had psychiatric hospitalizations of 2 weeks or longer were considered dropouts, unless they had achieved early remission. Early remission was achieved under predefined conditions, all of which had to be fulfilled: (1) the patient claimed recovery prior to session 45; (2) the therapist agreed; (3) the therapist's supervisor agreed; and (4) a blinded rater assessed that the patient no longer met the PTSD diagnosis (Clinician-Administered PTSD Scale [CAPS-5] score).[53]

To ensure integrity of the treatments, prior to the study, participating therapists were trained in either DBT-PTSD or CPT in 4-day workshops led by the respective treatment developers. All therapists had regular team consultations. The arms were balanced with respect to therapists' experience, age, and structural characteristics, such as the number of patients (eTable 1 in Supplement 1). Therapist adherence and competence were assessed by 2 independent raters (M.M.-E. and 1 nonauthor) who had received intensive training in both treatments and the rating procedure. They viewed a total of 258 videotapes (2 sessions from each patient who completed the study) and rated the therapists using scales that had been specifically developed to assess these characteristics in both arms. Interrater reliability for all scales yielded good to excellent results (intraclass correlations, 0.67-0.97).[54,55]

Diagnostic Procedures

Diagnoses of PTSD were established with the CAPS-5, cooccurring Axis I disorders with the Structured Clinical Interview for DSM-IV Axis I disorders,[56] and BPD with the International Personality Disorder Examination.[57] The concordance between the diagnoses of PTSD according to the CAPS-5 vs the Structured Clinical Interview was 100%. Interrater reliability for the diagnosis established with the CAPS-5 in the present sample was high (intraclass correlations, 0.81-0.89).[58]

Outcome Measures

The predefined primary outcome was the CAPS-5 score at 15 months, for which internal consistency (Cronbach α) was 0.93 in our sample.[58] Secondary outcomes included all psychopathology scales assessed at all major assessments and the Global Assessment of Functioning.[59] Rating scales included the PTSD Checklist for *DSM-5*,[60] the Borderline Symptom List (short version [BSL-23]),[61] the behavioral items of the BSL,[62] the Beck Depression Inventory-II,[63] and the Dissociation Tension Scale covering the last week[64] with the subscales for duration and intensity.

Assessments and Missing Data

Full assessments were conducted before the start of therapy and after 3, 6, 9, 12, and 15 months. The primary analyses were conducted on the intent-to-treat (ITT) population, which included all participants who were randomized and fulfilled the criteria for participating. Missing items (≤10%) were imputed using stochastic regression imputation based on all other items from the respective scale.[65,66] If more than 10% of the items were missing, multiple imputation on the scale level was applied. Given a nonmonotone missing pattern, the Markov chain Monte Carlo method was used for this purpose.[67] Multiple imputation was based on the SAS procedures MI (1000 runs) and MIANALYZE. The ITT analyses were supplemented with analyses according to protocol. Details regarding missing data for the primary outcome are provided in eTable 2 in Supplement 1.

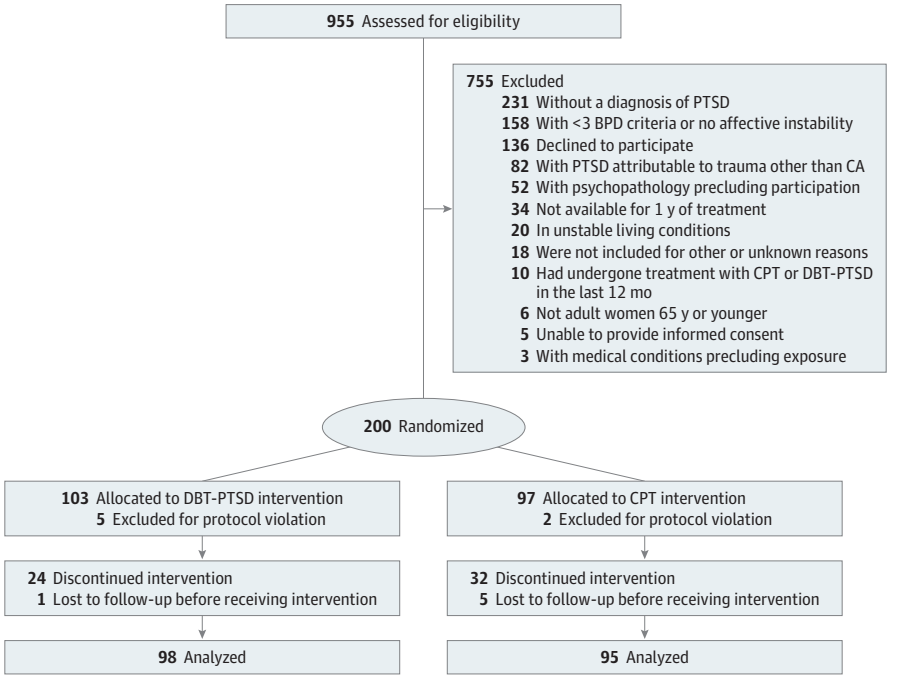
Statistical Analysis

The planned sample size was determined a priori from a power analysis. As described by Bohus et al,[47] an N of 180 or more would detect a medium-size superiority of DBT-PTSD over CPT with a statistical power of 0.80 or more. Mixed linear models were the predefined primary strategy for analyzing changes. Variables that were in line with the assumption of normality were modeled by the following mixed linear model (Equation 1) based on the unstructured covariance matrix:

$$\text{Level 1: } Y_{ij} = \pi_{0j} + \pi_{1j} Time_{ij} + r_{ij}, \text{ where } r_{ij} \sim N(0,\sigma^2)$$
$$\text{Level 2: } \pi_{0j} = \beta_{00} + \beta_{01} Group_j + u_{0j}, \pi_{1j} = \beta_{10} + \beta_{11} Group_j + u_{1j}$$
$$\text{where } \begin{pmatrix} u_{0j} \\ u_{1j} \end{pmatrix} \sim N\left[\begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} \tau_{00} & \tau_{01} \\ \tau_{01} & \tau_{11} \end{pmatrix}\right],$$
$$\text{with } Group = \begin{cases} 1, \textit{ for DBT} - \textit{PTSD} \\ 2, \textit{ for CPT} \end{cases},$$
$$\text{with } Time = 1, \ldots, 6.$$
$$i = \text{Time } (1, \ldots, 6),\ j = \text{Individual } (1, \ldots, 193).$$

Parameter estimation was based on restricted maximum likelihood estimates in SAS version 9.4 (SAS Institute) PROC

Figure 1. Patient Flow



BPD indicates borderline personality disorder; CA, childhood abuse; CPT, cognitive processing therapy; DBT-PTSD, dialectical behavior therapy for posttraumatic stress disorder; PTSD, posttraumatic stress disorder.

MIXED. Potential misspecifications were checked by plotting marginal residuals against predicted means and using Q-Q plots. Mixed models were complemented with the following clinically meaningful measures: symptomatic remission, defined as no longer meeting the diagnostic criteria of PTSD according to *DSM-5* vs not achieving this goal (ie, not experiencing remission or dropping out without having experienced remission); reliable improvement (on the CAPS-5), requiring that the improvement exceeds a threshold (calculated as SD-[$CAPS_{pre}$] × $\sqrt{2}$ × $\sqrt{}$(1 − reliability[CAPS]) × 1.96 = 7.29) compatible with chance variation and unreliability[68]; or reliable recovery, defined as reliable improvement plus symptomatic remission.[69]

Changes in percentages over time were evaluated using the McNemar test. Categorical data were compared using χ^2 tests. All *P* values ≤.05 (2-tailed) were considered statistically significant. Effect sizes for comparisons of continuous data before and after the intervention were calculated per Equation 2:

$$d = \left| \frac{Mean_{post} - Mean_{pre}}{\sqrt{Var_{post} + Var_{pre} - 2Cov_{post,pre}}} \right|.$$

Results

Patient Flow

Of 955 patients assessed for eligibility, 619 did not meet the inclusion criteria or met exclusion criteria, and 136 declined to participate (**Figure 1**). Of the 200 who were randomized, 7 were later excluded after they were found to be in violation of inclusion or exclusion criteria, in that they had no diagnosis of PTSD (n = 3), were pregnant at the time of randomization, had a brain tumor, had an established diagnosis of schizophrenia at the time of randomization, or did not have a female gender identity and sex. The final sample thus consisted of 193 participants (DBT-PTSD, 98; CPT, 95).

Overall, 62 of the 193 participants (32.1%) withdrew, with significantly more dropouts in the CPT than the DBT-PTSD group (37 [39.0%] vs 25 [25.5%]; *P* = .046). In 10 individuals (CPT, 8; DBT-PTSD, 2; *P* = .06), the reason was psychiatric hospitalization of 2 weeks or more. The numbers of dropouts in CPT vs DBT-PTSD were 20 vs 11 individuals from the start of therapy to 3 months, 6 vs 6 individuals from 3 months to 6 months, 8 vs 5 individuals from 6 months to 9 months, 3 vs 3 individuals from 9 months to 12 months, and 0 vs 0 individuals from 12 months to 15 months.

Patient Characteristics

Sociodemographic and clinical characteristics of participants are provided in **Table 1**. Briefly, mean (SD) age was 36.3 (11.1) years. The mean (SD) age at first abuse was 7.7 (4.2) years, and the mean (SD) duration of the abuse was 6.9 (6.0) years. Psychotropic medication was prospectively monitored. By the end of the treatment, prescription rates in the 2 groups were similar for all medication classes except for neuroleptics (DBT-PTSD, 7 [8.0%]; CPT, 17 [21.8%]; uncorrected *P* = .02); however, this was nonsignificant after Bonferroni correction. Pre-to-post changes in psychotropic medication were uncorrelated with pre-to-post changes in the primary and secondary outcomes and not significantly associated with either symptomatic remission or dropout rates.

Table 1. Patient Characteristics and Psychotropic Medication

Characteristic	Participants, No. (%)		
	Entire sample	DBT-PTSD	CPT
Age, mean (SD), y	36.3 (11.1)	37.0 (10.7)	35.5 (11.4)
Education[a]			
No graduation or still at school	11 (5.8)	7 (7.2)	4 (4.3)
Lower secondary school (Hauptschule)	30 (15.8)	16 (16.5)	14 (15.1)
Intermediate secondary school (Mittlere Reife)	67 (35.3)	33 (34.0)	34 (36.6)
High school graduation (Abitur)	75 (39.5)	37 (38.1)	38 (40.9)
Other	7 (3.7)	4 (4.1)	3 (3.2)
Marital status[b]			
Single	95 (49.7)	44 (45.8)	51 (53.7)
Married or similar relationship	49 (25.7)	25 (26.0)	24 (25.3)
Separated, divorced, or widowed	47 (24.6)	27 (28.1)	20 (21.1)
No. of Axis I disorders, mean (SD)			
Current	3.25 (1.43)	3.06 (1.31)	3.44 (1.53)
Lifetime	4.21 (1.54)	4.07 (1.45)	4.35 (1.62)
Co-occurring BPD	93 (48.2)	43 (43.9)	50 (53.6)
BPD criteria, mean (SD), No.	4.80 (1.64)	4.68 (1.63)	4.92 (1.65)
≥1 Suicide attempt, lifetime[c]	107 (57.5)	58 (63.0)	49 (52.1)
Nonsuicidal self-injury at least once in the last mo[d]	75 (39.1)	40 (40.8)	35 (37.2)
Index trauma			
Sexual abuse or sexual and physical abuse	144 (74.6)	75 (76.5)	69 (72.6)
Exclusively physical abuse	49 (25.4)	23 (23.5)	26 (27.4)
Repeated abuse[d]	174 (90.6)	86 (88.7)	88 (92.6)
Age at first abuse, mean (SD), y	7.69 (4.21)	7.67 (4.28)	7.71 (4.16)
Duration of abuse, mean (SD), y	6.90 (6.00)	6.36 (5.16)	7.44 (6.69)
Perpetrator known to the patient	182 (94.3)	94 (95.9)	88 (92.6)
Additional sexual or physical abuse in adulthood[e]	124 (67.8)	66 (71.7)	58 (63.7)
Prior psychotherapeutic or psychiatric treatment	172 (89.1)	85 (91.6)	87 (86.7)
Psychotropic medication at baseline[f]			
Any psychotropic medication	133 (69.3)	68 (69.4)	65 (69.2)
Antidepressants	103 (53.7)	52 (53.1)	51 (54.3)
Neuroleptics	55 (28.7)	24 (24.5)	31 (33.0)
Mood stabilizers[g]	4 (2.1)	1 (1.0)	3 (3.2)
Benzodiazepines	14 (7.3)	7 (7.1)	7 (7.5)
Other psychotropic medication	19 (9.9)	7 (7.1)	12 (12.8)
Psychotropic medication at postassessment			
Any psychotropic medication	84 (50.6)	42 (47.7)	42 (53.9)
Antidepressants	64 (38.6)	33 (37.5)	31 (39.7)
Neuroleptics	24 (14.5)	7 (8.0)	17 (21.8)
Mood stabilizers[g]	1 (0.6)	0 (0.0)	1 (1.3)
Benzodiazepines	8 (4.8)	4 (4.6)	4 (5.1)
Other psychotropic medication	10 (6.0)	5 (5.7)	5 (6.4)
Change in psychotropic medication from before therapy to postassessment	87 (52.4)	45 (51.4)	42 (53.9)

Abbreviations: BPD, borderline personality disorder; CPT, cognitive processing therapy; DBT-PTSD, dialectical behavior therapy for posttraumatic stress disorder.

[a] Data regarding education were available for 190 participants.

[b] Marital status was available for 191 participants.

[c] Data regarding suicide attempts (lifetime) were available for 186 participants.

[d] Data regarding nonsuicidal self-injury and repeated abuse were available for 192 participants.

[e] Data regarding additional sexual physical or sexual abuse in adulthood were available for 180 participants.

[f] Data regarding psychotropic medication at pretherapy assessment were available for 192 participants; psychotropic medication at 15 months and change in psychotropic medication data were available for 166 participants.

[g] Lithium, lamotrigine, carbamazepine, or valproate; atypical neuroleptics that are currently being used as mood stabilizers (ie, olanzapine, quetiapine, aripiprazole, risperidone, ziprasidone, asenapine, paliperidone, and lurasidone) have been subsumed under neuroleptics.

Treatment Integrity

Mean (SD) adherence to the respective manuals was good in both groups (DBT-PTSD, 4.1 [1.2] points; CPT, 3.9 [1.3] points). Mean (SD) therapeutic competence was likewise good (DBT-PTSD, 4.0 [0.9] points; CPT, 4.0 [0.9] points).

Primary Outcome

For both therapies, mean changes on the CAPS-5 score were significant, with unadjusted mean (SD) improvements of 19.4 (14.4) points ($P < .001$) in the DBT-PTSD group and 14.6 (14.8) points ($P < .001$) in the CPT group. These reductions correspond to large pre-to-post effect sizes (d, 1.35 and d, 0.98, respectively; **Table 2**). Comparisons of individual CAPS-5 scores before and after therapy (**Figure 2**) indicated that most participants in both groups showed improvement with respect to the primary outcome, and none showed reliable worsening.

Between-group comparison of the predefined primary outcome favored DBT-PTSD. For the ITT population, the mean

Table 2. Primary and Secondary Outcome Data Before Therapy vs Postassessment

Measure	Mean (SD)		Effect size, Cohen *d*						
	Pretherapy	Postassessment	Intent-to-treat population[a]	*P* value	Population according to protocol[b]	*P* value	Mixed linear models, β (SE)	Term	*P* value
Clinician Administered PTSD Scale									
DBT-PTSD	39.93 (10.84)	20.56 (15.81)	1.35	NA	1.66	NA	β_{10} = −4.84 (0.73)	Time	<.001
CPT	40.96 (8.95)	26.41 (16.04)	0.98	NA	1.25	NA	β_{01} = −0.30 (1.54)	Group	.85
Comparison	NA	NA	0.33	.02	0.21	.26	β_{11} = 0.93 (0.47)	Group × time	.047
Posttraumatic Stress Disorder Checklist for *DSM-5*									
DBT-PTSD	49.39 (11.46)	23.82 (17.86)	1.55	NA	2.34	NA	β_{10} = −6.98 (0.89)	Time	<.001
CPT	49.54 (11.04)	33.74 (19.60)	0.90	NA	1.34	NA	β_{01} = −1.24 (1.82)	Group	.50
Between	NA	NA	0.57	<.001	0.46	.04	β_{11} = 1.86 (0.57)	Group × time	.001
Dissociation Tension Scale-duration									
DBT-PTSD	24.13 (16.88)	14.04 (14.58)	0.79	NA	1.23	NA	β_{10} = −3.13 (0.74)	Time	<.001
CPT	23.96 (14.81)	20.87 (18.08)	0.20	NA	0.31	NA	β_{01} = −0.57 (2.45)	Group	.82
Comparison	NA	NA	0.50	<.001	0.30	.20	β_{11} = 1.17 (0.48)	Group × time	.02
Dissociation Tension Scale-intensity									
DBT-PTSD	2.82 (1.70)	1.77 (1.70)	0.82	NA	1.22	NA	β_{10} = −0.30 (0.08)	Time	<.001
CPT	3.12 (1.62)	2.61 (1.88)	0.33	NA	0.55	NA	β_{01} = 0.28 (0.27)	Group	.32
Comparison	NA	NA	0.39	.007	0.20	0.41	β_{11} = 0.09 (0.05)	Group × time	.09
Borderline Symptom List-23									
DBT-PTSD	2.01 (0.82)	1.14 (0.86)	1.11	NA	1.4	NA	β_{10} = −0.25 (0.04)	Time	<.001
CPT	2.04 (0.80)	1.63 (0.95)	0.47	NA	0.72	NA	β_{01} = −0.001 (0.12)	Group	.99
Comparison	NA	NA	0.55	<.001	0.27	.22	β_{11} = 0.08 (0.03)	Group × time	.003
Borderline Symptom List-behavioral items									
DBT-PTSD	0.34 (0.33)	0.18 (0.18)	0.54	NA	0.76	NA			
CPT	0.31 (0.28)	0.29 (0.25)	0.08	NA	0.34	NA	NA[c]	NA[c]	NA[c]
Comparison	NA	NA	0.50	<.001	0.39	.06			
Beck Depression Inventory-II									
DBT-PTSD	33.24 (11.20)	21.57 (14.04)	0.98	NA	1.37	NA	β_{10} = −3.20 (0.78)	Time	<.001
CPT	34.10 (10.81)	26.99 (15.09)	0.48	NA	0.76	NA	β_{01} = 0.33 (1.93)	Group	.86
Comparison	NA	NA	0.32	.02	0.17	.45	β_{11} = 0.86 (0.49)	Group × time	.09
Global Assessment of Functioning									
DBT-PTSD	50.75 (9.14)	60.13 (13.95)	0.67	NA	1.12	NA	β_{10} = 2.38 (0.62)	Time	<.001
CPT	49.19 (7.69)	55.25 (12.55)	0.51	NA	0.87	NA	β_{01} = −0.71 (1.39)	Group	.61
Comparison	NA	NA	0.26	.08	0.27	.16	β_{11} = −0.52 (0.40)	Group × time	.20

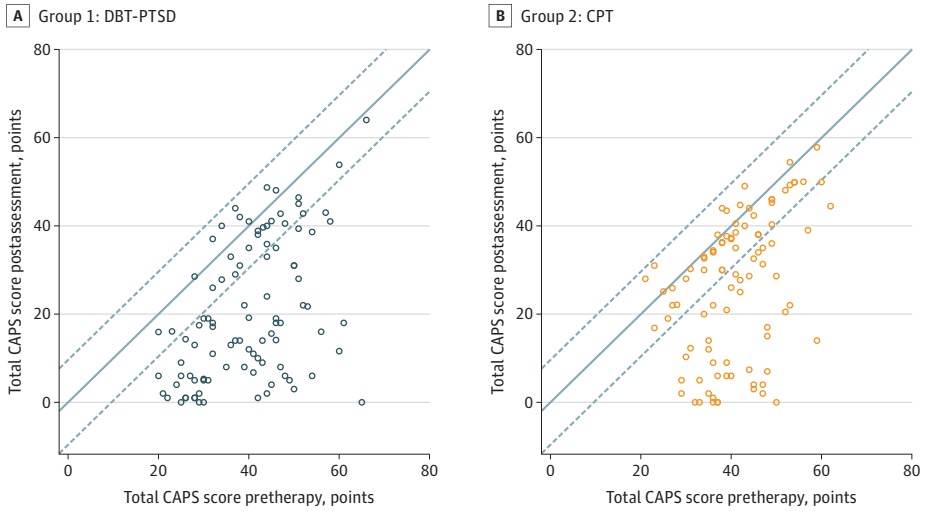
Abbreviations: CPT, cognitive processing therapy; DBT-PTSD, dialectical behavior therapy for posttraumatic stress disorder; NA, not applicable; PTSD, posttraumatic stress disorder.

[a] Intent-to-treat: n = 98 (DBT-PTSD), and n = 95 (CPT), respectively; besides the Dissociation Tension Scale–duration under CPT and the Borderline Symptom List–behavioral items under CPT all pre-to-post effect sizes *d* were statistically different from 0.

[b] According to protocol: n = 73 (DBT-PTSD), and n = 58 (CPT), respectively; besides the Dissociation Tension Scale–duration under CPT, all pre-to-post effect sizes *d* were statistically different from 0.

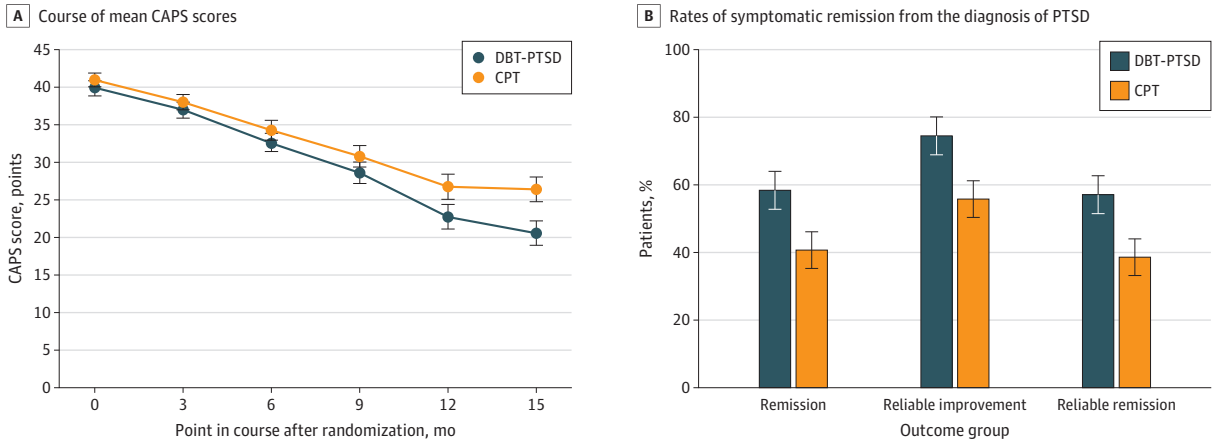
[c] Mixed linear models for the Borderline Symptom List–behavioral items are not reported because the assumption of linearity was not met and the Newton-Raphson algorithms used in generalized linear models did not consistently converge during the procedure of multiple imputation.

Figure 2. Individual Participant Scores



Total Clinician-Administered PTSD Scale for *DSM-5* (CAPS) scores of participants randomized to dialectical behavioral therapy for posttraumatic stress disorder (DBT-PTSD) or cognitive processing therapy (CPT) (intent-to-treat population) before therapy (month 0) vs postassessment (month 15). Values below the main diagonal indicate improvements; the dotted diagonals represent reliable change.

Figure 3. Dimensional and Categorical Treatment Outcomes



Scores and categories are based on Clinician-Administered PTSD Scale for *DSM-5* (CAPS-5) scores for dialectical behavioral therapy for posttraumatic stress disorder (DBT-PTSD; dark color) and cognitive processing therapy (CPT; light color). Error bars indicate standard errors of means. A, Course of mean CAPS scores from before therapy (month 0) to postassessment (month 15). B, Rates of symptomatic remission from the diagnosis of PTSD (not meeting the full criteria of posttraumatic stress disorder (PTSD) in the CAPS-5) of reliable improvement (improvement from before to after therapy that exceeds a threshold compatible with the unreliability of measurement) and reliable recovery (reliable improvement plus symptomatic remission).

change on the CAPS-5 scores was larger for DBT-PTSD than CPT, albeit with a small effect size (*d*, 0.33; *P* = .02). Similarly, the mixed linear model indicated a steeper slope of linear improvements for DBT-PTSD (β_{11}, 0.93 ± 0.47; *P* = .047; Table 2 and **Figure 3**). The more pronounced decline of CAPS-5 scores in the DBT-PTSD group was mirrored by a higher percentage of participants achieving symptomatic remission (52 of 89 observed cases [58.4%] vs 35 of 86 observed cases [40.7%]; *P* = .02), reliable improvement (73 [74.5%] vs 53 [55.8%]; *P* = .006), and reliable recovery (52 of 91 observed cases [57.1%] vs 34 of 88 observed cases [38.6%]; *P* = .01). However, the percentage of participants achieving early remission was higher for CPT than DBT-PTSD (9 [9.5%] vs 2 [2.0%]; *P* = .03).

Secondary Outcomes

Changes in the PTSD Checklist for *DSM-5* were large in both groups. Mean changes in the ITT population were larger for the DBT-PTSD group (DBT-PTSD: *d*, 1.55; CPT: *d*, 0.90; between-group effect size *d*, 0.57; *P* < .001). This finding was supported by the significant group × time interaction in the mixed linear model, indicating a more pronounced improvement in the DBT-PTSD group for self-rated severity of PTSD symptoms (β_{11}, 1.86 ± 0.57; *P* = .001).

Findings regarding dissociation were less homogeneous. While duration of dissociative symptoms (Dissociation Tension Scale) declined in both groups, decline in the intensity of dissociative symptoms was significant only for DBT-PTSD.

Mean changes were large for DBT-PTSD (*d*, 0.79 and *d*, 0.82 for the duration and intensity of dissociation, respectively) and small for CPT (*d*, 0.20 and *d*, 0.33, respectively). Between-group effect sizes were significant for both duration and intensity of dissociation (*d*, 0.50; *P* < .001; *d*, 0.39; *P* = .007). Mixed linear models partially supported these findings (β_{11}, 0.09 ± 0.05; *P* = .02 and β_{11}, 1.17 ± 0.48, respectively; *P* = .09 for the group × time interactions; Table 2).

Pre-to-post effect sizes in the BSL-23 were large for DBT-PTSD (*d*, 1.11) and medium for CPT (*d*, 0.47). The difference between the groups was significant (between-group effect size: *d*, 0.55; *P* < .001). While the BSL-behavioral items score involving frequencies of dysfunctional behaviors, such as self-harm, high-risk behaviors, or consumption of drugs, declined in both groups, the decline in the DBT-PTSD group was significant (*d*, 0.54; *P* < .001), while that for CPT was not (*d*, 0.08; *P* = .42). This decline was more pronounced under DBT-PTSD (between-group effect size: *d*, 0.50; *P* < .001).

Improvements of Beck Depression Inventory–II scores were large for DBT-PTSD (*d*, 0.98) and medium for CPT (*d*, 0.48). This difference of pre-to-post differences was small and significant (*d*, 0.32; *P* = .02), but the group × time interaction in the mixed linear model was not significant. With respect to the Global Assessment of Functioning, medium improvements were observed (DBT-PTSD: *d*, 0.67; CPT: *d*, 0.51), but there were no significant between-group effects (Table 2). The means (SDs) for all dimensional scales and assessment points and the length of hospitalization by condition are provided in eTable 3 and 4 in Supplement 1, respectively.

Results pertaining to the analyses according to protocol are summarized in Table 2. No differences in any outcome variables were noted between the 3 sites (eTable 5 in Supplement 1).

No suicides occurred during the observation period. One suicide attempt was noted in the CPT group.

Discussion

Dialectical behavior therapy for PTSD (DBT-PTSD) is designed as a phase-based treatment specifically for patients with highly symptomatic CA-associated PTSD and complicating conditions, such as emotion dysregulation and other features of BPD. This randomized clinical trial compared the efficacy of DBT-PTSD with that of CPT, which is one of the best available treatments for PTSD but is not specifically designed for this population. Improvements in the primary outcome measure were large and significant for both treatments but more pronounced in the DBT-PTSD group. The same results were seen for other aspects of psychopathology closely associated with a history of CA, such as dissociation, self-harm, and high-risk behaviors. Furthermore, participants in the DBT-PTSD group were more likely to achieve symptomatic remission, reliable improvement, and reliable recovery and were less likely to drop out of treatment.

The large pre-to-post effect sizes in both treatment groups parallel the effect sizes observed in previous studies of both CPT and DBT-PTSD.[41-44,70] Similarly, the low rates of suicidal acts and the absence of significant symptom exacerbations in both groups are in line with previous studies.

Cognitive processing therapy did not perform as well as it has in PTSD studies in general.[41,44] This might be because of the relatively high dropout rate within the first 3 months. It is unclear how sessions 1 to 4, which were added to the CPT protocol for safety reasons, affected treatment dropout. On the other hand, high dropout rates might be explained by clinical characteristics of the study population (in that all participants met at least 3 BPD criteria, including affective instability, and 48% had co-occurring BPD). These characteristics might require specifically tailored interventions for this population, as provided by DBT-PTSD.

Strengths

Strengths of this study included measures to control for potentially confounding variables. Both groups received equal dosage and frequency of therapy, the process of therapist training was guided by the treatment developers, training and experience of the therapists were balanced across treatment groups, and structured observer-based scales were used to assess treatment integrity. In line with the updated CONSORT statement, randomization was concealed to all persons involved,[71] and raters were blinded.

We tried to balance developers' bias by including the CPT developer (P.A.R.) as a senior trainer and consultant for CPT supervisors. Therapists in both groups had similar experience and competence and received the same amounts of training and supervision. Assessments of adherence and competence revealed good treatment integrity to both manuals.

Limitations

Nevertheless, allegiance effects cannot be completely ruled out, and the findings need to be replicated by independent research groups. In the DBT-PTSD arm, the treatment developers were part of the consultation teams, while in the CPT arm, the supervisors were experienced in cognitive behavior therapy but did not have more experience in CPT than the therapists.

We emphasize that the study population consisted of patients whose PTSD was associated with CA and who had severe problems in emotion regulation and features of BPD, so the findings cannot be extended to PTSD in general. It also remains unknown whether our results can be generalized to patients of any age, sex, or gender identity. It is further unclear whether the improvements achieved and the superiority of DBT-PTSD over CPT will persist in the long term. These limitations should be addressed by future research.

Given the dropout rate of 32%, the results may be affected by attrition bias. To minimize potential bias, the primary analysis was based on the ITT sample.

Finally, the observed effects might have been confounded by intercurrent treatments. However, this seems unlikely since, with the exception of inpatient crisis interventions, only CPT and DBT-PTSD were allowed during the study period. Use of medication was unrestricted, but neither hospitalization nor changes in psychotropic medication were significantly associated with the outcome variables.

Conclusions

The study shows that even severe forms of CA-associated PTSD that include multiple co-occurring mental disorders and emotion dysregulation can be treated efficaciously. Future studies should strive for a better definition of patient groups that might profit from current therapies. In particular, additional research is required to test whether treatment efficacy might extend beyond adult women, and whether the DBT-PTSD protocol could be condensed to reduce cost burdens and patient burdens and facilitate dissemination.

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REFERENCES

1. Cutajar MC, Mullen PE, Ogloff JR, Thomas SD, Wells DL, Spataro J. Psychopathology in a large cohort of sexually abused children followed up to 43 years. *Child Abuse Negl*. 2010;34(11):813-822. doi:10.1016/j.chiabu.2010.04.004

2. Gilbert R, Widom CS, Browne K, Fergusson D, Webb E, Janson S. Burden and consequences of child maltreatment in high-income countries. *Lancet*. 2009;373(9657):68-81. doi:10.1016/S0140-6736(08)61706-7

3. Hailes HP, Yu R, Danese A, Fazel S. Long-term outcomes of childhood sexual abuse: an umbrella review. *Lancet Psychiatry*. 2019;6(10):830-839. doi:10.1016/S2215-0366(19)30286-X

4. Kessler RC, McLaughlin KA, Green JG, et al. Childhood adversities and adult psychopathology in the WHO World Mental Health Surveys. *Br J Psychiatry*. 2010;197(5):378-385. doi:10.1192/bjp.bp.110.080499

5. Pérez-Fuentes G, Olfson M, Villegas L, Morcillo C, Wang S, Blanco C. Prevalence and correlates of child sexual abuse: a national study. *Compr Psychiatry*. 2013;54(1):16-27. doi:10.1016/j.comppsych.2012.05.010

6. Scott KM, Smith DR, Ellis PM. Prospectively ascertained child maltreatment and its association with DSM-IV mental disorders in young adults. *Arch Gen Psychiatry*. 2010;67(7):712-719. doi:10.1001/archgenpsychiatry.2010.71

7. Grant BF, Chou SP, Goldstein RB, et al. Prevalence, correlates, disability, and comorbidity of DSM-IV borderline personality disorder: results from the Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions. *J Clin Psychiatry*. 2008;69(4):533-545. doi:10.4088/JCP.v69n0404

8. Scheiderer EM, Wood PK, Trull TJ. The comorbidity of borderline personality disorder and posttraumatic stress disorder: revisiting the prevalence and associations in a general population sample. *Borderline Personal Disord Emot Dysregul*. 2015;2(1):11. doi:10.1186/s40479-015-0032-y

9. Pagura J, Stein MB, Bolton JM, Cox BJ, Grant B, Sareen J. Comorbidity of borderline personality disorder and posttraumatic stress disorder in the U.S. population. *J Psychiatr Res*. 2010;44(16):1190-1198. doi:10.1016/j.jpsychires.2010.04.016

10. Lenzenweger MF, Lane MC, Loranger AW, Kessler RC. DSM-IV personality disorders in the National Comorbidity Survey Replication. *Biol Psychiatry*. 2007;62(6):553-564. doi:10.1016/j.biopsych.2006.09.019

11. Heffernan K, Cloitre M. A comparison of posttraumatic stress disorder with and without borderline personality disorder among women with a history of childhood sexual abuse: etiological and clinical characteristics. *J Nerv Ment Dis*. 2000;188(9):589-595. doi:10.1097/00005053-200009000-00005

12. Shea MT, Zlotnick C, Weisberg RB. Commonality and specificity of personality disorder profiles in subjects with trauma histories. *J Pers Disord*. 1999;13(3):199-210. doi:10.1521/pedi.1999.13.3.199

13. Zanarini MC, Frankenburg FR, Dubo ED, et al. Axis I comorbidity of borderline personality disorder. *Am J Psychiatry*. 1998;155(12):1733-1739. doi:10.1176/ajp.155.12.1733

14. McLean LM, Gallop R. Implications of childhood sexual abuse for adult borderline personality disorder and complex posttraumatic stress disorder. *Am J Psychiatry*. 2003;160(2):369-371. doi:10.1176/appi.ajp.160.2.369

15. Karatzias T, Murphy P, Cloitre M, et al. Psychological interventions for ICD-11 complex PTSD symptoms: systematic review and meta-analysis. *Psychol Med*. 2019;49(11):1761-1775. doi:10.1017/S0033291719000436

16. Herzog JI, Thome J, Demirakca T, et al. Influence of severity of type and timing of retrospectively reported childhood maltreatment on female amygdala and hippocampal volume. *Sci Rep*. 2020;10(1):1903. doi:10.1038/s41598-020-57490-0

17. Teicher MH, Khan A. Childhood maltreatment, cortical and amygdala morphometry, functional connectivity, laterality, and psychopathology. *Child Maltreat*. 2019;24(4):458-465. doi:10.1177/1077559519870845

18. Lyssenko L, Schmahl C, Bockhacker L, Vonderlin R, Bohus M, Kleindienst N. Dissociation in psychiatric disorders: a meta-analysis of studies using the dissociative experiences scale. *Am J Psychiatry*. 2018;175(1):37-46. doi:10.1176/appi.ajp.2017.17010025

19. Naismith I, Zarate Guerrero S, Feigenbaum J. Abuse, invalidation, and lack of early warmth show distinct relationships with self-criticism, self-compassion, and fear of self-compassion in personality disorder. *Clin Psychol Psychother*. 2019;26(3):350-361. doi:10.1002/cpp.2357

20. McDonagh-Coyle A, Friedman MJ, McHugo GJ, et al. Randomized trial of cognitive behavioral therapy for chronic PTSD in adult female childhood sexual abuse survivors. *J Consult Clin Psychol*. 2005;73(3):515-524. doi:10.1037/0022-006X.73.3.515

21. Clarke SB, Rizvi SL, Resick PA. Borderline personality characteristics and treatment outcome in cognitive-behavioral treatments for PTSD in female rape victims. *Behav Ther*. 2008;39(1):72-78. doi:10.1016/j.beth.2007.05.002

22. Feeny NC, Zoellner LA, Foa EB. Treatment outcome for chronic PTSD among female assault victims with borderline personality characteristics: a preliminary examination. *J Pers Disord*. 2002;16(1):30-40. doi:10.1521/pedi.16.1.30.22555

23. Hembree EA, Cahill SP, Foa EB. Impact of personality disorders on treatment outcome for female assault survivors with chronic posttraumatic stress disorder. *J Pers Disord*. 2004;18(1):117-127. doi:10.1521/pedi.18.1.117.32767

24. Holder N, Holliday R, Pai A, Surís A. Role of borderline personality disorder in the treatment of military sexual trauma-related posttraumatic stress disorder with cognitive processing therapy. *Behav Med*. 2017;43(3):184-190. doi:10.1080/08964289.2016.1276430

25. Kredlow MA, Szuhany KL, Lo S, et al. Cognitive behavioral therapy for posttraumatic stress disorder in individuals with severe mental illness and borderline personality disorder. *Psychiatry Res*. 2017;249:86-93. doi:10.1016/j.psychres.2016.12.045

26. Bradley R, Greene J, Russ E, Dutra L, Westen D. A multidimensional meta-analysis of psychotherapy for PTSD. *Am J Psychiatry*. 2005;162(2):214-227. doi:10.1176/appi.ajp.162.2.214

27. Ronconi JM, Shiner B, Watts BV. Inclusion and exclusion criteria in randomized controlled trials of psychotherapy for PTSD. *J Psychiatr Pract*. 2014;20(1):25-37. doi:10.1097/01.pra.0000442936.23457.5b

28. Harned MS, Chapman AL, Dexter-Mazza ET, Murray A, Comtois KA, Linehan MM. Treating co-occurring Axis I disorders in recurrently suicidal women with borderline personality disorder: a 2-year randomized trial of dialectical behavior therapy versus community treatment by experts. *J Consult Clin Psychol*. 2008;76(6):1068-1075. doi:10.1037/a0014044

29. Harned MS, Korslund KE, Linehan MM. A pilot randomized controlled trial of dialectical behavior therapy with and without the dialectical behavior therapy prolonged exposure protocol for suicidal and self-injuring women with borderline personality disorder and PTSD. *Behav Res Ther*. 2014;55:7-17. doi:10.1016/j.brat.2014.01.008

30. American Psychological Association. Clinical practice guideline for the treatment of posttraumatic stress disorder (PTSD) in adults. Published 2017. Accessed August 9, 2019. https://www.apa.org/ptsd-guideline/ptsd.pdf

31. International Society for Traumatic Stress Studies. Posttraumatic stress disorder prevention and treatment guidelines: methodology and recommendations. Published 2019. Accessed September 2, 2019. https://istss.org/getattachment/Treating-Trauma/New-ISTSS-Prevention-and-Treatment-Guidelines/ISTSS_PreventionTreatmentGuidelines_FNL-March-19-2019.pdf.aspx

32. US Department of Veteran Affairs. VA/DOD Clinical practice guideline for the management of posttraumatic stress disorder and acute stress disorder. Published 2017. Accessed August 15, 2019. https://www.healthquality.va.gov/guidelines/MH/ptsd/VADoDPTSDCPGFinal012418.pdf

33. Berliner L, Bisson J, Cloitre M, et al. New ISTSS prevention and treatment guidelines. Published 2019. Accessed August 9, 2019. http://istss.org/treating-trauma/new-istss-prevention-and-treatment-guidelines

34. De Jongh A, Resick PA, Zoellner LA, et al. Critical analysis of the current treatment guidelines for complex PTSD in adults. *Depress Anxiety*. 2016;33(5):359-369. doi:10.1002/da.22469

35. Cloitre M, Courtois CA, Charuvastra A, Carapezza R, Stolbach BC, Green BL. Treatment of complex PTSD: results of the ISTSS expert clinician survey on best practices. *J Trauma Stress*. 2011;24(6):615-627. doi:10.1002/jts.20697

36. Cloitre M, Koenen KC, Cohen LR, Han H. Skills training in affective and interpersonal regulation followed by exposure: a phase-based treatment for PTSD related to childhood abuse. *J Consult Clin Psychol*. 2002;70(5):1067-1074. doi:10.1037/0022-006X.70.5.1067

37. Cloitre M, Stovall-McClough KC, Nooner K, et al. Treatment for PTSD related to childhood abuse: a randomized controlled trial. *Am J Psychiatry*. 2010;167(8):915-924. doi:10.1176/appi.ajp.2010.09081247

38. Harned MS, Gallop RJ, Valenstein-Mah HR. What changes when? the course of improvement during a stage-based treatment for suicidal and self-injuring women with borderline personality disorder and PTSD. *Psychother Res*. 2018;28(5):761-775. doi:10.1080/10503307.2016.1252865

39. Rosner R, Rimane E, Frick U, et al. Effect of developmentally adapted cognitive processing therapy for youth with symptoms of posttraumatic stress disorder after childhood sexual and physical abuse: a randomized clinical trial. *JAMA Psychiatry*. 2019;76(5):484-491. doi:10.1001/jamapsychiatry.2018.4349

40. Foa EB, Hembree EA, Rothbaum BO. *Prolonged Exposure Therapy for PTSD: Emotional Processing of Traumatic Experiences*. Oxford University Press; 2007.

41. Resick PA, Galovski TE, Uhlmansiek MO, Scher CD, Clum GA, Young-Xu Y. A randomized clinical trial to dismantle components of cognitive processing therapy for posttraumatic stress disorder in female victims of interpersonal violence. *J Consult Clin Psychol*. 2008;76(2):243-258. doi:10.1037/0022-006X.76.2.243

42. Bohus M, Dyer AS, Priebe K, et al. Dialectical behaviour therapy for post-traumatic stress disorder after childhood sexual abuse in patients with and without borderline personality disorder: a randomised controlled trial. *Psychother Psychosom*. 2013;82(4):221-233. doi:10.1159/000348451

43. Steil R, Dyer A, Priebe K, Kleindienst N, Bohus M. Dialectical behavior therapy for posttraumatic stress disorder related to childhood sexual abuse: a pilot study of an intensive residential treatment program. *J Trauma Stress*. 2011;24(1):102-106. doi:10.1002/jts.20617

44. Chard KM. An evaluation of cognitive processing therapy for the treatment of posttraumatic stress disorder related to childhood sexual abuse. *J Consult Clin Psychol*. 2005;73(5):965-971. doi:10.1037/0022-006X.73.5.965

45. Resick PA, Nishith P, Weaver TL, Astin MC, Feuer CA. A comparison of cognitive-processing therapy with prolonged exposure and a waiting condition for the treatment of chronic posttraumatic stress disorder in female rape victims. *J Consult Clin Psychol*. 2002;70(4):867-879. doi:10.1037/0022-006X.70.4.867

46. Resick PA, Wachen JS, Dondanville KA, et al; and the STRONG STAR Consortium. Effect of group vs individual cognitive processing therapy in active-duty military seeking treatment for posttraumatic stress disorder: a randomized clinical

trial. *JAMA Psychiatry*. 2017;74(1):28-36. doi:10.1001/jamapsychiatry.2016.2729

47. Bohus M, Schmahl C, Fydrich T, et al. A research programme to evaluate DBT-PTSD, a modular treatment approach for complex PTSD after childhood abuse. *Borderline Personal Disord Emot Dysregul*. 2019;6:7. doi:10.1186/s40479-019-0099-y

48. Resick PA, Monson CM, Chard KM. *Cognitive Processing Therapy for PTSD: A Comprehensive Manual*. Guilford Press; 2016.

49. Linehan MM. *DBT Skills Training Manual*. Guilford Press; 2014.

50. Ehlers A, Clark DM, Hackmann A, McManus F, Fennell M. Cognitive therapy for post-traumatic stress disorder: development and evaluation. *Behav Res Ther*. 2005;43(4):413-431. doi:10.1016/j.brat.2004.03.006

51. Gilbert P. *Compassion-Focused Therapy: Distinctive Features (CBT Distinctive Features)*. Routledge; 2010. doi:10.4324/9780203851197

52. Hayes SC, Strosahl KD, Wilson KG. *Acceptance and Commitment Therapy: The Process And Practice of Mindful Change*. Guilford Press; 2011.

53. Weathers FW, Blake DD, Schnurr PP, Kaloupek DG, Marx BP, Keane TM. The Clinician-Administered PTSD Scale for *DSM-5* (CAPS-5). Published 2013. Accessed January 5, 2014. http://www.ptsd.va.gov

54. Dittmann C, Müller-Engelmann M, Resick PA, et al. Adherence rating scale for cognitive processing therapy–cognitive only: analysis of psychometric properties. *Behav Cogn Psychother*. 2017;45(6):661-670. doi:10.1017/S1352465816000679

55. Dittmann C, Müller-Engelmann M, Stangier U, et al. Disorder- and treatment-specific therapeutic competence scales for posttraumatic stress disorder intervention: development and psychometric properties. *J Trauma Stress*. 2017;30(6):614-625. doi:10.1002/jts.22236

56. First MB, Spitzer RL, Gibbon M, Williams JBW, Benjamin LS. *User's Guide for the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I)—Clinical Version*. American Psychiatric Press; 1997.

57. Loranger AW, Sartorius N, Andreoli A, et al. The international personality disorder examination: the Health Organization/Alcohol, Drug Abuse, and Mental Health Administration international pilot study of personality disorders. *Arch Gen Psychiatry*. 1994;51(3):215-224. doi:10.1001/archpsyc.1994.03950030051005

58. Müller-Engelmann M, Schnyder U, Dittmann C, et al. Psychometric properties and factor structure of the German version of the clinician-administered PTSD scale for *DSM-5*. *Assessment*. Published May 1, 2018. doi:10.1177/1073191118774840

59. Endicott J, Spitzer RL, Fleiss JL, Cohen J. The global assessment scale: a procedure for measuring overall severity of psychiatric disturbance. *Arch Gen Psychiatry*. 1976;33(6):766-771. doi:10.1001/archpsyc.1976.01770060086012

60. Weathers FW, Litz BT, Keane TM, et al. The PTSD Checklist for DSM-5 (PCL-5). Published 2013. Accessed January 5, 2014. https://www.ptsd.va.gov/professional/assessment/adult-sr/ptsd-checklist.asp

61. Bohus M, Kleindienst N, Limberger MF, et al. The short version of the Borderline Symptom List (BSL-23): development and initial data on psychometric properties. *Psychopathology*. 2009;42(1):32-39. doi:10.1159/000173701

62. Bohus M, Limberger MF, Frank U, Sender I, Gratwohl T, Stieglitz RD. Development of the Borderline Symptom List. *Psychother Psychosom Med Psychol*. 2001;51(5):201-211. doi:10.1055/s-2001-13281

63. Beck A, Steer R, Brown G. *Beck Depression Inventory–II Manual*. Psychological Corporation; 1996.

64. Stiglmayr C, Schimke P, Wagner T, et al. Development and psychometric characteristics of the Dissociation Tension Scale. *J Pers Assess*. 2010;92(3):269-277. doi:10.1080/00223891003670232

65. Enders CK. A primer on the use of modern missing-data methods in psychosomatic medicine research. *Psychosom Med*. 2006;68(3):427-436. doi:10.1097/01.psy.0000221275.75056.d8

66. Rubin DB. Multiple imputation after 18+ years. *J Am Stat Assoc*. 1996;91(434):473-489. doi:10.1080/01621459.1996.10476908

67. Schafer JL. *Analysis of Incomplete Multivariate Data*. Chapman and Hall; 1997. doi:10.1201/9781439821862

68. Christensen L, Mendoza JL. A method of assessing change in a single subject: an alteration of the RC index. *Behav Ther*. 1986;17:305-308. doi:10.1016/S0005-7894(86)80060-0

69. Clark DM, Canvin L, Green J, Layard R, Pilling S, Janecka M. Transparency about the outcomes of mental health services (IAPT approach): an analysis of public data. *Lancet*. 2018;391(10121):679-686. doi:10.1016/S0140-6736(17)32133-5

70. Steil R, Dittmann C, Müller-Engelmann M, Dyer A, Maasch AM, Priebe K. Dialectical behaviour therapy for posttraumatic stress disorder related to childhood sexual abuse: a pilot study in an outpatient treatment setting. *Eur J Psychotraumatol*. 2018;9(1):1423832. doi:10.1080/20008198.2018.1423832

71. Schulz KF, Altman DG, Moher D; CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *BMC Med*. 2010;8:18. doi:10.1186/1741-7015-8-18

Supplementary Online Content

Bohus M, Kleindienst N, Hahn C, et al. Dialectical behavior therapy for posttraumatic stress disorder (DBT-PTSD) compared with cognitive processing therapy (CPT) in complex presentations of PTSD in women survivors of childhood abuse: a randomized clinical trial. *JAMA Psychiatry*. Published online July 22, 2020. doi:10.1001/jamapsychiatry.2020.2148

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Description of study treatments

Dialectical behavior therapy for posttraumatic stress disorder (DBT-PTSD)
DBT-PTSD is a multi-component phase-based program based on the principles, modes and functions of dialectical behavior therapy (DBT) that has been supplemented by trauma-focused cognitive-behavioral interventions, and by specific techniques from compassion focused therapy and from acceptance and commitment therapy.
DBT-PTSD is structured into seven treatment phases, each composed by modules, which allow individual adaptation to the patient's specific symptoms: During the first three treatment phases (Commitment, Trauma Model and Motivation, Skills and Cognitive Elements) patients learn to identify their typical escape strategies in response to trauma-related stimuli, and to use DBT-skills. Phase 4 focuses on skills-assisted exposure to traumatic memories. Exercises on acceptance of the past and grief are the core of the fifth phase (Radical Acceptance). Phase 6 focuses on improvement of psychosocial aspects as well as relapse reduction. The final phase is focussing on the process of farewell.

Cognitive Processing Therapy (CPT)
CPT is an established trauma-focused cognitive therapy aiming at challenging dysfunctional trauma-related cognitions and emotions.
CPT starts with psycho-education about PTSD and treatment rationale. The patient writes a statement on her beliefs why the worst event happened, and how it has affected her beliefs about herself, others and the world. Then, worksheets supporting the patient in identifying and changing dysfunctional trauma-related beliefs are introduced with regard to thoughts about the trauma, and about beliefs about self, others and the world currently.
Treatment, modified for this study, followed a session-by-session protocol. The first 4 sessions aim at elaborating a case history, the patient's specific problem behavior, and emergency plans. Sessions 5 to 16 encompass the original 12 CPT core sessions. Strictly following the CPT manual, each new session introduced a new worksheet or focused on a new theme such as trust or safety in the second part of the treatment. In line with the manual the therapist introduced the next theme, even when the previous theme was not completely worked through. To allow for an individualized, in-depth treatment of themes that have not been completely worked through, therapists and patients identified stuck points that were not sufficiently addressed during the previous sessions. From session 17, these individual stuck points were challenged in depth using the worksheets and the patients' stuck point logbook from the 12 CPT core sessions. The stuck point logbook is a list of relevant stuck points collected after analyzing the impact statement and during the following session. Thus, the session focus from session 17 differed between patients. For example, for some patients guilt regarding the index trauma was still a relevant theme while for others trust issues were more important. After all stuck points related to the index trauma had been addressed, the patient was asked to write a new impact statement that was compared to the first one from the beginning of treatment.
After this, if the patient had experienced more than one trauma cluster another traumatic event could be addressed. In this case, the patient wrote a new impact statement regarding this traumatic event. When all relevant trauma related stuck points were addressed and PTSD symptoms had decreased the remaining sessions could be used to address themes related to patient's life style, for example problems related to work, marriage or friendship.

eTable 1. Therapist characteristics.

	All therapists	Therapists in the DBT-PTSD group	Therapists in the CPT group	DBT-PTSD vs CPT: *P*-value
Number of therapists, n	49	26	23	*P*=.78[a]
Sex of therapist: female (n)	87.8% (43)	88.5% (23)	87.0% (20)	*P*>.99[b]
Age in years, mean (SD)	32.67 (5.18)	32.78 (5.82)	32.55 (4.49)	*P*=.92[c]
Number of cases per therapist during the study period, mean (SD)	4.08 (2.28)	3.81 (2.02)	4.39 (2.55)	*P*=.46[c]
Previous experience with the treatment delivered in the study (years), mean (SD)[d]	1.12 (1.90)	1.23 (2.04)	1.00 (1.77)	*P*=.94[c]
Number of previously treated out-patients with the treatment later delivered in the study (n)[e]				*P*=.32[f]
- none	23.3% (10)	21.7% (5)	25.0% (5)	
- 1 or 2	44.2% (19)	43.5% (10)	45.0% (9)	
- 3 to 5	11.6% (5)	4.4% (1)	22.0% (4)	
- 6 to 10	2.3% (1)	4.4% (1)	0.0% (0)	
- more than 10	18.6% (8)	26.1% (6)	10.0% (2)	
Pilot case of DBT-PTSD or CPT preceding the trial (n)	60.0% (27)	48.0% (12)	75.0% (15)	*P*=.08[b]
Number of previously treated out-patients with a diagnosis of PTSD[e]				*P*=.07[f]
- none	15.9% (7)	25.0% (6)	5.0% (1)	
- 1 or 2	27.3% (12)	37.5% (9)	15.0% (3)	
- 3 to 5	31.8% (14)	20.8% (5)	45.0% (9)	
- 6 to 10	9.1% (4)	4.2% (1)	15.0% (3)	
- more than 10	15.9% (7)	12.5% (3)	20.0% (4)	
Number of previously treated out-patients with a diagnosis of BPD[e]				*P*=.17[f]
- none	11.9% (5)	21.7% (5)	0.0% (0)	
- 1 or 2	31.0% (13)	34.8% (8)	26.3% (5)	
- 3 to 5	26.2% (11)	17.4% (4)	36.8% (7)	
- 6 to 10	11.9% (5)	8.7% (2)	15.8% (3)	
- more than 10	19.1% (8)	17.4% (4)	21.1% (4)	

[a] Exact binomial test for testing the null "half of the therapists belong to one treatment group".
[b] Fisher's exact test
[c] Mann-Whitney U test
[d] i.e. previous experience with outpatient DBT-PTSD for those who delivered DBT-PTSD during the study and i.e. previous experience with outpatient CPT for those who delivered CPT during the study
[e] Including pilot cases
[f] Chi-squared test

eTable 2: Number of observed cases per assessment for the primary outcome (CAPS).

	T1 Mean (SD), number of observed cases	**T2 Mean (SD), number of observed cases**	**T3 Mean (SD), number of observed cases**	**T4 Mean (SD), number of observed cases**	**T5 Mean (SD), number of observed cases**	**T6 Mean (SD), number of observed cases**
DBT-PTSD	39.93 (10.84) n_{obs}=97[a]	36.99 (10.98) n_{obs}=83	32.54 (10.96) n_{obs}=75	28.60 (14.01) n_{obs}=69	22.72 (15.80) n_{obs}=69	20.56 (15.81) n_{obs}=65
CPT	40.96 (8.95) n_{obs}=95	38.01 (9.94) n_{obs}=73	34.27 (12.92) n_{obs}=69	30.80 (13.94) n_{obs}=60	26.75 (16.35) n_{obs}=60	26.41 (16.04) n_{obs}=53

[a] The total score of the CAPS at T1 was missing for one participant due to an incomplete assessment of the CAPS.

eTable 3: Means and standard deviations (SD) for the primary and secondary outcome data at all assessments.

	T1 Mean (SD)	**T2** Mean (SD)	**T3** Mean (SD)	**T4** Mean (SD)	**T5** Mean (SD)	**T6** Mean (SD)
CAPS						
DBT-PTSD	39.93 (10.84)	36.99 (10.98)	32.54 (10.96	28.60 (14.01)	22.72 (15.80)	20.56 (15.81)
CPT	40.96 (8.95)	38.01 (9.94)	34.27 (12.92)	30.80 (13.94)	26.75 (16.35)	26.41 (16.04)
PCL-5						
DBT-PTSD	49.39 (11.46)	41.29 (13.52)	39.37 (14.29)	33.29 (17.01)	28.46 (17.97)	23.82 (17.86)
CPT	49.54 (11.04)	45.56 (13.62)	42.03 (16.65)	36.57 (18.44)	34.74 (19.75)	33.74 (19.60)
DSS-7d						
DBT-PTSD	24.13 (16.88)	20.68 (15.84)	18.83 (15.13)	16.89 (14.84)	14.43 (14.05)	14.04 (14.58)
CPT	23.96 (14.81)	25.02 (16.76)	23.13 (17.36)	20.55 (17.08)	19.20 (17.93)	20.87 (18.08)
DSS-7i						
DBT-PTSD	2.82 (1.70)	2.51 (1.80)	2.32 (1.74)	2.16 (1.85)	1.85 (1.72)	1.77 (1.70)
CPT	3.12 (1.62)	3.21 (1.78)	2.95 (1.78)	2.75 (1.85)	2.45 (1.95)	2.61 (1.88)
BSL-23						
DBT-PTSD	2.01 (0.82)	1.67 (0.74)	1.49 (0.73)	1.33 (0.82)	1.21 (0.84)	1.14 (0.86)
CPT	2.04 (0.80)	1.87 (0.88)	1.75 (0.84)	1.72 (0.89)	1.56 (0.99)	1.63 (0.95)
BSL-BI						
DBT-PTSD	0.34 (0.33)	0.20 (0.18)	0.17 (0.16)	0.16 (0.16)	0.17 (0.18)	0.18 (0.18)
CPT	0.31 (0.28)	0.27 (0.25)	0.27 (0.27)	0.29 (0.25)	0.26 (0.25)	0.29 (0.25)
BDI-II						
DBT-PTSD	33.24 (11.20)	30.16 (11.40)	27.66 (12.09)	24.96 (13.04)	21.50 (13.88)	21.57 (14.04)
CPT	34.10 (10.81)	32.96 (11.34)	30.67 (11.79)	28.63 (13.82)	26.16 (15.46)	26.99 (15.09)
GAF						
DBT-PTSD	50.75 (9.14)	50.70 (11.83)	53.76 (9.34)	56.15 (9.41)	58.47 (12.11)	60.13 (13.95)
CPT	49.19 (7.69)	50.47 (8.53)	51.02 (10.68)	53.07 (9.88)	55.30 (11.12)	55.25 (12.55)

BDI-II=Beck Depression Inventory-II. BSL-23=Borderline Symptom List. BSL-BI=behavioral items of the Borderline Symptom List. CAPS=Clinician Administered PTSD-scale. CPT=cognitive processing therapy. DBT-PTSD=dialectical behavior therapy for posttraumatic stress disorder. DSS-7d=Dissociation Tension Scale – duration. DSS-7i= Dissociation Tension Scale – intensity. GAF=Global Assessment of Functioning. PCL-5= Posttraumatic Stress Disorder Checklist for DSM-5.

eTable 4: Hospitalization during treatment.

	0: No hospitalization	1: Hospitalized for less than a week	2: Hospitalized for at least one week, but less than two weeks	3: Hospitalized for at least two weeks
DBT-PTSD	91	2	2	2
CPT	83	3	1	8

eTable 5: Potential impact of the study site on the change scores of primary and secondary assessments of outcome.

	T1 Mean (SD)	T6 Mean (SD)	Change Score Mean (SD)	ANOVA[1] Effect of Site on the Change-Score	GLM[2] Effect of Site*Treatment on the Change-Score
CAPS					
Berlin (n=63)	37.11 (8.90)	21.58 (14.44)	15.54 (13.30)		
Frankfurt (n=64)	40.36 (9.94)	22.88 (15.43)	17.48 (13.93)	F(2,190)=0.47	F(2,187)=0.15
Mannheim (n=66)	43.68 (9.96)	25.76 (18.21)	17.92 (16.83)	*P*=.63	*P*=.87
PCL-5					
Berlin	51.10 (10.40)	28.76 (19.87)	22.35 (16.93)		
Frankfurt	46.55 (11.77)	27.57 (18.24)	18.99 (17.40)	F(2,190)=0.58	F(2,187)=0.10
Mannheim	50.73 (11.06)	29.76 (20.07)	20.97 (18.70)	*P*=.56	*P*=.91
DSS-7d					
Berlin	24.08 (15.79)	18.08 (17.60)	6.00 (15.90)		
Frankfurt	19.15 (14.74)	13.13 (12.68)	6.02 (11.69)	F(2,190)=0.35	F(2,187)=0.38
Mannheim	28.75 (15.73)	20.89 (18.51)	7.86 (15.79)	*P*=.71	*P*=.69
DSS-7i					
Berlin	3.01 (1.70)	2.30 (1.85)	0.71 (1.55)		
Frankfurt	2.48 (1.60)	1.74 (1.52)	0.75 (1.20)	F(2,190)=0.26	F(2,187)=0.33
Mannheim	3.40 (1.59)	2.51 (2.02)	0.89 (1.56)	*P*=.77	*P*=.73
BSL-23					
Berlin	2.21 (0.73)	1.42 (1.00)	0.79 (0.86)		
Frankfurt	1.77 (0.88)	1.25 (0.86)	0.52 (0.82)	F(2,190)=1.51	F(2,187)=0.47
Mannheim	2.09 (0.74)	1.47 (0.95)	0.62 (0.90)	*P*=0.22	*P*=.63
BSL-BI					
Berlin	0.38 (0.32)	0.28 (0.26)	0.10 (0.34)		
Frankfurt	0.24 (0.26)	0.18 (0.16)	0.06 (0.28)	F(2,190)=0.63	F(2,187)=0.38
Mannheim	0.36 (0.33)	0.24 (0.22)	0.12 (0.26)	*P*=0.53	*P*=.68
BDI-II					
Berlin	35.67 (9.56)	24.16 (14.92)	11.50 (13.47)		
Frankfurt	30.49 (12.87)	23.14 (14.90)	7.36 (12.94)	F(2,190)=1.47	F(2,187)=0.11
Mannheim	34.83 (9.68)	25.39 (14.67)	9.43 (14.41)	*P*=0.23	*P*=.89
GAF					
Berlin	50.14 (6.93)	57.09 (13.09)	-6.94 (12.18)		
Frankfurt	53.19 (9.47)	59.86 (14.05)	-6.67 (14.22)	F(2,190)=0.96	F(2,187)=0.14
Mannheim	46.71 (7.61)	56.26 (13.19)	-9.54 (12.73)	*P*=0.38	*P*=.69

[1]ANOVA=Analysis of Variance used for testing the null "The change score does not depend on the site".
[2]GLM=Generalized Linear Model used for testing the null "The change score does not depend on the two-way interaction of site*treatment".
BDI-II=Beck Depression Inventory-II. BSL-23=Borderline Symptom List. BSL-BI=behavioral items of the Borderline Symptom List. CAPS=Clinician Administered PTSD-scale. CPT=cognitive processing therapy. DBT-PTSD=dialectical behavior therapy for posttraumatic stress disorder. DSS-7d=Dissociation Tension Scale – duration. DSS-7i= Dissociation Tension Scale – intensity. GAF=Global Assessment of Functioning. PCL-5= Posttraumatic Stress Disorder Checklist for DSM-5.

Study Protocol[1]

RELEASE Protocol
Final Version - 08/10/2013

Treatment of psychosocial and neural sequelae in adults with a history of childhood interpersonal violence: a multicenter randomized controlled trial

RELEASE-Study

Planned intervention: Evaluation of the efficacy of a 12-month outpatient treatment program: dialectical behavior therapy for post-traumatic stress disorder (DBT-PTSD)

Key words: 12-month outpatient treatment program: Cognitive processing therapy (CPT)

Indication: Female patients suffering from post-traumatic stress disorder following interpersonal violence before the age of 18 with emotion dysregulation

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The study is conducted in accordance with the Helsinki Declaration and with ICH-GCP, and in accordance with the applicable legal and regulatory requirements including the archiving of all essential documents.

[1] The randomized controlled trial was part of a larger research consortium comprising several independent sub-projects (e.g. health economics, neural activation patterns). The study protocol and the amendments submitted to the review board which refer to the comparative efficacy of DBT-PTSD and CPT are described here. Those parts of the study protocol and amendments, that exclusively refer to the independent sub-projects will be published elsewhere.

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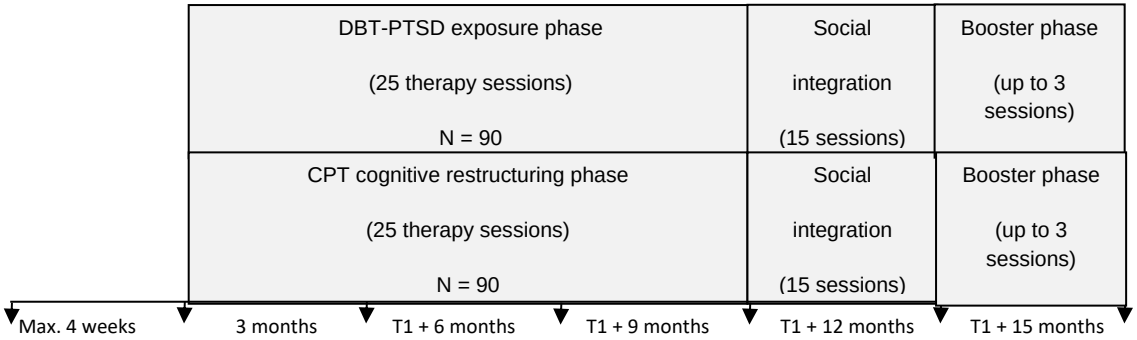
TABLE OF CONTENTS

ABSTRACT

Title	Treatment of psychosocial and neural sequelae in adults with a history of childhood interpersonal violence: a multicenter randomized controlled trial
Short title	RELEASE
Study code	RELEASE
Study Protocol version	V02 dated [08/10/2013]
Indication	Female patients suffering from post-traumatic stress disorder (PTSD) following interpersonal violence before the age of 18 with emotion dysregulation.
Target parameters	Aim: Evaluation of the efficacy of a 12-month outpatient treatment program, dialectical behavior therapy for post-traumatic stress disorder (DBT-PTSD), in female patients with PTSD following interpersonal violence during childhood and severe emotion dysregulation. Primary outcome: Post-traumatic symptoms (CAPS, Blake et al., 1995). Secondary outcome: Borderline Symptoms (ZAN-BPD, Zanarini et. al., 2002, BSL-23, Bohus et al., 2009); General Symptom Severity (SCL-90-R, Derogatis et al., 1992); Social Functioning Level (GAF, Endicott et al., 1976); Health Economy (questionnaire and interview on health economy, Wagner et al., in press); and Quality of Life (WHOQOL-BREF, Angermeyer, Kilian & Matschinger, 2000); EQ-5D (EuroQol Group, 1990); SWLS (Glaesmer et al., 2011).
Reference	12-month outpatient treatment with a trauma-focused, established treatment program, cognitive processing therapy (CPT) in female patients with PTSD following interpersonal violence in childhood and suffering from severe emotion dysregulation.
Study design	Multicenter, randomized, controlled trial
Study population	Inclusion criteria: • Gender: female • Minimum age: 18 years • Diagnosis of post-traumatic stress disorder (PTSD) following sexual or physical abuse before the age of 18, according to the criteria of DSM-5 (CAPS for DSM-5, Blake et al., 1995; Weathers et al., 2013) • Sexual abuse or physical violence as index trauma • Diagnosis of borderline personality disorder (BPD) or sub-clinical BPD (4 out of 9 DSM-IV criteria, including criterion 6: affective instability) as per the International Personality Disorder Examination (IPDE; Loranger et al., 1994) • Must be able to participate in treatment over a period of one year, with weekly sessions; no planned absence of more than 4 weeks

	(e.g. planned inpatient treatment) • Patient must have capacity to understand the nature and scope of the clinical trial • Written informed consent <u>Exclusion criteria:</u> • Lifetime diagnosis of schizophrenia or bipolar I disorder according to DSM-IV • Mental retardation • Severe psychopathology requiring immediate treatment in a different setting (e.g. serious physical illness, body mass index below 16.5) • Acute alcohol and substance dependence according to DSM-IV without abstinence for a period of at least 2 months (substitution is not an exclusion criterion) • Medical conditions contradicting exposure treatment • Life-threatening behavior in the last 2 months (defined as achieving a value of 5 in the corresponding question in the SBDI) (Borgmann & Bohus, 2012) • Instability in the current life circumstances (defined as homelessness or on-going victimisation by the perpetrator(s)) • CPT or DBT-PTSD treatment during the last year • Pregnancy
Number of patients	180 (60 per study center; 90 per treatment program (DBT-PTSD, CPT)
Trial duration	Total duration: 3 years Duration of the clinical phase: (excluding preparation phase) 2 years, 8 months FSI (first subject in): Q1/2014 LSI (last subject in): Q3/2015 LSO (last subject out): Q3/2016 DBL (database lock): Q3/2016 Statistical analysis completed: Q3/2016 Completion of study report: Q4/2016
Statistical evaluation	Analysis of the comparative efficacy of the two treatments is carried out by means of modelling the primary outcome using hierarchical linear modelling (HLM). To compare the effectiveness of the two groups, the interaction between the group (DBT-PTSD vs. CPT) and time are tested for significance. To test the moderator hypothesis, the model is extended to include the interaction of time*group*(initial severity).
Number of centers	3
Financing	Sponsored by the Federal Ministry of Education and Research (BMBF); FKZ: 01KR1303A

Flow chart / collection instruments



Baseline measurements / randomization / adverse events							
Inclusion and exclusion criteria	*						
Randomization	*						
Socio-biographical anamnesis	*						
Adverse events		*	*	*	*	*	*
Medication [a]	*a	*a	*a	*a	*a	*a	*a
PTSD / BPD symptoms / diagnostic testing over course							
CAPS (60-90 min)	*		*	*	*	*	*
IPDE BPD (45 min)	*					*	
SKID I (90 min)	*					*	
SBDI (30 min)	*					*	
MACE (60min)	*						*
ZAN-BPD (30 min)	*					*	
CTQ (12 min)	*						
ETI-SF (8 min)	*						
TSI (10 min)		*		*		*	
TRGI (10 min)		*	*	*	*	*	

DTS (8 min) [a]		* [a]	* [a]	* [a]	* [a]	* [a]	*
PCL (8 min) [a]	*	* [a]	* [a]	* [a]	* [a]	* [a]	*
BSL-23 (8 min) [a]		* [a]	* [a]	* [a]	* [a]	* [a]	*
Session questionnaire [a]		* [a]	* [a]	* [a]	* [a]	* [a]	*
Suicidality/crisis protocol [a]		* [a]	* [a]	* [a]	* [a]	* [a]	*
Diary card [a;c]		* [a;c]	* [a]	* [a;c]	* [a]	* [a;c]	
ASQ (8 min) [b]		* [b]	* [b]	* [b]	* [b]	* [b]	*
PTCI (8 min) [b]		* [b]	* [b]	* [b]	* [b]	* [b]	*
General psychopathology							
SCL-90-R (13 min)		*	*	*	*	*	*
BDI-II (8 min)		*	*	*	*	*	*
FDS (9 min)		*	*	*	*	*	*
BIS (8 min)		*				*	*
DSS 7 days (8 min) [a]		*	*	*	*	*	*
Physical sensation		*	*	*	*	*	
Sexuality		*	*	*	*	*	
Health economy / quality of life / social functioning level							
WHOQOL-BREF (5-10	*		*	*	*	*	*
EQ-5D (3 min)	*		*	*	*	*	*
SF-36 (5-10 min)	*		*	*	*	*	*
SWLS (2 min)							
Health economy (questionnaire 25 min, interview 15 min)	*		*	*	*	*	*
Belief in change [a]		*	*	*	*	*	*
Social functioning level GAF	*	*	*	*	*	*	*
fMRI exam		*				*	
Time per assessment point in min. for patients	Approx. 7 hours	Approx. 3 hours fMRI: 2 hours	Approx. 5 hours	Approx. 5 hours	Approx. 5 hours	Approx. 7 hours fMRI: 2 hours	Approx. 5 hours

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[a)] These instruments are recorded weekly before and after each therapy session.

[b)] These instruments are recorded once every month.

[c)] Electronically-recorded diaries: at the assessment points T1, T3 and T5.

CAPS: Clinician-Administered PTSD Scale (Blake et al., 1995; Weathers et al., 2013; German version, Schnyder & Moergeli, 2002)
IPDE: International Personality Disorder Examination (Loranger et al.,1994)
SKID I: Structured Clinical Interview for DSM-IV (Wittchen, Wunderlich, Gruschwitz & Zaudig, 1997)
SBDI: Severe Behavioral Dyscontrol Interview (Borgmann & Bohus, 2008, 2012)
MACE: Modified Adverse Childhood Experience Scale (unpublished; ACE scale by Teicher & Parigger, 2011)
CTQ: Childhood Trauma Questionnaire (Bernstein et al., 1994)
DTS: Davidson Trauma Scale (Davidson et al., 1997)
PCL: Post-traumatic Stress Disorder - Checklist (Weathers et al., 1993)
BDI-II: Beck Depression Inventory II (Hautzinger, Keller & Kühner, 2006)
SCL-90-R: Symptom Checklist-90R (Derogatis, 1992, German version, Franke, 1995)
BSL-23: Borderline Symptom List (Bohus et al., 2009)
FDS: Questionnaire on Dissociative Symptoms (Spitzer, Stieglitz & Freyberger, 2005)
ASQ: Affective Style Questionnaire (Hofmann & Kashdan, 2010)
BIS: Barrat Impulsiveness Scale (Patton, Stanford & Barratt, 1995)
PTCI: Post-traumatic Cognitions Inventory (Foa et al., 1999)
ETI-SF: Early Trauma Inventory (German version: Wingenfeld et al., 2011)
SWLS: Satisfaction With Life Scale (Glaesmer et al., 2011)
WHOQOL-BREF: German version from the WHO for measurement of quality of life (Angermeyer, Kilian & Matschinger, 2000)
EQ-5D: EuroQoL Group (1990).
SF-36: (Hays, Sherbourne & Mazel, 1993)
Health economics: Interview and questionnaire (Wagner et al., in press)
TSI: Trauma Symptom Inventory (Briere, 1995)
TRGI: Trauma-Related Guilt Inventory (Kubany et al., 1996)

FURTHER ABBREVIATIONS

BMBF	Bundesministerium für Bildung und Forschung (German Federal Ministry of Education and Research)
CRF	Case Report Form
CPT	Cognitive Processing Therapy
DBL	Database Lock
DBT	Dialectic Behavior Therapy for Post-Traumatic Stress Disorder
EK	Ethics Committee
FSI	First Subject In
GCP	Good Clinical Practice
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
ISF	Investigator Site File
KKS	Koordinierungszentrum für Klinische Studien (Clinical Trial Coordination Centre)
LSI	Last Subject In
LSO	Last Subject Out
Q	Quarter
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
TMF	Trial Master File

1. INTRODUCTION

In addition to main project A (randomized controlled trial), the overall project also consists of additional sub-projects B and C, that will be published elsewhere.

1.1 Scientific background and rationale

Project A: Evaluation of an outpatient treatment program for post-traumatic stress disorder (PTSD) with severe emotion dysregulation following interpersonal violence in childhood: a randomized controlled trial.

Experiences of interpersonal violence in childhood and adolescence can lead to a variety of psychological problems in adulthood. Over a long-term observation period, affected women were found to be at particularly high risk of developing post-traumatic stress disorder (PTSD) (Cutajar et al., 2010). PTSD is a psychiatric disorder that manifests itself in a stressful and involuntary re-living of traumatic events, avoidance of stimuli associated with the trauma, and generally elevated levels of arousal. In those who have been victims of violence in their childhood, this disorder is often very complex and is associated with the development of further psychiatric disorders. These patients often experience the symptoms, or the full picture, of borderline personality disorder (BPD). Those affected can only poorly regulate their intense feelings, and injure themselves, for example, or develop suicidal ideation in order to end the unpleasant feelings (sometimes triggered by memories). In addition, those affected exhibit pronounced disorders of temporal and spatial coordination and self-perception (termed “dissociative symptoms”). This results in reduced recovery rates as well as frequent in-patient treatments with extended admission durations. In the literature, these symptoms are also discussed under the term “complex PTSD”.

Despite the high clinical relevance, the quantity of empirically-based data in relation to psychotherapeutic treatment of this set of symptoms is still limited. The discussions on appropriate treatment continue to be highly controversial. Especially in German-speaking regions of the world, a thorough preparation phase, termed the “stabilisation” phase, is recommended before engaging with traumatic memories. There was, however, no evidence found on the efficacy of these purely stabilising interventions in the only study published in this regard (Lampe et al., 2008). Nevertheless, this approach is still very widespread in the health-care infrastructure of German-speaking regions, consuming vital resources in the health-care sector.

In meta-analyses of PTSD psychotherapy studies, large effects on post-traumatic symptoms in general could be determined for trauma-focused cognitive-behavioral therapy and “Eye Movement Desensitisation and Reprocessing” (EMDR) (Bisson & Andrew, 2007; Bradley et al., 2005). However, it is unclear to what extent these results can be applied to the treatment of PTSD with emotion dysregulation following interpersonal violence. In the few studies which are available for this patient group, patients with other severe symptoms such as dissociation or self-harming behaviors were often excluded (Bradley et al., 2005). Currently, there are only 8 randomized controlled trials worldwide on the treatment of PTSD following experiences of interpersonal violence in childhood and adolescence. The results from these studies support the efficacy of Cognitive Processing Therapy (CPT; Chard, 2005; Resick et al., 2008) and a combination of emotion regulation training and engaging with the traumatic memories (Cloitre et al., 2002, 2010). Even in these studies, however, it remains unclear how effective the treatment is for patients with an additional BDP diagnosis, as there is little evidence for this sub-population. The only study including this information showed that all patients with an additional BPD diagnosis discontinued a primary exposure-based therapy (McDonagh et al., 2005).

A promising approach to the treatment of patients suffering from PTSD with comorbid borderline symptoms includes techniques from dialectical behavior therapy (DBT, Linehan

1993), an evidence-based therapy for BPD previously studied in 9 randomized controlled trials (Zanarini, 2009). However, in a study by Harned et al. (2008), it was demonstrated that only 13% of the borderline patients receiving treatment showed full remission of the comorbid PTSD after one year of DBT treatment without additional, specific interventions for the comorbid PTSD. In an open study, Harned et al. (2012) treated 13 borderline patients with PTSD using a trauma-focused exposure treatment in addition to the on-going standard DBT treatment given on an outpatient basis. An inclusion criterion was that patients exhibited control over so-called stage-I problematic behaviors, such as serious self-harm. Intent-to-treat analyses showed significant improvements in PTSD symptoms and in most secondary outcomes with medium-to-large pre-post effect sizes. Cloitre et al. (2010) reported on the benefits of DBT skills training given prior to a prolonged exposure therapy for adult PTSD patients with interpersonal trauma in childhood.

Against this background, dialectical behavior therapy of post-traumatic stress disorder (DBT-PTSD) was developed specifically for PTSD patients with emotion regulation disorder, negative self-concept, and interpersonal problems, working in close collaboration with Marsha Linehan (Seattle, USA), the developer of the standard DBT treatment, at the Central Institute for Mental Health in Mannheim (Bohus et al., 2011; Steil et al., 2011; Bohus et al., 2013). The efficacy of DBT-PTSD was evaluated in a randomized controlled trial in an inpatient treatment setting. The inpatient treatment concept for DBT-PTSD was tested against a TAU waiting list. The DBT-PTSD treatment was demonstrated to be significantly more effective compared to the waiting list with large effect sizes between the groups regarding PTSD symptoms and medium-to-large effect sizes regarding the depressive symptoms, general psychopathology, borderline symptoms and social adaptation. Patients currently exhibiting self-harming behaviors and severe PTSD symptoms (CAPS > 90) were included in the study. Despite intensive exposure-based interventions, there was a significant reduction in self-harming behavior and no increase in suicidality (Bohus et al., 2013). Therefore, we assume that DBT-PTSD is very effective for treating patients with severe PTSD and a comorbid borderline disorder, and is superior to cognitive processing therapy, especially in these patients.

Since inpatient treatment is very expensive and only accessible to a limited number of patients, the main objective of this multicenter research project is to investigate the efficacy of DBT-PTSD on an outpatient basis as compared to CPT.

1.2 Risk-benefit assessment

There may be an increase in distress brought about during diagnosis and treatment. Experience shows, however, that this is temporary. All diagnosticians and therapists are experienced psychologists that have been specially trained for the trial. All diagnosis and treatment steps are regularly monitored. The diagnosticians assess the current stress level after each session, and are available to talk further if needed. If necessary, emotion regulation techniques will be taught and, if required, emergency management will be discussed e.g. providing the telephone number of the psychiatric hospital for use in emergency situations. Patients will be provided with the contact details of their therapist, which can be contacted in case of an emergency. In addition, a detailed emergency plan will be developed when treatment is started. Patients will also be provided with the study coordinator's telephone number in the patient information materials, which they can contact if they have any questions. In the long term, the treatment sessions can be expected to reduce symptomatology.

2. AIMS AND OUTCOMES

2.1 Primary aim and primary outcome

The primary aim of Project A and the overall project is to evaluate the efficacy of a 12-month outpatient treatment program: Dialectical Behavior Therapy for Post-traumatic Stress Disorder (DBT-PTSD). Over the study, the treatment program is tested against a well-established PTSD treatment: Cognitive Processing Therapy (CPT). Patients with PTSD following interpersonal violence in childhood and severe emotion dysregulation were accepted onto the treatment program.

Hypothesis 1: Improvement in PTSD symptoms is more pronounced in DBT-PTSD treatment than in CPT treatment.

Primary outcome: Clinician-Administered PTSD Scale (CAPS, Blake et al., 1995)

A secondary aim of Project A is to evaluate moderators for the general and specific efficacy of treatment.

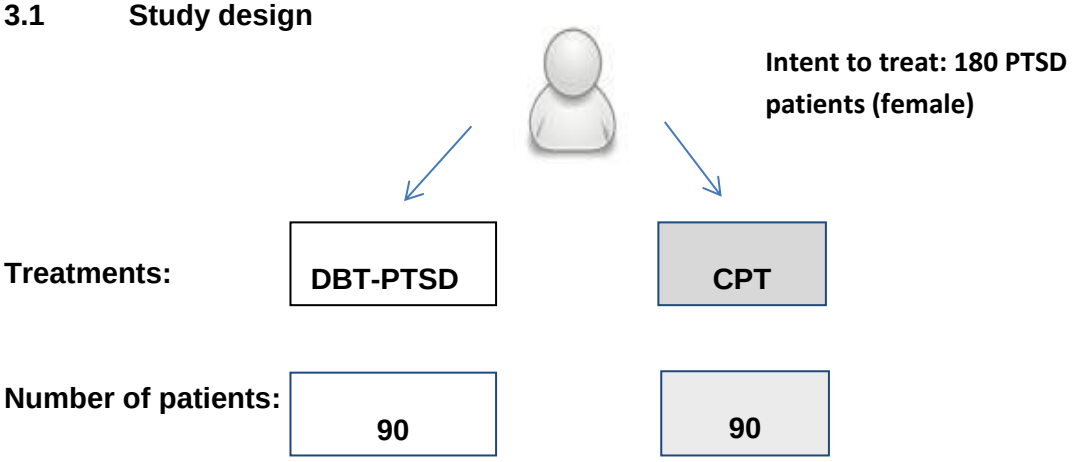
Hypothesis 2: Superiority of DBT-PTSD over CPT correlates with the severity of borderline symptoms.

Secondary outcomes: Borderline symptoms (Zanarini Rating Scale for Borderline Personality Disorder (ZAN-BPD; Zanarini et al. 2002), Borderline Symptom List (BSL-23, Bohus et al., 2009), General Symptom Severity (SCL-90-R, Derogatis et al., 1992), Social Functioning Level (GAF, Endicott et al., 1976), Health Economy (Interview and Questionnaire for Recording Health Economy, Wagner et al., in press), Quality of Life (WHOQOL, Angermeyer, Kilian & Matschinger, 2000, EQ-5D (EuroQuol Group, 1990), SF-36 (Hays et al., 1993), SWLS (Glaesmer et al., 2011).

In addition, the collected data will be used to determine potential moderator variables for general and differential treatment results: patient variables such as pre-treatment symptom severity, comorbid depression, severity of interpersonal trauma in childhood, age at onset and duration of traumatization, current age and educational level.

3. STUDY DESIGN

3.1 Study design



Dialectical Behavior Therapy for Post-Traumatic Stress Disorder (DBT-PTSD):

- 1 year one-on-one outpatient treatment with a maximum of 45 sessions of 50 minutes each
- Modular treatment approach: Single treatment sessions follow if-then algorithms
- Based on the principles and methods of Dialectical Behavior Therapy (DBT)
- Integrates methods from trauma-focused cognitive treatment and exposure-based interventions
- Skills-supported exposure

Cognitive Processing Therapy (CPT):

- 1 year one-on-one out-patient treatment with a maximum of 45 sessions of 50 minutes each
- Linear treatment approach: Individual sessions follow a pre-defined protocol
- Integrates methods of cognitive restructuring and special interventions with regards to guilt, dysfunctional assumptions regarding safety, control, trust, self-worth and intimacy

A total of 180 patients with post-traumatic stress disorder (PTSD) following interpersonal violence that has occurred before the age of 18, also suffering from emotion regulation disorder are to be investigated in this multicenter, randomized, controlled trial. A total of 3 study centers are involved (Central Institute of Mental Health, Mannheim; Institute of Psychology of the Goethe University, Frankfurt; and the Institute of Psychology of the Humboldt University, Berlin). 60 patients are recruited per center: 30 for DBT-PTSD; and 30 for CPT treatment. After providing information on the study, explaining inclusion and exclusion criteria, and signing of consent forms for participation in the study, patients at the respective centers will be randomly assigned to the two treatment programs: DBT-PTSD and CPT. Participation in the study will last for a total of 16 months for each patient (including initial diagnosis and follow-up at 3 months). After inclusion in the study, a total of 5 assessment points are carried out, at 3-month intervals; primary and secondary outcomes are recorded at each assessment point (project A, B, C). The professional performing diagnostics is blinded with respect to the treatment which any given patient is assigned to. In addition, patients will receive questionnaires before and after each therapy session, as well as a monthly questionnaire on emotion regulation and trauma-related dysfunctional cognition. In addition to the weekly diary cards, the primary outcome variables (post-traumatic symptoms and borderline symptoms) and the extent of social isolation at the start of treatment (T1), 6 months after the start of treatment (T3), and at the end of treatment (T5) are recorded over a period of one week each using electronic diaries. The electronic diary is

used to record the variables of interest in real time while the subjects follow their normal daily routine. During the first 5 days, patients are asked to make entries each time they are confronted with a trauma-associated memory; over the subsequent 2 days, the extent of affective instability is measured using repeated queries. Each individual query takes less than 5 minutes or less than 2 minutes respectively. Social isolation involves evaluation of whether: (a) the patient's radius of action increases (km/day); and (b) how much time they spend at home (h/week). GPS is used (in combination with WLAN and CELL) to record the movement patterns of the patients. The data is encrypted using public key encryption and transferred to a secure server that meets the necessary data protection standards via an SSL-encrypted connection.

The general and specific therapeutic competencies, adherence scales (DBT-PTSD and CPT) and the therapeutic alliance are rated by trained clinical psychologists using videos.

3.2 Study duration and timeline

The total duration of the clinical trial will be 3 years. Recruitment of patients will start in January 2014 (first subject in (FSI)). The actual duration of the entire clinical trial or recruitment phase may vary. The end of study is defined as the “last patient out” (LPO).

Total duration	3 years
Duration of clinical phase	2 years, 8 months
Start of the preparatory phase	September 2013
FSI (first subject in)	Q1/ 2014
LSI (last subject in)	Q2/2015
LSO (last subject out)	Q3/2016
DBL (database lock)	Q3/2016
Completion of statistical analysis	Q3/2016
Completion of study report	Q4/2016

4. PATIENT AND CENTER CHOICE

4.1 Number of patients

As explained in Section 9.1 Sample size calculation, 180 subjects are to be included in the clinical trial, i.e. 90 subjects per treatment group. The recruitment and treatment of the subjects will be carried out in 3 study centers. The maximum number of subjects per center is 60 unless problem-solving measures are initiated due to recruitment difficulties at any given center (see below).

During the recruitment period (Jan 2014 – July 2015), the recruitment figures are reviewed by the Mannheim Study Center at 6-month intervals (on 01/07/2014, 01/01/2015, 01/06/2015). If less than 60% of the specified recruitment rate is reached, a problem-solving recommendation is developed working in collaboration with study management. If the recruitment rate is less than 30%, the study management reserves the right to stop payments of the per-case rates, or to discontinue payment if the patient is still excluded. The principal investigator of the trial reserves the right to apply the per-case flat rate(s) to another study center in the event of a delay in the recruitment process, in order to ensure that the overall recruitment goals of the study are achieved.

4.2 Study centers

This trial will be conducted as a multicenter study at the Central Institute of Mental Health, Mannheim, the Psychological Institute of the Goethe University, Frankfurt, and the Psychological Institute of the Humboldt University, Berlin.

4.3 Inclusion criteria

Individuals who meet the following criteria are eligible for inclusion in the clinical trial:

- Gender: female
- Minimum age: 18 years
- Diagnosis of post-traumatic stress disorder following sexual abuse or physical violence before the age of 18, according to the criteria of DSM-5 (collected using CAPS for DSM-5)
- Sexual abuse or physical violence as index trauma
- Diagnosis of BPD or sub-clinical BPD (at least 4 out of 9 DSM-IV criteria, including criterion 6: affective instability) as per the International Personality Disorder Examination (IPDE; Loranger et al., 1994)
- Must be able to participate in treatment over a period of one year, with weekly sessions; no planned absence of more than 4 weeks (e.g. planned inpatient stay)
- Subjects in the trial must have the capacity to understand the nature and scope of the clinical trial
- Written informed consent

4.4 Exclusion criteria

Any persons meeting one of the following criteria will not be included in the clinical trial:

- Lifetime diagnosis of schizophrenia or bipolar I disorder according to DSM-IV
- Mental retardation

- Severe psychopathology requiring immediate treatment in a different setting (e.g. serious physical illness, body mass index below 16.5)
- Acute alcohol and substance dependence according to DSM-IV without abstinence for a period of at least 2 months (substitution is not an exclusion criterion)
- Medical factors that make exposure treatment impossible
- Life-threatening behavior in the last 2 months (defined as achieving a value of 5 in the corresponding question in the SBDI (Borgmann & Bohus, 20082012)
- Instability in the current life circumstances (defined as homelessness or on-going victimisation by the perpetrator(s)).
- CPT or DBT-PTSD treatment during the year prior to initiation of treatment
- Pregnancy

4.5 Termination criteria

4.5.1 Exclusion of subjects

Treatment as part of the study will be discontinued for any given subject if one of the following reasons apply:

- A wish expressed by the subject.
- Non-attendance at 5 treatment sessions in a row.
- Inpatient crisis intervention of 2-week duration: Therapists are encouraged to contact the admitting hospital and assist with discharge preparations. If the inpatient intervention continues for a period of more than 2 weeks, participation in the study will be terminated and treatment as part of the trial will be terminated. However, further treatment outside of the framework of the trial is possible.
- Success-related discontinuation criterion: if the CAPS and BSL-23 values at two consecutive assessment points fall within a non-clinical range for any given subject, and the patient, therapists and supervisor all approve a success-related discontinuation, the treatment can be terminated early.

If any of the above criteria apply, the study management of each study center shall make a decision with regards to discontinuation of treatment as part of the study in the case of the affected subject of the clinical trial.

If a subject does not present at an assessment point, clarification should be sought as to whether this is due to the fact that she wishes to terminate participation. In any case, the reason for the termination and the date must be documented in the CRF and in the subject's record; the study sponsor must be informed. If the subject withdraws from further participation in the clinical trial at her own request, a reason for this should be requested and documented in as much detail as possible.

For those who terminate participation in the study, all persistent adverse events (AEs)/serious adverse events (SAEs) should be followed up until no signs or symptoms are presenting, or until the subject achieves a stable state. Subjects who terminate participation in the trial will not be replaced.

4.5.2 Early termination of participation of a study centre

Premature termination of a center's participation is possible if the sponsor notices that the trial is not being conducted in accordance with ICH-GCP and/or not in accordance with the Study Protocol, or the recruitment and/or quality of the data is insufficient.

If the clinical trial at a center is terminated prematurely, all study materials (completed, partially completed and blank CRFs, randomisation envelopes, etc.) must be returned to the study center at the Central Institute of Mental Health, Department of Psychosomatics and Psychotherapeutic Medicine, Mannheim.

5. TREATMENTS/INTERVENTIONS

5.1 Description of treatments/interventions

Project A: Description of treatment approaches: DBT-PTSD and CPT.

The treatments take place in the outpatient rooms of the 3 study centers. All therapy sessions are video-recorded.

Dialectical Behavior Therapy for Post-Traumatic Stress Disorder (DBT-PTSD)

DBT-PTSD is based on dialectical behavior therapy (DBT) with a modular treatment approach. It provides an algorithm for the treatment of female patients suffering from PTSD and emotion dysregulation following interpersonal violence in childhood.

DBT-PTSD as adapted for outpatient treatment has a total duration of 1 year and consists of a total of 45 individual sessions plus homework tasks and telephone consultations as required. As part of DBT-PTSD, patients learn emotion regulation skills. Methods of trauma-focused cognitive treatment and exposure-based interventions are predominantly used during parts one and two (of a total of three parts) of treatment. In the final (third) part of treatment, social problems and the reorganisation of living conditions in everyday life are addressed. Telephone consultations can be used for the purpose of crisis intervention, available to the patients as and when necessary.

The weekly supervisions aim to ensure adherence to the manual, in addition to supporting the therapists and for quality assurance.

As part of the therapy, the patients also regularly listen to the therapy sessions, recorded by USB MP3 stick, outside the therapy sessions. For this purpose, each patient in DBT-PTSD treatment is provided with a laptop by the respective study center, onto which the Morpheus software (developed specifically for this purpose) can be installed. The software allows users to play back recordings of treatment sessions with regular queries appearing in relation to the intensity of tension, stress, and feelings of guilt, shame, disgust, anger, fear, impotence and grief, queried both before and after the recording is played. During playback, the intensity of tension/stress is queried at regular intervals, provided on a scale of 0 to 100 (0 = not at all stressed, 100 = maximum possible stress). If the patient indicates a stress level equal to or greater than 70, the software automatically offers skills to stabilise stress levels. The software automatically generates statistics in relation to the patient's data, allowing for observation and documentation of therapeutic processes, which are then fed back into and addressed during therapy.

Cognitive processing therapy

Cognitive processing therapy (CPT) was originally developed by P. Resick for the treatment of adult victims of rape suffering from PTSD. It is manual-based and highly-structured therapy designed with the aim of reducing negative trauma-associated feelings, building up feelings of control and safety in the subject's own life and environment, and promoting more balanced and appropriate attitudes to oneself and to the environment. In essence, CPT is based on the assumption that the meaning of the experience of violence, rather than the experience of violence itself, causes the affected person to suffer. Through CPT, affected patients learn to identify their own dysfunctional cognitions of what has happened, and to question thoughts which they do not consider to be helpful; they can then replace these thoughts with more helpful and appropriate thoughts. Patients are guided during therapy to question and modify their thoughts. First of all, thoughts are addressed which relate to the causes of the experience of violence. Later over the course of treatment, there will be examination of the impact the experiences have on the affected patients in terms of safety, trust, power, control, self-esteem and intimacy.

In addition to cognitive techniques, the original CPT also includes an element of written exposure to the memories of the experience(s) of violence. Patients were instructed to write a detailed report on their trauma. However, the cognitive interventions without the written exposure have been shown to be equally as effective in reducing PTSD symptoms (Resick et al., 2008) as in the combination therapy (cognitive interventions plus written exposure).

In order to be able to better compare the two forms of treatment in the planned randomized controlled trial, the CPT was modified for the purposes of this study in collaboration with P. Resick, the person who developed the treatment program. The CPT now consists of 45 individual sessions plus homework tasks, and is conducted over a maximum period of 1 year. Each session follows a pre-defined session protocol. The sessions include psycho-education for PTSD, and addressing the consequences of the interpersonal violence suffered in childhood. The therapist explains the treatment approach to the patient. The patient then describes the impact that the experience of interpersonal violence has had on her life. Cognitive restructuring is then carried out, taking into account any feelings of guilt and shame. As a result, basic dysfunctional assumptions in relation to safety, trust, control and power, self-confidence and intimacy are addressed. At the end of the treatment, there is a return to the description of the impact of the interpersonal violence on the patient's life created at the beginning of treatment, and the areas of social problems and the reorganisation of living conditions in everyday life are addressed.

Also in the case of CPT, the weekly supervisions aim to ensure adherence to the manual, in addition to supporting the therapists and for quality assurance.

5.2 Risks due to treatment(s)/ intervention(s)

These are psychotherapeutic interventions, which are carried out according to evidence-based procedures. Although overall it can be expected that symptoms will improve, being confronted with traumatic memories, which forms part of the treatment approach, may initially lead to a worsening of symptoms and generally to significant stress for patients. The investigators and all therapists are specially trained in this respect, and can offer patients the appropriate support and care they need. In addition to the planned therapy sessions, telephone calls for times of crisis can also be offered. Inpatient admission for patients as part of crisis intervention can be provided at all three centers in a timely manner.

5.3 Randomization

Subjects are randomly assigned to the two treatment program in a 1:1 ratio per study site, i.e. following verification of inclusion and exclusion criteria and obtaining consent for participation, patients will be assigned a number for randomization, which determines which of the two treatment programs they will be assigned to. The randomization procedure is web-based, using the service provided by the University of Graz (www://randomizer.at). The professionals responsible for diagnosis over the course of treatment remain blind throughout the study with respect to the assignment of each subject.

The randomization list will be stored in a safe and confidential manner at the respective study center.

5.4 Blinding and unblinding

The assessors responsible for initial and follow-up diagnostics over the course of treatment remain blind to the treatment approach assigned to patients over the entire course of the trial. Randomization will be carried out by the respective study coordinator.

Once the trial has been completed (Database Lock Q3/16), all randomization lists are unblinded at the study center in Mannheim.

5.5 Previous illness and co-morbidities

Any further relevant diseases that were present at the time of providing information to patients about the study and obtaining consent are considered as concomitant diseases, and are documented on the relevant pages in the CRF. As this clinical trial is conducted with physically healthy individuals, there should be no physical co-morbidities requiring treatment. Comorbid psychiatric illnesses are recorded during initial diagnosis and documented in the CRF.

5.6 Previous and concomitant treatments

Any relevant additional treatment measures that the subject undergoes at the start or over the course of the clinical trial should be considered as concomitant treatment measures and must be documented on the respective pages in the CRF.

Psycho-pharmacological treatment is permitted, with information on medication and/or changes to medication being recorded weekly. No other concomitant psychotherapeutic treatments are allowed.

All additional medical treatments provided to subjects at the start or over the course of the clinical trial are to be considered concomitant treatment measures. These are to be documented on the respective pages in the CRF.

5.7 Emergency Treatment

If symptoms deteriorate dramatically over the course of the study, whereby hospitalization in a protected psychiatric facility is required, this measure will be initiated directly by the treating therapists. An emergency response plan will also be developed with each subject, determining the exact course of action to follow in the event of acute suicidality. As part of this, points of contact are also defined, which can be contacted if the therapist and study coordinator are not reachable by telephone.

6. METHODS OF ASSESSMENT

6.1 Time sequence

For each individual patient, the duration of the treatment is no more than 12 months from the start of treatment to the end of treatment. The booster phase has a duration of 3 months, and therefore corresponds to the 3-month period after the end of treatment. A screening phase is carried out prior to start of treatment (maximum 4 weeks prior to start of treatment).

6.2 Description of the study measures

6.2.1 Screening visits (T0-T6)

Initial and on-going diagnostic visits take place in the outpatient rooms of each of the three centers. The patients recruited are those who present at the respective outpatient departments of the three study centers for outpatient treatment and who fulfil the inclusion and exclusion criteria as described in Chapter 4.4/4.5. After detailed diagnostics is carried out, the study is explained to the patients by the respective study coordinator and written consent is obtained for each subject; following this, patients are admitted to the study (T0). Randomization is performed, whereby patients are randomly assigned to one of the two treatment approaches. There is a maximum interval of 4 weeks between randomization and first contact with the assigned therapist (see Flow chart, page 8). This is the first assessment point, at the start of treatment (T1). The individual examination instruments are shown in the flow chart on page 8. Further intermediate assessment points are carried out at three-month intervals after start of treatment (T2-T5), and at three months after end of treatment (T6) across all three study centers.

6.3 Planned treatment following end of trial

Patients have the option of having further outpatient treatment after the end-of-treatment date, whereby the therapist and treatment center must be changed after the end of the treatment. Subjects who terminate participation in the trial should be followed up until they achieve a stable condition for all persisting adverse events (AEs)/serious adverse events (SAEs).

7. METHODS OF DATA COLLECTION

Data is collected using Case Record Forms (CRFs), diagnostic interviews and self-assessments. Documents relating to data recording and all instruments will be made available to all three test centers by the Mannheim Study Center.

The CRFs and questionnaires should be completed using a blue pen so that the principal investigator can identify the original. The completed questionnaires at the assessment points for T0-T6 (see Flow chart on page 8) are to be scanned by the respective study centers, and the study centers in Frankfurt and Berlin will then send them to the study center in Mannheim electronically in a timely manner. The original documents are stored in the respective patient records at the study centers.

The questionnaires completed on a weekly basis before and after therapy sessions are initially stored in the patient file by the respective therapist, and are collected and scanned at regular intervals by study coordination staff. Representatives from the centers in Frankfurt and Berlin shall regularly send these documents in electronic form to the study center in Mannheim, where they will be verified using TELEform software, version 10.2, and automatically exported to SPSS for Windows (cf. Section 10.2).

7.1 Evaluation of Efficacy

Primary endpoints from Project A will be used for evaluating treatment efficacy.

7.2 Assessment of Safety

Adverse events are documented at each assessment point T0-T6. Should a serious adverse event occur, the treating therapist will immediately notify the principal investigator. All treating therapists will be provided with the corresponding contact information.

An emergency response plan in the event of acute suicidality will also be drawn up with all patients (see Chapter 5.7).

8. ADVERSE EVENTS

8.1 Definitions

8.1.1 Adverse event

According to GCP, an adverse event (AE) is defined as follows: any untoward medical occurrence in the patient or clinical trial subject administered a medicinal product and which does not necessarily have a causal relationship with this treatment. An AE may therefore be any adverse and unintended reaction, symptom or condition which is temporarily associated with the intervention, irrespective of whether these are related to the intervention. In psychotherapeutic studies, adverse events are rarely systematically documented. An exception to this are studies in which the indication itself is somatic or is directly related to medical interventions (e.g. in studies with patients who are struggling with substance abuse or are overweight).

No additional physical/medical examinations will be performed as part of this trial. As such, adverse events are documented solely with regard to psychological symptoms or changes. The following events are defined as adverse events:

- New psychological symptoms/complaints/impairments of wellbeing
- Attempted suicide
- Inpatient admission due to a deterioration in psychological condition requiring crisis intervention.

A pre-existing disease/symptom shall not represent an AE unless there has been an unfavourable change in its intensity, frequency, or quality. A change of this type must be documented by the responsible investigator.

Adverse events are classified as “severe” and “non-severe”.

8.1.2 Severe adverse event

Serious adverse events (SAEs) are defined as the following events, regardless of the intervention:

- Suicide

Or any other event,

- that leads to death,
- that is acutely life-threatening (i.e. subject is in acute danger of death at the time of an AE),
- or that leads to significant physical disability.

8.1.3 Intensity of adverse events

The **intensity** of an AE should be assessed by the investigator using the following classification:

Mild:	Any event that results in a slight impairment, i.e. activities of daily life can be carried out without any restriction.
Moderate/medium-grade:	Any event that results in a moderate impairment, i.e. activities of daily life are impeded.
Severe:	Any event that results in a significant impairment, i.e. it is not possible to carry out the activities of daily life.

8.1.4 Correlation and outcome of adverse events

In the case of each AE, the investigator will assess any possible association with the intervention:

Certain:	There is a justified assumption that the event is due to the intervention. The temporal correlation is plausible and an alternative cause is unlikely.
Likely:	There is a justified assumption that the event is due to the intervention. There is a temporal correlation and a known response pattern occurs, but there is another possible cause.
Possible:	There is a justified assumption that the event is due to the intervention. There is a temporal correlation; however, the response pattern is atypical. An alternative explanation seems to be more likely or there is significant uncertainty surrounding the cause of the event.
Unlikely:	There is only a remote possibility that there is a relationship between the adverse event and the intervention. Other conditions, including concomitant diseases, progression or change in course of disease, or a reaction to concomitant medication, may explain the reported adverse event.
No correlation	There is no temporal correlation to the intervention and the clinical condition of the subject; other treatment modalities or another aetiology offer a likely explanation for the AE.
Cannot be assessed:	It is not possible to assess the relationship.

The outcome of an adverse event at the time of last contact is classified as follows:

Recovered:	All signs and symptoms of the AE have disappeared without other sequelae at the time of the last examination
Improving:	The intensity of signs and symptoms has decreased since the last examination and/or the clinical picture has changed in a manner which is typical for improvement
Not recovered:	Signs and symptoms of the AE are more or less unchanged at the time of the examination
Recovered with sequelae:	Acute signs and symptoms of the AE have resolved, but there are still sequelae whose cause can be traced back to the AE

Fatal:	Has resulted in death. If there are multiple AEs, only the AE which has led to death (possibly in relation to the intervention) is classified as "fatal"
Unknown:	The outcome is unknown or implausible and the information cannot be supplemented or verified

8.2 Period of observation and documentation

All AEs reported by the trial subjects or observed by the investigator will be recorded during the clinical trial and must be documented in the CRF on the pages provided for this purpose. The AEs must also be recorded in the patient record.

In this clinical trial, all AEs occurring from the moment when the subject gives consent up to T6 (3 months after the end of treatment) will be documented in the CRF. Irrespective of whether or not any connection with the intervention is suspected, all subjects with AEs are observed until the AEs resolve or until a stable condition is reached.

8.3 Reporting of severe adverse events by the investigator

SAEs must be reported using the SAE form within 24 hours of becoming aware of it, or at the latest on the next working day, to the principal investigator (Prof. Dr. Martin Bohus). The initial report should be as detailed as possible and should include exact details of the SAE and an evaluation of the causal link between the AE and the intervention. The SAE form will be faxed to the study centre in Mannheim (fax number: 0621 1703 4405). All SAE reports should be forwarded to the responsible monitor and local ethics committee of the respective study centers.

9. STATISTICAL PROCEDURES

9.1 Sample size calculation

The sample size has been optimized on the basis on a formal sample size calculation for sub-project A (effectiveness comparison). The null hypothesis ("The progression of the CAPS total score over time is independent of the group allocation") is tested at the Bonferroni-corrected significance level of $\alpha_1 = 0.025$. For the sample size calculation, it was assumed that the relative efficacy of DBT-PTSD vs. CPT is significantly smaller, at d = 0.5, than the very large effect size that has been demonstrated in our pilot study comparing DBT-PTSD vs. standard treatment (Cohen's d = 1.5; Bohus et al., 2013). The effect size of d = 0.5 corresponds to a mean effect and an effect size f(V) of 0.354 for the group*time contrast in a general linear model with one between-subject factor and one within-subjet factor. Under these assumptions, 63 subjects per group are required to achieve a statistical power of 0.8. The drop-out rate of 30% used as the basis for the (conservative) power calculation results in a sample size of 90 subjects per study group. The assumed drop-out rate of 30% is in line with the review published by Hembre et al. (2003) on drop-out in treatment studies for post-traumatic stress disorder.

With a sample size of n = 90 per group, the study has sufficient statistical power to detect a small to medium effect (incremental explained variation of 10%; $\alpha_1 = 0.025$) with respect to the moderator hypothesis (relating to association between relative efficacy and symptom severity at baseline) with an 80% probability.

9.2 Variables to be included in the analyses

Project A: The primary outcome for investigation of the efficacy hypothesis is the total score of the Clinician-Administered PTSD scale (CAPS, Blake et al., 1995). The severity of borderline symptoms as a possible moderator of differential efficacy is operationalized by the total score of the Zanarini Rating Scale for Borderline Personality Disorder (ZAN-BPD; Zanarini et al., 2003) and the Borderline Symptoms List (BSL-23, Bohus et al., 2009).

Other secondary outcomes for analysis are: General Symptom Severity (SCL-90-R, Derogatis et al., 1992); Social Functioning Level (GAF, Endicott et al., 1976); Health Economy (Interview and Questionnaire to Record Health Economy, Wagner et al., in press); Quality of Life (QHOQOL, Angermeyer, Kilian & Matschinger 2000); EQ-5D (EuroQuol Group, 1990); SF-36 (Hays et al., 1993); SWLS (Glaesmer et al., 2011).

9.3 Definition of the study population to be examined

Treatment as part of the study will be discontinued if: (i) the subject declares a wish to this effect; or (ii) serious adverse events occur; or (iii) the subject fails to present at 5 consecutive therapy sessions; or (iv) the subject must be hospitalized for 2 weeks or more for crisis intervention; or (v) the subject's participation in the trial is terminated prematurely, which occurs where the value for CAPS (Blake et al., 1995) and BSL-23 (Bohus et al., 2009) fall below a clinically significant value on at least two assessment points in succession, and the subject, the therapist and the supervisor all approve a success-related discontinuation of trial participation.

According to the intent-to-treat approach used in the hierarchical linear models, all subjects who have been randomized will be included in the statistical analysis.

9.4 Statistical methods

The primary analysis of efficacy and the potential moderating effect of the severity of symptoms on differential efficacy is investigated using a hierarchical linear model (HLM). For this, the CAPS total score is modelled on the basis of the measurement timepoint (start of study, months 3, 6, 9, 12, and 15), the group, the interaction between time and group (for primary evaluation of the relative efficacy of the groups), and the initial severity. To test the moderator hypothesis, the model is extended to include the interaction of time*group*(initial severity). All model parameters are estimated based on the restricted maximum likelihood method (REML). The hierarchical linear model was selected as the primary evaluation method in accordance with the requirements of the Institute of Medicine (2008), which recommend this method to avoid a bias associated with drop-outs. In order to further minimise this bias, it is also investigated whether there is relationship between absence of data and the result. In particular, analysis in this respect will test whether the interaction between completer status, time, and group significantly improves the model adaptation (cf. Hedecker & Gibbons, 1997).

9.5 Interim analysis

No interim analysis is planned.

10. DATA MANAGEMENT

10.1 Data collection

It must be possible to verify all entries in the CRF using source documents. Irrespective of this, the patient record must contain a minimum of documentation to provide information on participation in the trial, and all the medical information necessary for adequate medical care outside the framework of the clinical trial.

The investigator is responsible for ensuring correct, timely and uninterrupted documentation. Incorrect entries must be deleted with a single strike-through so that the original entry remains readable. The correction is made next to the respective data field and the signature of the investigator or authorised member of the study team, date and reason for the change, if any, must be added next to the correction. The reason for the change can be omitted for self-explanatory corrections (e.g. transposition errors of numbers in date fields).

Each final CRF page from a visit must be signed once by the investigator and dated to confirm the accuracy of the data. The original of the CRF is sent in to the data management department at the Central Institute of Mental Health, Hospital for Psychosomatics and Psychotherapeutic Medicine, J 5, 68159 Mannheim.

10.2 Data handling

After a first visual check for plausibility, all documents are scanned. The Frankfurt and Berlin test centers will send their scanned documents to the study coordination department and its representatives in Mannheim, where they are verified using the TELEform Standard software, version 10.2, and automatically exported to SPPS, version 20.

On the basis of the visual plausibility check and the subsequent checks, queries are created. The respective centers must then respond to the queries, with support from the monitor if necessary.

After the study is completed, further checks are carried out to ensure that the data is plausible, consistent and complete. These checks in addition to a visual check by the responsible data manager lead to the creation of queries.

Any missing data or inconsistencies are reported to the centers, and must be clarified by the responsible investigator. As soon as there is no need for further corrections to be made to the database, it is confirmed and approved for statistical evaluation.

10.3 Storing and archiving data

In accordance with medical professional regulations, all important study documents (e.g. CRFs) must be archived for at least 10 years following the completion of the trial.

The study center at the Central Institute of Mental Health in Mannheim is responsible for archiving the TMF and CRFs.

The investigator stores all of the study documents, including the patient identification list and relevant correspondence, in the Investigator Site File (ISF). The ISF, all source documents and all other documents listed in Section 8 of the “ICH Consolidated Guideline on GCP” will be archived by the investigator following the standard or otherwise premature termination of the trial, in accordance with the legal requirements.

11. ETHICAL AND LEGAL ASPECTS

11.1 Good clinical practice

The procedures specified for the implementation, analysis and documentation of this clinical trial are intended to ensure that all parties adhere to the principles of Good Clinical Practice (GCP) and the ethical principles set out in the Helsinki Declaration. The trial will be carried out in accordance with all locally-applicable laws and regulations.

The provisions of the GCP guideline must be complied with, and the Federal Data Protection Act (BDSG) shall apply.

11.2 Approval of the Study Protocol and amendments to the Study Protocol

Prior to the start of the clinical trial, the Study Protocol, patient information and consent forms, as well as any other required documents will be submitted to the responsible Ethics Committee (EC).

Approval from the Ethics Committee is a prerequisite for the clinical trial to start. The opinion of the EC should include the title of the clinical trial (and short name, if applicable), the test locations and all other documents examined. The date on which the decision was made must be specified and the vote must be signed by a member of the ethics committee. The supporting evaluation documents are to be completed by a list of the members of the Ethics Committee who have been involved in the consultation, in addition to a confirmation that the EC is operating according to GCP principles (if necessary, the statutes of the EC can be filed together with the vote in place of this).

All correspondence (written and oral) with the responsible ethics committee must be documented and stored by the sponsor.

All ethical and legal requirements must have been met before the first subject is admitted to clinical trial.

Changes to the Study Protocol are to be made in writing and require the approval of all signatories to the Protocol. Any subsequent significant changes to the Study Protocol also require the approval of the responsible ethics committee.

11.3 Practicalities of informing study subjects and obtaining consent

Before a subject can be included in the clinical trial, the subject must be informed both verbally and in writing of the nature, significance and scope of the clinical trial in an intelligible form; subsequently, the subject is required to consent to participation in writing.

The subject will receive a copy of the clinical trial patient information and consent forms. The original copy is stored by the study coordinator. These documents must be produced in a language that the subject can understand. The documents shall include an indication of who has informed the subject.

Subjects will be notified of any new information that may affect their decision to participate in the study. Communication of any such information to subjects shall also be documented.

12. QUALITY CONTROL AND QUALITY ASSURANCE

12.1 Data protection

The data collected over the course of the clinical trial will be handled in accordance with the provisions of the German Data Protection Act (Bundesdatenschutzgesetz; BDSG).

During the clinical trial, subjects are identified only by an individual identification number (randomization number). When saving study data on a computer, the regulations of the Federal Data Protection Act will be observed; the data is handled in a strictly confidential manner. Organisational measures have been taken to ensure this data is protected, preventing it from being passed on to unauthorised third parties. Full compliance with the relevant provisions of the country-specific data legislation will be ensured.

By signing the written consent form for participation in the clinical trial, the subject releases the investigator from his/her confidentiality obligations with respect to representatives of the competent authorities (inspectors) and of the sponsor (monitors, auditors) in so far as these individuals may access the personal data to ensure that data has been correctly transferred in order to verify that the clinical trial is being implemented correctly.

The investigator is responsible for maintaining an identification list of the trial subjects (identification number and name of the subject) in order to make identification possible where necessary.

Patients who do not consent to the disclosure of their data in this pseudonymised form will not be included in this clinical trial.

12.2 Monitoring and audit

Monitoring is carried out by personal visits by a clinical monitor in accordance with the Standard Operating Procedures (SOPs) of the KKS Heidelberg. Before the first subject can be included, an initial visit to each study center will be conducted by the responsible monitor. This visit will include checking that all the essential documents are available, and that the prerequisites for the correct implementation of the trial are met. Over the course of regular visits, the responsible monitor will check the entries in the CRFs against the source documents. The investigator must ensure that the local monitor has free access to all the required documents, and must support their work at all times.

The local monitor shall carry out checks between visits, through frequent contact (letter, phone, email), as to whether the trial is being carried out in accordance with the Study Protocol and the legal requirements.

Details on the scope of monitoring are set out in the Monitoring Manual.

In accordance with ICH-GCP, the sponsor reserves the right to carry out audits.

The investigator must ensure that monitors and (if applicable) auditors have free access to all the required documents, and must support their work at all times.

12.3 Investigator responsibilities

The investigator must ensure that all personnel involved in the clinical trial at the study center are adequately informed with respect to the Study Protocol, any modifications to the Study

Protocol, the treatments carried out as part of the trial, and the responsibilities and tasks in relation to the trial.

The investigator shall keep a list of co-investigators and other qualified personnel who have been delegated important audit-related tasks by the investigator.

13. AGREEMENTS

13.1 Financing of the clinical trial

The clinical trial is funded by the BMBF (01KR1303A).

13.2 Reports

The study center shall prepare the final report in collaboration with all the principal investigators, study coordinators, and the biometrician. The study report will be completed in Q4/2016.

13.3 Registration of the clinical trial

The principal investigator shall ensure that this trail is registered at http://www.zks.uni-freiburg.de/uklreg/php/index.php prior to the start of the clinical phase (first subject in, FSI). The study is assigned a specific number (International Standard Randomised Controlled Trial Number; ISRCTN), which is a prerequisite for publication in prestigious scientific journals.

13.4 Publication

All data collected in connection with the clinical trial must be kept confidential until publication.

14. SIGNATURES

This Study Protocol has been critically reviewed by all the signatories and has been approved in its current version. The data contained within the Protocol is consistent with:

- the current version of the risk-benefit assessment for the intervention;
- the moral, ethical and scientific principles of clinical research in accordance with the Helsinki Declaration and the principles of GCP.

Each investigator will be informed in detail of any important or new findings, including intervention-related AEs.

In principle, the Study Protocol must be signed, as a minimum, by the client/principal investigator and the biometrician.

Date:	Signature:	
	Name (Printed):	
	Function:	Principal Investigator
Date:	Signature:	
	Name (Printed):	
	Function:	Medical Coordinator (Author)
Date:	Signature:	
	Name (Printed):	
	Function:	Biometrician
Date:	Signature:	
	Name (Printed):	
	Function:	Project Manager

15. DECLARATION BY THE INVESTIGATOR

I have read this Study Protocol and confirm that it describes all the information necessary for the clinical trial to be implemented correctly. I undertake to implement the clinical trial as defined in this Study Protocol.

I will only enrol the first subject onto the trial once all the ethical requirements for starting the clinical trial have been met. I undertake to obtain a written consent form for participation in the clinical trial from all subjects.

I understand the requirements in relation to the correct reporting of serious adverse events and undertake to document and report such events as stipulated.

I undertake to store all trial-related documents and source documents as described.

Date: Signature:

Name

(Printed):

Function: Investigator

Study center (address):

16. LITERATURE

Angermeyer, M.C., Kilian, R. & Matschinger, H. (2000). *WHOQOL-100 und WHOQOL-BREF. Handbuch für die deutsche Version der WHO Instrumente zur Erfassung von Lebensqualität.* Göttingen: Hogrefe.

Bernstein, D.P., Fink, L., Handelsman, L., Foote, J., Lovejoy, M.,…& Wenzel, K. (1994). Initial reliability and validity of a new retrospective measure of child abuse and neglect. The *American Journal of Psychiatry, 151*, 1132-1136.

Bisson, J. & Andrew, M. (2007). Psychological treatment of post-traumatic stress disorder (PTSD). *Cochrane Database of Systematic Reviews*, CD003388

Blake, D.D., Weathers, F.W., Nagy, L.M., Kaloupek, D.G., Gusman, F.D., Charney, D.S. & Keane, T.M. (1995). The development of a Clinician-Administered PTSD Scale. *Journal of Traumatic Stress, 8,* 75-90.

Bohus, M., Kleindienst, N., Limberger, M. F., Stieglitz, R. D., Domsalla, M., Chapman, A. L., . . .& Wolf, M. (2009). The short version of the Borderline Symptom List (BSL-23): development and initial data on psychometric properties. *Psychopathology, 42(1),32-39.*

Bohus M., Dyer, A. S., Priebe, K., Kruger, A. & Steil, R. (2011). Dialectical behavior therapy for posttraumatic stress disorder in survivors of childhood sexual abuse. *Psychotherapie, Psychosomatik, Medizinische Psychologie, 61(3-4)*, 140-147.

Bohus, M,, Dyer, A. S., Priebe, K., Krüger, A., Kleindienst, N., Schmahl, C., . . . & Steil, R. (2013). Dialectical Behaviour Therapy for Post-traumatic Stress Disorder after childhood sexual abuse in patients with and without borderline personality disorder: A randomised controlled trial. *Psychotherapy and Psychosomatics, 82*(4), 221-233.

Borgmann, E. & Bohus, M. (2012). *SBDI: Severe Behavioral Dyscontrol Interview. Interview zur Erfassung schwerwiegender Störungen der Verhaltenskontrolle*, from www.zi-mannheim.de/materialien.html.

Bradley, R., Greene, J. & Russ, E. (2005). A multidimensional meta-analysis of psychotherapy for PTSD. *The American Journal of Psychiatry, 162*, 214-227.

Briere, J. (1995). *Trauma Symptom Inventory professional manual.* Odessa, FL: Psychological Assessment Resources.

Chard, K. M. (2005). An evaluation of cognitive processing therapy for the treatment of posttraumatic stress disorder related to childhood sexual abuse. *Journal of Consulting Clinical Psychology, 73(5),* 965-971.

Cloitre, M. , Koenen, K. C., Cohen, L. R. & Han, H. (2002). Skills training in affective and interpersonal regulation followed by exposure: a phase-based treatment for PTSD related to childhood abuse. *Journal of Consulting and Clinical Psychology, 70*, 1067-1074.

Cloitre, M., Stovall-McClough, K.C., Nooner, K., Zorbas, P., Cherry, S., Jackson, C. L., . . . & Petkova, E. (2010). Treatment for PTSD related to childhood abuse: a randomized controlled trial. *The American Journal of Psychiatry, 167*, 915-924.

Cutajar, M. C., Mullen, P. E., Ogloff. J. R., Thomas, S. D., Wells, D. L. & Spataro, J. (2010). Psychopathology in a large cohort of sexually abused children followed up to 43 years. *Child Abuse & Neglect, 34*(11), 813-822.

Davidson, J. R. T., Book, S. W., Colket, J. T., Tupler, L. A., Roth, S., David, D. & Feldman, M. E. (1997). Assessment of a new self-rating scale for post-traumatic stress disorder. *Psychological Medicine, 27* (1), 153-160.

Derogatis, L.R. (1992). *SCL-90-R, administration, scoring & procedures manual-II for the R(evised) version and other instruments of the Psychopathology Rating Scale Series.* Townson: Clinical Psychometric Research, Inc.

Endicott, J., Spitzer, R. L. & Fleiss, J. L. (1976). The Global Assessment Scale: a procedure for measuring overall severity of psychiatric disturbance. *Archives of General Psychiatry, 33*, 766-771.

EuroQol Group. (1990). EuroQol-a new facility for the measurement of health-related quality of life. *Health Policy, 16*, 199-208

Foa, E. B., Ehlers, A., Clark, D. M., Tolin, D. F. & Orsillo, S. M. (1999). The posttraumatic cognitions inventory (PTCI): Development and validation. *Psychological Assessment, 11*, 303-314.

Franke, G. (1995). *SCL-90-R: Die Symptom-Checkliste von Derogatis - Deutsche Version*: Manual. Göttingen: Beltz Test.

Glaesmer, H., Grande, G., Braehler, E. & Roth, M. (2011). The german version of the Satisfaction with Life Scale – Psychometric properties and population based norms. *European Journal of Psychological Assessment, 27*(2), 127-132.

Harned M. S., Korslund, K. E., Foa, E. B. & Linehan, M. M. (2012). Treating PTSD in suicidal and self-injuring women with borderline personality disorder: Development and preliminary evaluation of a dialectical behavior therapy prolonged exposure protocol. *Behaviour Research and Therapy, 50*, 381-386

Hautzinger, M., Keller, F. & Kühner, Ch. (2009). BDI-II. Beck-Depressions-Inventar. Revision. 2. Auflage. Pearson Assessment: Frankfurt.

Hays, R. D. , Sherbourne, C. D. & Mazel, R. M. (1993). The Rand 36-item health survey 1.0. *Health Economics, 2*, 217-227

Hedecker, D. & Gibbons, R. D (1997). Application of random-effects pattern-mixture models for missing data in longitudinal studies. *Psychological Methods, 2*, 64-78.

Hofmann, S. G. & Kashdan, T. B. (2009). The Affective Style Questionnaire: Development and psychometric properties, *Journal of Psychopathology and Behavioral Assessment*, 32, 255-263

Institute of Medicine (2008). *Treatment of posttraumatic stress disorder: An assessment of the evidence*. Washington: The National Academics Press.

Kubany, E. S., Haynes, S. N., Abueg, F. R., Manke, F. P., Brennan, J. M., & Tahura, C. (1996). Development and validation of the Trauma-Related Guilt Inventory (TRGI). *Psychological Assessment, 8*, 428-444.

Lampe, A., Mitmansgruber, H., Gast, U., Schussler, G. & Reddemann, L. (2008). [Treatment outcome of psychodynamic trauma therapy in an inpatient setting]. *Neuropsychiatrie, 22(3)*, 189-197.

Linehan MM. *Cognitive-behavioral treatment of borderline personality disorder.* New York, NY, US: Guilford Press.; 1993

Loranger, A. W., Sartorius, N., Andreoli, A., Berger, P., Buchheim, P., Channabasavanna, S.M., … & Ferguson, B. (1994). The International Personality Disorder Examination: The World Health Organization/Alcohol, Drug Abuse, and Mental Health Administration international pilot study of personality disorders. *Archives of General Psychiatry, 51*, 215-224.

McDonagh, A., Friedman, M., McHugo, G., Ford, J., Sengupta, A., Mueser, K., …& Descamps, M. (2005). Randomized trial of cognitive-behavioral therapy for chronic posttraumatic stress disorder in adult female survivors of childhood sexual abuse. *Journal of Consulting and Clinical Psychology, 73*, 515-24.

Patton, J. H., Stanford, M. S. & Barratt, E. S. (1995). Factor structure of the Barratt impulsiveness scale. *Journal of Clinical Psychology, 51*(6), 768-774

Resick, P. A., Galovski, T. E., O'Brien Uhlmansiek, M., Scher, C. D., Clum, G. A. & Young-Xu, Y. (2008). A randomized clinical trial to dismantle components of cognitive processing therapy for posttraumatic stress disorder in female victims of interpersonal violence. *Journal of Consulting and Clinical Psychology, 76*(2), 243-258.

Schnyder, U. & Moergeli, H. (2002). German version of Clinician-Administered PTSD Scale. *Journal of Traumatic Stress, 15*,487-492

Spitzer, C., Stiegliltz, R.D. & Freyberger, H.J. (2005). Fragebogen zu Dissoziativen Symptomen. Göttingen: Huber-Verlag.

Steil, R., Dyer, A., Priebe, K., Kleindienst, N. & Bohus, M. (2011). Dialectical behavior therapy for posttraumatic stress disorder related to childhood sexual abuse: a pilot study of an intensive residential treatment program. *Journal of Traumatic Stress*, *24*(1), 102-106.

Teicher, A. & Parigger, A. (2011). *Modified adverse childhood experience scale.* Unpublished manuscript.

Wagner, T., Roepke, S., Marschall, P., Stiglmayr, C., Renneber, B., Gieb, D., … & Fydrich, T. (in press). Die Krankheitskosten der Borderline Persönlichkeitsstörung aus der gesellschaftlichen Perspektive. *Zeitschrift für Klinische Psychologie und Psychotherapie*.

Weathers, F. W., Blake, D. D., Schnurr, P. P., Kaloupek, D. D., Marx, B. P. & Keane, T. M. (2013). The Clinician-Administered PTSD Scale for DSM-5 (CAPS-5). http://www.ptsd.va.gov.

Weathers, F. W., Litz, B. T., Keane, T. M., Palmieri, P. A., Marx, B. P. & Schnurr, P. (2013). The PTSD Checklist for DSM-5 (PCL-5). http://www.ptsd.va.gov.

Wittchen, H.U., Zaudig, M. & Fydrich, T. (1997). *SKID. Strukturiertes Klinisches Interview für DSM-IV Achse I.* Göttlingen: Hogrefe

Wingenfeld, K., Driessen, M., Mensebach, C., Rullkoetter, N., Schaffrath, C., Spitzer, C., … & Heim, C. (2011). Die deutsche Version des "Early Trauma Inventory" (ETI). *Diagnostica, 57(1),* 27-38

Zanarini, M. C., Frankenburg, F. R., Dubo, E. D.,, Sickel, A. E., Trikha, A., Levin, A. & Reynolds, V. (1998). Axis I comorbidity of borderline personality disorder. *American Journal of Psychiatriy, 155*, 1733-1739.

Zanarini, M. C., Frankenburg F. R. & Vujanovic, A. A. (2002). Inter-rater and test-retest reliability of the Revised Diagnostic Interview for Borderlines. *Journal of Personality Disorders, 16(3)*, 270-276

Zanarini, M. C., Vujanovic, A. A., Parachini, E. A., Boulanger, J. L., Frankenburg, F. R. & Hennen, J. (2003). Zanarini Rating Scale for Borderline Personality Disorder (ZAN-BPD): a continuous measure of DSM-IV borderline psychopathology. *Journal of Personality Disorders, 17(3),* 233-242.

Zanarini, M. C. (2009). Psychotherapy of borderline personality disorders. *Acta psychiatrica Scandinavica, 120(5)*, 373-377.

Amendments[2]

RELEASE Study

[2] The randomized controlled trial was part of a larger research consortium comprising several independent sub-projects (e.g. health economics, neural activation patterns). Those parts of the amendments and the amendments submitted to the review board which refer to the comparative efficacy of DBT-PTSD and CPT are described here.

26/03/2014

File reference: 2013-635N-MA

Treatment of psychosocial and neural sequelae in adults with childhood interpersonal violence (RELEASE)

Amendment No. 2

With reference to the aforementioned study, we would like to give notification of the following changes:

In addition to the instruments specified to-date, the following self-assessment questionnaires are to be recorded at the beginning and end of treatment for subjects with post-traumatic stress disorder as well as for subjects who did not subsequently develop post-traumatic stress disorder as a result of physical and/or sexual abuse:

1. Self-esteem measurement: Rosenberg self-assessment scale (Rosenberg, 1965, German version Colani & Herzberg, 2003); the Rosenberg self-assessment scale is a one-dimensional assessment that uses 10 items to determine the overall self-esteem value.

2. Partner preference measurement: The partner characteristics questionnaire (unpublished) consists of 60 personality characteristics, which should be evaluated with respect to: a) the desirability of each point in a potential partner; b) the presence of each point in the case of a current partner; and c) the presence of each point in the case of the most recent ex-partner.

3. Sleep disorders measurement: The sleep questionnaire consists of 18 items (Pittsburgh Sleep Quality Index [PSQI], Buysse et al., 1989; Epworth Sleepiness scale [ESS], Johns, 1991). It measures the quality of sleep, normal sleep times, latency time in falling asleep, sleep duration, sleep medication taken, and sleepiness. The sleep questionnaire makes it possible to have a quick overview of the type and extent of the disorder.

4. Measuring the capacity to have self-compassion: The Self-Compassion Scale (SCS-D; Neff 2003, German version Hupfeld & Ruffieux, 2011) assesses the positive attitude toward oneself in difficult life circumstances. This personality characteristic is considered to be an effective protection factor that promotes emotional resilience. It consists of 26 items. The items assess the positive or negative aspects of self-kindness, compassion and mindfulness.

5. Measuring mindfulness: The Kentucky Inventory of Mindfulness Skills (KIMS; Baer et al. 2004) consists of 39 items for self-assessment of 4 mindfulness skills: observing; describing; acting with awareness; and accepting without judgement. The inventory relates to mindfulness in everyday life and to people without meditation experience.

   Since no individual instruments have been listed in the patient information, no changes have been carried out for this information.

References:
v. Collani G & Herzberg PY (2003). Zur Internen Struktur des globalen Selbstwertgefühls nach Rosenberg. Zeitschrift für Differentielle und Diagnostische Psychologie, 24, 9-22.
Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ (1989). The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice research. Psychiatry Res, 28.(2), 193-213.
Johns MW (1991). A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale, Sleep, 14(6): 540-545.
Hupfeld J & Ruffieux N (2011), Validierung einer deutschen Version der Self-Compassion Scale (SCS-D). Zeitschrift für Klinische Psychologie und Psychotherapie, 40(2), 115-123.
Baer RA, Smith, GT & Allen KB (2004). Assessment of mindfulness by self-report: The Kentucky Inventory of Mindfulness Skills Assessment, 11, 191-206.

002/06/2014

File reference: 2013-635N-MA

Treatment of psychosocial and neural sequelae in adults with childhood interpersonal violence (RELEASE)

Amendment No. 3

With reference to the aforementioned study, we would like to give notification of the following changes:

The inclusion criterion “Diagnosis of BPD or sub-clinical BPD” (at least 4 out of 9 DSM-IV criteria, including criterion 6: affective instability) as per the International Personality Disorder Examination (IPDE; Loranger et al., 1994)” has been modified.

As one of the main hypotheses of this study relates to the improvement of symptoms of a co-occuring borderline personality disorder, the number of BPD criteria has been reduced from 4 to 3 criteria (including criterion 6: affective instability) for the following reasons: 1. to increase the variance of BPD symptoms within the sample (greater power for moderator analyses); and 2. to increase the representativeness of the sample (external validity).

Furthermore, in addition to the instruments listed to-date, mental images are to be recorded using the questionnaire for mental images (Fragebogen für Vorstellungsbilder; FVB, unpublished) at the beginning and end of treatment: The questionnaire consists of 3 different sections and a total of 26 items to assess the content and characteristics of: a) pleasant mental images; b) unpleasant images; and c) images depicting injury and death. The questionnaire is fully standardised and provides the subject with formulated item responses. The individually perceived agreement with the different responses given should be evaluated on a scale ranging from 0-100 (e.g. 0 = not at all, 100 = extreme; or 0 = unclear/little detail, 100 = very clear/highly detailed). The timeframe for answering the questionnaire is approximately 15 minutes.

As the modified inclusion criterion and the list of questionnaires are not listed in the patient information, no changes have been made to this information.

15/12/2014

File reference: 2013-635N-MA

Treatment of psychosocial and neural sequelae in adults with childhood interpersonal violence (RELEASE)

Amendment No. 5

With reference to the aforementioned study, we would like to give notification of the following changes:

A. Changes with regard to termination and completer criteria:

1. Over the course of the first trial treatments, it became apparent that the termination criterion “Non-attendance at 5 treatment sessions in a row” was not clearly defined in the Study Protocol. Although weekly therapy sessions are the standard, this is not a fixed rule. We are clearly defining the termination criterion as an “interruption of more than 6 weeks of treatment”.
2. We would like to provide more detail for the termination criterion “In-patient crisis intervention of 2-week duration”: the criterion will only come into effect if the subject in question has attended at least one appointment with their therapist.
3. It has been established that a "completer", or subject considered to have finished their participation in the trial as standard, must have attended at least 80% of their therapy sessions, i.e. at least 36 sessions.

B. Changes with reference to diagnostic interviews and questionnaires

1. To-date, no study has been published in the literature in which sexual dysfunction in women following sexual abuse has been recorded in a structured and standardized manner with a diagnostic interview (e.g. Haase et al., 2009). This will be carried out for the first time as part of this study. The only structured interview of sexual dysfunction in the German-speaking world is the “structured interview for sexual dysfunction according to DSM-5 (SISEX; Hoyer & Frank-Noyon, 2014)”. In addition to a general part, in which information on the current experiences with respect to relationships, stress and sexual behavior is collected, SISEX consists of three sections: one relating to disorders of sexual interest and arousal; one relating to orgasm disorders; and lastly a section relating to genital-pelvic pain and penetration disorders. Each section begins with screening questions, whereby if negative responses are given, a section can be skipped. Furthermore, questions are asked at the end of each section in order to rule out other explanations for the symptoms, to understand their origin, and to establish their severity. SISEX takes approximately 20 minutes to complete. It should be carried out 3 months after the start of treatment and (3 months after the end of treatment).

Haase, A., Boos, A., Schönfeld, S., & Hoyer, J. (2009). Sexual dysfunction and sexual satisfaction in patients with post-traumatic stress disorder. *Verhaltenstherapie, 19,* 161-167

Hoyer, J. & Frank-Noyon, E. (2014). Structured interview for sexual dysfunction according to DSM 5: Part B Interview. Unpublished manuscript. Institute of Psychology. Technische Universität Dresden

2. Over the course of the first trial treatments, it also became clear that clinically-relevant dissociative symptoms and disorders are not uncommon. In a study recently published by Sack (2012), a prevalence rate of dissociative disorders of 53% was identified amongst borderline patients with comorbid post-traumatic stress disorder (PTSD) undergoing in-patient treatment. Prevalence rates for patients in treatment on an outpatient basis have not yet been recorded. Since these axis I disorders are not identified within the scope of SKID-I, but are highly significant for therapy, we would like to also carry out SKID-D. In order to keep the additional burden for subjects to a minimum during initial diagnosis, this interview should also be conducted at the interim measurement timepoint after 3 months. SKID-D (Gast et al., 2000) is the gold standard confirming a diagnosis. The semi-standardised interview allows for diagnosis of all the dissociative disorders listed in DSM-IV on the basis of operationalized criteria. Five chapters cover the occurrence and severity of the five major dissociative symptoms (amnesia, depersonalisation, derealisation, identity uncertainty, identity change). In addition to the answers, any dissociative features from the interview situation are also recorded. The interview will take 30 to 90 minutes, depending on the presenting symptoms.

Gast, U., Zündorf, F. & Hofmann, A. (2000). Structured clinical interview for DSMIV Dissociative Disorders (SKID-D). Göttingen: Hogrefe.

3. In one of the two therapy approaches examined (DBT-PTSD), the development of acceptance is an important component, which is why the "*Acceptance and Action Questionnaire II*" (AAQ-II; Bond et al., 2011) was recorded in these patients, and in the group of healthy subjects with experiences of violence before reaching 18 years of age. The AAQ-II consists of a total of 10 self-assessment items on a 7-level Likert scale from "never applies" to "always applies". The questionnaire records the avoidance of experiences and the associated passivity, on the one hand, and the acceptance of experiences and the associated ability to act, on the other (cf. attached).

Bond, F.W., Hayes, S.C., Baer, R.A., Carpenter, K.M., Guenole, N., Orcutt, H.K., Waltz, T., Zettl, R.D. (2011). Preliminary Psychometric Properties of the Acceptance and Action Questionnaire?II: A Revised Measure of Psychological Inflection and Experiential Avoidance. Behaviour Therapy, Volume 42, Issue 4, 676-688.

4. Recording the resilience factors (psychological resistance) is important for the comparison of the group of healthy women with experiences of interpersonal violence before reaching the age of 18 and the treatment group. The following instruments will be used: the Resilience Scale (Schuhmacher et al., 2004), which records resilience on the two scales of "Acceptance of Self and Life" and "Personal Competence". The scale for "Acceptance of Self and Life" focuses on characteristics such as adaptability, tolerance, a flexible view of oneself, and one's own way of life. "Personal competence" encompasses characteristics such as self-confidence, independence, control, agility, and endurance. In addition, the construct of post-traumatic maturation is recorded using the questionnaire "Post-traumatic Personal Maturation" (Maercker et al., 2001). The questionnaire includes five sub-scales (new opportunities, relationships with others, personal strengths, appreciation of life, and religious changes) and is called "a fulfilled life" as part of the study to prevent the title of the questionnaire from influencing how it is completed.

Schumacher, J., Leppert, K., Gunzelmann, T., Strauß, B., & Brähler, E. (2005). The resilience scale – a questionnaire to record psychological resilience as a personal characteristic. *Z Klin Psychol Psychiatr Psychother*, *53*, 16-39.

5. Initial diagnosis of the first subjects also showed that a considerable amount of time was required to complete and conduct the questionnaires and interviews as originally planned. For this reason, the number of assessment points was reduced or the instruments were shortened in the case of some interviews and questionnaires. The following changes have been made:

a. The “Modified Adverse Childhood Experience Scale (MACE)” specified in the test plan for T0 is to be carried out at T3, as this assessment point is less extensive.

b. The IPDE interview will now only be conducted at the beginning of treatment, and not at the end of treatment.

c. The ZAN interview will be carried out in the middle of treatment, at T3, in addition to at T0 and T5.

d. The SBDI interview has been shortened significantly, and now only takes 10 minutes. It is carried out at each assessment point to record any self-harm and suicidal behavior throughout the treatment period.

e. The life events checklist forms part of the CAPS interview specified in the Study Protocol.

f. The Health Economics Interview will be carried out at T1, close to the time when randomization is carried out, instead of at T0.

g. The Dissociative Symptoms Questionnaire is only recorded at the beginning of treatment (previously it was recorded at each assessment point from T1 onwards).

h. The BSI is a short form of the SCL-90-R. It is recorded at the beginning, middle and end of therapy (see also Annex; SCL-90-R was provided for each assessment point).

i. Sexuality was indicated in summarised form in the Study Protocol. The following questionnaires are used to record sexuality: .
“Multi-dimensional Sexuality Questionnaire” (Multidimensionaler Fragebogen zur Sexualität; MFS, Brenk-Franz & Strauss, 2011): The MFS includes 61 items to be assessed on a five-level Likert scale (“strongly disagree” to “strongly agree”). It includes the sub-scales of “self sexual evaluation”, “mental engagement with sexuality”, “internal sexual control” (in terms of self-efficacy with regard to sexuality in general), “sexual awareness”, “sexual motivation”, “sexual anxiety” “sexual self-confidence”, “sexual depression”, “external sexual control”, “perception of public reactions in relation to own sexuality”, “fear of sexual relations” and “sexual satisfaction”. It takes approximately 5 minutes to answer the MFS. The “Sexuality and Partnership Resources Questionnaire” (Ressourcen in Sexualität und Partnerschaft; RSP; Klingler & Loewit, 1996) includes 25 items to be assessed on a five-level Likert scale (from 1 = “very frequently excited by this” to 5 = “very rarely”). The RSP refers to the last 4 weeks and includes the sub-scales: “body feeling”, “tenderness”, “lust”, “love” and “communication”. It takes about 3 minutes in total to answer the questionnaire.

The “Questionnaire on sexual experiences and behavior - Version for Women” (Fragebogen zum sexuellen Erleben und Verhalten- Version für Frauen; FSEV-F; Ahlers et al., 2004) has been adapted for the RELEASE study by removing or adding to individual questions from the sub-scales. The questionnaire to be used includes 25 items with different response formats that query subjects in relation to the frequency of sexual behaviours and sexual dysfunction. The frame of reference is the past year. It takes approximately 5 minutes to answer the questionnaire.

The “Questionnaire relating to the feeling of beeing contaminated” (Fragebogen zur Erfassung des Gefühls der Beschmutztheit) is a self-constructed questionnaire that measures the intensity, volatility, uncontrollability, and stress

due to feelings of being contaminated over the past 3 months, on an 11-step scale.

Ahlers, C.J., Schaefer, G.A. & Beier, K.M (2004). Survey tools in clinical sex research. Sexuologie, 11 (3/4), 79-97.
Brenk-Franz, K. & Strauß, B. (2011). The Multi-dimensional Sexuality Questionnaire (MFS). Zeitschrift für Sexualforschung, 24, 256-271.
Klingler, O.J. & Loewit, K.K. (1996). Sexuality and Partnership Resources Questionnaire (RSP) – Conception and initial findings relating to validity. Zeitschrift für Differentielle und Diagnostische Psychologie, 17, Volume 4, p. 268-275.

j. The SF-36 is only recorded at the beginning and end of treatment (previously recorded at every assessment point except T1).

k. The number of assessment points for recording BSL-23 has been reduced from 6 to 3: at the beginning, middle and end of treatment (previously at every assessment point except T0).

l. DSS-7 and PCL are no longer recorded weekly, but rather at every assessment point.

m. CTQ will be collected close to time of randomization for T1 (previously at T0).

n. DTS is collected at the beginning and end of treatment (previously weekly).

o. The generalization of PTSD-associated symptoms to different areas of life (family life, leisure time, professional life) and potential avoidance of these are recorded using a self-constructed questionnaire (8 items), close to time of T1.

Mannheim, 12/02/2016

File reference: 2013-635N-MA

Treatment of psychosocial and neural sequelae in adults with childhood interpersonal violence (RELEASE)

Amendment No. 7

For the aforementioned study, we would like to give notification of the following changes and ask for your review:

1) Booster sessions following completion of psychotherapy

In addition to the maximum of 45 therapy sessions, all subjects in the trial can receive three booster sessions (3 therapy sessions of 50 minutes each) with their therapist. These sessions are to take place within three months of the end of the one-year period defined for the treatment. How these three sessions are spread in time over the three-month period is at the therapists' discretion. Patients who do not take part in these booster sessions will not be considered as having discontinued therapy.

Patients who are newly included in the study will receive this information during the oral and written information and clarification sessions for the overall trial before being included in the trial. The corresponding change in the patient information is highlighted grey.
Patients who have already been included in the trial will be informed by their therapists about the possibility of three additional refresher sessions. These patients will receive a supplementary page for their existing consent forms. Written consent will be obtained during the diagnostic sessions.

Bohus M. Dialectical behavior therapy for posttraumatic stress disorder compared with cognitive processing therapy in complex presentations of posttraumatic stress disorder in women survivors of childhood abuse. JAMA Psychiatry. Published online July 22, 2020. doi:10.1001/jamapsychiatry.2020.2148

Data Sharing Statement

Data

Data available: Yes
Data types: Deidentified participant data
How to access data: Available from the corresponding author upon request.
When available: With publication

Supporting Documents

Document types: None

Additional Information

Who can access the data: Researchers whose proposed use of the data has been approved.
Types of analyses: For any purpose.
Mechanisms of data availability: With a signed data access agreement
Any additional restrictions: -

From: **Dialectical Behavior Therapy for Posttraumatic Stress Disorder (DBT-PTSD) Compared With Cognitive Processing Therapy (CPT) in Complex Presentations of PTSD in Women Survivors of Childhood Abuse: A Randomized Clinical Trial**
JAMA Psychiatry. Published online July 22, 2020. doi:10.1001/jamapsychiatry.2020.2148

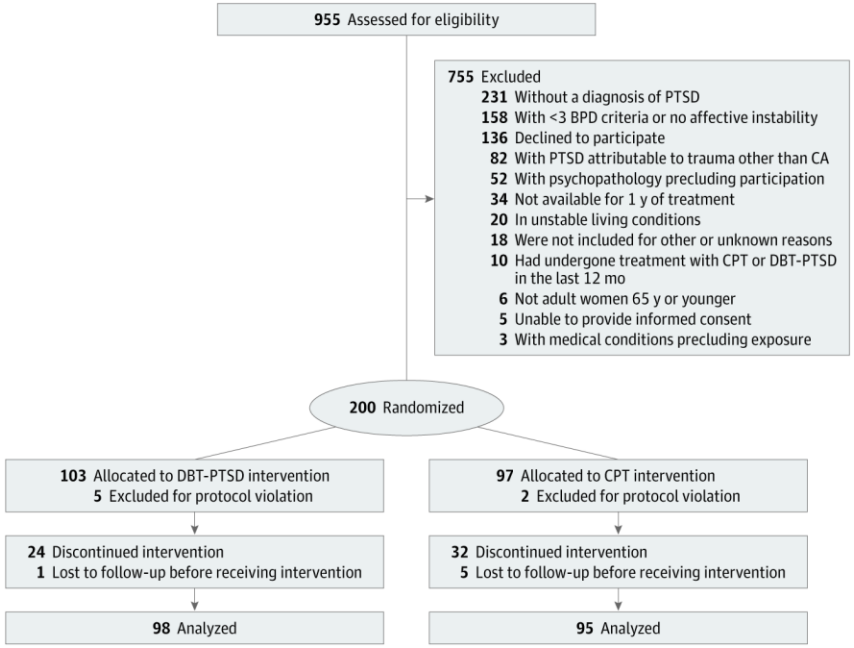


Figure Legend:

Patient FlowBPD indicates borderline personality disorder; CA, childhood abuse; CPT, cognitive processing therapy; DBT-PTSD, dialectical behavior therapy for posttraumatic stress disorder; PTSD, posttraumatic stress disorder.