



Sequence matters: Combining Prolonged Exposure and EMDR therapy for PTSD

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ABSTRACT

Objective: Investigating the influence of the sequence in which two evidence-based trauma-focused treatments are offered to PTSD-patients.

Methods: PTSD-patients were treated using an intensive eight-day treatment program, combining Prolonged Exposure (PE) and EMDR therapy. Forty-four patients received a PE session in the morning and an EMDR session in the afternoon, while 62 patients received the reversed sequence (EMDR followed by PE). Outcome measures were PTSD symptom severity and subjective experiences.

Results: Patients who received PE first and EMDR second showed a significantly greater reduction in PTSD symptoms. Patients preferred this sequence and valued the treatment sessions as significantly more helpful compared to patients in the EMDR-first condition.

Conclusion: The results of this explorative study are supportive of the notion that PE and EMDR therapy can be successfully combined, and that sequence matters. First applying PE sessions before EMDR sessions resulted in better treatment outcome, and better subjective patient's evaluations in terms of treatment helpfulness and preference.

1. Introduction

Several international treatment guidelines (e.g., National Institute for Clinical Excellence (NICE, 2018); World Health Organization (WHO, 2013)) recommend trauma-focused treatments as first-line psychotherapies for individuals with posttraumatic stress disorder (PTSD). Among the effective treatments are prolonged exposure therapy (PE), Cognitive Therapy, and Eye Movement and Desensitization and Reprocessing (EMDR) therapy (Cusack et al., 2016; WHO, 2013). Although PE and cognitive therapy have been found to be effective as stand-alone treatments, in many therapy programs a combination of cognitive-behavioral methods is applied. This approach is based on the assumption that a combination of multiple interventions with different working mechanisms could be more effective than a single treatment method (Bryant et al., 2008). In most treatment programs this concerns the use of a mixed cognitive behavioral treatment protocol, typically consisting of elements of both exposure and cognitive therapy. In general, these mixed programs have been found to be effective in reducing PTSD symptoms, as shown in meta-analyses (e.g., Cusack et al., 2016; Watts et al., 2013). However, studies that were

specifically set up to compare single versus combined treatments, led to mixed results. That is, some studies failed to find an additional effect of combined treatments on reduction of PTSD-symptoms (Foa et al., 2005; Marks et al., 1998; Moser et al., 2010), whereas others did find additional effects (e.g., Bryant et al., 2008; see for an overview Kehle-forbes et al., 2013).

One possible explanation for these conflicting findings is that in combined treatment protocols, usually diluted versions of exposure and cognitive therapy are delivered. Another possible explanation could be that the *sequence* in which interventions are offered matters. In the studies that did not find an additional effect of combining cognitive with PE therapy versus applied as stand-alone for PTSD (Foa et al., 2005; Marks et al., 1998), PE preceded cognitive therapy during sessions. In contrast, in the study of Bryant et al., (2008), cognitive therapy was offered first and was then followed by - and integrated with - PE therapy. However, to the best of our knowledge, the specific (differential) effectiveness of different sequences of evidence-based therapies for PTSD has never systematically been studied. In addition, while combinations of PE and cognitive therapy are common, outcome studies examining a combination of EMDR therapy with another first-line

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treatment for PTSD, are scarce, let alone studying its sequence effects.

Although PE and EMDR therapy share some commonalities, such as directly targeting trauma memories (Schnyder et al., 2015), it has been argued that PE and EMDR therapy are quite different in terms of the underlying working mechanism, and the way these treatments are applied (Lee et al., 2006). While during PE patients are instructed to confront themselves with the traumatic memories, and expose themselves *continuously* to the fearful stimuli to reach habituation or extinction (Foa and Kozak, 1986), in EMDR therapy sessions the patients are *distracted* from the disturbing memories by using a dual attention task, usually by using eye movements (De Jongh et al., 2019; De Jongh et al., 2013). Therefore, based on the different supposed working mechanisms of PE and EMDR therapy, it is conceivable that both treatments could complement each other.

Besides differences in working mechanisms, there may also be differences between PE and EMDR therapy in terms of preferences and perceived burden as experienced by patients. However, studies investigating these outcomes are scarce and non-existing when it comes to the sequence of different treatments offered to patients. This is important given the findings that when patients receive their preferred treatment, the treatment results may be better (Zoellner et al., 2019). Besides perceived burden, perceived helpfulness of a treatment program may also be a relevant factor to consider, because greater perceived helpfulness has been found to be related to a better treatment outcome (Cooper et al., 2017).

The purpose of the present study was to explore the effects of a brief trauma-focused treatment program consisting of PE and EMDR therapy, and more specifically the effectiveness of the sequence in which these two therapies were offered. The combination was provided within the context in which patients received eight treatment days within two weeks, with two therapy sessions per day; one exposure session and one EMDR session. In an open study containing 347 patients, we showed that our treatment program was highly effective in decreasing PTSD symptoms (Van Woudenberg et al., 2018). The rationale behind combining these two treatments was mainly clinically driven. In the start-up phase of our treatment program we offered patients either PE or EMDR therapy as stand-alone treatments. Although these treatment results were promising (see e.g. Bongaerts et al., 2017), observations of therapists using both methods were that both therapies have their own particular strengths, but also specific difficulties. For instance, some patients were too avoidant to bring up an emotionally charged memory, as is required for a successful session of EMDR therapy, while others stayed highly emotional and anxious after the exposure sessions, which sometimes interfered with the continuation of treatment. In this light, we consider it as important to examine whether a treatment program that combines two treatment methods could target and solve both commonly seen problems. Therefore, the purpose of the present study was to determine the effectiveness of a treatment program combining PE and EMDR therapy, and more specifically, to investigate the influence of the sequence (PE first, and then EMDR versus EMDR first and then PE therapy) in which these two evidence-based trauma-focused treatments are offered to people with PTSD, in terms of treatment outcome, i.e., a significant reduction of PTSD symptoms. The second aim was to explore patients' perceived burden, helpfulness and treatment preference concerning both combinations of therapy sequence. Because this was the first study that studied combinations of PE and EMDR therapy in a certain treatment sequence we had no empirically based hypotheses in this regard.

2. Method

2.1. Participants

The current study included 117 consecutive patients who were enrolled in an intensive treatment program for PTSD at the Psychotrauma Expertise Centre (PSYTREC), a mental health centre in Bilthoven, the

Netherlands, in the period of January and February 2017. Patients were referred to PSYTREC by their general practitioner, psychologist, or psychiatrist. The inclusion criteria for this study were fulfilling the diagnostic criteria of PTSD according to the DSM-IV-TR or DSM-5, as established by the CAPS, being at least 18 years old, and being able to speak and understand the Dutch language. Exclusion criterion was: a suicide attempt in the past three months.

Of the 117 patients, seven provided no informed consent, and one patient had missing data on the outcome measure. Further, three patients stopped prematurely with treatment. Because we were interested in the subjective experiences and outcome of the whole treatment program, we did not include these individuals in the analyses. In January 2017, patients ($N=44$) received Exposure therapy (EXP) in the morning and EMDR therapy in the afternoon (EXP-EMDR). In February 2017 treatment order was reversed, so that patients ($N=62$) received EMDR in the morning and Exposure therapy in the afternoon (EMDR-EXP).

2.2. Materials

The Dutch version of the PTSD Symptom Scale-Self Report (PSS-SR; Foa et al., 1993; Mol et al., 2005) assesses PTSD symptom severity during the past week. This version was DSM-IV based and contains 17 items, with a scoring range from 0-51 for the total scale, with higher scores representing higher PTSD symptom severity. Internal consistency of the PSS-SR is high. This scale was administered at pre-treatment (at the beginning of the first treatment day), and at post-treatment (nine days after the last treatment day).

To measure perceived burden and helpfulness, at the last treatment day, patients rated 5 questions using a 4-point Likert-type scale ranging from 0 (not at all) to 4 (very much). These were: 'How distressing were the EMDR sessions?', 'How distressing were the exposure sessions?', 'How much did the exposure sessions help you?', 'How much did the EMDR sessions help you?', 'How much did the sequence of treatment help you?'. Also, they were asked to make a forced choice regarding the sequence: EXP first vs EMDR first. Questions were analyzed separately, thus no total scores were calculated.

Comorbid psychiatric disorders and suicide risk were assessed using the Dutch version of Mini International Neuropsychiatric Interview (MINI; Overbeek et al., 1999; Sheehan et al., 1998). The MINI is a brief, structured interview to diagnose current and lifetime major Axis I disorders according to the DSM-IV. Items are scored with 'yes' or 'no', and suicide risk is reported as no risk, low, moderate, or high risk.

The Dutch version of the Clinician Administered PTSD Scale was administered during the intake session to assess whether participants met the diagnosis of PTSD. The CAPS is a semi-structured diagnostic interview and is considered the golden standard measure to establish PTSD diagnosis. This study was performed during the transition from DSM-IV to DSM-5, so for some patients CAPS-IV (Blake et al., 1995) was administered, while for other patients the CAPS-5 (Boeschoten et al., 2018; Weathers et al., 2017) was used.

2.3. Procedure

During intake, a psychologist assessed whether patients met the diagnostic criteria of PTSD using the CAPS and the MINI. Next, patients signed informed consent for using their demographic and clinical data for scientific purposes. After inclusion, participants were allocated to the treatment sequence group in two blocks, depending on the time of referral. More specifically, in January 2017, patients received EXP-EMDR, and in February 2017 patients received EMDR-EXP. Importantly, patients were assigned to the treatment groups based on the order of referral, not based on any clinical or demographic characteristic, nor based on patient's or clinician's preferences. Participants did not know beforehand which treatment sequence they would receive, and they were unaware that other groups received a different

order of treatment sessions. Also, psychologists at the intake were unaware of the treatment sequence groups participants were assigned to. Treatment was provided in closed groups: each two weeks, new treatment groups arrived and started treatment, and completed treatment within these two weeks. All participants in the group received the same treatment sequence. The two treatment sequence groups were similar with regard to content, duration, and location. The only difference was the order of the trauma-focused treatment sessions.

At the first treatment day, before the first treatment session, pre-treatment PSS-SR was completed. At the final treatment day, participants filled in the questions about their experiences of the treatment sessions and treatment sequence. Nine days after treatment, patients returned to the clinic for the post-treatment assessment (PSS-SR).

Participants signed an informed consent form for including their personal and clinical information for research purposes. Patients were free to choose whether they were agreed to participate or not, and patients who did and patients who did not agree to participate received the same treatment. Further, the study was performed in accordance with the precepts and regulations for research as stated in the Declaration of Helsinki and the Dutch Medical Research on Humans Act (WMO, 2001) concerning scientific research. That is, all data were collected using the standard assessment instruments and routine outcome monitoring procedure, the study lacked random allocation, and no additional 'physical infringement of the physical and/or psychological integrity of the individual' was to be expected (WMO, 2001).

2.4. Treatment

To the best of our knowledge, our treatment program is the first that combines PE and EMDR therapy. To prevent lowering the dosage of each of the treatment elements provided, we chose not to combine PE and EMDR therapy within the same session, or lower the number of sessions, but to provide each method while maintaining the common dosage (i.e., a minimum of eight sessions of 90 minutes each). Because we hypothesized that, based on their different working mechanism, both treatments could complement each other, we chose to provide both treatments at each treatment day, while each day targeting the same traumatic memory within those two sessions. Each treatment day, patients received one individual PE session of 90 minutes and one individual EMDR therapy session of 90 minutes. One treatment session was provided in the morning, the other in the afternoon. Thus, during the intensive treatment program, patients received eight sessions of PE and eight sessions EMDR therapy of 90 minutes each, in total.

The PE protocol largely followed the approach of Foa et al., (2007). According to this approach, patients were asked to imagine the memories of the traumatic events as vividly as possible, and to describe their traumatic memories in the present tense and in detail. During treatment sessions, in vivo exposure to feared but safe trauma-related stimuli was used. The EMDR therapy protocol used followed the eight phases approach of Shapiro (2018; De Jongh and Ten Broeke, 2013). During treatment, patients were asked to memorise the most distressing part of the experienced trauma while their working memory capacities are challenged by visually tracking the finger movements of the therapist and other stimuli to maximize the work load of the working memory, such as a light bar, clicking sounds, and/or hand-hold buzzers. Each day one specific traumatic situation was targeted. In the EXP-EMDR group, this traumatic situation was first processed using exposure therapy (morning session) followed by EMDR therapy (afternoon session). In the EMDR-EXP group, this order was reversed, so that participants first processed the memory using EMDR (morning session) followed by exposure therapy (afternoon session). Treatment sessions were employed by clinical psychologists, trained in both EMDR and PE therapy. Each session was provided by a different therapist, a so-called "therapist rotation" approach (see Van Minnen et al., 2018).

Between treatment sessions, patients engaged in four daily 90-minute sessions of group physical activities which varied from low to

high intensity. Furthermore, psycho-education about PTSD was provided in groups. Treatment duration was eight days; four consecutive days followed by a three-day break in which the participants returned to their homes, and then again four consecutive days. For more detailed information about the treatment program see (Van Woudenberg et al., 2018).

2.5. Data Analysis

SPSS version 24 was used to perform the statistical analysis. Descriptive information (e.g., age, gender, type of trauma, comorbidity) was explored first to gain an overview of the sample characteristics. Independent t-tests were conducted to analyze the difference in decline of PTSD symptoms (PSS-SR post-treatment minus PSS-SR pre-treatment) and treatment experiences between the two groups (EXP-EMDR and EMDR-EXP). For the forced choice question, a chi-square analysis was used.

3. Results

The mean age of the total sample was 38.75 ($SD = 11.12$) and 72.6% of the sample was female. All 106 participants had experienced multiple traumatic events. Most of them had been exposed to sexual ($n = 87$; 82.1%) and/or physical abuse ($n = 91$; 85.8%). Also, the majority of the patients suffered from one or more comorbid psychiatric disorders. More specifically, 71.4% had a mood disorder, 20.8% panic disorder, 32.1% social phobia, and 14.7% fulfilled the diagnostic criteria of alcohol dependence. Suicidal risk was moderate to high for 51% of the patients. The EXP-EMDR and EMDR-EXP group were compared on baseline characteristics (i.e., age, gender, and pre-treatment PSS-SR score). Independent samples t-tests did not reveal any significant differences between the EXP-EMDR group and EMDR-EXP group on age, $t(104) = -1.59$, $p = .114$ and pre-treatment PSS-SR score ($t(104) = -1.03$, $p = .304$). Pearson Chi-Square analyses did not yield any significant differences between the EXP-EMDR group and EMDR-EXP group with regard to gender ($\chi^2(1) = .181$, $p = .825$).

3.1. Treatment Outcome

Figure 1 represents the PSS-SR scores for both treatment conditions at pre- and post-treatment. Independent t-test showed that the EMDR-EXP group had a significantly smaller decline in PSS-SR scores compared to the EXP-EMDR group ($t(104) = 2.20$, $p = .030$, between group Cohen's $d = 0.54$).

3.2. Perceived burden, helpfulness and treatment preference

Subjective ratings were available of 73 participants ($n = 26$ in the EXP-EMDR group and $n = 47$ in the EMDR-EXP group, see Table 1). No significant differences between groups were found regarding the perceived burden of PE or EMDR therapy, but participants in the EXP-EMDR group rated the treatment as significantly more helpful compared to the EMDR-EXP group. This was true for both the EXP ($t(71) = 2.58$, $p = .012$) and the EMDR sessions ($t(71) = 2.79$, $p = .007$), as well as for the sequence of treatment ($t(71) = 2.39$, $p = .019$). The helpfulness of the sequence of the treatment was significantly related to the decline in PTSD symptom severity ($r = .59$, $p < .001$). With regard to preference, significantly more patients preferred the sequence EXP-EMDR (58.1%) than EMDR-EXP (41.9%); $\chi^2(1) = 22.94$, $p = < .001$.

4. Discussion

The primary aim of the present study was to investigate whether the sequence of a combination of first-line treatments of PTSD, i.e., prolonged exposure (PE) and EMDR therapy, influenced treatment

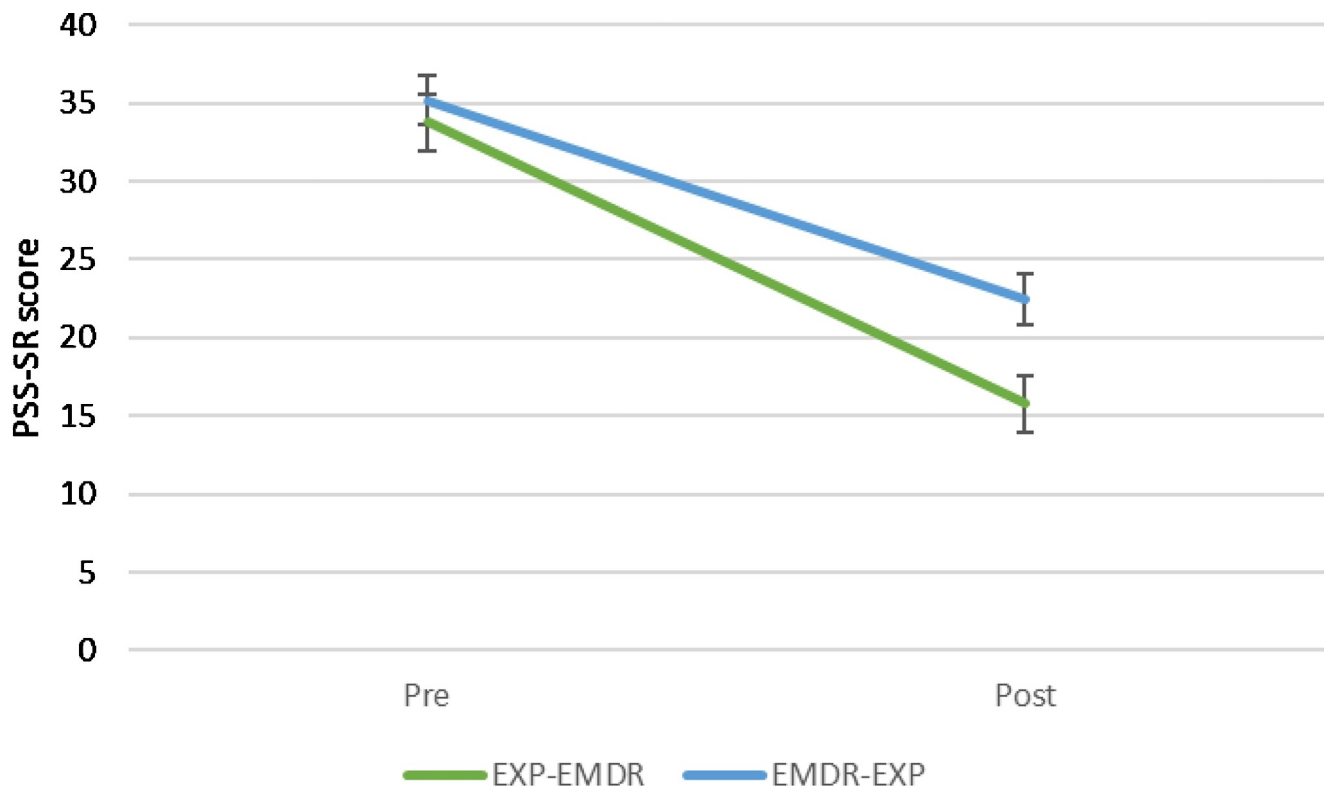


Fig 1. Pre- and post-treatment PTSD Symptom scale-self report (PSS-SR) scores.

Table 1
Perceived burden and helpfulness of treatment sessions.

	EXP-EMDR (n = 26)	EMDR-EXP (n = 47)	Between group effect sizes
	Mean (SD)		Cohen's d
<i>Burden</i>			
Exposure	3.23 (.82)	3.36 (.79)	0.16
EMDR	2.81 (.85)	2.83 (.87)	0.02
<i>Helpfulness</i>			
Exposure*	3.46 (.76)	2.94 (.87)	0.64
EMDR*	3.50 (.76)	2.91 (.91)	0.70
Sequence*	3.35 (.98)	2.74 (1.05)	0.60

* p < .05

outcome. Although both groups showed significant improvements in PTSD symptoms, interestingly, patients who received PE in the morning sessions and EMDR therapy in the afternoon sessions showed significantly better treatment results than patients who received the reversed order, with a moderate between group effect size. These findings are consistent with our previous outcome studies (Van Woudenberg et al., 2018; Wagenmans et al., 2018; Zoet, Wagenmans et al., 2018) which also showed the combination of treatments to be effective, and with other studies that successfully combined different trauma-focused therapies (Gurak et al., 2016; Kehle-forbes et al., 2013).

In line with its greater effectiveness, patients found the EXP-EMDR sequence significantly more preferable and helpful, and helpfulness of the sequence was related to a better treatment outcome, in line with findings of Cooper et al. (2017). Typically, during PE sessions, so called hotspots are addressed to fully activate the fear network. As a result, fear levels may be relatively high throughout the entire PE session, including the end of the session. In contrast, during EMDR sessions a decrease in fear levels is specifically aimed for, and patients may feel relieved and satisfied at the end of their session. Translated to clinical utility, it is clinically more intuitive to first induce high levels of fear by targeting hotspots in the traumatic memory (during PE sessions in the

morning), to use these hotspots as targets in the EMDR-sessions, and subsequently aim at a strong decrease in fear levels (during the EMDR-session in the afternoon). The fact that patients preferred this PE-EMDR order, and found it more helpful may also be due to this mechanism; patients may feel more comfortable with lower fear levels at the end of the day, so they could finish their treatment with a low level of arousal before they went to sleep. However, one would expect that patients in the EMDR-PE condition would rate the PE as more burdensome than in the PE-EMDR condition, which was not the case. No significant differences between groups were found regarding the perceived burden of PE or EMDR in the two sequence groups. This means that participants' ratings of the burden of PE and EMDR were independent of the sequence in which they were offered.

Another, more theoretical explanation for the finding that providing PE sessions in the morning was related to better treatment outcomes, is that previous research (Zuj et al., 2016) found that fear extinction learning ability is influenced by the hours since waking. Participants with more (severe) PTSD symptoms responded significantly better to extinction learning when this extinction learning task was planned earlier on the day; that is, more close to their awakening time. In our EXP-EMDR condition, the PE sessions were also planned more closely to the awakening hours than in the EMDR-EXP condition.

What we consider a strength of the study is that when combining two stand-alone treatment approaches, we were capable of maintaining each original dose (i.e., 90 minutes per session). Further strengths of the current study are the high number of included patients, and the variety of the sample population, for instance in trauma characteristics, which makes our findings more generalizable to the commonly seen clinical PTSD patient population. On the other hand, the intensive nature of our treatment program limits making generalizations to other contexts and treatment settings, and combining PE and EMDR in regular weekly scheduled sessions has still to be studied. A further limitation is that our findings are in favor of the combination that had the larger clinical 'face validity'. Although they were explicitly instructed *not* to do so, it cannot be ruled out that the therapists have emphasized in their

communication (consciously or unconsciously) with patients that the reversed order was more 'difficult', and thereby influenced and guided the ratings of patients. Similarly, the fact that patients rated their preferences at post-treatment and without experiencing the other treatment sequence, can be considered a limitation, in that treatment outcome may have affected their ratings. Also, of quite some participants, the subjective ratings of the treatment sequence were missing, what limits the generalisability of our findings. Maybe the most important limitation is that, albeit patients were not allocated to the two sequence groups on clinical grounds, our study design was uncontrolled. Therefore, our findings are explorative in nature, and should be considered in that context. Future studies using randomized controlled designs are needed.

Together with our clinical findings suggesting that sequence of interventions matters and influences outcome, we should be careful with integrating several effective PTSD treatment elements in clinical practice because 'these all look alike', share commonalities and lead to the same treatment results (e.g. Wampold, 2019). When applying and combining two different treatments, it is important to consider in what way the treatments and its underlying working mechanisms can reinforce each other. Careful studies are needed, and in future studies it might be interesting to study several variants of treatment combinations, and optimize its enhancement conditions.

Clinical or methodological significance of the article

Effective trauma-focused treatments, such as Prolonged Exposure (PE) and Eye Movement Desensitization and Reprocessing (EMDR therapy) can be successfully combined. However, the sequence of the interventions matters: PE followed by EMDR sessions was more effective and had higher perceived helpfulness than EMDR sessions followed by PE.

CRedit authorship contribution statement

Agnes Van Minnen: Conceptualization, Methodology, Formal analysis, Writing - original draft, Supervision. **Eline M. Voorendonk:** Investigation, Formal analysis, Writing - review & editing. **Linda Rozendaal:** Software, Validation, Writing - review & editing. **Ad de Jongh:** Conceptualization, Methodology, Writing - review & editing, Supervision.

Declaration of Competing Interest

A.v.M. receives income for published book chapters on PTSD and for the training of postdoctoral professionals in prolonged exposure. A.d.J. receives income from published books on EMDR therapy and for the training of postdoctoral professionals in this method. E.V. and L.R. have no competing interests.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.psychres.2020.113032](https://doi.org/10.1016/j.psychres.2020.113032).

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