Choosing the right track: improving PTSD treatment outcomes for patients with childhood abuse-related posttraumatic stress disorder

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Chapter 4

Impact of dissociation on the effectiveness of psychotherapy for post-traumatic stress disorder: a meta-analysis

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Abstract

Background: Many patients with Post-Traumatic Stress Disorder (PTSD) suffer from dissociative symptoms. The question of whether these dissociative symptoms negatively influence the effectiveness of psychotherapy for PTSD is unresolved.

Aim: To determine the influence of dissociative symptoms on psychotherapy outcome in PTSD.

Method: We conducted a systematic search in Cochrane, Embase, PILOTS, PsycINFO, Pubmed and Web of Science for relevant clinical trials. A random-effects meta-analysis examined the impact of dissociation on psychotherapy outcome in PTSD.

Results: Twenty-one trials (of which 9 randomized controlled trials) with 1,714 patients were included. Pre-treatment dissociation was not related to treatment effectiveness in patients with PTSD (Pearson's correlation coefficient = .04, 95% confidence interval: -.04; .13). Between-study heterogeneity was high but was not explained by moderators such as trauma focus of the psychotherapy or risk of bias score. There was no indication for publication bias.

Conclusions: We found no evidence that dissociation moderates the effectiveness of psychotherapy for PTSD. The quality of some of the included studies was relatively low, emphasizing the need for high-quality clinical trials in patients with PTSD. The results suggest that pre-treatment dissociation does not determine psychotherapy outcome in PTSD.

Pre-registered at Prospero: CRD42018086575.

Introduction

In the DSM-5, a dissociative subtype was added to the classification criteria of Post-Traumatic Stress Disorder (PTSD). This subtype describes patients who meet diagnostic criteria for PTSD, and additionally have persistent or recurrent symptoms of depersonalization (i.e., experience of unreality or detachment from one's thoughts, feelings, sensations, body or actions, e.g. unreal or absent self) and derealisation (i.e., experience of unreality or detachment from one's surroundings, e.g. dreamlike or foggy; APA, 2013). The addition of a dissociative subtype to the DSM-5 was based on multiple sources of evidence, pertaining to factor analyses, brain activation patterns and response to treatment (Friedman, 2013). Approximately 14 percent of the patients with PTSD meet criteria for the dissociative subtype (Stein et al., 2013). While this subtype was only recently added to the DSM-5, research on dissociative symptoms in the context of trauma dates back to the 19th century (Janet, 1894). Several studies have shown that PTSD is associated with high levels dissociation, both compared to nonclinical samples and patients with other psychiatric disorders (Kratzer et al., 2018; Lyssenko et al., 2018; Özdemir, Celik, & Oznur, 2015; Putnam et al., 1996). Additionally, several studies have shown that dissociation is strongly related to the other PTSD symptoms and that these clusters wax and wane together, also in response to treatments (Harned, Korslund, Foa, & Linehan, 2012; Lynch, Forman, Mendelsohn, & Herman, 2008; Rothbaum, Astin, & Marsteller, 2005; Taylor et al., 2003; Zoet, Wagenmans, van Minnen, & de Jongh, 2018). A review of brain-imaging studies has shown that dissociative symptoms/states are related to activation of brain areas related to neurological overmodulation of affect (Lanius et al., 2010). This overmodulation of affect could, amongst others, reduce emotional engagement with the trauma memory, which is considered to be a relevant factor in understanding the effectiveness of current psychotherapies for PTSD (Schnyder et al., 2015). This lack of engagement may be specifically relevant for exposure-based psychotherapy as fear activation is thought to be a crucial mechanism underlying the treatment effect (Cooper et al., 2017a; Ebner-Priemer et al., 2009; Foa & McLean, 2016; Jaycox, Foa, & Morral, 1998; Lanius et al., 2010; Pittig, Treanor, LeBeau, & Craske, 2018).

Currently, there is no consensus about 1) whether patients with PTSD and who dissociate benefit as much from psychotherapy as PTSD-patients who do not dissociate and 2) whether some forms of psychotherapy are particularly ineffective for patients with PTSD and dissociation. Some authors have suggested that treatment programs need to be tailored for PTSD-patients with dissociative symptoms, because, due to their limited emotion regulation capacities, trauma-focused treatments might even lead to an increase in PTSD symptoms, overall distress and functional impairment (Lanius et al., 2010). Others have argued that there is no evidence for an impeding effect of dissociation on the effectiveness of psychotherapy for PTSD (van Minnen et al., 2012). The aim of this study is to provide more clarity to this ongoing debate by quantifying the moderating effect of dissociation on the effectiveness of psychotherapy for PTSD in a meta-analysis.

Method

This project was pre-registered at Prospero (https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=86575).

Search strategies

We conducted systematic searches in the following data-bases up to the 28th of August 2018: Cochrane trials register, Embase, PILOTS, PsycINFO, Pubmed and Web of Science. Relevant results during the search from review articles, book chapters and studies were searched for further studies and additionally, key authors and research groups were contacted via email to request any data relevant to the study. Search terms were based on (mesh) terms for PTSD [AND] dissociation [AND] psychotherapy and were adapted to every specific search engine to ensure inclusion of all relevant studies. The search includes the following terms for: (A) PTSD: Posttrauma* Stress Disorde*, Post-Trauma* Stress Disorde*, Post Trauma* Stress Disorde*, DESNOS, CA-PTSD, C-PTSD, PTSD (B) dissociation: Dissocia* Depersonali* Derealization* Derealisation* Fugue* Psychogenic amnesia and (C) psychological treatment: Psychotherap*, Therap*, Posttraumatic Growth, Interven*, Treat*, Exposure, EMDR, CBT, STAIR, Recover*. We manually searched for studies in prior meta-analyses and reviews to ensure that no studies were missed in the systematic search. We de-duplicated data of the search following the protocol of Bramer and colleagues (2016).

Inclusion criteria

The criteria for individual papers for inclusion were: (1) inclusion of patients of 18 years of age and older; (2) assessment of PTSD according to the DSM-5, DSM-IV, DSM-III-R or DSM-III criteria; (3) evaluation of psychotherapy with PTSD symptom severity as main outcome; (4) inclusion of validated self-report measures or structured clinical interviews to assess both PTSD symptom severity and dissociation severity; (5) assessment of PTSD symptom severity at pre and post-treatment; (6) assessment of pre-treatment dissociation severity; (7) inclusion of at least 10 participants per treatment condition which is analysed; (8) published in a peer-reviewed journal; and (9) written in English, Dutch, German, Italian, Spanish or French.

Data extraction and risk of bias assessment

Eligible studies were screened twice and data were extracted twice by two independent screeners. All discrepancies were resolved through discussion and consensus. Risk of bias of the studies was assessed independently by two of the authors using the Cochrane risk of bias tool, which resulted in a methodological score for each study included (Higgins, Green, & Cochrane Collaboration., 2008). The Cochrane scale assesses sources of bias including selection bias, detection bias and attrition bias. We added two items to this measure about: 1) the type of the PTSD measurement (clinical interview versus self-report); and 2) treatment integrity (whether the original article reported on treatment integrity, yes versus no). Consequently, the adapted Cochrane scale consisted of 8 items (see supplement Table S1). Two raters scored each item, and their scores were summed into a risk of bias score (range

0-16; with higher scores indicating higher risk of bias). The risk of bias score was used as a moderator. High bias scores were not considered an exclusion criterion for further analysis.

Potential moderators

To investigate potential moderators of the effect of dissociation on psychotherapy outcome, we coded several study characteristics: (1) completely trauma-focused treatment (yes versus no); (2) randomized controlled trial (yes versus no); (3) sample size (continuous variable); and (4) risk of bias score (continuous variable). The potential moderators were independently coded by two authors and differences were resolved through discussion and consensus.

We compared treatments that were exclusively trauma-focused versus those that were not. Since dissociation is thought to be due to failing emotion regulation capacities, exposure to traumatic memories would result in emotional overmodulation and consequently impede fear activation and emotional learning. This may prevent the therapeutic effect of exposure, unless emotion regulation or other coping skills are also addressed (Lanius et al., 2010). The treatment was coded as trauma-focused if it comprised only evidence-based trauma-focused treatment strategies as described in the manuscript (i.e. prolonged exposure, cognitive processing therapy or eye movement desensitization and reprocessing). Treatments that also comprised other treatment components (i.e. physical activity or stabilization) or treatments that did not include trauma-focused treatment strategies were coded as not exclusively trauma-focused. If a trial included both types of treatments, we extracted the effect size for the two conditions separately for this moderation analysis (see supplement Figure S3 for details).

Statistical analysis

The R package meta was used for all analyses (Schwarzer, 2010). The effect of dissociation on PTSD treatment was determined using pooled effect sizes of the moderating effect of dissociation measured with the Pearson's correlation coefficient (*r*) between pre-treatment dissociation and change in PTSD symptoms from pre- to post-treatment (post-treatment minus pre-treatment PTSD symptom severity score). A positive correlation would indicate a negative relationship between dissociation and treatment effectiveness, whereas a negative correlation would indicate a positive effect of dissociation on treatment effectiveness. Where needed, we calculated the reported effect size from the data provided into *r* as common metric. In case we were unable to calculate the effect size from the publication, we contacted the researchers for additional data. We contacted 38 researchers of whom 27 responded. Twelve of these researchers did not provide the data for various reasons (e.g. no access to data, no time to get data, not willing to share data). Fifteen researchers provided the requested data. Twelve of these studies met the inclusion criteria and were included in the meta-analysis. We used a random effects model that allows heterogeneity between studies (assessed with the Q index) and performed a rank test to detect asymmetry in the funnel plot which is an indication of publication bias. If we had any indications of publication bias either by the rank tests or by visual inspection, we used a trim and fill procedure to

correct for bias due to missing studies. In case of a statistically significant main finding of dissociation on treatment effectiveness, we performed the fail-safe tests of Rosenthal and Orwin to assess the robustness of the results. We conducted moderation analyses with a meta-regression approach by fitting mixed effect models including potential treatment moderators to test for differences in the effect size associated with characteristics of the studies.

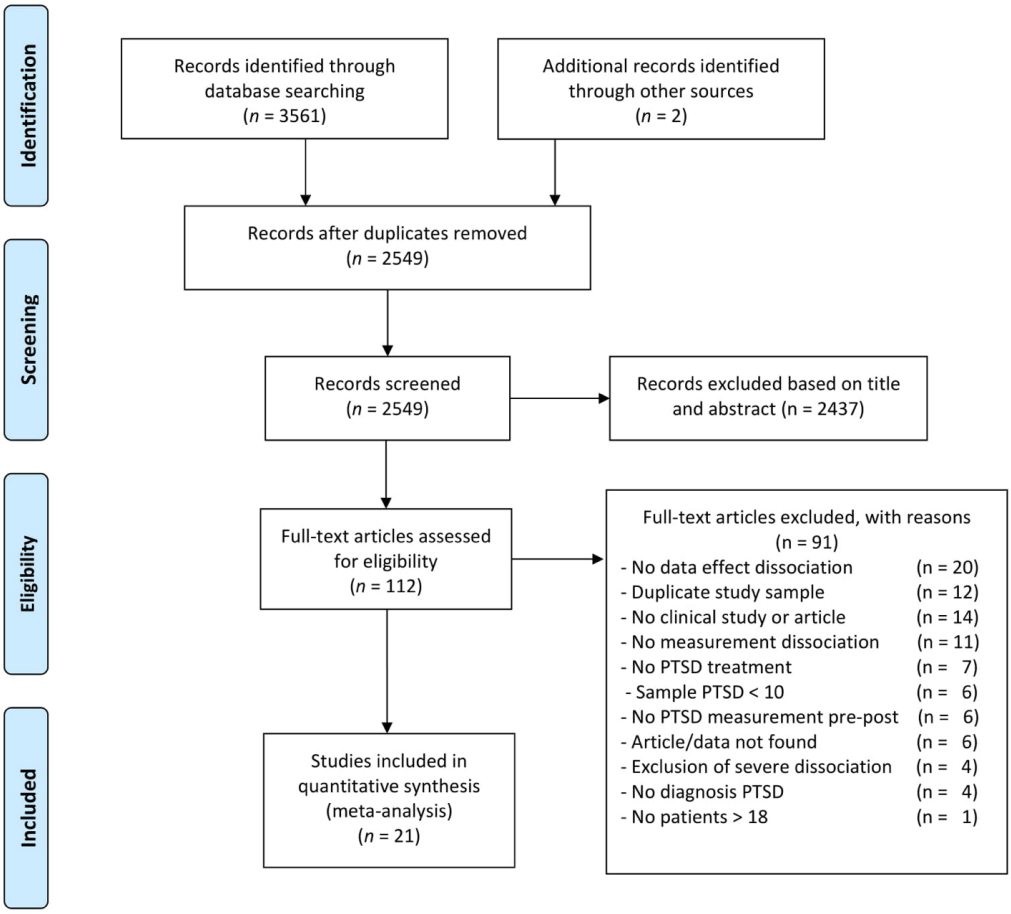

Figure 1. Flowchart of inclusion of studies.

Results

Selection and inclusion of studies

The systematic searches yielded a total of 3,563 papers (2,549 after removal of duplicates). Of these 2,549 papers, 2,437 were excluded based on title and abstract as they did not meet inclusion criteria. 112 full-text papers were retrieved of which 91 were excluded because they did not meet the inclusion criteria (see Figure 1 for details). The remaining 21 articles were included in this meta-analysis. Note that none of the included studies used severe levels of dissociation or diagnosis of dissociative (identity) disorder as exclusion criterion.

Characteristics of included studies

The 21 included studies contained a total of 1,714 patients from 9 RCTs and 12 uncontrolled clinical trials or treatment cohort studies. Table 1 shows the study characteristics and potential moderator variables (see supplement Table S2 for more study details).

Risk of bias score

The overall risk of bias of the included studies was modest (M = 6.6; SD = 2.94). Table 2 lists item and total scores for the risk of bias scores for each of the included studies. Agreement between two independent assessors regarding risk of bias of individual studies was high (Cohen's Kappa = .81, SE = .04, $p < .001$).

Effect of dissociation on PTSD treatment

Figure 2 depicts the main results of the meta-analysis. The pooled correlation between pre-treatment dissociation and decrease in PTSD symptoms during treatment was .04 (95% *CI:* -.04; .13, p =.32). The heterogeneity between studies was moderately high: I^2 = 68.90, $p < .001$. Visual inspection of the funnel plot did not indicate asymmetry in any direction (see Figure 3), which was confirmed by Kendall's tau based on the rank correlation (p = .46) and by Eggers' test (p = .25). The funnel plot shows two potential outliers: Harned et al. (2014) (positive effect of dissociation) and Abramowitz et al. (2016) (negative effect). The study sample of Harned et al. (2014) was very small and the drop-out was high. The study of Abramowitz et al. (2016) was an open study with a relatively small sample size. Therefore, both studies may have yielded an effect size that is not so reliable.

Table 1. Selected characteristics of studies examining the effect of dissociation on PTSD psychotherapy treatment outcome

Study	Treatments	Effect size	Female (%)	Age *M (SD)*	Measure PTSD; DSM	Measure dissociation	Moderators			
							Trauma focus	Design	Sample size	Bias score
Abramowitz et al. (2010)	Hypnotherapeutic olfactory conditioning	NR	0	41.2 (12.2)	IES-R; DSM-IV	DES	No	No RCT	36	11.0
Bae et al. (2016)	EMDR	1.27 Com.	59	34.9 (11.6)	CAPS; DSM-IV	CAPS subtype items + decreased awareness	Yes	No RCT	60	8.0
Cloitre et al. (2012)	Stair/NST; Support/NST; Stair/support	1.97 ITT	100	36.4 (9.40)	CAPS; DSM-IV	TSI-DIS averaged score	No	RCT	75	3.0
Gantt et al. (2007)[1]	Art, hypnosis, video therapy	NR	77	38 (14)	IES; DSM-IV	DES	No	No RCT	53	11.0
Haagen et al. (2018)	EMDR, NET, other interv.	.36 Com.	3.1	39.8 (10.1)	IES-R; DSM-IV	DES	No	No RCT	64	8.0
Hagenaars et al. (2010)	PE	3.07 Com.	83	35.75 (11.74)	CAPS; DSM-IV	DES	Yes	No RCT	36	4.0
Halvorsen et al. (2014)	NET + TAU	.95 Com.	31	35.55 (11.05)	CAPS; DSM-IV	CAPS subtype items	TAU: No NET: Yes	RCT	81	5.0
Harned et al. (2014)	DBT + DBT-PE	1.8 ITT	100	32.6 (12.0)	PSS; DSM-IV	DES	No	RCT	12	3.0
Kleindienst et al. (2016)	DBT-PTSD	NR	100	37.3 (10.5)	CAPS; DSM-IV	DES	No	RCT	24	4.5
Kratzer et al. (2018)	EMDR + em. reg. group	1.81 Com.	88	47.9 (10.5)	IES-R; DSM-IV	DES	No	No RCT	150	8.5
Lampe et al. (2014)[1]	PITT + psychodyn. Group	NR.	100	40.72 (10.0)	IES; DSM-IV	DES	No	No RCT	88	9.0
Lynch et al. (2008)[1]	NR	NR	83	36 (9.99)	PDS; DSM-IV	DES	No	No RCT	127	8.5
Murphy et al. (2015)	Group + indiv CBT	NR	1	NR	PSS; DSM-IV	DES	No	No RCT	244	11.0
Pabst et al.[1] (2014)	NET; TBE	.95 Com	100	29.91 (10.11)	PDS; DSM-IV	DES	TBE: No NET: Yes	RCT	36	3.0
Resick et al. (2012)	CPT; CPT-C; WA	1.68 ITT	100	35.4 (12.4)	CAPS; DSM-IV	TSI-DIS	Yes	RCT	117	3.0
Steele et al. (2018)	Treatment program	.70 Com.	29	42.94 (11.63)	Missisipi scale for PTSD	DES	No	No RCT	62	10.0
Steuwe et al. (2016)	NET + SIC	.70 ITT	90.9	34.9 (9.71)	PDS; DSM-IV	DES	No	No RCT	11	7.5
van Emmerik et al. (2008)[1]	CBT; SWT	.79 ITT	65	40.87 (11.97)	IES; DSM-IV	DES	Yes	RCT	50	6.5
Van Minnen et al. (2016)	PE; EMDR	1.67 Com.	54	41.2 (10.5)	CAPS; DSM-IV	CAPS subtype items	Yes	RCT	82	6.0
Wolf et al. (2016)	PE; PCT	NR	100	44.79 (9.44)	CAPS; DSM-IV	TSI subtype items averaged score	PCT: No PE: Yes	RCT	137	2.5
Zoet et al. (2018)	EMDR + PE + sport	2.03 Com.	70	38.16 (10.90)	CAPS; DSM-IV	CAPS subtype items	No	No RCT	169	5.0

Meth: methodological, Com: completely, PCT: present-centered therapy, CPT: cognitive processing therapy, CPT-C: cognitive therapy only, WA: written trauma accounts only, RCT: randomized controlled trial, EMDR: eye movement desensitization and reprocessing, Stair: skills

training in affective and interpersonal regulation, NST: narrative story telling, NET: narrative exposure therapy, PE: prolonged exposure, DBT; dialectical behaviour therapy, DBT-PTSD: dialectical behaviour therapy for PTSD, TBE: treatment by experts of borderline disorder, CBT: cognitive behavioural therapy, SWT: structured writing therapy, Av: Average, wk: weeks, CAPS: clinician-administered PTSD scale, IES: impact of events scale, PSS: PTSD symptom scale, PDS: post-traumatic stress diagnostic scale, TSI-DIS: trauma symptom inventory-dissociation, DES: dissociative experiences scale, DES-T: DES-taxon, FDS: German version of the dissociative experiences scale, ITT: intention to treat, Interv: interventions, Com: completers, Em. reg.: emotion regulation focused, PITT: Psychodynamic imaginative trauma therapy, psychodyn: psychodynamic, diss: dissociation, NR: not reported.

[1]Note: These studies provided additional data for a sub-sample of patients who met inclusion criteria of this meta-analysis so patient characteristics stated in this table are an estimation based on complete study sample

Table 2. Risk of bias scores of included studies with higher scores indicating a higher risk of bias.

	Item								
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**Total**
Abramowitz *et al.* (2010)	1 \ 1	1 \ 1	1 \ 1	1 \ 1	2 \ 2	2 \ 2	2 \ 2	1 \ 1	**11.0**
Bae *et al.* (2016)	1 \ 1	1 \ 1	0 \ 0	1 \ 1	0 \ 0	2 \ 2	2 \ 2	1 \ 1	**8.0**
Cloitre *et al.* (2012)	0 \ 0	0 \ 1	2 \ 2	0 \ 0	0 \ 0	0 \ 0	0 \ 0	0 \ 1	**3.0**
Gantt *et al.* (2007)	1 \ 1	1 \ 1	1 \ 1	1 \ 1	2 \ 2	2 \ 2	2 \ 2	1 \ 1	**11.0**
Haagen *et al.* (2018)	1 \ 1	1 \ 1	0 \ 0	1 \ 1	0 \ 0	2 \ 2	2 \ 2	1 \ 1	**8.0**
Hagenaars *et al.* (2010)	1 \ 1	1 \ 1	0 \ 0	1 \ 1	0 \ 0	0 \ 0	0 \ 0	1 \ 1	**4.0**
Halvorsen *et al.* (2014)	1 \ 1	1 \ 1	2 \ 1	0 \ 0	0 \ 0	0 \ 0	2 \ 2	0 \ 1	**5.0**
Harned *et al.* (2014)	1 \ 1	1 \ 1	1 \ 1	0 \ 0	0 \ 0	0 \ 0	0 \ 0	1 \ 1	**3.0**
Kleindienst *et al.* (2016)	1 \ 1	0 \ 0	0 \ 0	0 \0	2 \ 2	0 \ 0	2 \ 2	0 \ 1	**4.5**
Kratzer *et al.* (2018)	1 \ 1	1 \ 1	1 \ 1	1 \ 1	0 \ 0	2 \ 2	2 \ 1	1 \ 1	**8.5**
Lampe *et al.* (2014)	1 \ 1	1 \ 1	1 \ 1	1 \ 1	0 \ 0	2 \ 2	2 \ 2	1 \ 1	**9.0**
Lynch *et al.* (2008)	1 \ 1	1 \ 1	1 \ 1	1 \ 1	0 \ 0	2 \ 2	2 \ 1	1 \ 1	**8.5**
Murphy *et al.* (2015)	1 \ 1	1 \ 1	2 \ 2	2 \ 2	2 \ 2	0 \ 0	2 \ 2	1 \ 1	**11.0**
Pabst *et al.* (2014)	1 \ 1	1 \ 1	1 \ 1	1 \ 1	0 \ 0	2 \ 1	0 \ 0	0 \ 1	**3.0**
Resick *et al.* (2012)	0 \ 1	0 \ 0	2 \ 2	0 \ 0	0 \ 0	0 \ 0	0 \ 0	0 \ 1	**3.0**
Steele *et al.* (2018)	1 \ 1	1 \ 1	1 \ 1	1 \ 1	2 \ 2	2 \ 1	2 \ 1	1 \ 1	**10.0**
Steuwe *et al.* (2016)	1 \ 1	1 \ 1	1 \ 1	0 \ 0	0 \ 0	2 \ 2	2 \ 1	1 \ 1	**7.5**
Van Emmerik *et al.* (2008)	0 \ 0	1 \ 1	1 \ 1	0 \ 0	0 \ 0	2 \ 2	2 \ 2	0 \ 1	**6.5**
Van Minnen *et al.* (2016)	0 \ 1	0 \ 1	2 \ 2	0 \ 0	2 \ 2	0 \ 1	0 \ 0	0 \ 1	**6.0**
Wolf *et al.* (2016)	1 \ 1	1 \ 1	0 \ 0	0 \ 0	0 \ 0	0 \ 0	0 \ 0	0 \ 1	**2.5**
Zoet *et al.* (2018)	1 \ 1	1 \ 1	0 \ 0	0 \ 0	0 \ 0	0 \ 0	2 \ 2	1 \ 1	**5.0**

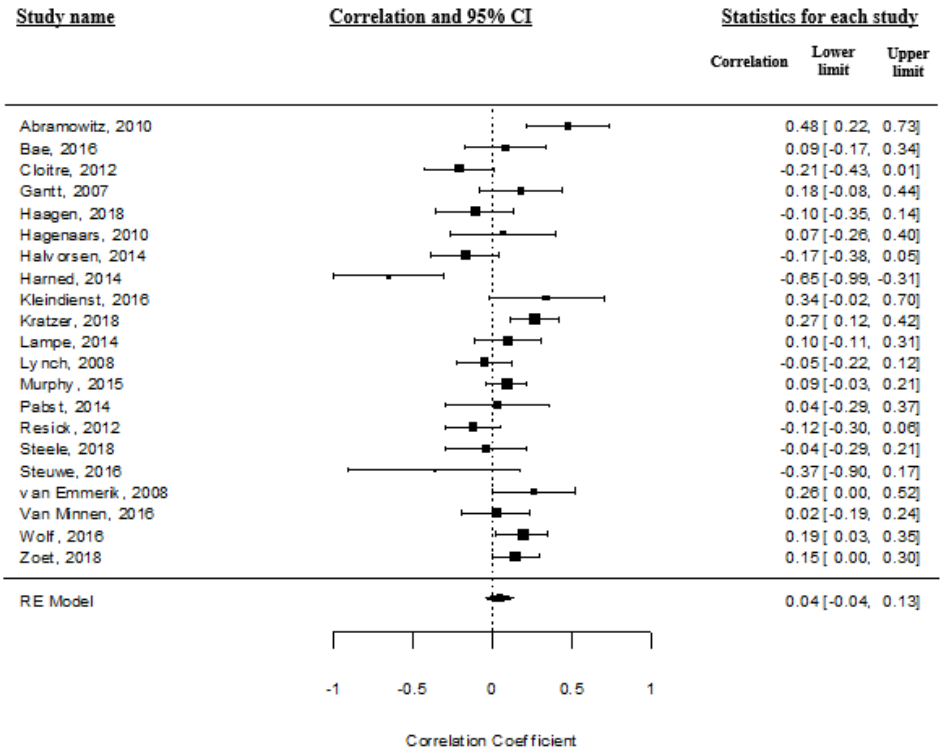

Figure 2. Pearson's Correlation coefficient (*r*) between baseline dissociation and change in PTSD symptoms from pre to post-treatment

Table 3. Effect of dissociation on improvement in PTSD symptoms and moderation analyses

	N	Pearson's r	95% CI	p
Overall outcome	21	.04	-.04; .13	.32
Moderation analyses				
Trauma-focused	8	.06	-.11; .22	.76[1]
Not trauma-focused/combination	16	.02	-.09; .14	
RCT	9	-.03	-.17; .11	.18[1]
No RCT	12	.10	-.02; .21	
Sample size	21	.001	-.001; .002	.38
Risk of bias score	21	.03	-.002; .06	.07

[1]p-value indicates whether effect size of subgroups differ significantly. A positive correlation (Pearson's correlation) indicates negative effect of dissociation on PTSD improvement.

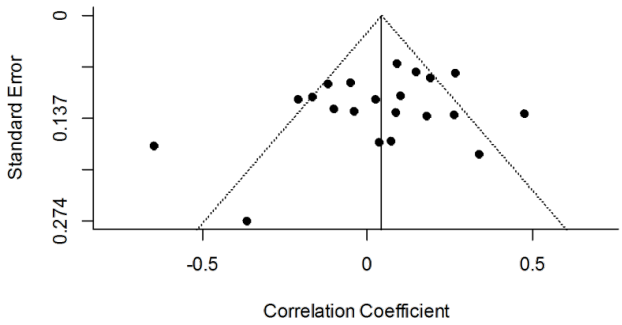

Figure 3. Funnel plot with Pearson's correlation coefficient between dissociation and change in PTSD symptoms from pre to post-treatment

Effect of potential moderators of the effect of dissociation on PTSD treatment outcome

Table 3 shows the results of the moderation analyses. We did not find that a higher risk of bias resulted in a larger effect of dissociation, although this effect was borderline significant (slope r =.03, CI: -.002; .06, p = .07). In addition, we found no difference in the effect of dissociation on the effectiveness of completely trauma-focused treatments compared to non-trauma-focused/multi-component treatments (p = .76). Similarly, we did not find that the effect of dissociation was different for randomized controlled trials compared to non-randomized studies (p = .18), nor did we find an effect of sample size (p =.38).

To explore the effect of risk of bias on the results, we performed a post-hoc analysis including only studies with a low-moderate risk of bias (i.e. risk of bias score ≤ 8 (n = 14)). The correlation between pre-treatment dissociation and decrease in PTSD symptoms during treatment for higher quality studies was -.01 (95% *CI*: -.13; .10, p =.80) and not different from the results derived over all studies.

Discussion

We found no evidence for a moderating effect of dissociation on psychotherapy outcome in patients with PTSD. Furthermore, differences between studies in the effect size of dissociation on treatment outcome were not explained by study characteristics. We conclude that comorbid dissociative symptoms do not reduce the effectiveness of psychotherapy in patients with PTSD. Although we did not specifically examine the dissociative subtype of PTSD, the present findings suggest that this subtype may not be associated with worse treatment outcomes as was suggested by the introduction of this subtype in the DSM-5.

Most included studies found non-significant effects of dissociation on the treatment outcome, which corresponds to the null finding of this meta-analysis. The results from the studies reported in this meta-analysis may differ from the conclusion from the individual papers. Some of these studies were hampered by methodological limitations, including incorrect moderation analyses. We assessed dissociation as treatment moderator. Some individual studies, however, did not test moderation, but reported the association between

dissociation and post-treatment PTSD severity. We were able to include a relatively large number of recently published clinical trials. The addition of the dissociative subtype to the DSM-5 seems to have increased awareness and research into dissociation. We found a moderately high heterogeneity among studies, indicating that the effect of dissociation varied due to systematic differences rather than chance. Despite this variation, the pooled effect size allows a uniform conclusion since the error bars (95% confidence intervals) of the effect sizes of most studies include the pooled effect size (Fletcher, 2007). Moreover, we did not find indications for publication bias.

We examined whether the following study characteristics explained the heterogeneity between studies: type of treatment (exclusively trauma focus or not), risk of bias score, study design and sample size. We observed no effect of type of treatment, study-design and sample size. Only a borderline significant effect of bias score was observed. The effect of dissociation on treatment outcome tended to be smaller in the higher-quality studies. No less than one third of the studies (33%) had a low study quality score, however a post-hoc analysis including only those studies with a low or moderate risk of bias again revealed no moderating effect of dissociation. We conclude that this meta-analysis provides no evidence for the idea that dissociation specifically reduces the effectiveness of trauma-focused treatment in those suffering from PTSD.

This study has some limitations. Firstly, a meta-analysis can only be as convincing as the quality of the individual studies. In most studies, the effect size of dissociation is based on completer samples (n = 19), thereby limiting the conclusions to patients who complete treatment. However, all included studies which reported on the effect of dissociation on treatment drop-out found that dissociation was not related to higher treatment drop-out (Bae, Kim, & Park, 2016; Cloitre, Petkova, Wang, & Lu, 2012b; Hagenaars, van Minnen, & de Rooij, 2010; Halvorsen, Stenmark, Neuner, & Nordahl, 2014; Lynch et al., 2008; Murphy, Elklit, Murphy, Hyland, & Shevlin, 2017; van Minnen et al., 2016; Wolf, Lunney, & Schnurr, 2016). Cloitre and colleagues (2012) even found that patients with high dissociation were less likely to drop-out from treatment. We observed quite a few studies of less than optimal quality, however, results were independent of study quality. Because we included several non-controlled clinical trials or cohort studies, we evaluated whether the effect sizes of the included treatments were comparable to previous meta-analyses of psychotherapy for PTSD. The psychotherapies of the included studies showed large within-subject effect sizes from pre to post-treatment (Cohen's d or Hedges' g) for treatment completers (M = 1.42) and intention-to-treat samples (M = 1.39). These effect sizes are comparable to those found in meta-analyses investigating the effectiveness of psychotherapy for PTSD as such (and including only randomized clinical trials (Lee et al., 2016a)). General limitations of the current studies in patients with PTSD are a lack of long-term follow-up measurements and the use of exclusion criteria (e.g. suicidality, psychosis or substance abuse) which limits the generalizability of the results. We encourage future studies to use non-restrictive in- and exclusion criteria (Ronconi et al., 2014). Secondly, most (67% of) studies measured dissociation broadly with the dissociative experience scale (DES), which includes

depersonalisation, derealisation, amnesia and absorption. Only a few studies measured the dissociative subtype (depersonalisation and derealisation) specifically (*n* = 5). Furthermore, a recent study indicated that the broad and specific measures have a large overlap and high correlation (Swart, Wildschut, Draijer, Langeland, & Smit, 2019). Future studies could focus on other instruments with a different timing of dissociation, for example within session (state) dissociation (Kleindienst et al., 2016). Thirdly, we exclusively focused on the effect of only one moderator, that is dissociation, on treatment effects. This specific hypothesis was based on clinical experience and theoretical considerations. Possibly, a combination of patient characteristics (i.e. dissociation, depressive symptoms and functional impairment) is more predictive of treatment responsiveness (Deisenhofer et al., 2018). Future work may consider examining combinations of moderators to detect patients who do not (fully) recover with psychotherapy and to detect differential treatment responses (DeRubeis et al., 2014). However, the sample sizes will need to be substantial and the risk of spurious or population-specific findings increases if research is not hypothesis-driven. Finally, we did not have the power to evaluate how moderators of the effect of dissociation interact. This could provide more insight into the effect of dissociation under specific conditions (Li, Dusseldorp, & Meulman, 2017).

Conclusions

Despite these limitations, the strength of our meta-analysis is that it is the first to systematically review the effect of dissociation on psychotherapy outcome in patients with PTSD across different types of psychotherapies. Psychotherapy for PTSD is generally effective but there is room for improvement since about half of the patients still meet criteria for PTSD after treatment (Bradley et al., 2005). About half of the clinicians believe that any degree of dissociation is a contraindication for psychotherapeutic treatment of PTSD (Becker, Zayfert, & Anderson, 2004; Ronconi et al., 2014). Importantly, the results of our meta-analysis contrast this supposition. We found that pre-treatment dissociation did not reduce the effectiveness of psychotherapy in patients with PTSD.