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Does complex PTSD predict or moderate treatment outcomes of three variants of exposure therapy?

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ABSTRACT

Background: One reason for the inclusion of Complex Posttraumatic Stress Disorder (CPTSD) in the 11th revision of the International Classification of Diseases (ICD-11) was its suspected relevance for treatment indications. We investigated whether CPTSD predicted and moderated treatment outcomes of Prolonged Exposure (PE), intensified PE (iPE) and Skills Training in Affective and Interpersonal Regulation followed by PE (STAIR + PE). We expected that CPTSD would predict worse treatment outcomes across treatments. Secondly, we expected that CPTSD would lead to better treatment effect in STAIR + PE compared to PE and iPE.

Methods: We analyzed 149 patients with childhood-abuse related PTSD from a randomized clinical trial. CPTSD diagnosis and symptom severity were measured with the International Trauma Questionnaire. The main outcome was change in clinician-assessed PTSD symptoms. Assessments took place at baseline, week 4, week 8, week 16 (post-treatment) and at a 6-and 12-month follow-up. Analyses were based on an intention-to-treat sample using mixed effect models.

Results: More than half (54 %) of the patients met criteria for CPTSD at baseline. CPTSD was related to more severe PTSD symptoms and higher comorbidity at baseline. CPTSD neither predicted nor moderated treatment outcome.

Limitations: Inclusion was limited to patients with PTSD related to childhood abuse. Replication is needed in different samples.

Conclusions: CPTSD is associated with more severe PTSD and with higher comorbidity. CPTSD did not predict treatment outcome and did not indicate differential treatment outcome of STAIR + PE compared to PE and iPE.

1. Introduction

In the 11th revision of the International Classification of Diseases (ICD-11), Posttraumatic Stress Disorder (PTSD) was divided into two sibling diagnoses: PTSD and Complex PTSD (CPTSD; World Health Organization, 2018). The ICD-11 now recognizes a 'basic' form of PTSD with core features as well as a complex form of PTSD, that has disturbances in self-organization (DSO) alongside the core features (Maercker et al., 2013). DSO consists of emotion regulation difficulties, interpersonal problems and negative self-concept (World Health Organization, 2018). There is an ongoing debate on whether CPTSD pertains to a distinct group of patients (e.g., Brewin et al., 2017) or rather reflects more severe PTSD (e.g., Resick et al., 2012; Wolf et al., 2015). In the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders

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(DSM-5) several CPTSD symptoms were added to the diagnostic criteria of PTSD, but a separate diagnosis of CPTSD was not included (Friedman, 2013).

Several terms have been used to describe the clinical picture of CPTSD, including 'disorders of extreme stress not otherwise specified' (DESNOS), 'posttraumatic personality disorder' and 'enduring personality change after catastrophic experience' (Classen, Pain, Field, & Woods, 2006; Wilson, Friedman, & Lindy, 2001; World Health Organization, 1992; Yehuda, 2002). All terms aim to describe patients who have been victim of severe, repeated and/or early traumatization (Brewin et al., 2017; Herman, 1992; World Health Organization, 2018; Yehuda, 2002). The experience of repeated, interpersonal trauma (particularly during childhood) interferes with emotional and cognitive development and may affect self-organization skills (Cloitre et al., 2009; Dvir, Ford, Hill, & Frazier, 2014; Lonergan, 2014).

An important reason to distinguish CPTSD as a separate diagnosis would be the relevance for treatment indications (Berliner et al., 2019; Brewin, 2019). For PTSD, trauma-focused treatments such as Prolonged Exposure (PE) are well established first-line interventions (Cusack et al., 2016; Watkins, Sprang, & Rothbaum, 2018). However, it has been suggested that trauma-focused treatments may be less effective in patients with CPTSD (Berliner et al., 2019; Karatzias & Cloitre, 2019) because DSO symptoms may interfere with tolerating the distress of trauma-focused treatment (Cloitre, Koenen, Cohen, & Han, 2002). Patients with CPTSD may need a multi-modular treatment that targets both DSO and core PTSD symptoms (Cloitre, Karatzias, & Ford, 2020; Karatzias & Cloitre, 2019). Skills Training in Affective and Interpersonal Regulation followed by PE (STAIR + PE) is a multi-modular treatment for CPTSD (Cloitre et al., 2002, 2010). Symptoms related to DSO, such as emotion regulation and interpersonal dysfunction are addressed in the first phase (STAIR), followed by PE. Others, however, argue that patients with CPTSD respond well to trauma-focused treatment (De Jongh et al., 2016; Landy, Wagner, Brown-Bowers, & Monson, 2015; Resick et al., 2012). The empirical evidence on whether a CPTSD diagnosis predicts and/or moderates treatment outcome is limited. Three meta-analyses investigated the effectiveness of psychotherapy for patients with probable CPTSD based on the presence of DSO(-related) symptoms (Karatzias, Murphy et al., 2019); on the presence of DESNOS or co-morbid personality disorder (Dorrepaal et al., 2014); or the presence of complex interpersonal trauma (Mahoney, Karatzias, & Hutton, 2019). These meta-analyses show that patients with CPTSD symptomatology do benefit from trauma-focused treatment, including group treatment, although their results may be less favorable than patients with 'simple' PTSD. The definitions of CPTSD in these meta-analyses were not identical, which is not surprising given the recency of the inclusion of CPTSD in the ICD-11. Moreover, these meta-analyses did not test the effect of CPTSD as predictor or moderator of treatment outcome.

Considering prediction, three studies tested whether symptom profiles of CPTSD or similar to CPTSD predict worse psychotherapy outcome. The first study found that meeting criteria for DESNOS was associated with less improvement of PTSD symptoms during an inpatient treatment program in patients with war trauma (Ford & Kidd, 1998). The second study found that 'simple' versus 'more complex' PTSD was not related to differences in treatment outcome of EMDR, PE or relaxation therapy (Taylor, Asmundson, & Carleton, 2006). The third study found no difference in benefit for those with CPTSD compared to non-CPTSD in an intensive trauma-focused treatment program (Voorendonk, De Jongh, Rozendaal, & Van Minnen, 2020). Given this limited evidence, we also searched for studies that investigated the predictive effect of the CPTSD dimensions. Interpersonal problems predicted poor treatment outcome in several studies (Ehlers et al., 2013; Sripada et al., 2019), but most of the studies found no evidence that interpersonal problems or emotion regulation difficulties predict treatment outcome (Cahill, Rauch, Hembree, & Foa, 2003; Hoeboer, De Kleine et al., 2020; Rizvi, Vogt, & Resick, 2009; Tarrier, Sommerfield, Pilgrim, & Faragher, 2000; van Minnen, Arntz, & Keijsers, 2002).

Considering moderation, a *moderator* is a baseline variable which interacts with the effect of treatment condition on improvement over time and indicates for whom treatment A is likely to work better than treatment B – and vice versa (Hayes & Rockwood, 2017; Kraemer, 2016). A non-significant *predictor* variable may still be a relevant *moderator* (Kazdin, 2007; Kraemer, 2016). Hypothetically, a CPTSD diagnosis may be differentially related to outcome of treatments that specifically address DSO (i.e., STAIR) but not to treatments that do not (i.e., PE). No studies so far have investigated whether CPTSD moderates treatment outcome, but one study with 104 participants showed that a combination of several CPTSD-related dimensions (i.e., interpersonal problems, anger and regulation of negative mood) resulted in more beneficial outcomes of STAIR + PE compared to support + PE and STAIR + support (Cloitre, Petkova, Su, & Weiss, 2016). Interestingly, when these dimensions were modeled separately they did not moderate outcome.

The aim of the current study was to investigate whether CPTSD predicts and/or moderates treatment outcomes in patients with PTSD related to childhood abuse. We investigated the effect of 1) CPTSD diagnosis (yes versus no), based on the ICD-11 criteria and 2) DSO symptom severity (continuous measure). Firstly, we expected that both CPTSD diagnosis and higher DSO symptom severity predict worse treatment outcome (i.e. across conditions). Secondly, we hypothesized that CPTSD diagnosis and DSO symptom severity moderate treatment outcome. In particular, we expected that CPTSD and more higher DSO symptom severity would be related to better treatment effects in STAIR + PE in comparison to PE and intensive PE (iPE).

2. Method

2.1. Design

This study includes the sample of a randomized clinical trial investigating PTSD treatment for adults with childhood trauma: the IMPACT study (Oprel et al., 2018). The trial was approved by the Medical Ethics Committee of Leiden University Medical Center (NL57984.058.16). More detailed information about the design and main results of the study including baseline characteristics can be found elsewhere (Oprel et al., 2021)

2.2. Participants and procedure

The sample of the IMPACT study consists of adults with: at least moderately severe PTSD; related to multiple traumata including childhood sexual and/or physical abuse; committed by a primary caretaker or an authority figure. The sample included 149 patients randomized to PE, iPE or STAIR + PE. PTSD was diagnosed using the Clinician Administered PTSD Scale (CAPS-5). Patients had to be fluent in Dutch. Exclusion criteria included ongoing litigation concerning disability compensation or admission or stay in The Netherlands; pregnancy; severe non-suicidal self-injury or severe suicidal behavior in the past three months; severe disorder in the use of alcohol or drugs in past three months; cognitive impairment (IQ < 70); current engagement in psychological treatment and changes in psychotropic medication in past two months. No additional in- or exclusion criteria were used for the current study. The trial is registered at the clinical trials registry, number ISRCTN03194113.

2.3. Assessment schedule

Demographic information, and PTSD diagnosis and severity were assessed during the baseline assessment (T0). PTSD symptoms were assessed at baseline (T0), after 4 weeks (T1) after 8 weeks (T2), post-treatment after 16 weeks (T3) and at a 6-month (T4) and 12-month (T5) follow-up. The effect of CPTSD and DSO severity on PTSD symptom change during the treatment phase (from T0 to T3) is the main

outcome of this study. The effect of CPTSD and DSO severity on the follow-up phase (T3-T5) is the secondary outcome. Note that any finding during this phase may be influenced by other sources than treatment condition since patients could seek further treatment after T4.

2.4. Treatment

PE was delivered in 16 weekly face-to-face sessions of 90 min. PE involved psychoeducation about PTSD, imaginal exposure and exposure in vivo (Foa, Hembree, & Rothbaum, 2007). iPE was delivered three times a week for four weeks in face-to-face sessions of 90 min, followed by two sessions after one and two months (14 sessions total). Except for the time format, iPE was similar to the PE condition. STAIR + PE was delivered in 16 weekly face-to-face sessions. The first eight 60-minutes sessions consisted of STAIR and included psychoeducation and emotion regulation and interpersonal skills training. The subsequent 90-minutes sessions (i.e. session 9-16) consisted of PE. Treatment dropout was defined as stopping treatment prematurely after randomization. Overall dropout of the three treatments was 24 %. In PE, 29 % of the patients dropped out, in iPE 27 % and in STAIR + PE 18 %.

2.5. Measures

The main outcome was change in clinician-rated PTSD symptom severity, measured with the CAPS-5 (Boeschoten et al., 2018). The CAPS-5 is a clinical interview that assesses DSM-5 PTSD diagnostic criteria and symptom severity with 20 items. Each item is scored on a five-point Likert scale (0–4). We used the total severity score which ranges between 0−80. The internal consistency of CAPS-5 total score was Cronbach's $\alpha = .88$ in a previous study studies (Weathers et al., 2018) and $\alpha = .75$ in the current study.

CPTSD diagnosis and symptom severity were determined using the updated version of the International Trauma Questionnaire ITQ (Cloitre et al., 2018). The ITQ is a self-report questionnaire that assesses PTSD symptoms with six items and Disturbance in Self Organization (DSO) with six items, using five-point Likert scales (0–4). Moreover, six items assess functional impairment associated with PTSD and DSO symptoms. PTSD symptoms consist of three two-item subscales: re-experiencing, avoidance and sense of threat. DSO symptoms also consist of three two-item subscales: affective dysregulation, negative self-concept and disturbances in relationships. For both subscales, an item score ≥ 2 is considered endorsement of a symptom. Diagnosis of CPTSD requires: 1) ≥ 1 symptom of each PTSD subscale; 2) ≥ 1 symptom of each DSO subscale; 3) endorsement of one item indicating functional impairment associated with PTSD and DSO symptoms. DSO severity can be assessed by summing the six DSO items with scores ranging from 0 to 24 (higher scores indicate greater severity). Internal consistency of this total score was high in the current sample (Cronbach's $\alpha = .81$).

2.6. Statistical analyses

We pre-registered a statistical analysis plan at the Center For Open Science (Hoeboer et al., 2020). We performed the analyses with R version 3.6.1. (R Core Team, 2018). The analyses were conducted on an intention-to-treat basis. Alpha was set at .05 for all analyses (two-tailed). We evaluated differences between demographic characteristics of patients with and without CPTSD diagnosis at baseline using t-tests and χ^2-tests of independence. We used package lme4 for modelling the linear mixed effect models (Bates, Machler, Bolker, & Walker, 2015). The models were estimated with random intercepts for persons and random slope effect of time to account for the dependency in the data within persons (Hox, 2002; Kato et al., 2005). We modelled the linear effect of time with a piecewise growth model with two separate slopes: one for the treatment phase from baseline to post-treatment (T0-T3; main outcome) and one for the follow-up phase from post-treatment to 1-year follow-up (T3-T5; secondary outcome). We used a separate slope for the follow-up period to account for the differences in the effect of time during the treatment phase compared to the follow-up phase.

For the first hypothesis, we performed two independent linear mixed effect models. In the first model, CAPS-5 was the dependent variable and CPTSD diagnosis, the two time-slopes, and the interaction effects between the time-slopes and CPTSD diagnosis were included as independent variables. In the second model, CAPS-5 was the dependent variable and DSO, the two time-slopes, and the interaction effects between the time-slopes and DSO were included as independent variables. For ease of interpretation, we mean-centered total symptom severity of DSO.

For the second hypothesis, we used the same models but added the following variables to the first model: condition (dummy coded), the interaction between the two time-slopes and condition, the interaction between CPTSD diagnosis and condition, and the three-way interactions between the two time slopes, condition and CPTSD diagnosis as independent variables. To the second model we added: condition, the interaction between the two time-slopes and condition, the interaction between DSO and condition, and the three-way interactions between the two time slopes, condition and DSO as independent variables. We used STAIR + PE as dummy-coded comparator in all moderation analyses, since we hypothesized that CPTSD would result in more beneficial effects of STAIR + PE compared to PE and iPE.

The assumptions of all analyses were met. We used semi-parametric bootstrapping to derive the estimated treatment trajectory with prediction intervals for patients with and without CPTSD based on the linear mixed effect models to account for the uncertainty in the variance of the parameters due to the random effects using R package Bootmer (Bates et al., 2015). We evaluated effect sizes of the linear mixed effect models with modelled data following the method of Feingold and t-to-d conversion using function lme-dscore from R package EMAtools (Feingold, 2013; Kleiman, 2017).

2.7. Sensitivity analyses

To assess the robustness of findings, we planned to conduct four sensitivity analyses. Firstly, to check whether results were influenced by differences in PTSD conceptualizations between the DSM-5 and ICD-11, we performed a sensitivity analysis with PTSD symptoms measured with the ITQ, following ICD-11 criteria, as outcome variable. Hence, the four models from the main analyses were repeated with ITQ PTSD subscale score (baseline to 1-year follow-up) as dependent variable. Secondly, to check whether results are influenced by patients who met DSM-5 PTSD criteria but who did not meet ICD-11 PTSD criteria, we performed a sensitivity analysis with a subset of patients who met ICD-11 PTSD criteria according to the ITQ. Thirdly, to check whether results were influenced by PTSD symptom severity, we performed a sensitivity analysis with baseline ITQ PTSD symptom severity as covariate in the four models from the main analyses. Fourthly, we checked whether results were influenced by baseline differences between patients with and without CPTSD by performing a sensitivity analysis with significant differences in baseline clinical/demographic characteristics between CPTSD and PTSD as covariates in the four models from the main analyses.

3. Results

3.1. Baseline differences

Table 1 lists the baseline characteristics for the total sample ($N = 149$) and the comparison of baseline characteristics for patients with ($n = 80$) and without ($n = 69$) CPTSD. Patients with CPTSD reported more childhood physical abuse, more frequently met criteria for current depression, psychotic disorder and personality disorder and suffered from more comorbid axis-1 diagnoses (in general) than patients without CPTSD.

Table 1
Baseline characteristics for the total sample and comparison of baseline characteristics for patients with and without CPTSD.

	Total (N = 149)	PTSD (n = 69)	CPTSD (n = 80)	t-test versus $\chi 2$
Demographic characteristics, Mean (SD)				
Age, y	36.86 (11.75)	36.07 (12.88)	37.55 (10.72)	$t(147) = .77$, $p = .45$
Duration of PTSD, y	15.06 (12.49)	14.19 (12.01)	15.83 (12.93)	$t(143) = .79$, $p = .43$
Mean number Axis-1 MINI diagnoses, excluding PTSD	3.12 (1.91)	2.16 (1.47)	3.95 (1.86)	$t(147) = 6.46$, $p < .001$
Demographic characteristics, No. (%)				
Gender (female)	114 (76.5)	54 (78.3)	60 (75.0)	$\chi^2(1) = .21$, $p = .64$
Marital status (married/cohabitating)	56 (37.6)	25 (36.2)	31 (38.8)	$\chi^2(1) = .10$, $p = .75$
Education (high)[1]	30 (20.1)	13 (18.8)	17 (21.3)	$\chi^2(1) = .13$, $p = .72$
Cultural background (non-Western)[2]	65 (43.3)	27 (39.1)	38 (47.5)	$\chi^2(1) = 1.06$, $p = .30$
Trauma category (single or multiple) DSM-5A criterion CAPS-5				
Childhood sexual abuse	108 (72.5)	47 (68.1)	61 (76.3)	$\chi^2(1) = 1.23$, $p = .27$
Childhood physical abuse	93 (62.4)	36 (52.2)	57 (71.3)	$\chi^2(1) = 5.75$, $p = .02$
Sexual abuse in adulthood	29 (19.5)	10 (14.5)	19 (23.8)	$\chi^2(1) = 2.03$, $p = .16$
Physical abuse in adulthood	42 (28.2)	16 (23.2)	26 (32.5)	$\chi^2(1) = 1.59$, $p = .21$
Axis-1 MINI diagnosis				
Current depression	85 (57.1)	30 (43.4)	55 (68.8)	$\chi^2(1) = 9.66$, $p = .002$
Severe suicidality past month	64 (43.0)	24 (34.8)	40 (50.0)	$\chi^2(1) = 3.50$, $p = .06$
Current bipolar disorder (type1/2)	10 (6.7)	6 (8.7)	4 (5.0)	NA
Disorder alcohol/drug use past year	34 (22.8)	17 (24.6)	17 (21.3)	$\chi^2(1) = .24$, $p = .62$
Current psychotic disorder	19 (12.8)	4 (5.8)	15 (18.8)	$\chi^2(1) = 5.59$, $p = .02$
Any personality disorder diagnosis	90 (60.4)	33 (47.8)	57 (71.3)	$\chi^2(1) = 8.50$, $p = .004$

PTSD = Posttraumatic stress disorder, CPTSD = Complex PTSD, SD = standard deviation, y = year, N = sample size, No. = number, NA = not applicable, MINI = Mini-International Neuropsychiatric Interview, DSM-5 = Diagnostic and statistical manual of mental disorders version five, CAPS-5 = Clinician-administered PTSD scale for DSM-5.
[1] High education = higher vocational education or university.
[2] Non-Western cultural background = at least one parent was not born in a Western country.

3.2. Dropout

Patients with CPTSD did not show a higher dropout rate (24 %) than patients without CPTSD (26 %): $\chi^2(1) = .11$, $p = .74$. More severe DSO symptoms at baseline were not related to higher dropout rates: $b = -.008$, *Wald* $\chi^2(1) = .06$, $p = .82$.

3.3. Predictor effects

CPTSD was related to more severe PTSD symptoms at baseline: $b = 8.67$, $t(162) = 5.70$, $p < .001$ $d = .90$. Those who suffered from CPTSD ($M_{estimated} = 44.53$, $SE_{estimated} = 1.04$) had higher CAPS-5 baseline scores than those without CPTSD ($M_{estimated} = 35.87$, $SE_{estimated} = 1.52$). However, we did not find that CPTSD was a significant predictor of outcome during the treatment phase: $b = .38$, $t(132) = .40$, $p = .69$ or follow-up phase: $b = -.05$, $t(172) = -.04$, $p = .97$ (see Fig. 1).

DSO severity was also related to higher CAPS-5 scores at baseline: $b = .81$, $t(162) = 5.99$, $p < .001$, $d = .94$, but it was no significant predictor of outcome during the treatment phase: $b = .02$, $t(133) = .26$, $p = .80$ or follow-up phase: $b = -.01$, $t(169) = -.14$, $p = .89$ (see Fig. 2 for illustration).

3.4. Moderator effects

We did not find that CPTSD diagnosis significantly moderated outcome (STAIR + PE versus PE/iPE) during the treatment phase: $b = -.42$, $t(133) = -.21$, $p = .83$ or follow-up phase: $b = 1.33$, $t(188) = .54$, $p = .59$. (see Fig. 3).

We also did not find that DSO severity was a significant moderator of outcome (STAIR + PE versus PE/iPE) during the treatment phase: $b = -.07$, $t(135) = -.39$, $p = .70$, or follow-up phase: $b = .42$, $t(193) = 1.85$, $p = .07$. (see Fig. 4 for illustration).

3.5. Sensitivity analyses

The results of the main analyses were replicated in the sensitivity analyses. In all sensitivity analyses, both CPTSD and DSO severity were significantly related to more severe PTSD symptoms at baseline, while we did not observe a significant prediction or moderation effect of CPTSD and DSO severity on the outcome during the treatment or follow-up phase.

4. Discussion

The aim of this study was to investigate whether CPTSD predicts or moderates trauma-focused treatment outcome in patients with PTSD

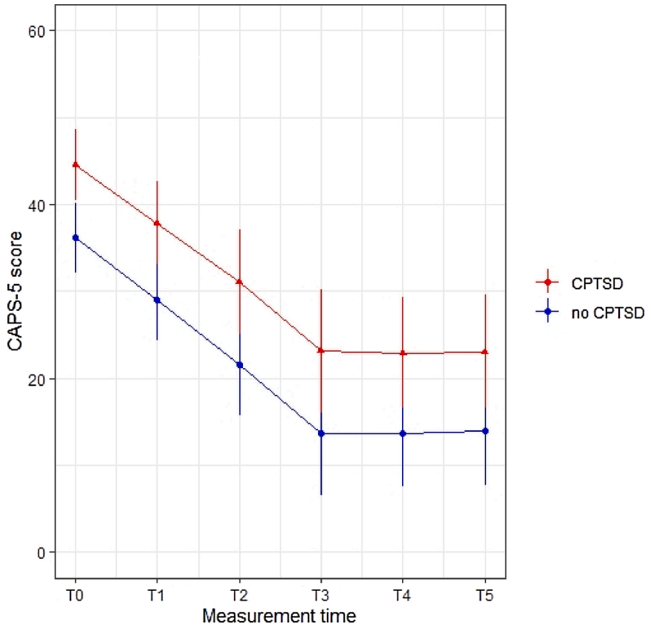

Fig. 1. Estimated treatment trajectory (baseline to 1-year follow-up) of patients with and without CPTSD based on the ITQ.
CPTSD = Complex Posttraumatic stress disorder, ITQ = International Trauma Questionnaire, CAPS-5 = Clinician-Administered PTSD scale for DSM-5, T0 = baseline, T1 = 4 weeks, T2 = 8 weeks, T3 = 16 weeks, T4 = 6 month follow-up, T5 = 12 month follow-up.

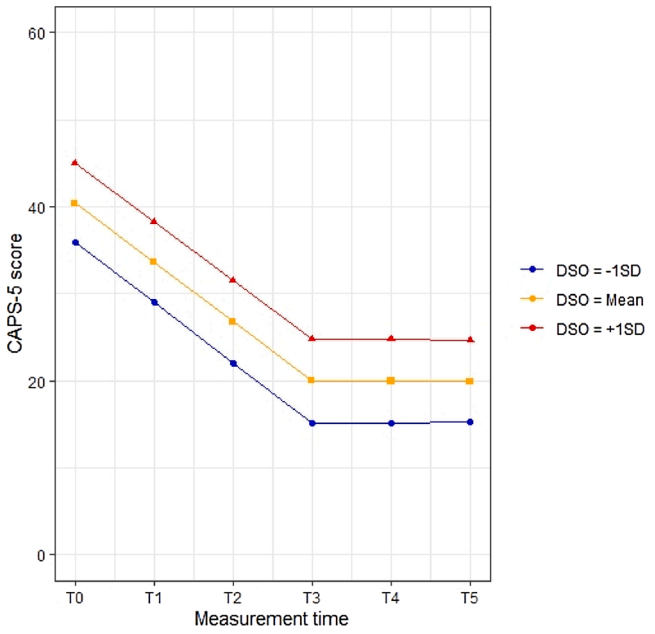

Fig. 2. Illustration of treatment trajectory (baseline to 1-year follow-up) of patients with average DSO, DSO one standard deviation below average and DSO one standard deviation above average measured with the ITQ. Estimations were based on probing of the interaction effect between DSO and Measurement time. DSO = Disturbances in self-organization, SD = standard deviation, ITQ = International Trauma Questionnaire, CAPS-5 = Clinician Administered PTSD scale for DSM-5, T0 = baseline, T1 = 4 weeks, T2 = 8 weeks, T3 = 16 weeks, T4 = 6 month follow-up, T5 = 12 month follow-up.

related to child abuse. We found that patients with CPTSD had more severe PTSD symptoms and a higher rate of comorbid diagnoses at baseline. However, patients with CPTSD did not benefit significantly less from three variants of exposure therapy than patients without CPTSD. In particular, patients with CPTSD did not benefit significantly more from STAIR + PE than from PE or iPE than patients with non-complex PTSD. The same pattern of findings was observed with the severity of disturbances in self-organization (DSO) as predictor and moderator.

Before treatment, patients with CPTSD reported more severe PTSD symptoms, more childhood physical abuse, met more axis-1 diagnoses and more frequently met criteria for a personality disorder than patients with non-complex PTSD. This finding is in line with previous studies, that found that CPTSD is characterized by more comorbid diagnoses (Cloitre et al., 2019; Elklit, Hyland, & Shevlin, 2014; Karatzias, Hyland et al., 2019; Powers et al., 2017), by higher PTSD symptom severity (Powers et al., 2017) and by more severe impairment (Bondjers et al., 2019; Brewin et al., 2017; Cloitre et al., 2019; Karatzias & Cloitre, 2019). Consequently, we conclude that CPTSD is a more severe form of PTSD (or PTSD with more comorbidities).

Our hypothesis that CPTSD and more severe DSO would predict worse outcome of (variants of) exposure therapy was not supported. These results were replicated in the sensitivity analyses, suggesting that the results were robust and not influenced by differences in PTSD conceptualizations between the DSM-5 and ICD-11. Given that patients with CPTSD suffered from more severe PTSD symptoms at baseline and showed similar decrease in PTSD symptoms compared to patients without CPTSD, our results could imply that patients with CPTSD are in need of more treatment sessions to reach the same endstate functioning. This is specifically relevant for those who experienced large symptom reductions during treatment, but still suffered from elivated symptoms post-treatment, as initial symptom change is highly predictive of symptom change during treatment continuation (Sripada, Ready, Ganoczy, Astin, & Rauch, 2020). The finding that CPTSD is not a relevant predictor of treatment outcome is consistent with another recent study which found no difference in treatment response between patients with CPTSD and non-complex PTSD (Voorendonk et al., 2020). Future studies are needed to replicate these findings across study populations, treatment settings and different types of treatments.

Our hypothesis that CPTSD diagnosis and DSO severity score moderate treatment outcome was not supported. These results were replicated in sensitivity analyses. Our expectation that patients with CPTSD would benefit more from STAIR + PE than from PE/iPE was based on the

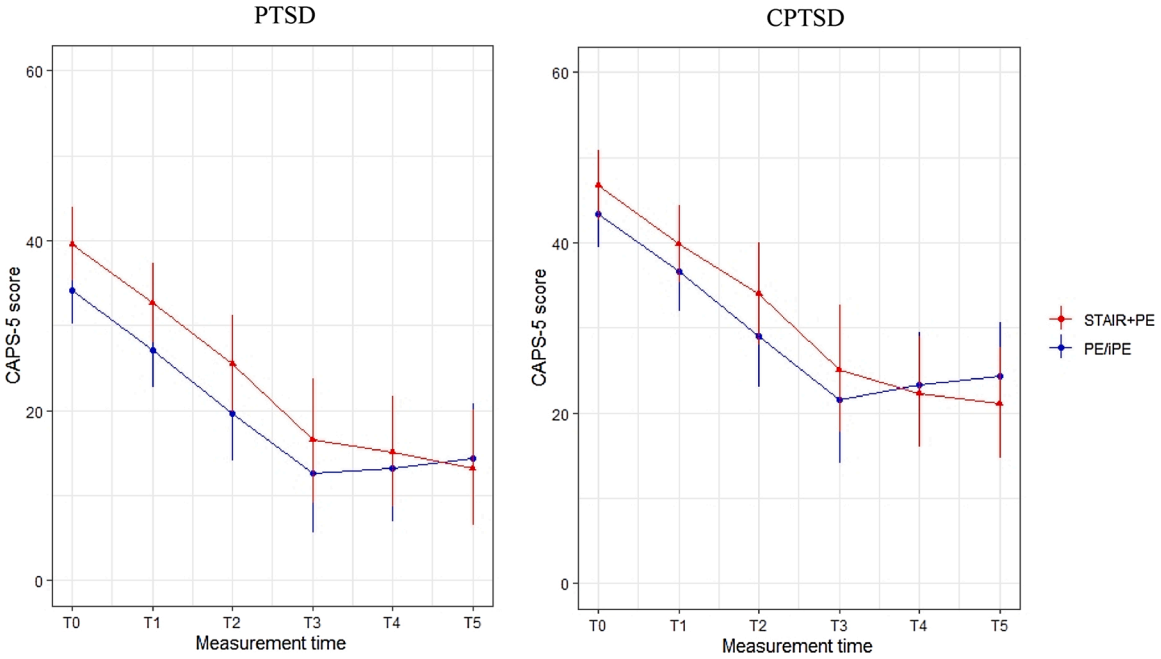

Fig. 3. Estimated treatment trajectory of STAIR + PE and PE/iPE for patients with PTSD (left panel) versus CPTSD (right panel) based on the ITQ.
STAIR + PE = Skills Training in Affective and Interpersonal Regulation followed by Prolonged Exposure, PE = Prolonged Exposure, iPE = intensified Prolonged Exposure, PTSD = Posttraumatic stress disorder, CPTSD = Complex PTSD, ITQ = International Trauma Questionnaire, CAPS-5 = Clinician Administered PTSD scale for DSM-5, T0 = baseline, T1 = 4 weeks, T2 = 8 weeks, T3 = 16 weeks, T4 = 6 month follow-up, T5 = 12 month follow-up.

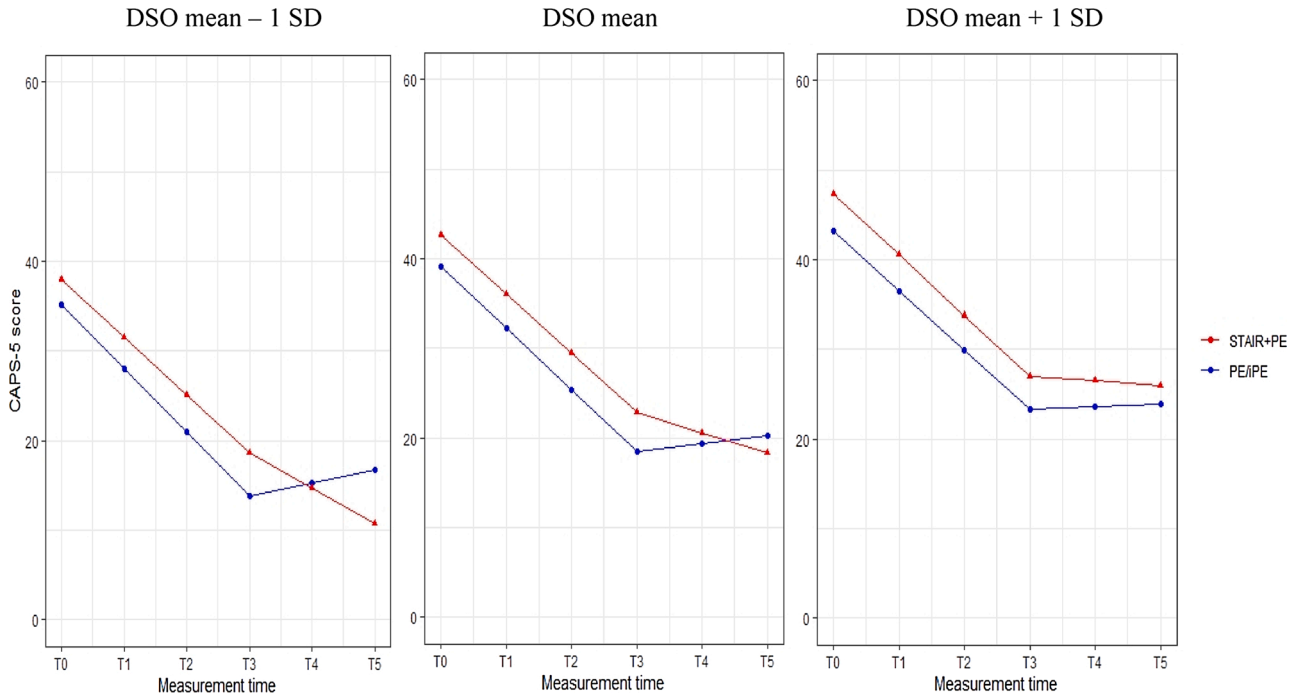

Fig. 4. Illustration of treatment trajectory (baseline to 1-year follow-up) of patients with average DSO (middle panel), DSO one standard deviation below average (left panel) and DSO one standard deviation above average (right panel) measured with the ITQ. Estimations were based on probing of the interaction effect between DSO, condition and measurement time.
SD = standard deviation, STAIR + PE = Skills Training in Affective and Interpersonal Regulation followed by Prolonged Exposure, PE = Prolonged Exposure, iPE = intensified Prolonged Exposure, DSO = Disturbances in self-organization, ITQ = International Trauma Questionnaire, CAPS-5 = Clinician-Administered PTSD scale for DSM-5, T0 = baseline, T1 = 4 weeks, T2 = 8 weeks, T3 = 16 weeks, T4 = 6 month follow-up, T5 = 12 month follow-up.

fact that STAIR targets DSO symptoms directly during the first phase of treatment. Left untreated, DSO symptoms may negatively influence the effectiveness of PE, but our results indicate that this is not the case. As reported elsewhere, DSO dimensions improved over the course of treatment in all three conditions (Oprel et al., 2021). Other recent studies have also shown that PE reduces DSO symptoms (Jerud, Zoellner, Pruitt, & Feeny, 2014; Jerud, Pruitt, Zoellner, & Feeny, 2016; van Toorenburg et al., 2020). However, a combination of CPTSD-related constructs was related to differential treatment effects in a previous study; women with a high symptom load relative to emotion regulation strength benefitted the least from support plus exposure (eight sessions exposure) and benefitted most from STAIR plus exposure (Cloitre et al., 2016). Granted that PE sessions may positively affect DSO symptoms, these differential findings might be explained by the higher dosage of PE in the current study (14–16 sessions) in comparison to this work (8 sessions). In the absence of a prediction or moderation effect, the construct of CPTSD does not seem to refer to a distinct disorder.

4.1. Limitations and strengths

The present study has several limitations. Firstly, patients were included based on DSM-5 PTSD criteria, not on ICD-11. Applying ICD-11 criteria would have resulted in a slightly different sample (Hansen et al., 2017; Hyland et al., 2016; O'Donnell et al., 2014). We do not expect this difference to be clinically relevant. Secondly, all patients had a current diagnosis of PTSD based on the experience of childhood abuse. A little more than half of our population scored positive on CPTSD, which is high compared to other chronically traumatized samples (Barbieri et al., 2019; Grossman et al., 2019; Vallieres et al., 2018). CPTSD is also common in veterans (Folke, Nielsen, Andersen, Karatzias, & Karstoft, 2019; Letica-Crepulja et al., 2020; Murphy et al., 2020), genocide survivors (Grossman et al., 2019) and refugees (Barbieri et al., 2019; Vallieres et al., 2018) and their response to treatment may be different. Thirdly, we used the self-report version of the ITQ, which may differ from a clinician-administered version which is currently being developed (Cloitre, Roberts, Bisson, & Brewin, 2017). Clinician-administered questionnaires are the golden standard for diagnosing PTSD (Boeschoten et al., 2018), but first results indicate that the clinician-administered version of the ITQ leads to similar results as the self-report version (Bondjers et al., 2019).

The strengths of the current study include the large sample size and multiple measurements within persons, the long-term follow-up measurements and the assessment of both CPTSD and DSO symptom severity. Furthermore, the sensitivity analyses increase the robustness of findings.

5. Conclusions

Since this is the first study to assess the prediction and moderation effect of CPTSD, future studies are needed to replicate our findings across samples and treatments. If replicated, these findings have important implications for clinical practice. Patients with CPTSD benefit from exposure therapies as well as patients with (non-complex) PTSD, implying that these treatments are indicated in patients with CPTSD related to childhood abuse. In other words, trauma-focused therapies should not be withheld from this patient population. Patients with CPTSD may benefit more from the implementation of existing treatments than from attempts to develop new treatments.

Author contribution statement

DACO and CMH coordinated the recruitment of participants and data collection of the dataset used for this study. CMH wrote the first draft of the manuscript and did the statistical analyses. RAdK, MS, DACO, AvM and WvdD contributed to the writing of the manuscript. All authors read and approved the final version.

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Declaration of Competing Interest

The authors report no declarations of interest.

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