# Great expectations: inhibitory learning and change processes in exposure therapy for PTSD

Kooistra, M.J.

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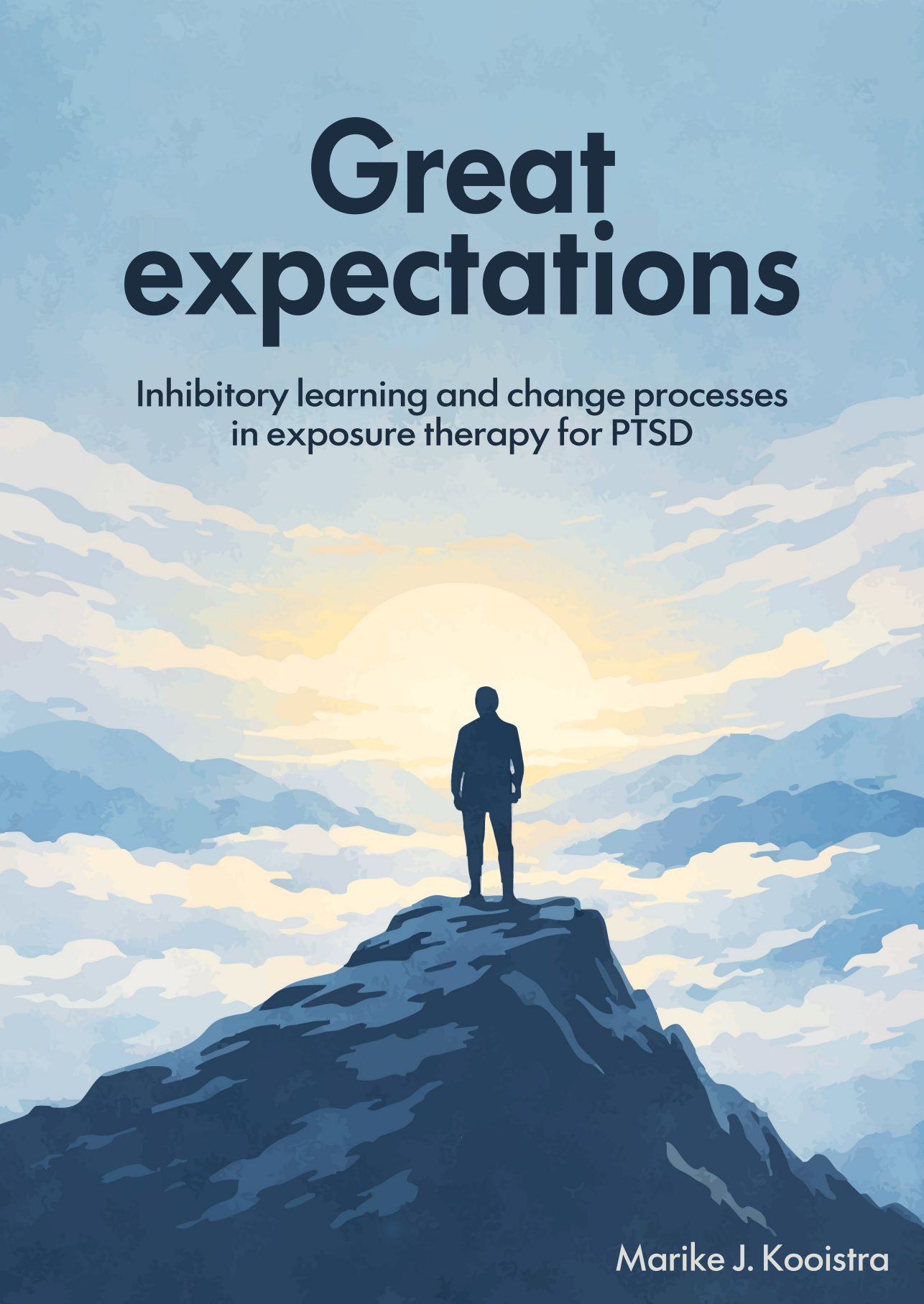
## Inhibitory learning and change processes in exposure therapy for PTSD



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Inhibitory learning and change processes in exposure therapy for PTSD

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**Take nothing on its looks; take everything on evidence.**
**There's no better rule.**

Charles Dickens, *Great Expectations*

# Chapter 1

# General introduction

# Introduction

It is estimated that 81.5% of the people in the Netherlands experience at least one potentially traumatic event during their lifetime, such as a serious traffic accident, physical violence or sexual assault (Hoeboer et al., 2025). Following such events, some people develop a posttraumatic stress disorder (PTSD). In the Netherlands, the estimated lifetime prevalence of PTSD is 11.1% (Hoeboer et al., 2025). Individuals with PTSD experience several symptoms associated with the traumatic event(s), including: 1) recurring intrusions, 2) persistent avoidance of thoughts, feelings or stimuli, 3) negative changes in cognitions and mood, and 4) changes in arousal and reactivity (American Psychiatric Association, 2022). See the vignette for a more detailed illustration of how these symptoms may manifest.

Multiple factors further increase the risk of developing PTSD, such as an interpersonal nature of the traumatic events (e.g., sexual assault), being female, and childhood adversity (Hoeboer et al., 2025; Kessler et al., 2017). Left untreated, PTSD can persist for many years, with delayed onset also possible (Kessler et al., 2017; Koenen et al., 2017). PTSD is a debilitating disorder, associated with substantial costs to the individual and society (Magruder et al., 2017; Warth et al., 2020). Moreover, PTSD has a high rate of comorbidity with other disorders, such as anxiety disorders and major depressive disorder (Hyland et al., 2021; Pietrzak et al., 2011; Walter et al., 2018). These findings highlight the need for effective treatments for PTSD.

**Prolonged Exposure**

Effective treatments for PTSD exist, with Prolonged Exposure (PE) being one of the first-choice treatments in multiple international guidelines (American Psychological Association, 2017; Federatie Medisch Specialisten, 2025; Hamblen et al., 2019; National Institute for Health and Care Excellence, 2018). PE includes several critical components (Foa et al., 2019). First, it includes psychoeducation about common reactions to trauma, PTSD symptoms and the treatment rationale. Second, PE includes repeated confrontations with objectively safe, trauma-related stimuli, situations, or people that the patient avoids (i.e., in vivo exposure). For example, after experiencing an assault, a patient might practice spending time around unfamiliar individuals who resemble the assailant's appearance or visit the location where the attack occurred. Third, PE includes repeatedly revisiting the traumatic memory (i.e., imaginal exposure), followed by emotional processing. During imaginal exposure, a patient is asked to recount the traumatic event out loud, with their eyes closed, in as much detail as possible. During the processing afterwards, the experience of recounting the event is discussed and the therapist provides support, psycho-education and explores erroneous thoughts that the patient might have

about themselves, other people and/or the world. Between sessions, patients are instructed to repeat in-vivo exposure exercises and listen to recordings of their imaginal exposure sessions on a daily basis.

**Vignette**

Charlotte is a 30-year-old woman who was sexually assaulted four years ago. Since then, she has experienced intrusion symptoms daily. She frequently re-experiences aspects of the event, often seeing the perpetrator's vividly face in her mind. She also has nightmares of being trapped and unable to escape. Charlotte tries to distract herself from thoughts of the assault by keeping herself busy, often by working extra hours or scrolling on her phone. Since the event, Charlotte avoids being alone with men she does not know well. She takes extra precautions when going out, such as planning her routes carefully or only meeting friends in familiar places. She finds it difficult to trust others, especially men, and often questions their intentions. She no longer goes jogging in the park, something she used to enjoy. She also avoids discussing the assault, fearing that people will not understand or will blame her. Charlotte is afraid that she will be harmed again and believes that she must always be on guard as the world is a dangerous place. She struggles with negative thoughts about herself, such as 'I am weak' and 'I should have done more to stop it'. Charlotte experiences arousal symptoms, including irritability, difficulty sleeping, and an exaggerated startle response, especially when someone unexpectedly appears behind her. Her symptoms have significantly impacted her daily life, making ordinary activities, such as commuting and socializing, feel exhausting and overwhelming. Charlotte's relationship with her partner has become strained, partly due to her withdrawal and her struggles with intimacy.



**Effectiveness of PE**

Multiple meta-analyses have shown that PE is an effective treatment that reduces PTSD symptoms, with these effects being relatively well maintained over time (Mavranezouli et al., 2020; McLean et al., 2022). It has been shown to be superior to waitlist, 'treatment as usual', and non-trauma focused treatment. On the longer term, PE also appears more effective than medication (particularly, antidepressants) (Lee et al., 2016; McLean et al., 2022). Besides reducing PTSD symptoms, PE has also been associated with improved quality of life (Kaur et al., 2024), increased perceived social support (Bourassa et al., 2020), and reductions in comorbid symptoms, such

as depressive and psychotic symptoms (Bont et al., 2016; Brown et al., 2018). PE is typically delivered in 8–15 weekly sessions, each lasting 90 minutes (Foa et al., 2019). Recently, there is growing interest in alternative delivery formats that may accelerate recovery and improve efficiency. For instance, intensive formats of PE (i.e., multiple sessions within one week) have been shown to be effective. Compared to weekly delivery, they are associated with a faster recovery and lower dropout rates (Levinson et al., 2022; McLean & Foa, 2024).

Despite PE's well-established efficacy and effectiveness, not all patients benefit sufficiently. A systematic review showed that after treatment for PTSD (including PE), 31% of patients still reported clinical symptom levels, and 59% reported subthreshold symptom levels (Larsen et al., 2019). Predicting who will benefit from treatment in advance is challenging (Barawi et al., 2020). Individuals with more severe symptoms or comorbidities often report higher symptom severity after treatment, but show a comparable rate of improvement (Barawi et al., 2020; Kline et al., 2021; van Minnen et al., 2015). Additionally, PE drop-out rates are generally high. While approximately 16–18% of patients drop out of psychological treatments for PTSD overall, estimates for PE range from 22% to 29% (Imel et al., 2013; Lewis et al., 2020; Varker et al., 2021). Although dropout occurs across all PTSD treatments, recent meta-analyses suggest that slightly more patients drop out from psychological treatments that are trauma-focused, including PE, than non-trauma-focused treatments (Hoppen et al., 2023; Lewis et al., 2020). Given that trauma-focused treatments also demonstrate the strongest efficacy, understanding and addressing the causes of dropout in these treatments remains a critical priority.

In summary, PE and related trauma-focused treatments are quite effective but there is ample room for improvement. Optimizing treatment effectiveness may be dependent on a better understanding of its mechanisms of change.

**Studying change mechanisms**

Identifying the mechanisms that drive symptom reduction could help refine interventions by ensuring that treatment targets the most critical change processes and by strengthening the therapeutic elements that facilitate these processes (Kazdin, 2007, 2009). Kazdin (2007, 2009) describes several recommendations for research on treatment mechanisms. First and foremost, using theory as a guide to understand the critical processes and how they drive change is essential. Second, to establish a treatment mechanism, several criteria must be met, and empirical research should be designed to rigorously test these criteria. These criteria include: 1) a strong association between the intervention, proposed mechanism and outcome; 2) specificity of this association, showing that the proposed mechanism is uniquely responsible for change; 3) consistency, demonstrating an observed result

repeatedly across studies, samples and conditions; 4) experimental manipulation, where direct manipulation of the proposed mechanism impacts the outcome; and 5) a timeline showing that change in the mechanism precedes the change in the outcome.

**Theories of exposure therapy for PTSD**

Multiple theories aim to explain the maintenance and recovery of PTSD, but two are particularly relevant for understanding how exposure therapy for PTSD is presumed to work. These two are the Emotional Processing Theory (EPT) and the Inhibitory Learning and Retrieval (ILR) model.



*Emotional processing theory*

EPT was first introduced as a framework for understanding the development and maintenance of anxiety-related disorders, including PTSD (Foa & Kozak, 1986). Inspired by the bio-informational theory of fear (Lang, 1979), EPT posits that fear is represented in memory as a cognitive structure. This structure includes representations of the fear stimuli (e.g., a knife), the fear responses (e.g., increased heart rate and muscle tension, running away), and their meaning (e.g., danger). Activation of one element generalizes to activate other elements in the structure. EPT makes a distinction between pathological and non-pathological structures. The fear structure is non-pathological if it becomes activated in the face of actual danger (e.g., a slashing movement with a knife) and elicits an appropriate response (e.g., moving away). The fear structure is considered pathological when it contains inaccurate associations that do not reflect reality, and when the structure becomes activated through stimuli or responses that are wrongfully viewed as dangerous (e.g., 'someone cutting food with a knife means danger') and elicits a maladaptive response (e.g., 'freezing'). Moreover, EPT posits that in PTSD, the structure also includes representations of someone's own reactions during and after the traumatic event and a meaning of self-incompetence. For example, freezing during the event may be interpreted as weakness. Two core dysfunctional cognitions are thought to underly PTSD (Rauch & Foa, 2006): negative cognitions about the self (e.g., 'I am weak'), and the world (e.g., 'the world is a dangerous place').

According to EPT, emotional processing is key to reducing symptoms, either via natural recovery or therapeutically. Emotional processing involves integrating corrective, realistic information into the fear structure, altering its pathological components. To do this, two conditions have to be met: a) the fear structure needs to be activated, and b) new information that is incompatible with the pathological elements must be presented and integrated. Repeatedly activating the fear structure (e.g., by talking about the traumatic event or confronting trauma-

reminders) in the absence of feared outcomes allows for recovery. Emotional processing is not directly observable; however, distress reduction[1] (in and over sessions) and change in posttraumatic cognitions may be indicators of effective processing. Although distress reduction was considered essential for corrective learning, empirical findings linking distress reduction to symptom improvement have been mixed (Cooper, Clifton, et al., 2017; Craske et al., 2008). Nevertheless, many current therapeutic procedures in PE are influenced by the assumption that distress reduction across repeated exposures indicates successful emotional processing, as reflected in session length, repetition of exposure exercises, the use of breathing exercises, and the use of exposure hierarchies. Throughout the PE treatment manual, therapists are instructed to monitor distress levels, to encourage their patients to continue exposure until their distress levels have decreased, and to move to more challenging exercises when distress levels during less challenging exercises have diminished.

Regarding changes in posttraumatic cognitions, EPT suggests that cognitions do not need to be explicitly addressed during exposure in order for them to change (Foa & McLean, 2016). For instance, someone who believes the world is completely dangerous may revise this belief after repeated in vivo exposures, like jogging alone in the park and experiencing that nothing bad happens, even if this belief was never directly addressed in therapy. A review of empirical studies shows that PE is related to decreases in posttraumatic cognitions and that this is related to PTSD symptom reduction (Brown, Belli, et al., 2019). These studies most often use the Posttraumatic Cognitions Inventory (PTCI; Foa et al., 1999) to measure posttraumatic cognitions about the self, world and self-blame. Findings on whether changes in posttraumatic cognitions temporally precede symptom reductions are, however, mixed (Brown, Belli, et al., 2019) and require further investigation.

*Inhibitory learning and retrieval model*

The premise of EPT that distress reduction is necessary for successful treatment has been questioned due to the inconsistent empirical findings (Craske et al.,

1 In EPT, this is often referred to as habituation, which involves a decrease in response to a stimulus after repeated exposure. Distress reduction, measured via subjective units of distress (SUDs), is commonly used to operationalize habituation. There is unclarity about what distress reduction precisely captures; it may reflect more than just the non-associative process of habituation. Throughout this dissertation, we therefore use 'distress reduction' to remain close to what is actually measured.

2008). The inhibitory learning and retrieval (ILR[2]) model of extinction offers a new perspective on the workings of exposure therapy, proposing refinements to the way it is conducted to enhance treatment efficacy (see Table 1 for an overview of these proposed refinements to exposure). This perspective has become increasingly influential in exposure therapy for anxiety and related disorders, including PTSD (Craske et al., 2008, 2014, 2022). The ILR model is based on classical conditioning paradigms, which posit that fear is acquired by the association of a conditioned stimulus (CS) with an inherently aversive, unconditioned stimulus (US), leading to a conditioned fear response (CR). In the context of PTSD, a trauma reminder (CS, e.g., knife) becomes associated with the traumatic experience (US, e.g., assault), triggering a fear response (CR). Repeated presentations of the CS in the absence of the US will lead to a reduction of the acquired fear response, a process called extinction[3]. Extinction is used in exposure therapy, where a patient is repeatedly exposed to innocuous but fear-provoking stimuli, in the absence of aversive outcomes. According to the ILR model, the original fear-excitatory associations (CS-US) are not fully erased or altered during extinction. Instead, a new, competing association is formed – one in which the CS no longer predicts danger (CS-noUS). This means the original fear excitatory association (CS-US) and the new inhibitory association (CS-noUS) coexist. Because the CS-US association is not erased, fear may return, also after apparent extinction. This would explain the return of fear that is sometimes seen after successful exposure therapy. Following the ILR model, exposure therapy should focus on developing new ***inhibitory associations*** that compete with initial fear-based associations and enhancing their retrievability to reduce the likelihood of fear returning. The effectiveness of exposure therapy thus depends on the strength and accessibility of the inhibitory associations.



2 The Inhibitory Learning and Retrieval model of extinction was first introduced as the Inhibitory Learning model of extinction (Craske et al., 2008, 2014) and is often referred to as Inhibitory Learning Theory (ILT) in earlier work, including some of our own. The model's name was later revised to include retrieval processes (Craske et al., 2022).

3 In earlier work, the terms extinction and habituation have occasionally been used interchangeably. However, extinction refers to an associative process characterized by a decrease in conditioned responding, whereas habituation is a non-associative process involving a reduction in responsiveness following repeated stimulus exposure.

**Table 1.** Strategies to enhance inhibitory learning (reproduced from Craske et al., 2014)

| Strategy | Description |
|---|---|
| Expectancy violation | Design exposures to violate specific expectations |
| Deepened extinction | Present two cues during the same exposure after conducting initial extinction with at least one of them |
| Reinforced extinction | Occasionally present the US during exposures |
| Variability | Vary stimuli and contexts |
| Remove safety behaviors | Decrease the use of safety signals and behaviors |
| Attentional focus | Maintain attention on the target CS during exposure |
| Affect labeling | Encourage the clients to describe their emotional experience during exposure |
| Mental reinstatement/ retrieval cues | Use a cue present during extinction or imaginally reinstate previous successful exposures |

Although there is overlap between EPT and the ILR model (see, for instance, Cooper et al., 2017), they highlight different mechanism variables. Craske et al. (2008, 2014) propose moving away from focusing on distress levels during exposure, suggesting instead a focus on expectancies to strengthen inhibitory learning. More specifically, in the context of PTSD, a patient needs to learn and remember that confrontation with trauma-related stimuli (CS) does not lead to their expected negative outcomes (e.g., 'I will be attacked', or 'I will go crazy'). Expectancy violation and expectancy changes are thus proposed to indicate successful learning. The focus should be on tolerating distress (i.e., 'I can handle it') to allow new learning, rather than attempting to reduce it. The retrievability of the inhibitory learning is enhanced by conducting exposure in a variety of contexts and with different stimuli. Table 2 provides an overview of EPT and ILR-informed exposure characteristics.

Although the ILR principles are based on a well-established empirically supported model (Craske et al., 2008, 2014; Pittig et al., 2016), studies testing these principles in clinical practice, especially in patients with PTSD, are lacking (Jacoby & Abramowitz, 2016; Weisman & Rodebaugh, 2018). At the start of this dissertation, maximizing expectancy violation and incorporating variability were proposed as the primary guiding principles to enhance exposure efficacy (Weisman & Rodebaugh, 2018).

**Table 2.** Characteristics of EPT and ILR-based exposure

| | EPT exposure | ILR exposure |
|---|---|---|
| Rationale | Emotional processing | Inhibitory learning and retrieval |
| View on distress | Reduction (distress diminishes over time) | Tolerance (distress can be experienced and withstood) |
| Change indices | 1) WS distress reduction<br>2) BS distress reduction<br>3) Posttraumatic cognitions | 1) Threat expectancies |
| Structure of exposure | Gradual, focus on repetition | Variable, focus on maximizing expectancy violation |

*Note.* WS = within session; BS = between session.



**Violating expectancies**

Threat expectancies are beliefs about the likelihood that confronting a feared stimulus will lead to a negative outcome (e.g., "If I go out in the dark, I will be attacked"). New learning is thought to occur when there is a discrepancy between expectation and reality (Rescorla & Wagner, 1972). In other words, stronger expectancy violations lead to greater inhibitory learning. Following the ILR model, exposure should thus focus on maximally violating expectancies (Craske et al., 2014, 2022). Expectancies are distinct from posttraumatic cognitions emphasized in EPT, as expectancies refer to specific, concrete expectations formulated in an 'if-then' statement, whereas posttraumatic cognitions are more general beliefs about the self, others, and the world.

*Expectancy violation during exposure*

Emerging studies are investigating whether there is an association between expectancies and symptom improvement during exposure, as is one of the requirements for establishing a mechanism of change (Kazdin, 2009). A large study in a sample of mixed anxiety disorders showed that the extent to which threat expectancies change is associated with symptom improvement (Pittig et al., 2022). In patients with PTSD, threat expectancies (e.g., 'If I do the exposure, I will go crazy') have been found to decrease over the course of treatment (de Kleine et al., 2017), although these changes in expectancies were not associated with reductions in PTSD symptoms. This study used a standardized measure to assess expectancies, which may not have captured the threat expectancies most relevant to individual patients throughout treatment. Further research is needed to clarify the relationship

between threat expectancies and symptom improvement, and particularly which expectancies must be violated for change to occur.

*Manipulating expectancy violation*

Another way of examining whether expectancy violation drives symptom reduction, is by *promoting* (i.e., manipulating) expectancy violation through therapeutic procedures and assessing whether it affects outcomes. Designing exposure as a hypothesis-testing mini-experiment, thereby emphasizing expectancies and their non-occurrence, may promote expectancy violation, which in turn is thought to strengthen inhibitory learning and enhance treatment effects (Craske et al., 2014, 2022). Support for the idea that expectancy violation enhances exposure outcomes is often drawn from two pre-clinical studies. One study found that administering one trial of expectancy-disconfirming exposure every two days was equally effective compared to daily repeated trials of non-disconfirming exposure, which was interpreted as evidence that expectancy violation enhanced treatment effects (Baker et al., 2010). Another study showed that exposure that continued until expected aversive outcomes dropped below a credibility of 5% was more effective than exposure focused on distress reduction for individuals with elevated anxiety sensitivity (Deacon et al., 2013). It is still unclear whether emphasizing expectancies and their non-occurrence will enhance exposure outcomes for PTSD.

**Incorporating variability**

Incorporating variability, across both contexts and stimuli, is presumed to enhance the generalization and retrievability of the inhibitory associations, thereby optimizing treatment efficacy (Craske et al., 2014, 2022). This is based on research on (non-emotional) learning which suggests that variability enhances memory retrievability and promotes generalization (Bjork & Bjork, 1992, 2006). Variability is presumed to offset context renewal (i.e., the return of fear in a different context after previous successful extinction). In the context of exposure therapy, context variability refers to varying the situations or environments in which exposure occurs (e.g., in different rooms, places, or varying times a day). Variability might also refer to varying distress levels during exposure which serve as an internal context (e.g., conducting exposures while being relatively calm vs. highly distressed). Stimulus variability refers to varying the specific features of the feared stimulus during exposure (e.g., in vivo exposure to different men in various social settings).

*Variability during exposure*

Only a small number of studies have assessed the association between variability during exposure and symptom improvement. Some empirical evidence suggests

that more variable in-session distress levels during exposure is associated with better treatment outcomes in adults with public speaking anxiety and contamination anxiety (Culver et al., 2012; Kircanski et al., 2012). Whether more variable levels of distress precede symptom improvement is still unknown and has not yet been investigated in samples of patients with PTSD.

*Manipulating variability*

Several laboratory and pre-clinical studies have shown that exposure in varying contexts (i.e., context variability) results in less return of fear than exposure in a single context, both in spider-fearful and healthy participants (Bandarian-Balooch et al., 2015; Dunsmoor et al., 2014; Shiban et al., 2015). Similarly, using multiple stimuli during exposure (i.e., stimulus variability) has been linked to reduced return of fear in spider-fearful individuals (Shiban et al., 2015). However, the order of stimulus presentation, gradual versus variable, has not been found to affect exposure outcomes in adults with obsessional thoughts, although this study may have been underpowered (Jacoby et al., 2019). Again, it remains unclear whether increasing variability (either in contexts or stimuli) as a therapeutic strategy optimizes exposure outcomes for PTSD.



**Examining ILR principles in PTSD**

In conclusion, further research is needed to determine whether principles from the ILR model enhance exposure therapy. Some proposed ILR-strategies have been tested in pre-clinical samples (e.g., samples with elevated levels of symptoms), but not yet in samples of patients with PTSD. Moreover, the exploration of a comprehensive PTSD treatment protocol that integrates multiple of these strategies is warranted. Below, we illustrate a suggested application of ILR-based exposure using Charlotte's case vignette.

**Aims and outline of the dissertation**

The aims of this dissertation are to 1) further understand the underlying mechanisms of action of exposure therapy for PTSD, and 2) to assess whether we can enhance the efficacy of exposure for PTSD by manipulating treatment elements proposed to promote inhibitory learning. In this dissertation, data from a large treatment study were analyzed, and additional studies were conducted, comprising studies with both experimental and observational designs.

**Chapter 2** investigates whether changes in posttraumatic cognitions temporally precede changes in PTSD symptoms during PE in patients with DSM-5 defined PTSD following childhood abuse, using data from the IMPACT study. The IMPACT study is a randomized controlled trial (RCT) comparing the effectiveness of different PE

treatment deliveries in 149 patients with PTSD. Given the emphasis on cognitive shifts in both EPT and ILR models, further investigation is needed to clarify their role in symptom improvement. **Chapter 3** investigates whether in-session distress variability precedes PTSD symptom improvement, also using data from the IMPACT study. **Chapter 4** assesses whether explicitly focusing on expectancy violation leads to better exposure outcomes in patients with PTSD, using data from the OPENup RCT study. In this study, 60 patients with PTSD received one session of exposure therapy followed by a one-week follow-up assessment. Patients were randomized to either exposure with an explicit focus on expectancy violation or exposure where expectancies were not explicitly addressed. **Chapter 5** presents results of a single case experimental design, OPENup SCED, where we evaluated the applicability and effects of a comprehensive, ILR adapted exposure therapy in patients with PTSD. The study consists of two single case experimental design studies where 19 patients with PTSD were tracked daily over the course of treatment and three-month follow-up. Patients either received ILR-based exposure or EPT-based exposure. When conducting our experimental studies, we discovered that, despite growing interest, no validated measure existed for assessing concrete negative expectancies. **Chapter 6** assesses the psychometric properties of a measure we developed, called 'Threat Appraisal in PTSD Scale' (TAPS), that aims to assess concerns for concrete trauma-related negative outcomes. We collected data from 309 non-clinical participants and 125 patients with PTSD. **Chapter 7** contains a summary and discussion of the main findings in this dissertation, the strengths and limitations, clinical implications and recommendations for future research.

**A suggested application of ILR-based exposure in Charlotte's case**

Charlotte follows exposure treatment for her PTSD symptoms based on ILR principles. In her first session, after having received psycho-education on PTSD and exposure therapy, Charlotte and her therapist identified her greatest fears when faced with trauma reminders. Charlotte was most afraid that someone would assault her again ('If I go jogging by myself, I will be assaulted again', 90% credibility). She also mentioned that she feared she would be unable to tolerate the distress she feels when thinking about the event ('If I think about the event, I will go crazy', which she further specified as being 'unable to hold a conversation and stand on her feet', 80% credibility). Exposure exercises (in vivo and imaginal) were designed as hypothesis testing experiments aimed to challenge these expectations. Charlotte and her therapist paid specific attention to elements that affect the likelihood of the feared outcome (i.e., safety signals). During exposure, she optimally tested her feared outcome by removing these safety signals or adding elements that increased the likelihood of the feared outcome. The exposure exercises followed a somewhat random order, i.e., they did not follow a gradual approach from least to most distressing. This would also allow Charlotte's distress levels to show a more variable pattern. Situations where Charlotte felt the feared outcomes were most likely to happen were prioritized (e.g., 'going jogging by myself without my phone') to maximize expectancy violation. Exposure was continued or repeated until the credibility of Charlotte's expectancies went down. After each exercise, her therapist asked Charlotte whether her feared outcome occurred and what she learned from this. Charlotte was instructed to practice her exposure exercises in different places and situations (e.g., at home, at varying times of the days). Charlotte's therapist also switched treatment rooms throughout the treatment and their appointments varied over the week.

# Chapter 2

# Changes in trauma-related cognitions predict subsequent symptom improvement during prolonged exposure in patients with childhood abuse-related PTSD

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## Abstract

Change in negative posttraumatic cognitions is a proposed mechanism through which Prolonged Exposure (PE) leads to symptom reduction of posttraumatic stress disorder (PTSD). A strong case for posttraumatic cognitions as a change mechanism in PTSD treatment can be made by establishing temporal precedence of change in cognitions. The current study examines the temporal relationship between change in posttraumatic cognitions and PTSD symptoms during PE, using the Posttraumatic Cognitions Inventory (PTCI). Patients with DSM-5 defined PTSD following childhood abuse (*N* = 83) received a maximum of 14–16 sessions of PE. Clinician-rated PTSD symptom severity and posttraumatic cognitions were assessed at baseline, week 4, 8, and 16 (post-treatment). Using time-lagged mixed effect regression models, we found that posttraumatic cognitions predicted subsequent PTSD symptom improvement. Notably, when using the items of an abbreviated version of the PTCI (PTCI-9), we found a mutual relationship between posttraumatic cognitions and PTSD symptom improvement. Crucially, the effect of change in cognitions on PTSD symptom change was greater than the reverse effect. The current findings corroborate change in posttraumatic cognitions as a change process during PE, but cognitions and symptoms cannot be completely separated. The PTCI-9 is a short instrument that appears suitable to track cognitive change over time.

*Keywords:* Posttraumatic stress disorder, Posttraumatic cognitions, Prolonged exposure therapy, Mechanisms of change

## Introduction

Negative posttraumatic cognitions have a central position in theoretical models of the development and maintenance of posttraumatic stress disorder (PTSD; (Ehlers & Clark, 2000; Rauch & Foa, 2006). Negative cognitions about the self (e.g., "I am weak" or "I am inadequate") and the world ("The world is a dangerous place") are thought to induce a sense of current threat, accompanied by intrusions, heightened arousal, and other emotions. Strategies to control this sense of threat (such as suppression of thoughts and feelings or avoiding situations or places) may alleviate symptoms in the short term but maintain negative cognitions, and thereby PTSD symptoms, in the long term. Many empirical studies have shown that negative posttraumatic cognitions are positively related to PTSD symptom severity (see for a meta-analysis Gómez de La Cuesta et al., 2019). Furthermore, prospective studies have indicated that negative posttraumatic cognitions predict later PTSD symptom severity (Dekel et al., 2013; Dunmore et al., 2001; Ehring et al., 2008; Shahar et al., 2013). Interestingly, one of the changes in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013) was the inclusion of 'persistent negative beliefs about oneself, others or the world' as a symptom criterion (Friedman, 2013). Recent network studies provide preliminary evidence that negative alterations in cognitions and mood form a central symptom cluster of PTSD which has strong connections to the other PTSD symptoms, such as re-experiencing or avoidance symptoms (Bartels et al., 2019; McBride et al., 2020). Given these findings, negative posttraumatic cognitions are important targets in the treatment of PTSD.

Prolonged exposure therapy (PE) is one of the treatments of choice for PTSD (Lewis et al., 2020; Mavranezouli et al., 2020; McLean et al., 2022). During PE, patients are repeatedly confronted with trauma-related stimuli they typically avoid, both trauma-related memories (imaginal exposure) and trauma-related objects and situations (in vivo exposure). Although the effectiveness of PE has been well established, less is known about the mechanisms that drive symptom reduction. Identifying these processes (i.e., mechanisms of change) may inform efforts to optimize treatment efficacy. Change in negative posttraumatic cognitions has been proposed to be a mechanism of change for a range of evidence-based trauma-focused treatments, including PE (Cooper, Clifton, et al., 2017; Kangaslampi & Peltonen, 2022; Sripada et al., 2016; Zalta, 2015). Many studies have shown that PE reduces negative trauma-related cognitions and concurrently improves PTSD symptoms (see for a review, Brown et al., 2019)

If negative trauma-related cognitions are indeed a change mechanism during PE, cognitions and symptoms need to not only be related, but cognitive change

needs to precede symptom change (Kazdin, 2007; Sripada et al., 2016). Establishing a timeline requires repeated assessments of the proposed mechanism and the treatment outcome measures; only then can temporal precedence be determined. The evidence for the temporal sequence of change in posttraumatic cognitions and symptoms during PE is not unequivocal. Some studies found that PTSD symptom alleviation was preceded by reductions in negative trauma-related cognitions and not vice versa (Cooper, Zoellner, et al., 2017; McLean, Yeh, et al., 2015; Zalta et al., 2014), but other studies found that cognitions and symptoms mutually influenced each other (Kumpula et al., 2017; McLean, Su, et al., 2015; Rauch et al., 2021). Various treatments were given alongside or in comparison with PE. Populations of these studies also differed (e.g., military veterans with PTSD, women with PTSD). However, none of these differences seem to be able to explain these discrepant findings and possible causes for these discrepancies should be further investigated.

All of the previously mentioned studies on the temporal relationship between posttraumatic cognitions and symptoms during PE used the Posttraumatic Cognitions Inventory (PTCI; Foa et al., 1999) to assess negative trauma-related cognitions. With 36 items, the PTCI may be considered a lengthy measure which is inconvenient for repeated assessments due to higher patient and therapist/researcher burden. Recently, a shorter version of the PTCI consisting of 9 items (PTCI-9; Wells et al., 2019) was developed and its psychometric properties were tested within different samples, such as trauma-exposed undergraduates, military veterans, and female civilians (Wells et al., 2019; Whiteman et al., 2022). Although the PTCI-9 appears to be a valid and reliable measure, it has not yet been used to track cognitive changes during treatment. As noted above, a shorter measure may be especially useful in the context of repeated assessment during treatment, as the burden for tracking these cognitions is lower, whilst still giving clinicians insights into the content and change of specific cognitions.

The aim of the present study was to examine the temporal relationship between changes in negative trauma-related cognitions and PTSD symptom change during PE in patients with PTSD related to childhood abuse. All prior studies in this field have investigated the relationship between PTCI changes and DSM-IV defined PTSD. In the current study, participants met DSM-5 defined PTSD criteria, and the Clinician Administered PTSD Scale for DSM-5 (CAPS-5; Boeschoten et al., 2018) was used for the assessment of symptom change. We expected that a decrease in trauma-related cognitions would lead to a subsequent decrease in clinician-rated PTSD symptoms but not vice versa. Additionally, we carried out the same analyses but instead used the nine items of the short version of the PTCI (PTCI-9; Wells et al., 2019), derived from the full PTCI. We expected the same pattern of findings. Furthermore, we carried out a sensitivity analysis in which we repeated the main analysis, but now

after excluding the symptom cluster 'negative changes in cognitions and mood' from the CAPS-5 total score. Given that the conceptualization of PTSD has been broadened in the DSM-5 to include this criterion, this sensitivity analysis tests whether any relationship between trauma-related cognitions and PTSD symptom change holds when the conceptual overlap is minimized.

## Methods

### Design

We use data from the IMPACT study, a multicenter randomized controlled trial that compared PE, intensive PE (iPE), and phase-based therapy (PBT) in a sample of childhood abuse-related posttraumatic stress disorder (CA-PTSD). The study was approved by the Medical Ethical Committee of Leiden University Medical Center (NL57984.058.16) and the study trial is registered at the ClinicalTrials.gov registry, number NCT03194113. For more details about the design and the main outcomes, we refer to the published study protocol and the primary outcome paper (Oprel et al., 2018, 2021).

### Participants

All participants met the following inclusion criteria: (1) age 18–65, (2) diagnosis of PTSD established with the Clinician Administered PTSD Scale for DSM-5 (CAPS-5; Boeschoten et al., 2018) with at least moderate severity of PTSD symptoms (CAPS-5 score ≥ 26), and at least one specific memory of the traumatic event, (3) an index traumatic event related to sexual abuse and/or physical abuse that occurred before the age of 18 years old and was committed by a primary caretaker or an authority figure and (4) proficiency in the Dutch language. Exclusion criteria were: (1) involvement in a compensation case or legal procedures concerning admission or stay in The Netherlands, (2) pregnancy, (3) severe non-suicidal self-injury (NSSI) which required hospitalization during the past three months, (4) severe suicidal behavior: a suicide attempt during the past three months or acute suicidal ideations with serious intent to die with a specific plan for suicide and preparatory acts, (5) severe disorder in the use of alcohol or drugs in last three months, (6) cognitive impairment (estimated IQ < 70), (7) changes in psychotropic medication in the two months before inclusion, and (8) engagement in any current psychological treatment. For the current paper, we only used data from participants who were randomly allocated to the PE or iPE condition ($n$ = 99, see also Hoeboer et al., 2022). Participants in these conditions completed measures of trauma-related cognitions and PTSD symptoms at multiple timepoints during PE treatment, allowing us to study temporal change. Although the PBT condition also included PE, trauma-

related cognitions and PTSD symptoms were only assessed once during PE. This precludes the study of temporality of cognitions and symptoms during PE within this condition. Therefore our primary analyses were conducted on the PE and iPE conditions. Moreover, participants who only had data on one measurement (i.e., only a baseline measurement [T0]; *n* = 17) were excluded from the analysis.

The final sample of our primary analyses consisted of 83 participants (18 male, 64 female, 1 other) between the ages of 20 and 60 years (*M* = 36.4, *SD* = 11.4). Thirty-two participants (61.4%) had at least one parent who was born in a non-Western country. The mean duration of PTSD was 16.0 years (*SD* = 12.1). Regarding the traumatic events, 63 participants (75.9%) experienced childhood sexual abuse, 50 participants (60.2%) experienced childhood physical abuse, 19 participants (22.9%) experienced adulthood sexual abuse and 25 participants (30.1%) experienced adulthood physical abuse. Forty-three (51.8%) were randomized to the PE condition and 40 participants (48.2%) to the iPE condition. For a complete description of the sample, see Oprel et al., 2021).

**Measures**

*Posttraumatic cognitions*

Posttraumatic cognitions were measured with the Dutch translation of the Posttraumatic Cognitions Inventory (PTCI; Foa et al., 1999; van Emmerik et al., 2006). The PTCI is a 36-item, self-report questionnaire, and each item is rated on a 7-point Likert scale that ranges from 1 (*totally agree*) to 7 (*totally disagree*). For the total score of the PTCI, sum scores of the answers to 33 items are used and scores range from 33 to 231. The PTCI was shown to have good internal reliability, test-retest reliability, and strong convergent and discriminant validity (Foa et al., 1999; van Emmerik et al., 2006). Evidence in favor of the three-factor structure of the PTCI (i.e., negative cognitions about the self, world, and self-blame) has been inconsistent, which questions the validity of these subscales (Beck et al., 2004; Hyland et al., 2015; Sexton et al., 2018; Whiteman et al., 2022). Therefore, we decided to use total scores only in the current study. Internal consistency of the PTCI in the current sample was good, both at baseline (Cronbach's α = 0.95, McDonald's ω = 0.95), and after four weeks (Cronbach's α = 0.96, McDonald's ω = 0.97), eight weeks (Cronbach's α = 0.97, McDonald's ω = 0.97), and 16 weeks (Cronbach's α = 0.97, McDonald's ω = 0.97).

We also calculated PTCI-9 total scores (Wells et al., 2019). The PTCI-9 consists of items 1, 7, 22, 23, 25, 27, 31, 33, and 36 of the PTCI. Item selection for the PTCI-9 was, among other things, based on the highest loading items within each subscale (Wells et al., 2019). PTCI-9 total scores are calculated by taking the mean of these nine items (vs. the sum in the original PTCI), with total scores ranging from 1 to 7. The PTCI-9 was not administered separately but calculated from the full version of the PTCI. The

33-item and the 9-item PTCI total scores at baseline (T0) had a strong, significant correlation ($r$ = 0.94, $p$ < .001). We also calculated the correlation between the PTCI-9 and the original PTCI without the nine items that were included in the PTCI, to control for the item overlap. This correlation was also strong and significant ($r$ = 0.89, $p$ < .001). Over the different timepoints, the strength of these correlations increased slightly. Internal consistency of the PTCI-9 in our sample was good, both at baseline (Cronbach's α = 0.83, McDonald's ω = 0.84), after four weeks (Cronbach's α = 0.88, McDonald's ω = 0.87), eight weeks (Cronbach's α = 0.88, McDonald's ω = 0.88), and 16 weeks (Cronbach's α = 0.90, McDonald's ω = 0.90).



*PTSD symptoms*

The severity of PTSD symptoms was measured with the Dutch version of the Clinician Administered PTSD Scale for DSM-5 (CAPS-5; Boeschoten et al., 2018). The CAPS-5 is a 20-item clinical interview covering DSM-5 PTSD diagnostic criteria and PTSD symptom severity during the past week. Scores range from 0 to 80, where lower scores indicate lower PTSD symptom severity. The internal consistency of the CAPS-5 total score at baseline in the current study was moderately high, Cronbach's α = 0.75. We also calculated a CAPS-5 score that excluded symptoms referring to negative posttraumatic cognitions (i.e., CAPS-5 total score – CAPS-5 item 9 and item 10), hereafter referred to as CAPS-5$^{excl9\text{-}10}$.

**Procedure**

Participants were recruited in two outpatient units specialized in the treatment of trauma-related disorders. Potential participants had to complete a baseline assessment in which they received detailed information about the treatment and in which eligibility was checked. Eligible participants were then randomized (1:1:1) to receive PE, iPE, or PBT.

In the PE condition, participants received 16 weekly sessions of 90 min of PE. In the iPE condition, participants received three 90-min PE sessions per week over four weeks (12 sessions in total), followed by two monthly booster sessions. Sessions in the iPE condition were alternately provided by two therapists for practical reasons. The same treatment manual was used for PE and iPE. The manual was based on the protocol by Foa et al. (2007). The first session consisted of psychoeducation on PTSD and the construction of a case conceptualization. The second to the last session consisted of imaginal exposure (repeatedly recounting the traumatic event) and exposure in vivo (repeatedly approaching trauma-related stimuli). As homework assignment, participants were instructed to listen to audiotapes of the imaginal exposure and to complete in vivo assignments during the week. All therapists in the study had to complete PE training and pass an exam with pilot patients.

Therapists also received weekly group supervision (supervisors: RAdK and AvM). Independent observers rated a random selection of the PE sessions (135 sessions; ~10% of all PE sessions) on treatment adherence based on the Dutch translation of the original adherence rater checklist scale. Protocol adherence was high (Mean session elements completed = 90%, *SD* = 18%). Measurements of the CAPS-5 and PTCI took place at baseline (T0), after four weeks (T1), after eight weeks (T2), and after 16 weeks (T3). At T3, data on the PTCI was available for 62 participants, and data on the CAPS-5 was available for 68 participants. The reasons for missed measures were diverse. Of the 21 participants who did not complete all measures, ten dropped out of therapy.

**Statistical analyses**

To increase comparability between the PTCI and PTCI-9 variables, we first standardized these scores. In the first analysis, we used a time-lagged mixed effect regression model with CAPS-5 scores (time point X) as the dependent variable and the autoregressive effect of CAPS-5 scores (time point X-1) and cross-lagged standardized PTCI scores (time point X-1) as the independent variables. In the second analysis, we used a time-lagged mixed effect regression model with standardized PTCI scores (time point X) as the dependent variable and the autoregressive effect of standardized PTCI scores (time point X-1) and cross-lagged CAPS-5 scores (time point X-1) as independent variables.

For the first sensitivity analysis, we carried out the same analyses, but now with the PTCI-9 instead of the PTCI. To control for conceptual overlap between the predictor and outcome variable, we also re-ran these analyses, but now excluding the symptoms referring to negative cognitions from the PTSD symptom total score (i.e., items 9 and 10 of the CAPS-5). Finally, we checked whether the effect of PTCI scores on subsequent PTSD symptom reduction was different between conditions by adding condition and the interaction between condition and cross-lagged PTCI as independent variables in the model. We checked this with a similar model for the reversed effect of PTSD symptoms on subsequent PTCI scores. All models were tested with maximum likelihood estimation using the lme4 package (v1.1-28; Bates et al., 2015) in R (Version 4.0.1). Maximum likelihood estimation can handle missing data and can take the effect of dropout into account. The alpha level was set at 0.05 (two-sided).

The data-analysis plan of this study was registered at OSF (Center for Open Science; osf.io/qg9zv). Note that we had to change our statistical approach from a dynamic panel model to a mixed effect regression model due to convergence issues of the dynamic panel model. We have not made changes to the dependent and independent variables in the models.

Based on peer-review, we conducted additional post-hoc analyses including the PBT condition. All information related to these additional analyses is included in Appendix A of this chapter.

## Results

### Descriptives

We tested baseline differences between the participants who completed all measures ($n$ = 62) and those who did not ($n$ = 21). The two groups did not significantly differ on age, $t(81) = 1.42$, $p = .160$, or gender, $\chi 2\ (2) = 3.13$, $p = .209$. The group who completed all measures scored significantly lower on the CAPS-5 at baseline ($M_{T0}$ = 39.5, $SD_{T0}$ = 8.4) compared to the group who did not ($M_{T0}$ = 44.4, $SD_{T0}$= 9.5), $t(81) = 2.23$, $p = .028$. Furthermore, the group who completed all measures also scored significantly lower on the PTCI at baseline ($M_{T0}$= 129.1, $SD_{T0}$ = 36.6) compared to the group who did not ($M_{T0}$= 152.6, $SD_{T0}$= 40.1), $t(81) = 2.47$, $p = .016$.

CAPS-5 scores decreased over the course of treatment ($M_{T0}$ = 40.7, $SD_{T0}$= 8.9; $M_{T3}$ = 17.3, $SD_{T3}$ = 15.5). Scores of the PTCI ($M_{T0}$ = 135.1, $SD_{T0}$ = 38.7; $M_{T3}$ = 102.2, $SD_{T3}$ = 44.6) and items of the PTCI-9 ($M_{T0}$ = 3.8, $SD_{T0}$ = 1.2; $M_{T3}$ = 2.9, $SD_{T3}$ = 1.4) also decreased over the course of treatment. See Table 1 for more details.

**Table 1.** Descriptive information on PTCI, PTCI-9, and CAPS-5 measures by each measurement timepoint.

| | | PTCI | PTCI-9 | | CAPS-5 |
|---|---|---|---|---|---|
| | $n_{PTCI}$ | *M (SD)* | *M (SD)* | $n_{CAPS}$ | *M (SD)* |
| T0 | 83 | 135.1 (38.7) | 3.8 (1.3) | 83 | 40.7 (8.9) |
| T1 | 81 | 124.1 (45.2) | 3.6 (1.4) | 81 | 29.6 (15.1) |
| T2 | 73 | 114.5 (45.8) | 3.3 (1.4) | 75 | 23.5 (16.2) |
| T3 | 62 | 102.2 (44.6) | 2.9 (1.4) | 68 | 17.3 (15.5) |

*Note.* $n_{PTCI}$ = the number of participants who have completed the Posttraumatic Cognition Inventory; PTCI = the original Posttraumatic Cognitions Inventory; PTCI-9 = items of the short version of the Posttraumatic Cognitions Inventory; $n_{CAPS}$ = the number of participants who have completed the Clinician Administered PTSD Scale for DSM-5; CAPS-5 = total score of the Clinician Administered PTSD Scale for DSM-5; Following the scale instructions, total scores of the PTCI-33 are calculated by *summing* 33 items whereas total scores of the PTCI-9 are calculated by *averaging* 9 items.

### Mixed regression models of posttraumatic cognitions and PTSD symptom change

The results of the mixed effect regression models can be found in Table 2. We first assessed the autoregressive effect of CAPS-5 and the cross-lagged effect of the standardized PTCI on CAPS-5. We found that both the auto-regressive effect, $b$ = 0.49, $SE$ = 0.08, $t$ = 6.28, $p$ < .001, Cohen's $d$ = 0.96, and the cross-lagged effect, $b$ = 4.27, $SE$ = 1.14, $t$ = 3.75, $p$ = < .001, Cohen's $d$ = 0.70, were significant. In other words, more negative posttraumatic cognitions at timepoint X-1 were related to a smaller reduction in PTSD symptoms at timepoint X. This effect did not differ for PE compared to iPE, $b$ = 0.27, $SE$ = 0.83, $t$ = 0.31, $p$ = .750. The reversed effect of CAPS-5 on the next measurement's PTCI was not significant, $b$ = 0.01, $SE$ = 0.00, $t$ = 1.61, $p$ = .109. This effect also did not differ for PE compared to iPE, $b$ = 0.04, $SE$ = 0.09, $t$ = 0.46, $p$ = .647.

**Table 2.** Time-lagged mixed effect models with cognitions and change in symptoms

| Model and variable | B | *SE* | *t* | *p* | *d* |
|---|---|---|---|---|---|
| Predicting CAPS-5 from time-lagged PTCI | | | | | |
| Intercept | 9.40 | 4.03 | 2.33 | .021 | |
| Time | -.47 | 1.10 | -0.43 | .668 | -0.11 |
| CAPS-5 autoregression | 0.49 | 0.08 | 6.28 | <.001 | 0.96 |
| Lagged PTCI | 4.27 | 1.14 | 3.75 | <.001 | 0.70 |
| Predicting PTCI from time-lagged CAPS-5 | | | | | |
| Intercept | -0.43 | 0.21 | -2.03 | .043 | |
| Time | 0.01 | 0.06 | 0.25 | .801 | 0.05 |
| PTCI autoregression | 0.79 | 0.06 | 14.23 | <.001 | 2.27 |
| Lagged CAPS-5 | 0.01 | 0.00 | 1.61 | .109 | 0.25 |

*Note.* CAPS-5 = total score of the Clinician Administered PTSD Scale for DSM-5; PTCI = the original Posttraumatic Cognitions Inventory.

### Sensitivity analyses

Using the PTCI-9 as the independent variable, we found that the PTCI-9 significantly predicted subsequent CAPS-5 scores, $b$ = 4.30, $SE$ = 1.02, $t$ = 4.22, $p$ < .001, Cohen's $d$ = 0.79. The reversed effect of CAPS-5 on the next measurement's PTCI-9 was also significant, albeit with a smaller effect size, $b$ = 0.01, $SE$ = 0.00, $t$ = 2.54, $p$ = .012, Cohen's $d$ = 0.39.

Using the PTCI as the independent variable and CAPS-5$^{excl9\text{-}10}$ as the dependent variable, we found that the PTCI significantly predicted subsequent CAPS-5$^{excl9\text{-}10}$ scores, $b$ = 3.50, $SE$ = 0.99, $t$ = 3.52, $p$ < .001, Cohen's $d$ = 0.64. The reverse effect,

CAPS-5$^{excl9-10}$ predicting PTCI, was not significant, $b$ = 0.01, $SE$ = 0.00, $t$ = 1.72, $p$ = .087. The results of these sensitivity analyses can be found in Table 3.

**Table 3.** Sensitivity analyses

| Model and variable | B | *SE* | *t* | *p* | *d* |
|---|---|---|---|---|---|
| Predicting CAPS-5 from time-lagged PTCI-9 | | | | | |
| Intercept | 8.97 | 3.84 | 2.34 | .020 | |
| Time | -0.51 | 1.09 | -0.47 | .668 | -0.11 |
| CAPS-5 autoregression | 0.50 | 0.07 | 7.21 | <.001 | 1.11 |
| Lagged PTCI-9 | 4.30 | 1.02 | 4.22 | <.001 | 0.79 |
| Predicting PTCI-9 from time-lagged CAPS-5 | | | | | |
| Intercept | 0.46 | 0.21 | -2.19 | .030 | |
| Time | -0.01 | 0.06 | -0.09 | .926 | -0.02 |
| PTCI-9 autoregression | 0.76 | 0.05 | 14.68 | <.001 | 2.27 |
| Lagged CAPS-5 | 0.01 | 0.00 | 2.54 | .012 | 0.39 |
| Predicting CAPS-5$^{excl9-10}$ from time-lagged PTCI | | | | | |
| Intercept | 6.97 | 3.59 | 1.94 | .521 | |
| Time | -0.16 | 1.02 | -0.16 | .848 | -0.04 |
| CAPS-5$^{excl9-10}$ autoregression | 0.51 | 0.08 | 6.82 | <.001 | 1.05 |
| Lagged PTCI | 3.50 | 0.99 | 3.52 | <.001 | 0.64 |
| Predicting PTCI from time-lagged CAPS-5$^{excl9-10}$ | | | | | |
| Intercept | -0.44 | 0.21 | -2.12 | .035 | |
| Time | 0.02 | 0.06 | 0.29 | .776 | 0.06 |
| PTCI autoregression | 0.80 | 0.01 | 14.98 | <.001 | 2.40 |
| Lagged CAPS-5$^{excl9-10}$ | 0.01 | 0.00 | 1.72 | .087 | 0.27 |

*Note.* CAPS-5 = total score of the Clinician Administered PTSD Scale for DSM-5; CAPS-5$^{excl9-10}$= total score of the Clinician Administered PTSD Scale for DSM-5 minus item 9 and item 10; PTCI-9 = the short version of the Posttraumatic Cognitions Inventory; PTCI = the original Posttraumatic Cognitions Inventory.

## Discussion

The present study aimed to assess the temporal relation between posttraumatic cognitions and PTSD symptom improvement during PE in patients with PTSD following childhood abuse. We primarily tested whether a change in trauma-related cognitions (full version PTCI) predicted subsequent DSM-5 defined PTSD symptom change (CAPS-5). Secondly, we tested whether a change in trauma-related cognitions, as measured with the items of an abbreviated version of the trauma-

related cognitions questionnaire (PTCI-9), predicted PTSD symptom change. Our results indicate that the reduction of negative trauma-related cognitions indeed precedes PTSD symptom change. When using the items of the PTCI-9, we found a bidirectional relationship, but notably, the effect of cognitions on symptoms was greater than the reverse (i.e., the effect of symptoms on cognitions). The interpretation of our findings did not change when we controlled for the conceptual overlap between trauma-related cognitions and DSM-5 defined PTSD symptoms.

As hypothesized and in line with cognitive theories (Ehlers & Clark, 2000; Rauch & Foa, 2006), we found that posttraumatic cognitions predicted subsequent PTSD symptom reduction. This finding is in line with earlier work (Cooper, Zoellner, et al., 2017; Kumpula et al., 2017; McLean et al., 2019; McLean, Su, et al., 2015; McLean, Yeh, et al., 2015; Rauch et al., 2021; Zalta et al., 2014). When we used the full version of the PTCI to measure negative posttraumatic cognitions, we did not find the reversed effect, i.e., PTSD symptoms did not predict subsequent changes in cognitions. Some earlier work also found a unidirectional temporal relationship between PTSD cognitions and symptoms (Cooper, Zoellner, et al., 2017; McLean, Yeh, et al., 2015; Zalta et al., 2014). Given that temporal precedence is one of the requirements for establishing a mechanism of change (Kazdin, 2007), our findings provide support for cognitions as a change mechanism. However, we found a bidirectional temporal relationship between PTSD cognitions and symptoms when we measured cognitions using the items from the PTCI-9. A bidirectional temporal relationship was also found in some earlier studies (Kumpula et al., 2017; McLean, Su, et al., 2015; Rauch et al., 2021), suggesting that cognitions and symptoms mutually influence each other. Of note, when looking at the effect sizes of our analyses, we see a similar pattern across our analyses: the effect of posttraumatic cognitions on subsequent PTSD symptoms is almost twice as large as the reversed effect. We thus find evidence that change in cognitions predict subsequent symptom reduction, but it is difficult to disentangle posttraumatic cognitions as a change mechanism from the overarching PTSD symptomatology.

We extend earlier work by also testing the predictive value of the items from an abbreviated version of the PTCI, i.e., the PTCI-9. This shortened instrument could promote the tracking of cognitive changes during trauma-focused treatment in routine clinical care. Given the very high correlation between the PTCI and the PTCI-9, the PTCI-9 appears to be a suitable alternative to the PTCI. That said, whether the temporal relationship between cognitions and symptoms was uni- or bidirectional depended on the version of the PTCI. This difference cannot be easily explained. The broader range of items in the PTCI appear to be less affected by PTSD symptom change. Importantly, our findings imply that it matters how cognitions are measured and future research should be aware of this. More work with the PTCI-9 is warranted

to see how findings with this instrument relate to findings when the full version is used and to validate its use in PTSD research, specifically in treatment studies.

It is important to note that change in negative posttraumatic cognitions is not proposed to be a mechanism of change that is specific to PE. Any treatment that accomplishes change in trauma-related cognitions proposedly leads to reductions in PTSD symptoms (Rauch & Foa, 2006). Indeed, empirical studies show that changes in trauma-related cognitions are relevant in other treatments too, such as cognitive (processing) therapy, written exposure therapy, present-centered therapy, and pharmacotherapy (Gobin et al., 2018; Kleim et al., 2013; Lee et al., 2021; McLean et al., 2019; Scher et al., 2017; Schumm et al., 2015). This is further supported by our exploratory analyses which included the PBT condition (STAIR followed by PE). Change in cognitions predicted subsequent changes in PTSD symptoms across all conditions and we found no significant interaction between treatment conditions and the effect of cognitions on PTSD symptoms.



Our current findings underline the importance of cognitive change for symptom alleviation, but future work should address whether promoting cognitive changes could improve treatment efficacy. Interestingly, in Inhibitory Learning Theory (ILT) it is proposed that maximizing expectancy violation could improve exposure efficacy (Craske et al., 2008, 2014, 2022). Expectancy violation (or prediction error) is thought to be crucial for the learning of inhibitory non-threat associations and refers to a mismatch between the expectancy of an aversive outcome and its non-occurrence. Translated to exposure therapy for PTSD, testing specific expectancies (e.g., "If I think back at the trauma, I will lose control and hurt someone") and directing attention to the non-occurrence of this outcome might promote new learning. Although related, expectancy violation and change in posttraumatic cognitions might be distinct processes. Repeated violation of specific expectancies is thought to lead to a change in the more generalized beliefs (Knowles & Tolin, 2022). For example, repeated violation of the expectancy to lose control upon exposure to the trauma memory may lead to change in the more general belief that one is weak or inadequate. Whether the application of ILT principles indeed improves the efficacy of exposure therapy for PTSD remains to be established (de Kleine et al., 2017). Future works should address whether promoting cognitive changes within sessions (i.e., expectancy violation) can improve treatment efficacy in PTSD. Moreover, aside from tracking changes in both expectancies and beliefs, it would be interesting to investigate established change mechanisms concurrently, such as belief change and between-session habituation (Cooper, Clifton, et al., 2017). Studies with larger sample sizes are necessary for this.

The current study is not without its limitations. Firstly, we did not measure our variables at the session level, but rather at a 4-week interval during treatment. Using

more frequent assessments (such as at the session level) increases the accuracy of the timeline between the proposed mechanism and the proposed outcome (see also Hagenaars et al., 2010). More frequent assessments would have been especially useful in the iPE condition. Secondly, due to a lack of measurement timepoints, our statistical analyses were not able to separate within-person from between-person effects, while this is important when investigating mechanisms of change (Falkenström et al., 2020). In the context of negative trauma-related cognitions and PTSD symptoms, this means that change in posttraumatic cognitions affects change in PTSD symptoms, within one person. Between-person effects demonstrate that, on average, those with more change in negative trauma-related cognitions have more change in PTSD symptoms, but do not clarify whether a change in trauma-related cognitions is related to fluctuations in PTSD symptoms over time within a patient. Dynamic panel models can distinguish within-from between-person effects and we have used this approach previously to investigate within- and between-session habituation as PE's mechanisms of change (Hoeboer et al., 2022). We found that, when looking at within-person effects, within-session habituation was predictive of PTSD symptom reduction, contrary to what previous studies using combined within- and between-effect statistical approaches found (for a review, see Asnaani et al., 2016). The use of the short PTCI-9 may increase the feasibility of more frequent assessments of cognitions and facilitate taking the crucial next step of separating within-from between-person effects. A third limitation is that participants in our study did not actually fill out the PTCI-9. To calculate the PTCI-9 score, we used the necessary items from the administered PTCI. We cannot exclude the possibility that participants would have filled out the items differently if only those nine items had been administered. Finally, a limitation of the current study is the missing data at later timepoints. Although the reasons for missing data varied, it was not completely random (we found significant differences in PTSD symptomatology and posttraumatic cognitions at baseline between participants who completed all measures and those who did not), which limits generalizability.

The strengths of this study include the fact that we investigated the temporality of cognitive change on PTSD symptoms in the context of a randomized clinical trial with few exclusion criteria (Oprel et al., 2021). This resulted in a culturally diverse, multimorbid sample with PTSD following childhood abuse, which serves the ecological validity of the current findings. No previous study has assessed the temporality of posttraumatic cognitions and symptom reduction in a sample of patients with PTSD related to childhood abuse specifically. These are patients who have often experienced multiple traumas early in life which affects how they view themselves and the world. Given their chronicity, these negative cognitions may be more difficult to treat. Yet, here we show that even in this early-traumatized sample

cognitions change during PE and predict symptom reduction. Finally, this study is the first on this topic that assessed PTSD using DSM-5 criteria.

To conclude, negative trauma-related cognitions predict subsequent PTSD symptom reduction during PE, also when taking the conceptual changes made in the DSM-5 into account. Negative trauma-related cognitions can also be tracked with an abbreviated version of the PTCI. Symptoms and cognitions might mutually affect one another and more research is necessary to further elucidate the temporal relation between cognitive changes and symptom alleviation. Nevertheless, the findings confirm the importance of posttraumatic cognitions for achieving PTSD symptom improvement as changes in cognitions may indicate subsequent symptom reduction. As such, clinicians are encouraged to track cognitions throughout treatment, as this can inform them on treatment effectiveness and assist in tailoring interventions (e. g., repeated exposure in vivo assignments to challenge a specific cognition). We highlight the need to assess negative posttraumatic cognitions on a session level which can be accomplished more easily with the use of short measures such as the PTCI-9.

# Appendix A

## Additional analyses including the PBT condition (*N* = 129)

## Introduction

**Aim:**
Change in posttraumatic cognitions is thought to be a mechanism of change for a range of (trauma-focused) treatments, and thus not to be specific for PE. Therefore we carried out additional analyses, including participants from the PBT condition. The aim of these additional analyses were to examine the temporal relationship between changes in negative trauma-related cognitions in PTSD symptom change during trauma-focused therapy (Prolonged Exposure (PE), intensive Prolonged Exposure (iPE) and, Skills Training in Affective and Interpersonal Regulation (STAIR) followed by PE (PBT)). We expected similar outcomes to the outcomes of our main analyses. Furthermore, we expected to not find differences between treatment conditions.

## Methods

NB. This section only contains information that is necessary to understand our additional analyses. All other methods are described in our main manuscript.

**Participants**
The IMPACT study consisted of 149 participants diagnosed with PTSD following childhood abuse. Full in- and exclusion criteria can be found in the main manuscript. For the additional, post-hoc, analyses we used data from participants in all three conditions. Participants who only had data on one assessment (i.e., only a baseline measurement [T0]; *n* = 20) were excluded from the analyses, as temporality cannot be assessed with one timepoint. The final sample of our additional analyses consisted of 129 participants.

**Phase-based treatment**
The phase-based treatment (PBT) was delivered in 8 weekly 60-minute STAIR sessions, followed by 8 weekly 90-minute PE sessions. The STAIR sessions followed the protocol by Levitt and Cloitre (2005). The first four STAIR sessions focused on improving emotion regulation strategies and the following for STAIR sessions focused on improving interpersonal skills. The PE sessions in this conditions were

similar to the PE sessions of the other conditions (see main manuscript). In the PBT condition, one therapist was assigned to each patient.

**Statistical analyses**

We repeated all our primary analyses, only now with our sample including the PBT condition (*N* = 129). See main manuscript for details.

## Results

See Table A1 for descriptive information on CAPS-5 and PTCI across timepoints. Both the CAPS-5 and the PTCI decreased over the course of treatment.



**Table A1.** Descriptive information on PTCI, PTCI-9 and CAPS-5 measures by each measurement timepoint, including the PBT condition

| | | PTCI | PTCI-9 | | CAPS-5 |
|---|---|---|---|---|---|
| | $n_{PTCI}$ | *M* (*SD*) | *M* (*SD*) | $n_{CAPS}$ | *M* (*SD*) |
| T0 | 129 | 140.3 (37.3) | 4.0 (1.2) | 129 | 41.5 (9.3) |
| T1 | 127 | 132.4 (43.9) | 3.8 (1.4) | 127 | 31.9 (14.5) |
| T2 | 115 | 123.1 (45.7) | 3.5 (1.5) | 117 | 27.3 (15.8) |
| T3 | 96 | 107.9 (46.4) | 3.1 (1.5) | 104 | 18.0 (15.1) |

*Note.* $n_{PTCI}$ = the number of participants who have completed the Posttraumatic Cognition Inventory; PTCI = the original Posttraumatic Cognitions Inventory; PTCI-9 = items of the short version of the Posttraumatic Cognitions Inventory; $n_{CAPS}$ = the number of participants who have completed the Clinician Administered PTSD Scale for DSM-5; CAPS-5 = total score of the Clinician Administered PTSD Scale for DSM-5; Following the scale instructions, total scores of the PTCI-33 are calculated by *summing* 33 items whereas total scores of the PTCI-9 are calculated by *averaging* 9 items.

**Additional mixed effect regression models, including the STAIR condition.**

Including the PBT condition, we first predicted the CAPS-5 from the CAPS-5 autoregression and the lagged standardized PTCI. We found that both the auto-regressive effect, $b = 0.47$, $SE = 0.06$, $t = 7.73$, $p < .001$, Cohen's $d = 1.12$, and the cross-lagged effect, $b = 4.59$, $SE = 0.85$, $t = 5.38$, $p = < .001$, Cohen's $d = 1.04$, were significant. This effect did not differ across conditions, $b = -0.41$, $SE = 0.79$, $t = -0.51$, $p = .610$. The reversed effect of CAPS-5 on next measurement's PTCI was not significant, $b = 0.00$, $SE = 0.00$, $t = 1.18$, $p = .241$. This effect also did not differ across conditions, $b = 0.00$, $SE = 0.00$, $t = -0.34$, $p = .735$. Outcomes can be found in Table A2. The interpretation of these outcomes does not differ from the main outcomes.

**Table A2.** Time-lagged mixed effect models with cognitions and change in symptoms, including PBT condition (N = 129)

| Model and variable | B | *SE* | *t* | *p* | *d* |
|---|---|---|---|---|---|
| Predicting CAPS-5 from time lagged PTCI | | | | | |
| Intercept | 13.88 | 3.23 | 4.30 | <.001 | |
| Time | -2.00 | 0.89 | -2.26 | .026 | -0.42 |
| CAPS-5 autoregression | 0.47 | 0.06 | 7.73 | <.001 | 1.12 |
| Lagged PTCI | 4.59 | 0.85 | 5.38 | <.001 | 1.04 |
| Predicting PTCI from time lagged CAPS-5 | | | | | |
| Intercept | -0.22 | 0.18 | -1.23 | .218 | |
| Time | -0.06 | 0.05 | -1.14 | .257 | -0.19 |
| PTCI autoregression | 0.85 | 0.04 | 19.55 | <.001 | 2.45 |
| Lagged CAPS-5 | 0.00 | 0.00 | 1.18 | .241 | 0.14 |

*Note.* CAPS-5 = total score of the Clinician Administered PTSD Scale for DSM-5; PTCI = the original Posttraumatic Cognitions Inventory.

**Sensitivity analyses, including the STAIR condition**

Using the PTCI-9 as independent variable, we found that the PTCI-9 significantly predicted subsequent CAPS-5 scores, $b = 4.18$, $SE = .80$, $t = 5.20$, $p < .001$, Cohen's $d = 0.95$. The reversed effect of CAPS-5 on next measurement's PTCI-9 was also significant, albeit with a smaller effect size, $b = 0.01$, $SE = 0.00$, $t = 2.58$, $p = .014$, Cohen's $d = 0.29$.

Using the PTCI as independent variable and CAPS-$5^{excl9\text{-}10}$ as dependent variable, we found that the PTCI significantly predicted subsequent CAPS-$5^{excl9\text{-}10}$ scores, $b = 3.58$, $SE = 0.74$, $t = 4.83$, $p < .001$, Cohen's $d = 0.63$. The reverse effect, CAPS-$5^{excl9\text{-}10}$ predicting PTCI, was not significant, $b = 0.00$, $SE = 0.00$, $t = 1.27$, $p = .205$. Results of these sensitivity analyses can be found in Table A3.

The interpretation of these outcomes does not differ from the main outcomes.

**Table A3.** Sensitivity analyses

| Model and variable | B | *SE* | *t* | *p* | *d* |
|---|---|---|---|---|---|
| Predicting CAPS-5 from time lagged PTCI-9 | | | | | |
| Intercept | 12.80 | 3.17 | 4.04 | <.001 | |
| Time | -1.99 | 0.89 | -2.24 | .027 | -0.41 |
| CAPS-5 autoregression | 0.51 | 0.06 | 8.68 | <.001 | 1.20 |
| Lagged PTCI-9 | 4.18 | 0.80 | 5.20 | <.001 | 0.95 |
| Predicting PTCI-9 from time lagged CAPS-5 | | | | | |
| Intercept | -0.32 | 0.18 | -1.78 | .077 | |
| Time | -0.07 | 0.05 | -1.27 | .207 | -0.21 |
| PTCI-9 autoregression | 0.77 | 0.04 | 17.14 | <.001 | 2.08 |
| Lagged CAPS-5 | 0.01 | 0.00 | 2.48 | .014 | 0.29 |
| Predicting CAPS-5$^{excl9\text{-}10}$ from time lagged PTCI | | | | | |
| Intercept | 10.26 | 2.87 | 3.58 | <.001 | |
| Time | -1.53 | 0.82 | -1.87 | .064 | -0.32 |
| CAPS-5$^{excl9\text{-}10}$ autoregression | 0.53 | 0.06 | 8.81 | <.001 | 1.05 |
| Lagged PTCI | 3.58 | 0.74 | 4.83 | <.001 | 0.63 |
| Predicting PTCI from time lagged CAPS-5$^{excl9\text{-}10}$ | | | | | |
| Intercept | -0.22 | 0.17 | -1.30 | .194 | |
| Time | -0.06 | 0.05 | -1.11 | .269 | -0.19 |
| PTCI autoregression | 0.86 | 0.04 | 20.36 | <.001 | 2.56 |
| Lagged CAPS-5$^{excl9\text{-}10}$ | 0.00 | 0.00 | 1.27 | .205 | 0.16 |

*Note.* CAPS-5 = total score of the Clinician Administered PTSD Scale for DSM-5; CAPS-5$^{excl9\text{-}10}$= total score of the Clinician Administered PTSD Scale for DSM-5 minus item 9 and item 10; PTCI-9 = the short version of the Posttraumatic Cognitions Inventory; PTCI = the original Posttraumatic Cognitions Inventory.

# Chapter 3

# Distress variability during exposure therapy and its relationship with PTSD symptom decline

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## Abstract

*Background and objectives:* Inhibitory Learning Theory (ILT) framework implies that in-session distress variability may promote extinction learning and thereby enhance exposure therapy efficacy. Thus far, research has mainly focused on in-session distress reduction. The aim of the current study was to assess whether in-session distress variability predicts next session PTSD symptom decline in PTSD patients receiving prolonged exposure (PE).
*Methods:* Eighty-six patients with PTSD received 14 to 16 sessions of PE. Using dynamic panel models, we assessed the temporal relation (i.e., within-persons) between in-session distress variability and PTSD symptom decline. Moreover, we assessed the averaged relation (i.e., between-persons) between in-session distress variability and PTSD symptom decline.
*Results:* Temporal analyses showed that in-session distress variability did not precede PTSD symptom improvement. Averaged analyses showed that distress variability was related to PTSD symptom improvement.
*Limitation*: The operationalization of distress variability appeared to deviate from its theoretical conceptualization.
*Conclusions:* In absence of distress reduction, distress variability can vary. However, our findings suggest that in-session distress variability does not drive symptom reduction during PE. In contrast, averaged over participants, distress variability was related to symptom improvement, suggesting that those with a more variable distress pattern across sessions show better treatment response. More empirical work is needed to shed light on the effect of distress variability during exposure sessions on treatment outcome and to offer grounds for clinical recommendations.


*Keywords*: PTSD, Prolonged Exposure, Inhibitory Learning, Distress variability, Change Mechanisms

## Introduction

Prolonged exposure (PE) is an effective treatment for posttraumatic stress disorder (PTSD) but a substantial amount of patients do not improve sufficiently (Larsen et al., 2019; McLean et al., 2022). Understanding the underlying mechanisms of successful PE can help to optimize treatment outcomes of PTSD. Fear extinction is thought to be one of the most important mechanisms of action during PE and Inhibitory learning theory (ILT; Craske et al., 2008, 2014, 2022) posits that fear reduction through extinction is accomplished by the formation of inhibitory associations that compete with the original fear-eliciting associations. One of the strategies that have been proposed in ILT to strengthen the inhibitory associations, is to increase variability – in stimuli used during exposure as well as in contexts wherein exposure takes place. Following ILT, it has also been suggested that varying levels of distress during exposure sessions promote treatment effectiveness (Craske et al., 2022; Knowles & Olatunji, 2019). However, somewhat contradictory, the ILT framework also de-emphasizes the role of (in-session) distress patterns. How distress variability relates to exposure effectiveness requires further examination.



Variability of distress levels has been proposed to be linked to beneficial treatment outcomes in different ways (Culver et al., 2012). First, it might allow the inhibitory association to be coupled with a variety of internal states during exposure. This variety of internal states is thought to increase the retrievability of the inhibitory association outside the exposure context, thereby strengthening the inhibitory association and making it more stable. Some suggest that variation in internal states may be viewed as context variability (Culver et al., 2012), which has been associated with a reduced return of fear after extinction in human laboratory studies (Bandarian-Balooch et al., 2015; Dunsmoor et al., 2014). Second, increased variability of in-session distress levels may provide multiple opportunities for patients to disconfirm aversive expected outcomes during exposure. The violation of expected outcomes has been shown to be crucial for learning (Rescorla & Wagner, 1972) and has been associated with enhanced extinction learning in laboratory settings (Brown et al., 2017; Gromer et al., 2022) and (sub-clinical) exposure outcomes (Deacon et al., 2013).

Greater variability of in-session distress levels has been related to better treatment outcomes in adults with public speaking – and contamination anxiety (Culver et al., 2012; Kircanski et al., 2012) and in clinically anxious children, diagnosed with e.g., obsessive compulsive disorder and generalized anxiety disorder (Kircanski & Peris, 2015; Waters et al., 2015). Conversely, a study that manipulated variability in exposure intensity in a sample of adults with an unacceptable obsessional thought did not find that in-session distress variability predicted treatment outcomes (Jacoby

et al., 2019). Another study also found no effect of fear variability on exposure therapy treatment outcome in a sample of pediatric OCD patients (Benito et al., 2018). These inconsistencies warrant a closer examination of the proposed effect of in-session distress variability on treatment outcomes, especially in clinical samples such as PTSD patients, which have not been studied before.

Prior to ILT, rather than in-session distress variability, in-session distress reduction was presumed to be an important index of change during PE. In-session distress reduction (often referred to as within-session habituation or WSH) was thought to provide new information that is incompatible with the pre-existing information about the feared stimuli, thereby weakening links between stimuli and fear responses (Foa & Kozak, 1986). However, since its conceptualization, multiple studies have not found that in-session distress reduction was related to long-term outcomes of PE (see for a review Asnaani et al., 2016). In line with ILT, some studies suggest that in-session distress reduction is not an important target to achieve during PE (Brown, Zandberg, et al., 2019; Sripada & Rauch, 2015).

In-session distress reduction is generally operationalized as the difference between the peak of distress in the session and the distress at the end of the session. However, distress levels may drop earlier in the exposure session, enabling corrective learning to occur, and may increase again as the session continues. For example, after an initial decrease in distress when recounting the traumatic event, the patient might subsequently focus on other distressing parts of the memory (Foa et al., 2007), causing an increase in distress. As such, corrective learning could have occurred, but this would not be reflected in in-session distress reduction from the peak to the end of the session. Possibly, variability of distress levels better captures the process of corrective learning during exposure therapy.

It should also be noted that most studies examining the relationship between in-session distress reduction and symptom decline only looked at between-person effects, and not at within-person effects. That is, these studies have examined whether those with more in-session distress reduction on average have lower PTSD symptoms following treatment. However, within-person effects are thought to be especially relevant for indices of change (Falkenström et al., 2020; Kazdin, 2007), as these effects provide more convincing evidence that a change in the proposed mechanisms leads to a subsequent change in the targeted outcome. Indeed, we recently showed that in-session distress reduction was predictive of next-session reduction in PTSD symptoms when testing the within-person effects (Hoeboer et al., 2022). In other words, in-session distress reduction preceded PTSD symptom improvement and appeared to be an indicator of change during PE. It should still be clarified how patterns of in-session distress present themselves, how they relate to each other, and to treatment outcome.

The aim of the current study was twofold. First, we aimed to provide descriptive information on levels of in-session distress variability and distress reduction throughout PE. Little is known about the session-to-session distress patterns during PE, as averaged effects over treatment are generally reported. We evaluated descriptive statistics (e.g., frequencies, mean, etc.) of distress variability and distress reduction indices across all sessions and examined the relationship between these two variables. Second, we aimed to assess whether in-session distress variability predicted change in PTSD symptoms, through temporal (within-person) analyses. Following ILT, we expected that in-session variability of levels of distress predicted next session change in PTSD symptoms. To enhance comparability with previous findings on this relationship, we carried out additional analyses to assess the between-person effect of distress variability on change in PTSD symptoms.



## Methods

### Design

The IMPACT study is a randomized controlled trial comparing the effectiveness of standard PE, intensified PE (iPE), and phase-based treatment (PBT), in which PE was preceded by Skills Training in Affective and Interpersonal Regulation (STAIR). For more information on the design and other outcomes of the IMPACT study, we refer to previously published papers (Oprel et al., 2018, 2021). The IMPACT study has been approved by the Medical Ethical Committee of Leiden University Medical Center (NL57984.058.16).

### Participants

Participants were diagnosed with posttraumatic stress disorder following childhood abuse (CA-PTSD) established with the Clinician Administered PTSD Scale (CAPS-5; Boeschoten et al., 2018) with at least moderate severity of PTSD symptoms (CAPS-5 score ≥26) and at least one specific memory of the traumatic event. The index trauma had to be related to sexual abuse and/or physical abuse that occurred before the age of 18 and was committed by a primary caretaker or an authority figure. Participants had to be between ages 18 and 65 and proficient in the Dutch language. Exclusion criteria were: (1) involvement in a compensation case or legal procedures concerning admission or stay in The Netherlands, (2) pregnancy, (3) severe non-suicidal self-injury (NSSI) which required hospitalization during the past three months, (4) severe suicidal behavior: a suicide attempt during the past three months or acute suicidal ideations with serious intent to die with a specific plan for suicide and preparatory acts, (5) severe disorder in the use of alcohol or drugs in last three months, (6) cognitive impairment (estimated IQ < 70), (7) changes in

psychotropic medication in the two months before inclusion, and (8) engagement in any current psychological treatment.

The IMPACT study sample consisted of 149 participants. For the current study, we excluded participants in the PBT condition ($n$ = 50) as PE in this condition was preceded by emotion regulation skills training. This skills training may influence the proposed working mechanism of the subsequent PE and may thereby affect the outcomes of the analysis. Furthermore, we excluded participants who did not complete at least 2 treatment sessions ($n$ = 13), as this was a requirement for the temporal analyses. Our final sample, therefore, consisted of 86 participants, most of whom were female (79%), and with ages ranging from 20 to 60 years ($M$ = 36.8, $SD$ = 11.5). Power analyses for sample size justification were conducted for the parent trial (Oprel et al., 2021). We previously did a study using a similar statistical method and comparable estimated effect sizes (medium effects; Cohen's $d$ = 0.5) and found to have sufficient power to detect significant effects using a sample of $N$ = 86 (Hoeboer et al., 2022).

In total, our dataset included 1069 therapy sessions. The first session ($n$ = 86) included psychoeducation and treatment planning. From the second session onwards, sessions included imaginal exposure ($n$ = 983). On average, participants completed 12.4 sessions ($SD$ = 3.6), with a minimum of 3 and a maximum of 16.

**Procedure**

Eligibility for the study was assessed during a baseline assessment. After this baseline assessment, patients were randomly allocated to one of the three treatment conditions with a 1:1:1 ratio (PE, iPE, and PBT). Patients in the PE condition received a maximum of 16 weekly, 90-min sessions. Patients in the iPE condition received a maximum of 14 90-min sessions, starting with 12 sessions over 4 weeks and followed by two sessions after one and two months. Exposure in the iPE condition was delivered by two therapists due to practical considerations. The treatment manual for both conditions was based on the protocol described by Foa et al. (2007). In both conditions, the first session consisted of psycho-education and a case conceptualization. The other sessions consisted of 60-min imaginal and in-vivo exposure. Between sessions, patients were instructed to perform homework assignments (e.g., listening to audiotape recordings of the imaginal exposure or performing in-vivo exercises).

All therapists were trained in the protocol and had to pass an exam with pilot patients to ensure competency in the exposure protocol. To further ensure the therapist's adherence to the treatment protocol, they received weekly group supervision (supervised by RAdK and AvM). The therapists had at least a master's degree in psychology and on average 10 years of experience in mental health

services. A random selection of PE sessions (approximately 10% of the total PE sessions) was rated by independent observers for treatment adherence based on the Dutch translation of the original adherence rater checklist scale. Protocol adherence was high (*M* session elements completed = 90%, *SD* = 18%).

The majority of patients completed 14 sessions (*n* = 55, 64%), but only a few participants completed session 15 (*n* = 18, 21%) and session 16 (*n* = 15, 17%), mostly because the iPE condition contained 14 sessions. Due to insufficient observations in these sessions (*n* = 33), they were omitted from our temporal analyses.

**Measures**

*PTSD symptoms*

Self-reported PTSD symptoms, the primary outcome of this study, were measured with the weekly version of the PTSD checklist for DSM-5 (PCL-5; Blevins et al., 2015). The PCL-5 consists of 20 self-report items that are rated on a 5-point Likert scale ranging from 0 (not at all) to 4 (extremely). The total PCL-5 score ranges from 0 to 80, with higher scores indicating higher symptom severity. The PCL-5 is considered to have good psychometric properties with high Cronbach's α (.94) in previous studies (Blevins et al., 2015). The PCL-5 was administered at the start of each session and was completed with reference to the index trauma. It should be noted that we did not have PCL-5 scores for each session in the iPE condition as the PCL-5 was administered once a week. For the iPE condition, this meant that the PCL-5 was administered every three sessions (as participants received three sessions per week). In total, we had PCL-5 data for 782 sessions.

*In-session distress indices*

From the second PE session onwards, participants rated subjective units of distress (SUD) for every 10 minutes of the in total 60-minute exposure (7 in-session time points) on a scale from 0 (*no distress*) to 100 (*maximum distress*). In line with previous work (Culver et al., 2012; Jacoby et al., 2019; Kircanski et al., 2012; Waters et al., 2015) in-session variability of distress was calculated for each session by taking the standard deviation of SUDs within a specific session (hereafter referred to as VAR-SD). Also in line with previous work (Badour et al., 2017; Harned et al., 2015; Hendriks et al., 2018; Hoeboer et al., 2022), in-session distress reduction (hereafter referred to as WSH) was calculated for each session by subtracting the SUD end (i.e., the last reported SUD score within a session) from the SUD peak (i.e., the highest reported SUD score within a session). Contrary to previous work, we did not average these outcomes across all sessions, as we used the data per session for our within-subjects analyses. For our post hoc between-subject analyses, we did average these outcomes across all sessions. In total, there were 933 sessions with SUD data.

**Statistical analyses**

The data analysis plan of this study was pre-registered at the open science framework (OSF; osf.io/n26xm). The first aim of this study was to provide descriptive information on distress variability and its relationship with distress reduction. We calculated the within-person correlation between VAR-SD and WSH across the 933 sessions for which SUDs data was available. We also calculated frequencies of the amount of distress variability and distress reduction. We created separate groups for the level of distress variability and distress reduction (low, medium, and high) based on the 33$^{rd}$ and 66$^{th}$ percentiles. This provided categories for within session distress variability and distress reduction, allowing us to plot distress patterns of (1) high variability and high reduction, (2) high variability and low reduction, (3) low variability and high reduction, and (4) low variability and low reduction. Sessions within the medium groups were not plotted, as these were hard to interpret and not very insightful.

For our second aim, to assess whether in-session variability in SUD levels predicted next session PTSD symptom reduction, we used dynamic panel models based on maximum likelihood estimation (Allison et al., 2017). This allowed us to assess within-person effects. Models were fitted using the Lavaan and dpm package (Rosseel, 2012) in Rstudio (version 2022.12.0). First, we assessed the effect of in-session distress variability on PTSD outcome. We used PCL-5 scores as dependent variable with the auto-regressive effect of the PCL-5 scores and the cross-lagged effect of distress variability (VAR-SD) per session as independent variable. To illustrate with an example, PCL-5 scores of session 4 were predicted by PCL-5 scores of session 3 and VAR-SD scores of session 3. As the iPE condition had fewer PCL-5 measurement points (session 1, 4, 7, 10, 12, 13, and 14), PCL-5 scores of session 4 were in this condition predicted by PCL-5 scores of session 1 and VAR-SD scores of session 3. To test temporality, we ran the reversed model with PCL-5 as the independent variable and VAR-SD as dependent variable. We also ran additional analyses to test the effect of condition on the relationship between VAR-SD and PTSD symptoms, as (1) the delivery format of exposure therapy in the two conditions might affect the outcomes of our analysis and (2) the PCL-5 was not administered in every session in the iPE condition which may have affected the autoregressive effect. We initially planned to evaluate whether distress variability added predictive value over in-session distress reduction when both variables were entered in the model, but this model did not converge.

Post hoc (i.e., after preregistration), we conducted additional analyses to assess the between-person effect of distress variability across sessions ('averaged distress variability') on PTSD symptom improvement. This was tested using a dynamic panel model, with PCL-5 scores as dependent variable, the autoregressive effect of the

PCL-5 score and the averaged distress variability (fixed effect) as independent variables.

## Results

Means and standard deviation of PCL-5 scores, within-session distress variability, and distress reduction can be found in Table 1. Over treatment, PCL-5 scores decreased from 54.15 (*SD* = 12.65) in session 1 to 31.22 (*SD* = 23.10) in session 14. On average, distress variability was larger in early sessions (session 1; *M* = 16.71) compared to later sessions (session 14; *M* = 9.38) and varied between participants (range *SD*s of VAR-SD across sessions is 8.42–10.03). SUD-WSH also decreased over the course of treatment and varied between participants (see Table 1).



**Table 1.** Descriptive information per session of PTSD symptomatology and within-session distress variability and – reduction

| | PCL-5 | | | SUD: VAR-SD | | | SUD: WSH | | |
|---|---|---|---|---|---|---|---|---|---|
| Session | *N* | *M* | *SD* | *N* | *M* | *SD* | *N* | *M* | *SD* |
| 1 | 85 | 54.29 | 12.72 | | | | | | |
| 2 | 43 | 55.93 | 12.59 | 86 | 16.71 | 8.54 | 86 | 25.48 | 23.81 |
| 3 | 44 | 54.25 | 15.74 | 85 | 16.38 | 10.03 | 85 | 24.94 | 26.53 |
| 4 | 83 | 50.61 | 15.32 | 83 | 14.47 | 8.97 | 83 | 22.35 | 21.00 |
| 5 | 42 | 46.95 | 17.87 | 79 | 14.55 | 9.89 | 79 | 23.99 | 21.72 |
| 6 | 40 | 46.10 | 18.42 | 73 | 13.36 | 9.41 | 73 | 21.63 | 20.73 |
| 7 | 73 | 42.93 | 18.83 | 73 | 15.16 | 8.57 | 73 | 20.41 | 18.76 |
| 8 | 35 | 38.03 | 21.71 | 69 | 14.26 | 8.84 | 69 | 18.96 | 17.63 |
| 9 | 33 | 34.94 | 21.17 | 64 | 13.78 | 8.92 | 64 | 18.91 | 19.51 |
| 10 | 66 | 36.50 | 20.42 | 64 | 13.62 | 8.70 | 64 | 21.20 | 21.67 |
| 11 | 28 | 34.07 | 23.94 | 63 | 13.39 | 8.42 | 63 | 19.53 | 17.89 |
| 12 | 62 | 32.08 | 20.07 | 60 | 11.85 | 8.44 | 60 | 19.67 | 21.30 |
| 13 | 62 | 30.35 | 20.95 | 56 | 11.09 | 8.68 | 56 | 15.02 | 16.58 |
| 14 | 54 | 31.22 | 23.10 | 46 | 9.38 | 8.81 | 46 | 15.07 | 19.22 |

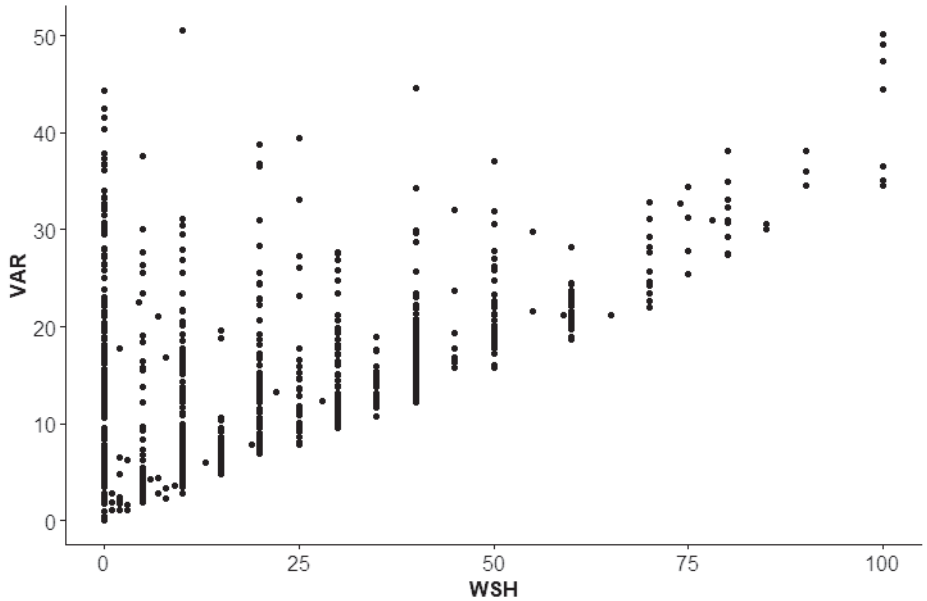
*Note.* PCL-5 = PTSD checklist for DSM-5; SUD = subjective units of distress; VAR-SD = variability operationalized as the standard deviation of SUDs per session (Kircanski et al., 2012); WSH = within-session habituation/distress reduction.

**Association between within-session distress reduction an variability**

As expected, the within-person correlation showed that within-session distress variability (VAR-SD) and within-session distress reduction (WSH) were significantly and positively correlated ($r = 0.53$, $p < 0.001$). However, an absence of distress reduction (i.e., SUD-WSH = 0) could co-occur with a wide range of in-session distress variability (i.e., VAR-SD varies between 0 and 45; see Figure 1).

To gain more insight in divergent or convergent distress variability and – reduction patterns, we created three groups for distress variability and – reduction (i.e., low, medium and high) based on their approximate 33rd percentiles (see Table 2). A pattern of high distress variability and high distress reduction was most common (*n* = 175, 18.8%), followed closely by a pattern of low distress variability and low distress reduction (*n* = 160, 17.1%). Approximately a tenth of the sessions (*n* = 83, 8.9%) show a pattern of high distress variability and low distress reduction.

**Figure 1.** Relation between in-session distress variability and reduction




*Note.* VAR = distress variability (original operationalization, Kircanski et al., 2012); WSH = within-session habituation/distress reduction.

Surprisingly, we found through visual inspection (see Figure 2) that the operationalization of distress variability by calculating the standard deviation of distress levels in a session (as was done in previous studies; Culver et al., 2012;

Jacoby et al., 2019; Kircanski et al., 2012; Waters et al., 2015) did not always capture the ups-and-downs pattern, which is crucial for the theoretical concept of distress variability (as it suggests opportunities for corrective learning). For instance, the top right graph of Figure 2 shows a session (green line) that is assigned to high variability, but this session merely shows an increase in distress levels. Merely increasing distress levels within the relatively high variability group was not a rare occasion (see Appendix A, Figure A1). Figure 2 shows what we theoretically expect a pattern within a category to look like, the average of distress patterns within a category, and distress patterns of five randomly selected sessions. Especially in the 'high variability and low reduction' category, the plots indicate that VAR-SD does not fully align with theory. To further develop the field, we came up with alternative metrics for distress variability (post hoc), which are discussed in Appendix B.

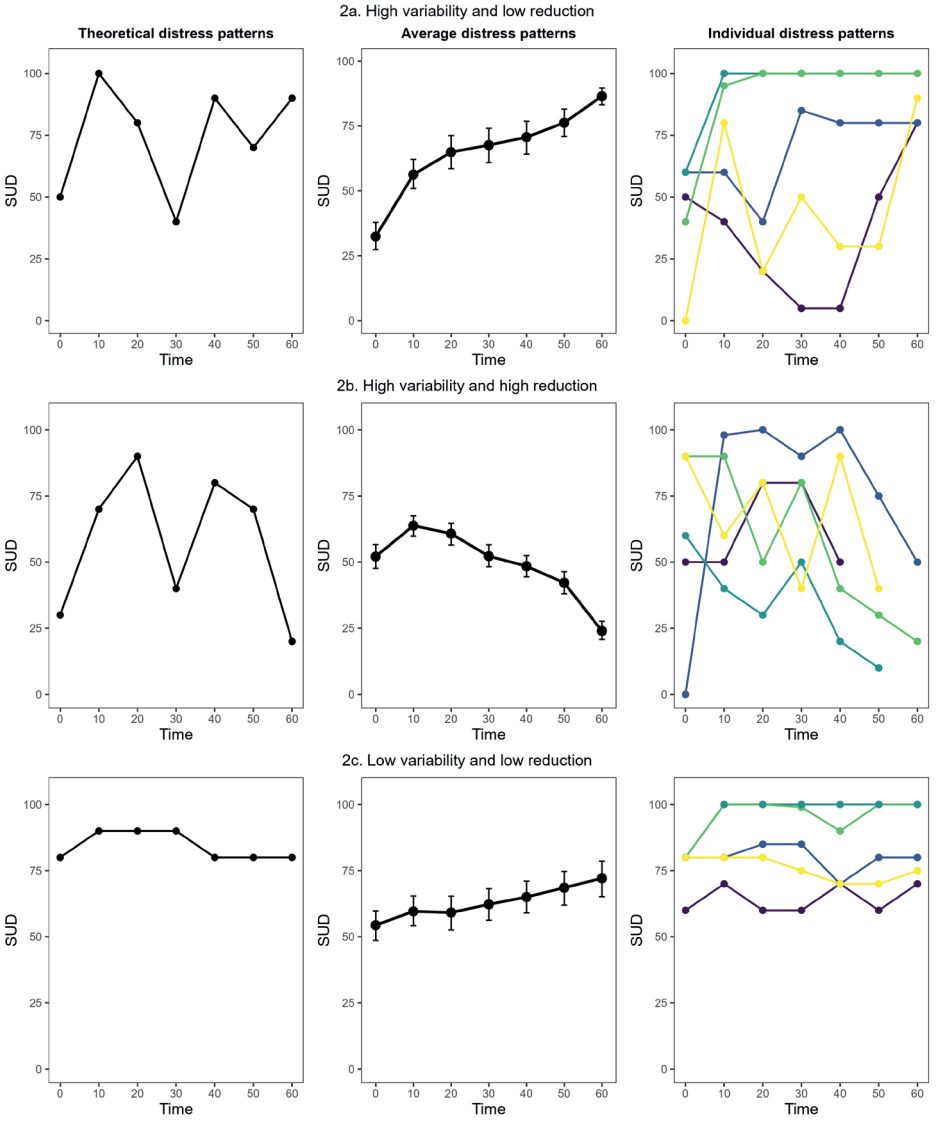


**Table 2.** Three group crosstabulation of distress variability and distress reduction

| | | VAR-SD | | | |
|---|---|---|---|---|---|
| | | Low | Medium | High | Total |
| | | *n* (%) | *n* (%) | *n* (%) | *n* (%) |
| WSH | Low | 160 (17.1) | 59 (1.6) | 83 (8.9) | 302 (32.4) |
| | Medium | 149 (16.0) | 127 (13.6) | 53 (5.7) | 329 (35.3) |
| | High | 0 (0) | 127 (13.6) | 175 (18.8) | 302 (32.4) |
| | Total | 309 (33.1) | 313 (33.5) | 311 (33.3) | 933 (100) |

*Note.* VAR-SD = distress variability; WSH = within-session habituation/distress reduction. In this table, *n* refers to the number of sessions.

**Figure 2.** Examples of SUD trajectories




*Note.* Plots on the left depict the pattern that is theoretically expected within a category (based on hypothetical data). Plots in the middle show the averaged distress pattern with the 95% Confidence Interval. Plots on the right show distress patterns of five randomly selected sessions.

**Temporal analyses**

Outcomes of the temporal analyses can be seen in Table 3. Within-session distress variability (VAR-SD) was not significantly related to lower PTSD symptoms in the next session, $b$ = -0.05, $SE$ = 0.05, $z$ = -0.95, $p$ = .345. We found no evidence for differences between the two treatment conditions (PE vs. iPE)[1], $b$ = 0.08, $SE$ = 0.06, $z$ = 1.36, $p$ = .172. The reversed effect was also not significant, i.e., PTSD symptoms were not significantly related to less within-session distress variability (VAR-SD) in the next session, $b$ = 0.05, $SE$ = 0.03, $z$ = 1.61, $p$ = .108. We refer to Appendix B for the temporal analyses with the alternative distress variability metrics.

**Table 3.** Temporal analyses of PTSD symptoms and distress variability

| Temporal effect | Estimate | SE | *z*-value | *p*-value |
|---|---|---|---|---|
| Predicting PCL-5 from VAR-SD | | | | |
| Lagged VAR-SD | -0.05 | 0.05 | -0.95 | .345 |
| Autoregressive PCL-5 | 0.70 | 0.05 | 15.55 | <.001 |
| Predicting VAR-SD from PCL-5 | | | | |
| Lagged PCL-5 | 0.05 | 0.03 | 1.61 | .108 |
| Autoregressive VAR-SD | 0.24 | 0.04 | 5.55 | <.001 |

*Note.* PTSD = posttraumatic stress disorder; PCL-5 = PTSD checklist for DSM-5; VAR-SD = in-session distress variability following original operationalization (Kircanski et al., 2012).

**Between-person analyses**

Correcting for the autoregressive effect of PTSD symptoms, averaged distress variability (VAR-SD) was a significant predictor of a decrease in PTSD symptoms over the course of treatment, $b$ = 0.12, $SE$ = 0.03, $z$ = 3.71, $p$ < .001.

## Discussion

In this study we aimed to provide descriptive information on in-session distress variability and distress reduction during PE, and to assess whether in-session distress variability predicted next session PTSD symptom improvement. We found

1 Based on a reviewer's suggestion we ran a sensitivity analysis on the PE condition only ($n$ = 44). In this model, within-session distress variability (VAR-SD) was not significantly related to lower PTSD symptoms in the next session, $b$ = -0.09, $SE$ = 0.06, $z$ = -1.41, $p$ = .159. Nor did we find evidence for the reversed effect: PTSD symptoms were not significantly related to less within-session distress variability (VAR-SD) in the next session, $b$ < 0.01, $SE$ = 0.04, $z$ = 0.06, $p$ = .954.

that sessions that contained no in-session distress reduction could have a wide range of in-session distress variability. That is, some PE sessions show distress variability but not reduction. In-session levels of distress variability were not predictive of next session PTSD symptom decline. Our post hoc analyses showed that the average level of distress variability over the sessions was related to better treatment outcomes (i.e., more PTSD symptom improvement) during treatment.

The positive relation between distress variability and distress reduction was not surprising, as reduction is a form of variability. More to our surprise, when looking at distress patterns that had a relatively high score on distress variability in our dataset, these also contained sessions marked by a steady in- or decrease in distress. It seems that participants with such distress patterns did not have multiple opportunities to disconfirm aversive expected outcomes regarding the infinite duration or intensity of distress (i.e., they did not show more 'ups' and 'downs'), yet scored high on this variability index. This operationalization of variability (calculating the standard deviation of in-session distress levels) does not fully align with our theoretical starting point that variability would better capture the process of corrective learning during exposure therapy than distress reduction (i.e., WSH). Up until now, studies on distress variability in adult samples have been carried out in clinical analogue populations (Culver et al., 2012; Jacoby et al., 2019; Kircanski et al., 2012). Suggestively, distress patterns may be different in clinical samples, where lack of in-session ups-and-downs may be more common. We explored alternative operationalizations of within-session distress variability that could better capture the up-and-down pattern (see Appendix B). Arriving at a suitable metric that captures distress variability proved to be difficult and distress variability and distress reduction are not entirely separable. Our alternative metrics further the field, but future research (across different samples) is needed.

Our hypothesis that in-session distress variability predicted next-session PTSD symptom improvement was not confirmed, neither with the original conceptualization of distress variability nor with our alternative conceptualizations. This is in line with two earlier studies (Benito et al., 2018; Jacoby et al., 2019), but not with several others (Culver et al., 2012; Kircanski et al., 2012; Waters et al., 2015). One difference between the studies that found an effect and ours is that these studies assessed averaged distress variability. However, especially temporal (or, within-person) effects are important when assessing change mechanisms, as they are more indicative of change processes than averaged effects (Falkenström et al., 2020; Kazdin, 2007). In our post hoc analysis, we found that averaged (or, between-person) distress variability was related to better treatment outcome. Our findings indicate that, on average, patients who show more distress variability show more improvement in PTSD symptoms. However, a patient who showed more variability

in one session did not show more next-session improvement. Therefore, in-session distress variability may reflect who responds well to treatment in general, rather than it being a mechanism of change during PE.

Taken together with our previous study, which showed that more in-session distress reduction (i.e., WSH) was related to more next-session PTSD symptom reduction (Hoeboer et al., 2022), the results of this study suggest that reduction in distress is a better predictor of PTSD symptom reduction than distress variability. This is in line with the original propositions of 'emotional processing theory' (Foa & Kozak, 1986), but not with several other earlier studies (see for a review Cooper, Clifton, et al., 2017). Partly based on these earlier findings, striving for in-session distress reduction has been de-emphasized in ILT (Craske et al., 2008, 2014). Moreover, ILT proposes to sometimes use strategies designed to maintain heightened in-session distress levels (Craske et al., 2014). Clinically, our current findings suggest that exposure interventions for PTSD do not need to be tailored to increase in-session distress variability.



Crucially, although increasing distress variability has been linked to the inhibitory learning approach, this approach also posits that we should move away from distress levels as a yardstick for successful exposure sessions and rather focus on the reduced credibility of the expected aversive outcome. Distress variability is difficult to control and operationalize in clinical settings. Multiple factors can cause distress variability, such as exposure length and stimulus. In contrast, several studies conducted in pre-clinical samples have suggested that a focus on the disconfirmation of expected outcomes enhances extinction learning and could thereby optimize exposure therapy outcomes (Brown et al., 2017; Deacon et al., 2013). However, other recent studies that aimed to translate these findings to more clinical populations have reported mixed results (Buchholz et al., 2022; de Kleine et al., 2017; Elsner et al., 2022; Krause et al., 2022). Therefore, the processes of expectancy violation and corrective learning during exposure therapy also warrants further investigation.

The current study also has some limitations. Variability has mostly been assessed in clinical analogue studies, while the current study used a clinical PTSD sample (with multiple traumas). Although the use of this sample increased ecological validity, it decreased the controllability of the variables under investigation. Importantly, extinction theory is about extinction processes on a single stimulus (e.g., a loud tone; CS) with an outcome specifically related to this CS (e.g., startle reflex; CR). In the current work, the exposure stimulus (trauma memory) could vary between sessions and the outcome index (PCL-5) assessed weekly PTSD symptoms, which may or may not have a direct link to the CS targeted in the prior exposure session. More studies with a single stimulus and an outcome directly linked to that stimulus

are needed to gain further insight into the effect of distress variability in clinical samples. Second, distress variability was measured in-session with 10-min intervals. Possibly, this is too infrequent to capture changes in distress. Related to this, the metrics we used to capture distress variability might not reflect the theoretical conceptualization of allowing for more corrective learning. The cause of distress change (i.e., reduction due to escape behavior or learning, see also Benito et al., 2018) is also unknown in the current study and future studies may benefit from function-based coding of distress (for instance via video-ratings, Alpert et al., 2021; Alpert, Hayes, et al., 2023 for examples). Third, we used the most commonly used peak-end operationalization of WSH

(Cooper, Clifton, et al., 2017; Foa & McLean, 2016; Hendriks et al., 2018; Nacasch et al., 2015). However, this metric may not fully capture the process of within-session distress reduction as this calculation misses instances of reduction that appear earlier in the session (Benito et al., 2018). As with distress variability, the operationalization of in-session distress needs refining and more granular indices of exposure processes are needed to ground adaptations in therapeutic procedures. Fourth, we conducted the averaged analyses post hoc and these outcomes should be interpreted with caution, and be replicated in studies with a priori hypotheses. Additionally, we did not have PCL-5 data for each session in the iPE condition, resulting in less power and lower precision in the assessment of change processes in this condition. Future work may more easily overcome these challenges by administering abbreviated measures, such as the 4- or 8-item PCL-5 (Price et al., 2016), although the decreased amount of variance due to fewer items may decrease power again (i.e., smaller differences are harder to detect). Finally, the current study is a re-analysis of data from the IMPACT study and the findings of the current study should be replicated in other samples. Notwithstanding these limitations, the current study is the first to assess the effect of distress variability on exposure treatment outcome in a clinical sample of PTSD patients.

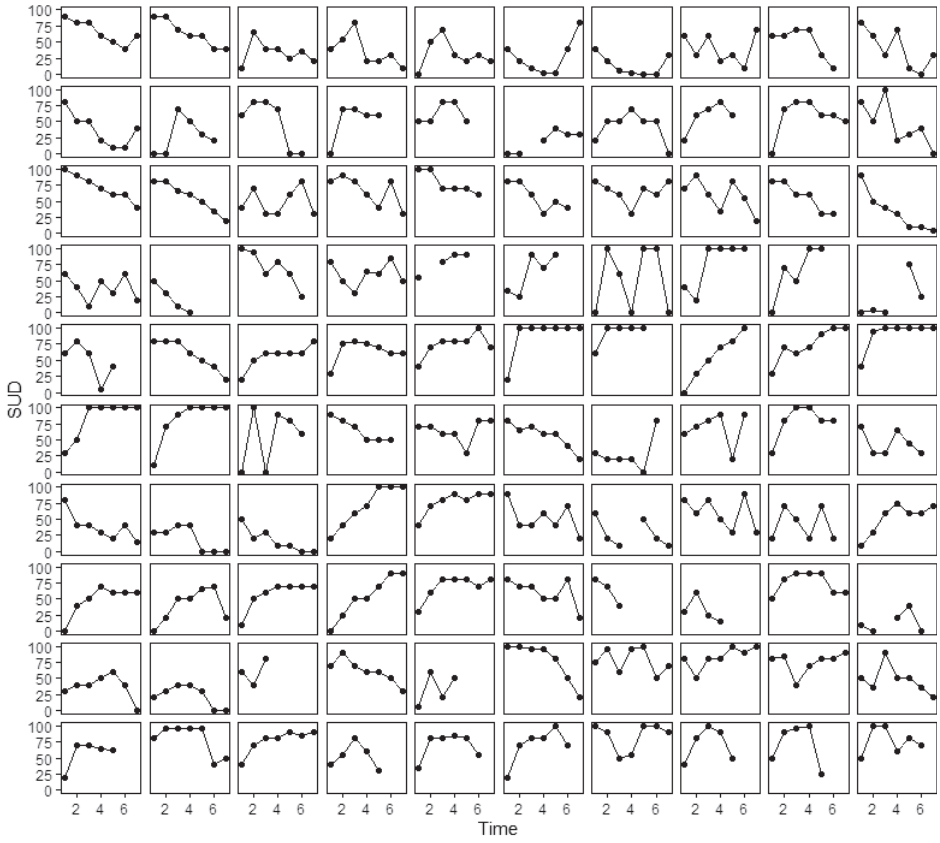
The results of this study showed that in-session distress variability during PE did not predict subsequent PTSD symptom decline. Averaged levels of distress variability were related to a greater decline in PTSD symptoms. On a conceptual level, the operationalization of distress variability requires further investigation. We argue that distress variability is not a predictor of symptom decline during exposure therapy for PTSD and that more research should be conducted on the temporal relationship between in-session distress patterns and symptom change to ground clinical recommendations on exposure procedures.

# Appendix A

## Visual inspection of high distress variability patterns

We plotted the distress patterns of 100 random sessions that had relatively high distress variability to show that VAR-SD (as was done in previous studies; Culver et al., 2012; Jacoby et al., 2019; Kircanski et al., 2012; Waters et al., 2015) does not always capture the ups-and-downs-pattern and that patterns with only 'ups' in this group are not a rare occasion.

**Figure A1.** Individual session patterns of distress with high distress variability, random selection (n = 100)



# Appendix B

## Alternative metrics for in-session distress variability

## Introduction

Based on visual inspection of in-session distress patterns (also see Figure 2 [ms.] and Figure A1), we found that the operationalization of distress-variability via the standard deviation of SUD scores per session (Culver et al., 2012; Jacoby et al., 2019; Kircanski et al., 2012; Waters et al., 2015) was not in line with how distress variability is theoretically thought to improve treatment outcomes. Namely, some sessions showed a pattern where there were no (multiple) opportunities to disconfirm expected aversive outcomes, but were still relatively high in variability. Moreover, distress variability and reduction overlap, both theoretically and mathematically. Sessions that have a large distress reduction by definition have a large variability if one uses the SUD-SD metric. Although some overlap between the variability and reduction constructs may remain, they should be clearly distinguishable. We therefore explored other operationalizations of distress variability. We explore two alternative metrics: 1) the average of absolute difference scores between subsequent time points within a session (VAR-abs), i.e., the sum of ups-and-downs in a session , and 2) the residual sum of squares of the linear regression across SUD timepoints (VAR-RSS), i.e., the variation of SUD scores controlled for the general pattern of SUDs decline (or increase) within a session. First, we assessed whether these alternative operationalizations better captured the theoretical concept of distress variability, by visual inspection and their relationship with WSH. Second, we assessed whether distress variability using these alternative metrics was predictive of PTSD symptom improvement.

## Methods

### Measures

During each exposure session, subjective units of distress (SUDs) was rated by participants every 10 minutes. We created two alternative metrics for within-session distress variability. The first alternative metric for in-session distress variability was calculated by taking the absolute difference between each subsequent time point in a session and then by averaging these differences into one score (VAR-abs). The second alternative metric was calculated by fitting a linear regression across the SUDs for each session and taking the residual sum of squares (RSS) of this model

as distress variability (VAR-RSS), thereby creating a metric that is not contaminated by the general time effect of the in-session distress pattern.

### Statistical analyses

We re-ran our main analyses (post-hoc, after pre-registration), but now with the alternative metrics for distress variability. We used dynamic panel models based on maximum likelihood estimation (Allison et al., 2017). This allowed us to assess within-person effects. Models were fitted using the Lavaan and dpm package (Rosseel, 2012) in Rstudio (version 2022.12.0). We used PCL-5 scores as dependent variable with the auto-regressive effect of the PCL-5 scores the cross-lagged effect of distress variability per session as independent variable, using VAR-abs in one analysis and using VAR-RSS in another analysis. Additionally, we ran the reversed models, with the alternative distress variability metrics as the outcome variable, and cross-lagged PCL-5 and auto-regressive distress variability as predictors.



## Results

### Descriptives

See Table B1 and B2 for the correlations between the in-session distress metrics. VAR-SD (the original operationalization of distress variability; Culver et al., 2012; Kircanski et al., 2012) showed strong, significant correlations with VAR-abs and VAR-RSS. The novel metrics also exhibit a decrease in their correlations with WSH; with VAR-RSS demonstrating a slightly more pronounced difference than VAR-abs.

**Table B1.** Within-person correlations of in-session distress metrics

| | VAR-SD | VAR-abs | VAR-RSS | WSH |
|---|---|---|---|---|
| VAR-SD | . | . | . | . |
| VAR-abs | .76** | . | . | . |
| VAR-RSS | .66*** | .68*** | . | . |
| WSH | .53*** | .46*** | .44*** | . |

*Note.* VAR-SD = in-session distress variability following original operationalization; VAR-abs = first alternative metric for distress variability; VAR-RSS = second alternative metric for distress variability; WSH = within-session habituation/distress reduction.

**Temporal analyses**

See table B2 for outcomes of the temporal analyses with the alternative VAR metrics. VAR-abs was not significantly related to lower PTSD symptoms in the next session, *b* = -0.03, *SE* = 0.02, *z* = -1.38, *p* = .166. The reversed effect was also not significant, i.e., PTSD symptoms were not significantly related to lower VAR-abs in the next session, *b* = 0.13, *SE* = 0.07, *z* = 1.88, *p* = .060. VAR-RSS was not significantly related to lower PTSD symptoms in the next session, *b* < -0.01, *SE* < 0.01, *z* = -1.82, *p* = .06. The reversed effect was also not significant, i.e., PTSD symptoms were not significantly related to lower VAR-RSS in the next session, *b* = 2.94, *SE* = 2.92, *z* = 1.01, *p* = .314.

**Between-person analyses**

Correcting for the autoregressive effect of PTSD symptoms, the averaged VAR-abs over sessions was a significant predictor of a decrease in PTSD symptoms over the course of treatment, *b* = -0.12, *SE* = 0.03, *z* = -3.60, *p* <.001, as well as the averaged VAR-RSS, *b* < -0.01, *SE* < 0.01, *z* = -3.53, *p* <.001.

**Table B2.** Temporal analyses of alternative distress variability metrics

| Temporal effect | Estimate | SE | *z*-value | *p*-value |
|---|---|---|---|---|
| Predicting PCL-5 from VAR-abs | | | | |
| Lagged VAR-abs | -0.03 | 0.02 | -1.38 | .166 |
| Autoregressive PCL-5 | 0.68 | 0.04 | 15.84 | <.001 |
| Predicting VAR-abs from PCL-5 | | | | |
| Lagged PCL-5 | 0.13 | 0.07 | 1.88 | .060 |
| Autoregressive VAR-abs | 0.14 | 0.04 | 3.51 | <.001 |
| Predicting PCL-5 from VAR-RSS | | | | |
| Lagged VAR-RSS | <-0.01 | <0.01 | -1.82 | .060 |
| Autoregressive PCL-5 | 1.04 | 0.01 | 72.17 | <.001 |
| Predicting VAR-RSS from PCL-5 | | | | |
| Lagged PCL-5 | 2.94 | 2.92 | 1.01 | .314 |
| Autoregressive VAR-RSS | 0.39 | 0.3 | 11.98 | <.001 |

*Note.* PCL-5 = PTSD checklist for DSM-5; VAR-abs = first alternative metric for distress variability; VAR-RSS = second alternative metric for distress variability.

## Brief discussion

In this appendix, we have explored alternative metrics that aim to capture in-session distress variability. The high within-person correlation between the different distress variability metrics support the notion that they are reflecting a similar construct,

indicating that the new metrics may be valid alternatives. When using the alternative metrics, the correlation with WSH decreased somewhat - albeit to a limited extent. It is possible that distress variability and distress reduction may not be further disentangled. The outcomes of the temporal analyses with these alternative metrics offer no new interpretations. We refer to our main manuscript for a more in-depth discussion on distress variability.

# Chapter 4

# Maximizing expectancy violation and exposure outcomes in patients with PTSD

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## Abstract

*Background:* It has been proposed that maximizing expectancy violation enhances the efficacy of exposure therapy. The clinical utility of expectancy violation remains unclear and it has not yet been studied in PTSD.
*Objective:* We aimed to test whether explicitly focusing on expectancy violation leads to superior exposure outcomes.
*Method:* Adult treatment-seeking patients with PTSD ($N$ = 60) were randomly assigned to one 90-minute exposure session focusing on either expectancy violation or a control condition without an expectancy focus. Assessments occurred before the session and one week later, measuring changes in fear responses during a script-driven imagery task, and PTSD symptoms.
*Results:* Using multilevel analyses, we found no between-condition differences. On average, fear responses to the imagery and PTSD symptoms decreased over time. The expectancy violation condition exhibited a greater decrease in threat appraisal, which appeared to mediate symptom reduction.
*Conclusions:* We found no evidence that explicitly focusing on expectancy violation led to superior immediate effects. However, it may lead to more changes in expectancies which could affect symptom improvement over an extended period. Further research is needed to determine whether emphasizing expectancy violation in exposure therapy for PTSD is advantageous.


*Keywords*: Posttraumatic stress disorder, exposure therapy, expectancy violation, inhibitory learning, mechanisms of change

## Introduction

Although it has been known for decades that exposure therapy is effective for PTSD (McLean et al., 2022), the discussion about how exposure works is still ongoing. Exposure therapy for PTSD (Foa et al., 2019) consists of systematic and repeated confrontations with (a) the fear-provoking traumatic memories (imaginal exposure) and (b) trauma-related situations, objects, or stimuli that are typically avoided or causing distress (in vivo exposure). While many patients with PTSD benefit from exposure therapy, approximately 30% report residual symptoms at a clinical level, indicating that there is room for improvement (Carpenter et al., 2018; Larsen et al., 2019; Springer et al., 2018). To improve efficacy, exposure therapy's mechanisms of action and how to engage them need to be clarified.

One proposed mechanism is inhibitory learning, which is based on extinction processes (Craske et al., 2008, 2014, 2022). In laboratory settings, during extinction, a fear-eliciting conditioned stimulus (CS) is repeatedly presented in the absence of the unconditioned stimulus (US), leading to a reduction of the conditioned response (CR; i.e., fear). The original fear excitatory association (CS-US) is not forgotten or erased, but rather a second, non-threat association (CS-noUS; i.e., inhibitory association) is learned (Bouton, 1993; Craske et al., 2022), which competes for retrieval with the fear excitatory association. Inhibitory learning refers to the formation of these inhibitory associations. Strengthening these associations and their retrievability during exposure therapy is thought to be a promising approach to increase response rates and to reduce relapse rates.

The inhibitory retrieval model (Craske et al., 2014, 2022) posits that a mismatch between expectancies and outcome drives the formation of inhibitory associations (Craske et al., 2014). This is based on research showing that the strength of new learning was influenced by the magnitude of prediction error (i.e., the discrepancy between expectation and outcome; Rescorla & Wagner, 1972). In the context of exposure therapy for PTSD, expectancies refer to the perceived likelihood that the confrontation with a feared stimulus will lead to a negative outcome (e.g., 'If I go out on the street, I will be assaulted'). The mismatch between the threat expectancy before exposure and the actual experience during exposure is called expectancy violation. It is proposed that maximally violating expectancies during exposure promotes the learning of inhibitory associations and may thereby optimize treatment efficacy (Craske et al., 2014; Weisman & Rodebaugh, 2018). The inhibitory retrieval model has been mostly tested among individuals with anxiety disorders (Craske et al., 2014; de Jong et al., 2019). In PTSD, it is also theorized to be one of the central principles (Cooper, Clifton, et al., 2017; Craske et al., 2014), but fewer studies have assessed this. How expectancy violation can be promoted during

exposure treatment of PTSD is not yet known. The best investigated treatment for PTSD, prolonged exposure (PE; Foa et al., 2019) does not explicitly identify CSs that predict the US nor is the CS-noUS association emphasized after exposure. Possibly, exposure where attention is paid to the identification and non-occurrence of the anticipated negative outcome could enhance exposure outcomes. This could be accomplished by presenting the exposure sessions as 'experiments' – to test the hypothesis that the US occurs.

To identify mechanisms of change, two types of studies are needed. Firstly, treatment studies that establish a (temporal) link between the mechanism and treatment outcome, and secondly, experimental studies that manipulate the proposed mechanism (Kazdin, 2007), for instance, by adapting exposure delivery and active elements (Cohen et al., 2023). Thus far, studies that have linked expectancy violation to exposure treatment outcome have yielded mixed results. In PTSD, we found that imaginal exposure led to expectancy violation, yet the degree of expectancy violation was not related to PTSD symptom reduction after treatment (de Kleine et al., 2017). The analysis of a large number of exposure records ($N$ = 8,484) from patients suffering from various anxiety disorders, showed that exposure consistently led to expectancy violation and that expectancies changed following exposure (Pittig et al., 2022). Not expectancy violation (i.e., the mismatch between expectancies and outcomes) but rather the expectancy *change* (i.e., the updating of expectancies after their violation) was related to treatment outcome, suggesting that violation is an important step to establish expectancy change, which in turn leads to symptom reduction.

In experimental paradigms wherein expectancy violation was manipulated, findings have also been mixed. An analogue study on interoceptive exposure for panic symptoms showed that an exposure session that continued until expectancies were low (<5%) outperformed a regular exposure session based on fear reduction (Deacon et al., 2013), with the caveat that participants in the experimental group also received more exposure trials, complicating the comparison between conditions. Conversely, two studies on spider phobia and claustrophobia found that the use of cognitive techniques prior to exposure that reduce the perceived likelihood of the aversive outcome (thereby limiting the magnitude of expectancy violation), did not negatively affect exposure outcomes (Buchholz et al., 2022; Krause et al., 2022). Studies testing the effect of exposure therapy delivery with an emphasis on expectancy violation are scarce and most have been carried out in (small) analog samples (Jacoby & Abramowitz, 2016). Given its potential to improve exposure outcomes (Craske et al., 2008, 2014, 2022), it is crucial to investigate whether explicitly focusing on expectancy violation during exposure will enhance outcomes, especially in clinical samples such as PTSD.

The aim of the current study was to examine whether exposure that explicitly focuses on expectancy violation improves the efficacy of PTSD treatment. We carried out a clinical assay (one-session treatment protocol; Rodebaugh et al., 2013). Closely mimicking the timeframe of fear conditioning studies, the clinical assay consisted of one session of exposure therapy followed by a one-week follow up measurement. In a treatment-seeking PTSD sample, we examined whether exposure with an explicit focus on expectancy violation (experimental condition; EXP) led to better outcomes than exposure wherein no explicit attention was paid to expectancies and their violation (control condition; CTL). We assessed pre-to post-intervention changes in fear-related responses (subjective distress and psychophysiology) to a personalized trauma-imagery task, which has shown to be sensitive to change after one exposure session (Tuerk et al., 2018; Wangelin & Tuerk, 2015). We expected that fear-related responses would significantly decrease from pre – to post-exposure session, and that this decrease would be greater in the EXP condition. Furthermore, we examined whether treatment condition affected pre – to post-exposure session change in self-reported PTSD symptoms, and hypothesized that participants in the EXP condition would show greater change. Measuring individualized threat expectancy violations in both conditions was problematic, as it would require identifying expectancies and thereby undermine our manipulation. Therefore, we used a general cognitive measure to assess threat appraisals related to PTSD outcomes. We assessed whether change in threat appraisal mediated intervention effects, and expected that especially in the EXP condition, intervention effects would be driven by change in threat appraisal. Between-condition baseline differences in treatment credibility and expectancy were checked, and to gather information about acceptability of exposure procedures, treatment burden and experience were assessed post intervention.



## Methods

### Design

The current study was a clinical assay (one-session treatment protocol) comparing exposure with an explicit focus on expectancy violation (EXP) to a control condition (CTL). A clinical assay has been developed as an alternative to large clinical trials and uses a 'quick win, fast fail' approach (Rodebaugh et al., 2013). This paradigm has previously been used in studies aimed at optimizing treatment for social anxiety disorder, panic disorder, and spider phobia (Davis et al., 2017; Hutschemaekers et al., 2020; Rodebaugh et al., 2013; Salkovskis et al., 1999; Shiban et al., 2013).

Assessments occurred at four timepoints: online questionnaires a week before the first lab visit (T0), the lab visit (T1), an exposure session the same day (T2), and

a final lab visit a week later (T3). This study was approved by the Medical Ethical Committee of Leiden University Medical Centre (NL73480.058.20).

**Randomization**

Participants were randomly allocated to a treatment condition (i.e., EXP vs CTL). Randomization was carried out through a computer-generated randomization list by an independent researcher. Randomization was stratified on PTSD symptom severity, i.e., low vs. high scores on the PCL-5 (cut-off = 50). Participants were not blind to treatment conditions. However, all treatment information was presented in such a way that the direction of the hypotheses was unclear.

**Participants**

Participants were recruited from two outpatient clinics specializing in the treatment of trauma-related disorders from November 2020 to December 2022. Inclusion criteria were: (1) A current PTSD diagnosis (DSM-5 criteria); (2) self-reported PTSD symptoms above clinical cut-off (i.e., PCL-5 score > 31); (3) at least one specific memory related to the index trauma; (4) age between 18 and 70 years. Exclusion criteria were: (1) current trauma-focused treatment; (2) significant suicidal ideations/serious self-injurious behavior or enactment of suicidal behaviors or serious self-injurious behavior within 3 months before intake; (3) intellectual disability; (4) severe substance use disorder; (5) somatic illness that interfered with exposure interventions or planned assessments; (6) pregnancy; (7) unstable regimen of psychotropic medication within 6 weeks before enrollment; (8) no commitment to refrain from using sedative medication/alcohol on the assessment days; and (9) insufficient command of Dutch language. Informed consent was obtained from all patients. An a-priori power analysis revealed that 52 participants would suffice to detect large effects with a power of .80 and alpha of .05. We decided to include 60 participants.

**Exposure session**

All participants received one 90-minute session of standardized exposure therapy conducted by a therapist trained in exposure therapy for PTSD (MA level or higher). The rationale was delivered through a 3-minute animation video that the therapist and the patient watched together. The traumatic event targeted (i.e., target trauma) in the exposure sessions was similar to the event described in the trauma-imagery (see below).

The exposure session in the EXP condition employed an inhibitory learning-based approach, where expectancies and their non-occurrence were explicitly formulated and tracked, using the session form introduced by Craske et al. (2014). The session

started with psychoeducation, which focused on the process of expectancy violation. Feared negative outcomes (i.e., the US) were identified using the session form ('What are you most worried will happen?') and were modified as needed to ensure they were specific and testable during the exposure session (e.g., 'I will suffocate'). Participants also provided a likelihood rating for this outcome. Outcomes related to intolerable distress ('I will be unable to function') were further specified to testable outcomes through tests of goal-directed actions (e.g., completing a simple task; see also Craske et al., 2022). The patient then continued with the exposure exercise ('What is your goal?'). The exposure exercises were designed in a way that allowed the feared outcome to be tested. Examples of feared outcomes were 'not being able to stop hyperventilating', 'losing control', 'fainting', and 'dying'. The first exercise was the same for every participant (recounting the event from beginning to end twice, with a suggested duration of approximately 20 minutes). Therapists were allowed to deviate from the number of repetitions if patients required more or less time to complete their recounts. In follow-up exposure exercises, the exposure target was the stimulus thought to be most associated with the feared outcome in session (i.e., principal CS), for instance, recounting a specific part of the traumatic memory. Attention was paid to the removal of safety signals, as these eliminate or decrease expectancies and thereby minimize expectancy violation. For instance, the therapist would leave the room while the patient completed the exposure exercise if this would increase the perceived likelihood of the occurrence of the feared outcome. Crucially, after each exposure exercise, attention was paid to the recognition and the non-occurrence of the anticipated negative outcome, to promote consolidation of the new learning (i.e., the CS-noUS association). Following the Craske et al. (2014) session form, participants answered the following questions: 'Did what you were most worried about occur'? (dichotomous, yes/no), 'How do you know?', and 'What did you learn?'. Therapists were instructed to complete a minimum of three exposure exercises in 60 minutes, with a minimum of 45 minutes of exposure. Prior to the start of exposure, expectancies were generally high ($M$ = 67.9, $SD$ = 22.7). Expectancies were violated in 81 of the 88 exposure exercises (92.0%).

The exposure session in the CTL condition employed a habituation-based approach (Foa et al., 2019). The session started with psycho-education, which was focused on habituation and emotional processing. No anticipated negative outcomes were identified. In-session exposure was prolonged, i.e., participants were asked to recount the traumatic event repeatedly and as vividly as possible for 60 minutes. Following initial repetitions, therapists guided patients towards hotspots. After the prolonged exposure, the experience was processed, during which attention was paid to the in-session distress levels, experiences, and thoughts or potential novel insights about the trauma. As opposed to the EXP condition, no expectancy-based

session form was used in this condition, as tracking of expectancies in-session would automatically emphasize expectancies and their non-occurrence. Therapists were instructed to complete a minimum of 45 minutes of prolonged exposure.

Treatment adherence was high. All sessions included standardized psychoeducation (specific for both conditions) and imaginal exposure. In all EXP sessions, hypothesis-testing mini experiments were conducted, where 28 sessions (90.3%) contained three or more separate exercises, two sessions (6.5%) contained two exercises, and one contained only one exercise (3.2%). Twenty-seven of the CTL sessions (93.1%) contained a minimum of 45 minutes of imaginal exposure. One of the participants who received less than 45 minutes imaginal exposure dropped out of the treatment and the study. The other participant received 37 minutes of imaginal exposure due to low SUD levels (three consecutive SUDs of 0). To assess potential contamination between conditions, we randomly selected 20% of CTL treatment sessions to verify whether therapists refrained from addressing expectancies. All therapists consistently adhered to the CTL protocol by not addressing expectancies or their violation.

**Trauma imagery**

We used a similar imagery task as described in previous studies (Tuerk et al., 2018; Wangelin & Tuerk, 2015). The trauma-imagery task has been shown to be a reliable and standardized way to measure physiological reactivity to trauma-reminders (Pineles et al., 2013; Pole, 2007). During T1, the researcher interviewed the participant and gathered information about the Criterion-A traumatic target event (Foa et al., 2019; Wangelin & Tuerk, 2015). Participants were asked to provide sensory information, as well as their thoughts and feelings experienced during the target traumatic event. This information was then incorporated in a 3-minute personalized trauma script, which the researcher constructed and recorded in another room. For baseline measurement, a standardized 9-minute neutral script was used, in which the arrival to a fictional museum was described. All scripts were recorded by the same female researcher. Both the neutral and the personalized script started with the following sentence: 'Imagine, as vividly as possible, the following scene…'.

The imagery task itself took place in a therapy room. The scripts were played on a computer and presented through noise-cancelling headphones. The participant was instructed to sit still in a comfortable position with both feet on the ground while listening to the scripts. Participants were asked to close their eyes if possible. Some participants indicated this was too difficult and kept their eyes open. The participant first listened to the neutral script, followed by the personalized trauma script. The imagery task was administered at T1 and at T3.

**Measures**

*Imagery task*

**Psychophysiology.** Heart rate (HR) and skin conductance (SC) were continuously measured during the imagery task using the VU Ambulatory Monitoring System (VU-AMS; de Geus et al., 1995) and data were stored using the Data Analysis and Management Software (VU-DAMS). To measure HR, three single-use Ag/AgCl (pre-gelled with isotonic gel) electrodes were placed on the chest (beneath right collarbone, on the left bottom rib, beneath the right bottom rib). To measure SC, two single-use Ag/AgCl electrodes were placed on the inside of the intermediate phalanges of the middle and index fingers of the non-dominant hand. We used the PhysioDataToolbox (Version 0.6.3) to pre-process and clean the HR and SC data (Sjak-Shie, 2022). We applied an ECG signal analyzer to the raw ECG data with a 1 Hz high-pass filter and a 50 Hz lowpass filter. The R-peaks were detected automatically (with a minimum R-peak value of 0.5 mV and a minimum distance between R-peaks of 0.3s). We applied an SC signal analyzer to the raw SC data with a low-pass filter with a cut-off of 2 Hz. HR and SC data were inspected visually and corrected manually in case of artifacts and/or misidentified R-peaks. Following previous studies (Castro-Chapman et al., 2018; Goodman & Griffin, 2018; Kearns & Engelhard, 2015; Tuerk et al., 2018; Wangelin & Tuerk, 2015), mean HR (beats-per-minutes or BPM) and mean skin conductance level (SCL; micro Siemens) were calculated for both scripts (neutral and trauma) and both timepoints (T1 and T3). Following Wangelin and Tuerk (2015), physiological reactivity (HR-R and SCL-R) was calculated as the difference in mean HR and mean SCL between the neutral script (first three minutes) and the trauma script (i.e., mean trauma script – mean neutral script).

**Subjective distress.** Subjective distress was measured using the 0–100 Subjective Units of Distress Scale (SUDS; Wolpe, 1990). In line with the Prolonged Exposure protocol (Foa et al., 2019), the patient first identified SUDS anchor points at 0, 25, 50, 75 and 100. SUD start, peak and – end scores were collected during the neutral script and the trauma script. We used the $SUD_{peak}$ scores during the trauma scripts at T1 and T3 to assess pre – to post intervention change in subjective distress.

*Self-report clinical measures*

**Self-reported posttraumatic stress symptoms.** Symptoms were measured with the weekly version of the PTSD Checklist for DSM-5 (PCL-5; Blevins et al., 2015). The PCL-5 is a 20-item self-report questionnaire. Items are scored on a 5-point Likert scale, ranging from 0 (not at all) to 4 (extremely). PCL-5 total scores range from 0 to 80. The PCL-5 is considered to have good psychometric properties. The PCL-5 was administered at T0 and T3. Internal consistency at T0 was good ($\alpha = .86$).

**Posttraumatic cognitions.** Posttraumatic cognitions were measured with the Posttraumatic Cognition Inventory (PTCI; Foa et al., 1999). The PTCI is a 36-item questionnaire, where items are scored on a 7-point Likert scale. The total PTCI score ranges from 33 to 231. The psychometric properties are considered to be good and internal consistency at T0 was excellent (α = .95).

**Life events.** The Life Events Checklist for DSM-5 (LEC-5; Weathers et al., 2013) was used to assess traumatic life events that were experienced in our sample and was administered at T0. The questionnaire consists of 16 items on potential traumatic events.

**Threat appraisals relevant to PTSD** were measured via 24-items measure of concern about negative, concrete, outcomes that might happen when confronted with a trauma-reminder (e.g., 'not being able to stop crying', 'getting a heart attack', 'becoming a victim again'). The wording of the items was based on the Appraisal of Social Concerns questionnaire (ASC; Telch et al., 2004), a reliable and valid questionnaire that assesses specific threat appraisals in social anxiety disorder, and adapted to PTSD-related threat appraisals (based on patient data from a previous study, Oprel et al., 2021, and expert consultation). For each item, participants were instructed to rate how concerning an outcome would be when confronted with a trauma-reminder, ranging from 0 (not at all) to 100 (extremely). The total score was calculated by averaging the item ratings, where a higher score reflected a higher concern for threatening outcomes. Threat appraisals were measured at T1 and at T2 (at the end of the exposure session). At T1, participants had a mean score of 37.5 (*SD* = 18.4, range: 2.1-79.6). Most participants (91.7%) had at least one item where they had an concern equal to or above 60. The internal consistency was excellent (α = .91). Threat appraisals at T1 had a medium, significant correlation with the baseline PCL-5 ($r$ = .37, $p$ = .004) and the PTCI ($r$ = .41, $p$ < .001). All items, including their descriptives, can be found in Appendix A of this chapter.

*Treatment measures*

**Treatment credibility and expectancy.** The credibility and expectancy of the exposure session was measured with the 6-item Credibility/Expectancy Questionnaire (CEQ; Devilly & Borkovec, 2000), adjusted for PTSD. The first three items assess treatment credibility and the others assess expectancy. Four items are rated on a 9-point scale and two are rated from 0-100%. In order to make one composite score for each scale (credibility and expectancy), items were first normalized (i.e., each item ranging from 0 to 1), before summing them to create total scores. Total scores for both scales range from 0 to 3. Higher scores reflect higher credibility and expectancy. The psychometric properties of the CEQ are good

(Devilly & Borkovec, 2000). The CEQ was administered after psycho-education and before the start of exposure (i.e., during T2).

**Patient – and therapist experience and treatment burden.** Using similar procedures as a previous study (van den Berg et al., 2016), patient and therapist experience was assessed with the following question: 'How do you look back on the exposure session?', using a VAS with a range from 0 ('negative') to 100 ('positive'). Treatment burden was assessed with the following question: 'How burdensome did you find the exposure session?', using a VAS with a range from 0 ('not at all') to 100 ('extremely'). For therapists, these questions were asked directly after the exposure session (T2). For patients, these questions were asked at the one-week follow-up (T3).

**Procedure**

Eligible participants were patients with PTSD who were about to start trauma-focused treatment. In and exclusion criteria were checked by a researcher. DSM-5 PTSD diagnosis was ascertained by clinical interview by the intaker of the treatment facility, either by CAPS-5 (Boeschoten et al., 2018) or SCID-5-S (Arntz et al., 2017). Participants were randomized to one of the two treatment conditions.

Participants filled out the online baseline questionnaires (T0) at some point during the week preceding the on-site baseline assessment. The baseline assessment (T1) started with obtaining written informed consent. Participants then filled out the threat-expectancies questionnaire and they subsequently did the imagery task. After approximately a 30-minute break, the participants received one standardized exposure session (T2). All exposure sessions were audio-recorded to control for treatment integrity. After the rationale of the exposure session was explained, participants were asked to fill out the credibility/expectancy questionnaire (CEQ; (Devilly & Borkovec, 2000) to assess treatment expectancy and rationale credibility. At the end of the session, participants rated their threat-expectancies again. Approximately one week after the exposure session (in days: $M$ = 7.9, $SD$ = 2.7), the follow-up assessment took place (T3). During this assessment, participants completed another set of questionnaires and the imagery task. Approximately one day to one month after participating in this study (T3), participants continued with trauma focused treatment at the treatment site.

**Statistical analyses**

As the treatment data (CEQ, experience and burden) were non-normally distributed, we conducted a nonparametric Mann Whitney U test to test between-condition differences in these measures. Following Wangelin & Tuerk (2015), before carrying out our main analyses, we checked whether participants showed significant increases (i.e., reactivity) in fear levels and physiology (HR and SC) during the imagery task (i.e., manipulation check), by conducting three paired sample t-tests, with HR, SC and SUD as the dependent variable and script type (neutral script and trauma script) as the independent variable.

To assess the effect of condition on physiological reactivity and distress during the imagery task across time (primary aim), we conducted a multilevel mixed model analysis. Outcome measures, HR-R, SCL-R, and $SUD_{peak}$, were entered as the dependent variable in three separate models. Time (T1 and T3) and its interaction with treatment condition (EXP vs. CTL), were entered as independent variables. We used a similar multilevel model to assess the effect of condition and time on self-reported PTSD symptoms (PCL-5). Following recommendations from

Fitzmaurice et al. (2012), as this study is a randomized trial and we can therefore assume that conditions are similar at baseline, we excluded the main effect of condition from the multilevel models to increase power. To control for multiple testing, we applied the Benjamini-Hochberg procedure (or false discovery rate; FDR) on these multilevel analyses. We assessed whether threat appraisal change differed between the two conditions, through a multilevel model with condition and time as the independent variables and threat appraisal as the dependent variable. Finally, we assessed whether threat appraisal measured at T2 mediated the relationship between condition and exposure outcomes measured at T3, by running separate mediation models for each outcome measure. Following recommendations by Hayes & Rockwood (2017), all mediation models controlled for baseline (T1) levels of threat appraisal and outcome measures.

Multilevel analyses were tested with maximum likelihood estimation using the lme4 package (v1.1-28; Bates et al., 2015) in R (Version 4.0.1). Mediation analysis were carried out using Hayes' PROCESS macro in SPSS (Hayes, 2017). A bias-corrected bootstrapping was used (10,000 iterations) to obtain 95% confidence intervals (CIs) to infer statistical significance (the CIs do not include zero). Other analyses were conducted using SPSS (v.27). Alpha levels were set at .05 (two-sided). The data-analysis plan of this study was registered at the open science framework (OSF; osf.io/fzja7).

## Results

### Participants

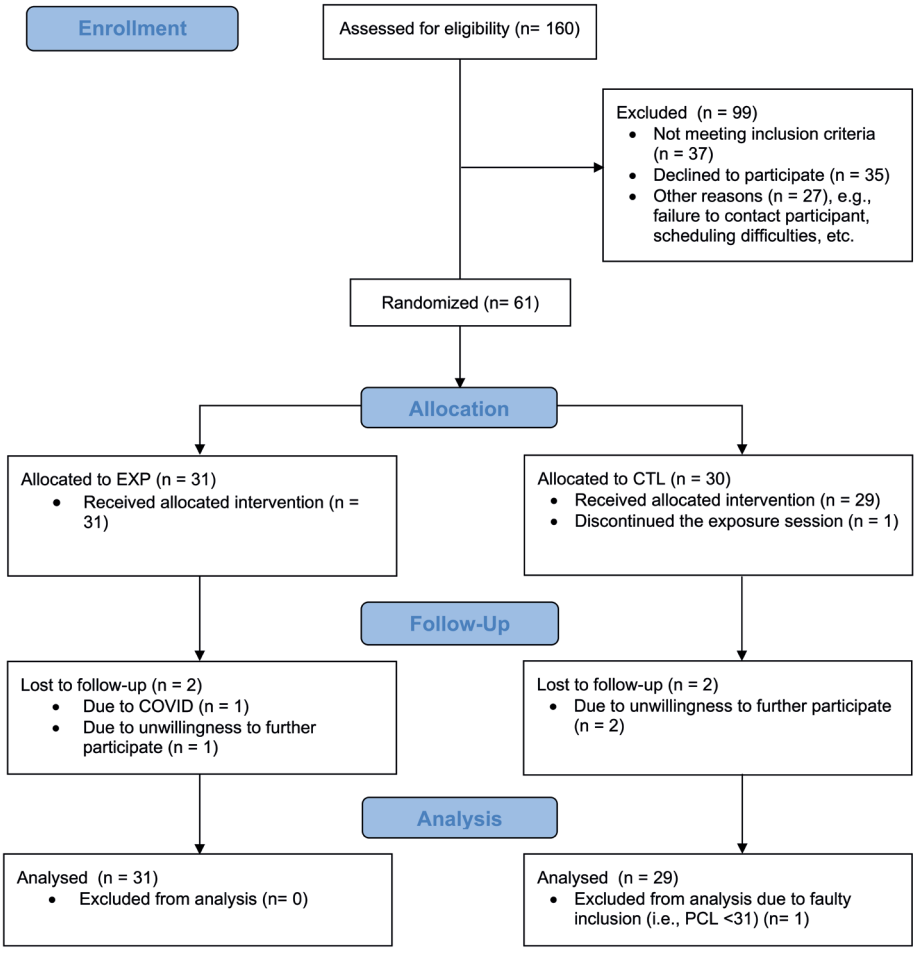
The sample consisted of 60 participants ($M_{age}$ = 39.7; $SD_{age}$ = 12.5), including 41 women, 18 men and one non-binary person. See Figure 1 for the study flowchart. One participant was replaced after receiving the intervention, as this participant failed to fill out the online questionnaires prior to the lab visit, and during the lab visit we found out that this participant did not meet inclusion criteria (i.e,. the PCL-5 total score was below 31). One participant in the CTL condition discontinued the exposure session, but all other participants received and finished the exposure session (i.e., the intervention). In both conditions, two participants were lost to follow-up. One of these participants was unable to attend the second study visit (T3) as this person was infected by the corona virus and lockdown rules at the time prohibited in-person meetings. This participant did fill out the follow-up questionnaires (T3) at home. The other three participants did not want to continue with the study.

The sample characteristics are listed in Table 1. As assessed with the LEC-5, fifty-three participants (88.3%) reported a direct experience or witnessing sexual assault and 54 participants (90.0%) reported physical violence. Participants reported to have directly experienced or witnessed an average of 8.4 potentially traumatic events (*SD* = 4.6). No significant between-condition differences were found at baseline.

### Treatment credibility and expectations

On average, participants thought that the provided treatment was quite credible (*M* = 2.2, *SD* = 0.5), with no between condition differences (*U* = 405.5, *p* = .518). Their expectations of the treatment were more towards the positive end of the scale (*M* = 1.9, *SD* = 0.5), and did not differ significantly between conditions (*U* = 413.5, *p* = .560).

**Figure 1.** CONSORT participant flow diagram




### Physiological reactivity during imagery task

At T1, participants showed a significant increase in HR from the neutral script ($M$ = 74.3, $SD$ = 10.2) to the trauma script ($M$ = 77.8, $SD$ = 9.8), $t(56) = -5.29$, $p < .001$, Cohen's $d$ = -0.70; HR reactivity (HR-R), $M$ = 3.3, $SD$ = 5.2. Participants also showed a significant increase in SCL from the neutral script ($M$ = 7.8, $SD$ = 4.8) to the trauma script ($M$ = 8.1, $SD$ = 4.7), $t(56) = -.49$, $p = .003$, albeit to a weaker extent (Cohen's $d$ = -0.37); SCL reactivity (SCL-R), $M$ = 0.4, $SD$ = 1.3. Peak distress levels ($SUD_{peak}$) strongly and significantly increased from the neutral ($M$ = 38.6, $SD$ =27.7) to the trauma script ($M$ = 73.3, $SD$ = 23.4), $t(59) = -11.275$, $p < .001$, Cohen's $d$ = -1.52.

**Table 1.** Baseline characteristics of participants

| | Total (*N* = 60) | EXP (*n* = 31) | CTL (*n* = 29) |
|---|---|---|---|
| | *n* (%) | *n* (%) | *n* (%) |
| Gender (woman) | 41 (68.3) | 22 (71.0) | 19 (65.5) |
| Education (high)[a] | 19 (31.6) | 7 (22.6) | 12 (41.3) |
| Cultural background (non-Western)[b] | 16 (26.7) | 8 (25.8) | 8 (27.6) |
| Work/occupation | | | |
| Employed | 16 (26.7) | 7 (22.6) | 9 (31.0) |
| Student | 3 (5.0) | 2 (6.5) | 1 (3.4) |
| Incapacitated/on disability | 18 (30.0) | 8 (25.8) | 10 (34.5) |
| Unemployed | 20 (33.3) | 12 (38.7) | 8 (27.6) |
| Retired | 3 (5.0) | 2 (6.5) | 1 (3.4) |
| Target trauma | | | |
| Sexual abuse as child | 24 (40.0) | 11 (35.5) | 13 (44.8) |
| Sexual abuse as adult | 10 (16.7) | 5 (16.1) | 5 (17.2) |
| Physical abuse as child | 13 (21.7) | 7 (22.6) | 6 (20.7) |
| Physical violence as adult | 11 (18.3) | 6 (19.4) | 5 (17.2) |
| Deathly accident | 2 (3.3) | 2 (6.5) | 0 (0.0) |
| | *M (SD)* | *M (SD)* | *M (SD)* |
| Age | 39.7 (12.5) | 39.7 (13.7) | 39.6 (11.3) |
| PTSD severity (PCL-5) | 55.2 (10.8) | 55.5 (12.8) | 54.9 (8.4) |
| Negative cognitions (PTCI) | 157.3 (35.0) | 162.1 (38.5) | 152.1 (30.7) |

*Note.* EXP = experimental condition; CTL = control condition; PCL-5 = PTSD Checklist for DSM-5; PTCI = Posttraumatic Cognitions Inventory.

[a] High education = higher vocational education or university.

[b] non-Western cultural background = at least one parent who was not born in a Western country.

**Pre- to post exposure session change on outcome measures**

The change of the outcome measures from pre- to post exposure session can be found in Table 2. Mean scores and participant's individual trajectories are shown in Figure 2. For the primary outcome measures (i.e., fear responses to the trauma script), no significant interaction effects of time and condition were found, indicating that change from T1 to T3 on fear responses to the trauma script was similar between conditions. We found a significant time effect for HR-R, $b$ = -2.43, $SE$ = 0.65, $t$ = -3.72, $p$ < .001, Cohen's $d$ = -0.88, and $SUD_{peak}$, $b$ = -6.71, $SE$ = 2.98, $t$ = -2.25, $p$ = .028, Cohen's $d$ = -0.51, indicating that these outcome measures significantly decreased from pre-exposure session to post-exposure session. Effect sizes were medium to large. No

significant time effect was found for SCL-R, *b* = -0.10, *SE* = 0.21, *t* = -0.47, *p* = .640. The results of the multilevel model analyses with random intercepts are shown in Table 3.

Regarding the secondary outcome measure, we found no significant interaction effects of time and condition, indicating that change in PTSD symptomatology from T1 to T3 was similar between conditions. As threat appraisal did seem to differ between conditions at baseline, we added condition as a main effect to this model as well. We found a significant time effect for the PCL-5, *b* = -6.79, *SE* = 1.71, *t* = -3.97, *p* < .001, Cohen's *d* = -0.91. We found a significant effect of time on threat appraisal, *b* = -15.09, *SE* = 2.23, *t* = -6.78, *p* < .001, and a significant interaction of time by condition, *b* = 10.19, *SE* = 3.16, *t* = 3.23, *p* = .002, Cohen's *d* = 0.85, suggesting that those who were in the EXP condition had a larger decrease in threat appraisal compared to those in the control condition (see also Table 2 and Figure 3). We have reported the unadjusted *p*-values in this section, the corrected *p*-values can be found in Table 3.

**Table 2.** Change in outcome measures from pre- to post exposure session

| | Total | | EXP | | CTL | |
|---|---|---|---|---|---|---|
| | *N* | *M (SD)* | *n* | *M (SD)* | *n* | *M (SD)* |
| HR-R | | | | | | |
| T1 | 58[a] | 3.3 (5.2) | 31 | 4.4 (5.6) | 27[a] | 2.1 (4.5) |
| T3 | 55[b] | 0.8 (2.9) | 28[b] | 1.1 (3.2) | 27 | 0.5 (2.5) |
| SCL-R | | | | | | |
| T1 | 60 | 0.4 (1.3) | 31 | 0.6 (1.2) | 29 | 0.3 (1.5) |
| T3 | 55[b] | 0.3 (1.1) | 28[b] | 0.4 (1.3) | 27 | 0.2 (0.9) |
| $SUD_{peak}$ | | | | | | |
| T1 | 60 | 73.3 (23.4) | 31 | 73.7 (24.3) | 29 | 72.9 (22.8) |
| T3 | 56 | 66.5 (26.3) | 29 | 66.4 (24.2) | 27 | 66.5 (28.9) |
| PCL-5 | | | | | | |
| T0 | 60 | 55.2 (10.8) | 31 | 55.5 (12.8) | 29 | 54.9 (8.4) |
| T3 | 57 | 48.7 (12.5) | 30 | 48.2 (13.7) | 27 | 49.3 (11.2) |

**Table 2.** Change in outcome measures from pre- to post exposure session *Continued.*

| | Total | | EXP | | CTL | |
|---|---|---|---|---|---|---|
| | *N* | *M (SD)* | *n* | *M (SD)* | *n* | *M (SD)* |
| Threat appraisal | | | | | | |
| T1 | 59 | 37.5 (18.4) | 30 | 41.3 (20.5) | 29 | 33.4 (15.2) |
| T2 | 59 | 27.9 (18.6) | 30 | 27.4 (21.0) | 29 | 28.5 (16.1) |

*Note.* EXP = experimental condition; CTL = control condition; HR-R = Heart rate reactivity during imagery; SCL-R = Skin conductance level reactivity during imagery; SUD = subjective units of distress; PCL-5 = PTSD Checklist for DSM-5; T0 = baseline questionnaire (online); T1 = baseline assessment (on site); T2 = at the end of the exposure session; T3 = one week after the exposure session.

[a] HR data was missing for two participants at T1 (both in CTL condition) due to equipment problems that occurred during the assessment.

[b] Physiological data (HR and SCL) was missing for one participant at T3 due to equipment problems.



**Table 3.** Outcomes multilevel models

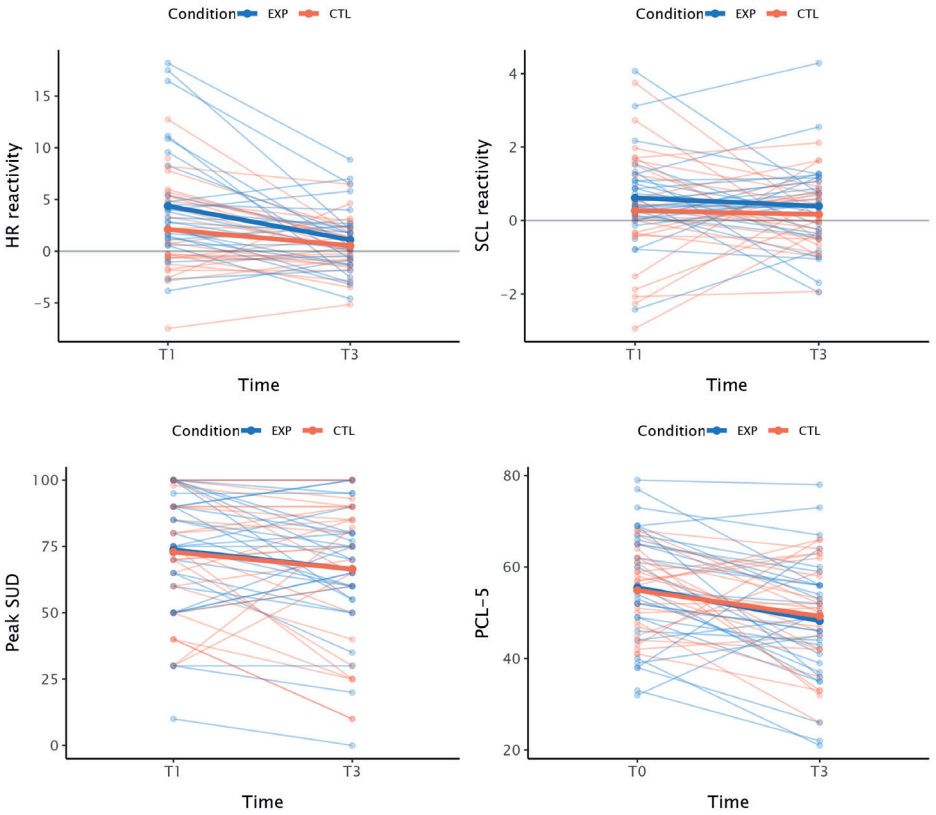
| | B | SE | *t* | *p* | *p** | *d* |
|---|---|---|---|---|---|---|
| HR-R | | | | | | |
| Intercept | 5.89 | 0.99 | 5.93 | <.001 | .002 | |
| Time | -2.43 | 0.65 | -3.72 | <.001 | .002 | -0.88 |
| Time*Condition | -0.26 | 0.55 | -0.48 | .635 | .731 | -0.10 |
| SCL-R | | | | | | |
| Intercept | 0.61 | 0.31 | 1.95 | .054 | .079 | |
| Time | -0.10 | 0.21 | -0.47 | .640 | .731 | -0.11 |
| Time*Condition | -0.14 | 0.16 | -0.90 | .369 | .492 | -0.20 |
| Peak SUD | | | | | | |
| Intercept | 79.74 | 4.79 | 16.66 | <.001 | .002 | |
| Time | -6.71 | 2.98 | -2.25 | .028 | .044 | -0.51 |
| Time*Condition | 0.55 | 3.15 | 0.17 | .863 | .863 | 0.03 |
| PCL-5 | | | | | | |
| Intercept | 61.78 | 2.64 | 23.43 | <.001 | .002 | |
| Time | -6.79 | 1.71 | -3.97 | <.001 | .002 | -0.91 |
| Time*Condition | 0.43 | 1.52 | 0.29 | .776 | .828 | 0.06 |
| Threat appraisal | | | | | | |
| Intercept | 57.61 | 4.57 | 12.61 | <.001 | .002 | |

**Table 3.** Outcomes multilevel models *Continued.*

| | B | SE | *t* | *p* | *p** | *d* |
|---|---|---|---|---|---|---|
| Time | -15.09 | 2.23 | -6.78 | <.001 | .002 | -1.78 |
| Condition | -19.30 | 6.51 | -2.97 | .004 | .007 | |
| Time*Condition | 10.19 | 3.16 | 3.23 | .002 | .004 | 0.85 |

*Note.* HR-R = Heart rate reactivity during imagery; SCL-R = Skin conductance level reactivity during imagery; SUD = subjective units of distress; PCL-5 = PTSD Checklist for DSM-5; *p** = corrected *p*-value with False Discovery Rate.

**Figure 2.** Changes in outcome measures across time per condition

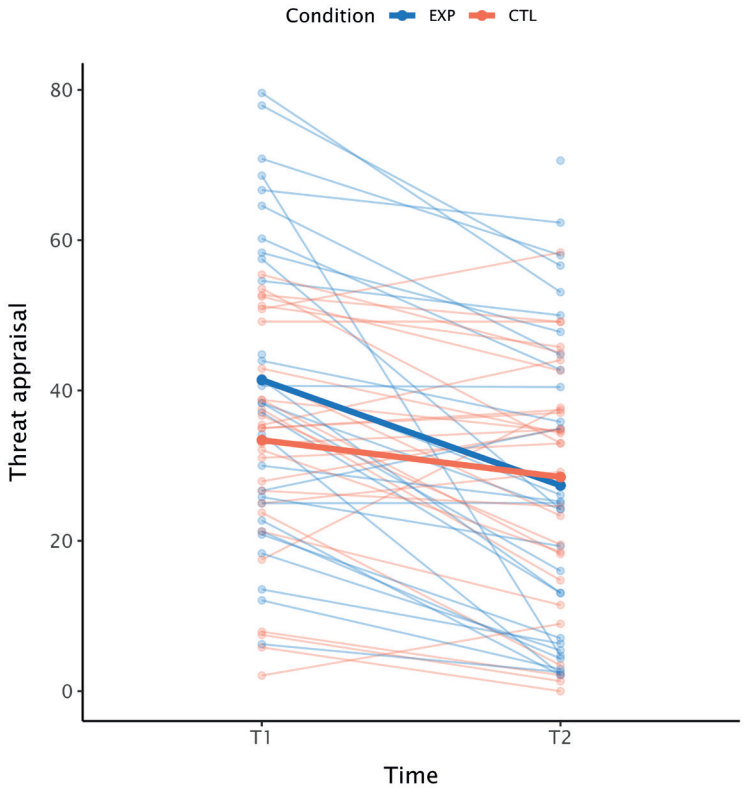



*Note.* HR = heart rate; SCL = skin conductance level; SUD = subjective units of distress; PCL-5 = PTSD Checklist for DSM-5; T1 = baseline assessment (on site); T3 = one week after the exposure session.

**Threat appraisal as mediator of exposure effects**

We expected that especially in the EXP condition, intervention effects would be driven by change in threat appraisal. In line with our hypotheses, the indirect effect of condition on both HR-R and PCL-5 through threat appraisal was significant, *b* = 0.56, *SE* = 0.27, 95% CI [0.01, 1.09] and, *b* = 2.60, *SE* = 1.27, 95% CI [0.69, 5.60], respectively. This suggests that the effect of condition on HR-R and PCL-5 was mediated by (lower) threat appraisal following exposure. The indirect effect of condition on $SUD_{peak}$ through threat appraisal (*b* = 3.61, *SE* = 2.19, 95% CI [-0.13, 8.49]) was non-significant. We did not assess a mediation with SCL-R, as there was no time effect with this outcome variable. Complete mediation outcomes (i.e., a, b, c and c' paths) can be found in Appendix B of this chapter.

**Figure 3.** Threat appraisal across time per condition




*Note.* T1 = baseline assessment (on site); T2 = end of the exposure session.

**Treatment acceptability**

On average, based on a 0-100 VAS scale, patients felt relatively positive about the exposure session, with no significant differences between conditions (EXP: *M* = 69.1, *SD* = 21.2; CTL: *M* = 66.3, *SD* = 25.6; *U* = 389.0, *p* = .859). Patients also found the exposure session quite burdensome, again with no significant differences between conditions (EXP: *M* = 83.9, *SD* = 19.1; CTL: *M* = 78.0, *SD* = 24.1; *U* = 443.0, *p* = .398). An open-ended question inquiring about the aspects that participants found most burdensome showed that participants mostly referred to exposure to the trauma memory (and not to specific treatment elements, per se).

As for the therapists, no significant between condition differences were found for how positively (EXP: *M* = 67.6, *SD* = 21.2; CTL: *M* = 73.8, *SD* = 18.0; *U* = 361.0, *p* = .193) nor how burdensome (EXP: *M* = 42.7, *SD* = 26.1; CTL: *M* = 33.2, *SD* = 22.8; *U* = 555.0, *p* = .120) they evaluated the session.

## Discussion

We found no differences in outcomes between two exposure conditions with or without an explicit focus on expectancy violation in a clinical sample of treatment-seeking PTSD patients using a single-session paradigm. Exposure outcomes were assessed through fear-related responses (heart rate reactivity, skin conductance reactivity and peak subjective distress) to a personalized imagery task. The secondary outcome was self-reported PTSD symptoms. Most of our participants had PTSD related to interpersonal violence. All measures, except skin conductance reactivity, decreased from pre – to post exposure session. We found some evidence that threat appraisals mediated exposure effects, indicating that more so in the expectancy violation condition, reduction in fear and PTSD symptoms was partly driven by a reduction in threat appraisal. Finally, therapists' and patients' experiences of the exposure sessions did not differ between conditions.

Based on the suggestion from the inhibitory retrieval approach (Craske et al., 2014, 2022) that a focus on prediction error might enhance exposure's efficacy, we expected that the expectancy violation condition would lead to more symptom reduction, but, surprisingly, we found no differences between conditions. Our finding also contrasts with an earlier study where exposure outcomes were superior when exposure continued until threat expectancies were low (Deacon et al., 2013). However, in line with our null-finding, other studies showed that the magnitude of expectancy violation was not associated with enhanced extinction learning or exposure outcomes (Buchholz et al., 2022; Jong et al., 2023; Krause et al., 2022; Stemerding et al., 2023). Furthermore, a wealth of studies demonstrate the efficacy of Prolonged Exposure, a specific exposure therapy protocol for PTSD without an

explicit focus on expectancy violation (McLean et al., 2022). In the current study, we do not find evidence that emphasizing the identification and the non-occurrence of negative expectancies during exposure leads to enhanced immediate PTSD-related treatment outcomes. As we used a single-session paradigm, we cannot rule out the possibility that one session was not sufficient to elicit longer term change.

Overlapping mechanistic constructs and varying construct operationalizations across the field make it difficult to study mechanisms (Benito et al., 2024; Cohen et al., 2023). We tried to elucidate how treatment delivery affected the mechanism of expectancy violation. Although we did not find significant differences between conditions in symptom reduction, our mediation findings suggest that especially in the EXP condition, intervention effects were driven by change in threat appraisal. More specifically, participants in the EXP condition showed a greater decrease in concern about potential PTSD-related negative outcomes, leading to more symptom reduction. These findings could suggest that focusing on threat expectancies and their violation during exposure enhances expectancy change (perhaps driven by enhanced awareness, see also Stemerding et al., 2023), which could subsequently drive symptom improvement (Pittig et al., 2022). Although, given unexpected baseline differences in threat appraisal between conditions, the alternative explanation that this reflects regression to the mean cannot be ruled out. As our control condition was not outperformed, alternative mechanisms might have played a bigger role here, such as distress habituation and more general cognitive change, i.e., cognitive change that is not related to CS-US predictions, such as negative views and judgments about oneself or the meaning of the trauma (Cooper, Clifton, et al., 2017). The effectiveness of treatment deliveries may also vary based on individual factors, such as differences in symptom presentations (e.g., varying levels of persistent negative beliefs or self-blame). Future research with larger sample sizes should assess multiple mediators simultaneously and assess what works best for whom.



It remains unclear whether it is advantageous to emphasize expectancies and their non-occurrence during (imaginal) exposure for PTSD. The inhibitory retrieval approach (Craske et al., 2022) attempts to target the principal CS-US association. As such, accurately identifying the most feared outcome (i.e., the US) is crucial. This requires that patients both recognize this outcome and can clearly articulate it. However, some patients have difficulty identifying their greatest fear, may have long-term feared outcomes that are untestable, or may have feared outcomes related to the inability to tolerate distress (Jacoby & Abramowitz, 2016; Scheveneels, Boddez, Van Daele, et al., 2019). This was also true for some patients in our study and may be more prevalent in complex clinical populations such as obsessive compulsive disorder (OCD) or PTSD, in comparison to specific phobia. Additionally, exposure

with an explicit focus on expectancy violation may work better for 'in vivo' than imaginal exposures, as expected outcomes are usually more concrete and easier to test in in vivo exposures (e.g., 'I will be assaulted again when going to crowded places'). Undoubtedly, cognitive changes, including the updating of expectancies, are central to the effectiveness of exposure therapy for PTSD (Brown, Belli, et al., 2019). However, as suggested by EPT (Cooper, Clifton, et al., 2017; Foa & Kozak, 1986), these changes may also occur implicitly, with patients modifying their cognitions at a level that does not require conscious awareness.

The current study has a number of limitations, including the single-session paradigm. A benefit of this paradigm is that we were able to isolate the effect of the manipulation more easily than in a large longitudinal trial with more confounding factors (e.g., doing homework, external stressors during the timeframe of treatment, etc.). However, we were unable to assess the effect over an extended period. Some expectancies may only be violated over repeated exposures. For instance, some patients are afraid that repeated exposure will lead to a mental catastrophe which makes them unable to take care of children or function at work. A full-scale RCT should be carried out, wherein the inhibitory retrieval model's posited strategies to enhance exposure outcomes are tested. Furthermore, this single session may have been insufficient for some patients to achieve meaningful improvements, which hinders comparisons between the delivery method of this session. It should also be noted that, on average, physiological reactivity at pretreatment was relatively low and some patients in our sample showed a blunted physiological response to the script-driven imagery, which may reflect dissociation (Carpenter et al., 2024; Sack et al., 2012). For these patients, a decrease of reactivity from pre to post treatment would actually not reflect better outcomes. Future studies using physiology during trauma-imagery should account for differential responding to trauma reminders in those suffering from PTSD. Crucially, we could not compare in-session threat expectancy violation between conditions, as it would have drawn attention to expectancies in the control group, undermining our manipulation. A more direct measure of the underlying mechanism would have been ideal, but it is still unclear how much simply measuring threat expectancies influences exposure outcomes. In the expectancy violation condition, we used the session form from Craske et al. (2014) to design exposure exercises. However, the form only includes pre-exposure perceived likelihood ratings, preventing us from tracking the degree of violation and its impact on outcomes. For our mediation analysis we used an unvalidated measure to operationalize threat appraisal, based on a validated measure to assess appraisal in social phobia (Telch et al., 2004). The results of our mediation analysis should thus be interpreted with caution. Finally, our study was powered to detect

large effects, as these were deemed clinically meaningful, but the study may have been underpowered to detect smaller differences between conditions.

The current study also has several strengths. Our study is the first that directly tests the effect of therapeutic procedures targeting expectancy violation on symptom reduction, while limiting dosage differences between conditions. We assess these effects in a clinical sample representative of routine clinical care (i.e., treatment-seeking PTSD patients). Additionally, few participants were lost to one-week follow-up. To assess exposure outcomes, we used a combination of measures, including self-report and psychophysiology. Finally, we test the acceptability of the exposure conditions, which has not been done previously. A recent meta-analysis suggested that the acceptability of exposure therapy is somewhat lower compared to other psychological interventions for PTSD (Hoppen et al., 2023). Given that exposure is, among others, the most effective treatment for PTSD, gaining insight into the therapeutic procedures that affect acceptability may be a crucial step in improving its efficacy.



To conclude, we found that exposure with an explicit focus on expectancy violation was not related to better outcomes. We also found that threat appraisal changes upon exposure, and more so in exposure that focuses expectancy violation. This, however, did not immediately transfer to PTSD symptomatology. Future work should address how to operationalize and measure threat expectancies and assess its long-term effects on exposure outcomes. More empirical work is necessary to assess whether the application of the inhibitory retrieval-based approach to exposure for PTSD is beneficial in routine clinical care.

# Appendix A

## Threat appraisal measure

The instructions and scoring of the threat appraisal measure was based on the Appraisal of Social Concerns questionnaire (ASC; Telch et al., 2004). Similar to the ASC, we chose to ask participants to rate their degree of concern about a negative anticipated outcome, aiming to capture its perceived likelihood and threat, whilst keeping the measure concise and easy to administer. Participants are asked to rate their level of concern for a negative outcome when confronted with a trauma reminder, ranging from 0 ('not at all concerned') to 100 ('extremely concerned'), where a score of 50 represents moderate concern.

**Table A1.** Overview of TAPS items, including their mean and rank at T1

| | | *M* (SD) | Rank |
|---|---|---|---|
| 1 | Screaming | 28.1 (31.6) | 19 |
| 2 | Throwing things | 30.7 (31.7) | 16 |
| 3 | Vomiting | 30.7 (32.3) | 16 |
| 4 | Having a heart attack | 19.5 (27.0) | 23 |
| 5 | Becoming a victim again/being in danger | 55.5 (37.8) | 3 |
| 6 | Choking | 28.7 (32.1) | 18 |
| 7 | Unable to move | 41.9 (36.1) | 8 |
| 8 | Fainting | 34.8 (30.7) | 13 |
| 9 | Not knowing where I am | 39.3 (32.8) | 10 |
| 10 | Hitting or kicking | 26.8 (33.1) | 20 |
| 11 | Unable to talk | 45.3 (34.1) | 7 |
| 12 | Unable to think (having a blackout) | 62.3 (32.4) | 1 |
| 13 | Swearing or cursing | 35.0 (36.7) | 11 |
| 14 | Unable to feel anything | 53.1 (34.5) | 4 |
| 15 | Hurting myself | 41.9 (37.2) | 8 |
| 16 | Wetting or soiling my pants | 12.1 (24.2) | 24 |
| 17 | Collapsing | 32.6 (31.1) | 14 |
| 18 | Dying | 22.3 (32.9) | 21 |
| 19 | Unable to stop crying | 48.2 (34.9) | 6 |
| 20 | Speaking gibberish | 32.3 (35.1) | 15 |
| 21 | Walking away or running away | 50.3 (34.5) | 5 |

**Table A1.** Overview of TAPS items, including their mean and rank at T1 *Continued.*

| | | *M* (SD) | Rank |
|---|---|---|---|
| 22 | Hurting someone else | 20.4 (30.2) | 22 |
| 23 | Moving uncontrollably | 35.0 (35.7) | 11 |
| 24 | Unable to function | 57.3 (34.2) | 2 |

*Note. M* = mean; *SD* = standard deviation; Rank = relative standing of the item based on highest mean.

# Appendix B

## Mediation analyses

**Table B1.** Results from mediation of threat appraisal between condition and exposure outcome variables.

| | B | SE | *t* | *p* | LLCI | ULCI |
|---|---|---|---|---|---|---|
| Model 1 | | | | | | |
| C → TA at T2 (a) | 9.48 | 3.27 | 2.90 | **.006** | **2.92** | **16.06** |
| TA at T2 → HRR at T3 (b) | 0.06 | .03 | 1.89 | .064 | -0.00 | 0.12 |
| C→ HRR at T3 (c) | 0.25 | 0.73 | 0.34 | .732 | -1.21 | 1.71 |
| C→ HRR at T3 (c') | -0.31 | 0.77 | -0.40 | .692 | -1.85 | 1.23 |
| C→ TA at T2→ HRR at T3 (a*b) | 0.56 | 0.27 | | | **0.01** | **1.09** |
| Model 2 | | | | | | |
| C → TA at T2 (a) | 8.72 | 3.13 | 2.78 | **.008** | **2.44** | **15.01** |
| TE at T2 → SUD at T3 (b) | 0.41 | 0.23 | 1.80 | .077 | -0.05 | 0.87 |
| C→ SUD at T3 (c) | 0.80 | 5.30 | 0.15 | .880 | -9.83 | 11.43 |
| C→ SUD at T3 (c') | -2.81 | 5.56 | -0.51 | .616 | -13.97 | 8.35 |
| C→ TA at T2→ SUD at T3 (a*b) | 3.61 | 2.19 | | | -.13 | 8.49 |
| Model 3 | | | | | | |
| C → TA at T2 (a) | 9.05 | 3.18 | 2.84 | **.006** | **2.66** | **15.43** |
| TA at T2 → PCL5 at T3 (b) | 0.29 | 0.12 | 2.37 | **.022** | **0.04** | **0.53** |
| C→ PCL5 at T3 (c) | 3.32 | 2.91 | 1.14 | .259 | -2.51 | 9.15 |
| C→ PCL5 at T3 (c') | 0.71 | 2.99 | 0.24 | .812 | -5.30 | 6.72 |
| C→ TA at T2→ PCL5 at T3 (a*b) | 2.60 | 1.27 | | | **0.69** | **5.60** |

*Note.* Model 1 is mediation model with heart rate reactivity as the outcome variable; Model 2 is mediation model with SUD peak as outcome variable; Model 3 is mediation model with the PLC-5 as outcome variable; a = effect of X on M; b = effect of M on Y; c = total effect of X on Y; c' = direct effect of X on Y controlling for M. The standard error and 95% CI for a*b are obtained by bootstrap with 50,000 re-samples. C = Condition; TA = Threat appraisal; HRR = Heart rate reactivity; SUD = subjective units of distress; PCL5 = PTSD symptomatology; T1 = baseline assessment (on site); T2 = at the end of the exposure session; T3 = one week after the exposure session; LLCI = lower bound of a 95% confidence; ULCI = upper bound of a 95% confidence interval; → **=** affects.

# Chapter 5

# Inhibitory retrieval-based exposure therapy for patients with PTSD: results from a single case experimental design study

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## Abstract

Exposure therapy is an effective treatment for Posttraumatic Stress Disorder (PTSD). The inhibitory retrieval (IR) approach to exposure utilizes strategies to optimize inhibitory learning and retrieval, but has yet to be systematically applied to PTSD. This randomized replicated single-case AB with follow-up design evaluated the applicability and effects of IR-based exposure therapy (12 sessions over four weeks) in patients ($n$ = 9) with DSM-5 defined PTSD. Daily measures of PTSD symptoms, negative expectancies and distress tolerance were collected during baseline, treatment and follow-up phases and analyzed using multilevel models for Single Case Experimental Designs (SCED). Results showed that PTSD symptoms significantly decreased over treatment compared to baseline ($b$ = - 0.22, $p$ <.001). Clinically meaningful symptom reductions were observed for most patients at post-treatment (56%) and follow-up (67%), as assessed with clinical interview. Negative expectancies significantly decreased over treatment in comparison to baseline ($b$ = - 0.60, $p$ =.001), while distress tolerance did not change significantly ($b$ = - 0.02, $p$ =.223). To explore specificity, a simultaneous study with a similar design ($n$ = 10) using Emotional Processing Therapy principles was conducted, yielding similar findings. This study provides initial evidence that IR-based principles can be effectively applied to exposure therapy for PTSD but does not indicate enhanced efficacy or unique effects on theorized change mechanisms. Future research should further examine change mechanisms to refine treatment approaches for PTSD.

*Keywords*: Posttraumatic stress disorder, Exposure therapy, Inhibitory learning and retrieval, Single case experimental design

## Introduction

Exposure therapy is one of the treatments of choice for posttraumatic stress disorder (PTSD; (Mavranezouli et al., 2020; McLean et al., 2022). It involves repeated exposure to traumatic memories (imaginal exposure) and to anxiety-provoking trauma-related situations (exposure in vivo). Exposure therapy for PTSD is commonly administered in accordance with the treatment manual of Prolonged Exposure (PE; Foa et al., 2019; McLean et al., 2022), a well-established approach rooted in Emotional Processing Theory (EPT; Rauch & Foa, 2006). Briefly summarized, EPT posits that exposure works through emotional processing, which is the process of integrating corrective information into an existing fear structure to alter emotional responses (Foa & Kozak, 1986; Foa & McLean, 2016). Emotional processing cannot be assessed directly; however changes in cognition and reductions in distress are proposed indicators of successful processing taking place. Substantial empirical evidence suggests that change in trauma-related cognitions is a reliable indicator of symptom improvement in PE (Alpert, Shotwell Tabke, et al., 2023; Brown, Belli, et al., 2019), but evidence for distress reduction has been mixed (Cooper, Clifton, et al., 2017). This has led to growing interest in alternative theoretical perspectives that challenge assumptions about the role of fear reduction and offer new directions for optimizing exposure therapy, particularly in light of suboptimal exposure outcomes for a group of patients (Larsen et al., 2019).



Based on principles of extinction learning, the inhibitory learning and retrieval (IR) approach to exposure posits to optimize exposure therapy by strengthening the formation and retrievability of inhibitory associations (Craske et al., 2008, 2014; Pittig et al., 2016). These associations are formed when a feared stimulus is repeatedly presented in the absence of the feared outcome, and they inhibit the original fear-excitatory associations (Bouton, 1993). The original association is not erased, and the development and retrievability of the competing inhibitory association is therefore essential for exposure therapy's effectiveness. The IR approach to exposure introduces several therapeutic strategies to strengthen inhibitory learning and retrieval. These strategies include maximizing expectancy violation, deepened extinction, incorporating variability, and removal of safety behaviors. The main differences between an EPT or IR approach to exposure are: (1) in the IR approach, expectancies (future-related if-then statements) are specified prior to exposure, and exposure is designed to test these expectancies, with their non-occurrence explicitly emphasized afterward; in contrast, the EPT approach does not focus on identifying expectancies prior to exposure, and (2) in the IR approach, stimulus, fear, and context variability is increased by, for example, focusing on several feared stimuli, while in the EPT approach gradual, repeated exposure is emphasized. Furthermore,

the IR approach emphasizes that inhibitory associations can develop independently of distress reduction, suggesting that exposure should prioritize tolerating distress rather than diminishing it.

Although the IR approach has been widely embraced, research evaluating comprehensive treatment protocols that apply IR principles is scarce. Multiple studies have examined the effect of individual strategies on exposure (see, for example: Deacon et al., 2013; Jong et al., 2023; Kooistra et al., 2025; McGlade & Craske, 2021; Scheveneels, Boddez, Vervliet, et al., 2019), with mixed results on outcomes. Only one study has examined the applicability of an IR-based approach to exposure therapy, encompassing multiple strategies, in a sample of patients with pathological health anxiety, using a case series design (Sauer et al., 2023). We thus have limited understanding of the effects of a full IR-based approach to exposure. An initial step in evaluating the IR approach as a way to optimize exposure is to examine its effects in clinical practice, particularly in patients suffering from complex disorders such as PTSD.

Therefore, the first aim of the current study is to investigate whether adopting an IR-based approach to exposure therapy for PTSD leads to clinically meaningful symptom change. The second aim is to test whether this approach leads to change in two proposed treatment mechanisms: expectancy change and distress tolerance. Multiple empirical studies have shown that greater expectancy change over the course of treatment is related to better treatment outcomes (e.g., de Jong et al., 2024; Pittig et al., 2022; Scheveneels & Carpentier, 2024). Expectancy violation, the mismatch between expectation and outcome, is presumed to drive expectancy change (Pittig et al., 2022). Several (clinical) studies have tested whether maximizing expectancy violation leads to better exposure outcomes, but so far, findings are mixed (Baker et al., 2010; Deacon et al., 2013; Krause et al., 2022; Scheveneels, Boddez, Van Daele, et al., 2019). In a previous study, we found that emphasizing expectancies and their non-occurrence during exposure for PTSD did not result in greater short-term symptom reduction, although it did appear to facilitate short-term expectancy changes (Kooistra, Schoorl, et al., 2025). In the current study, we will assess expectancies over a longer period, allowing us to test the effect of IR-based exposure on expectancy changes over the course of treatment. Distress tolerance, i.e., the idea that one can tolerate uncomfortable distressing feelings, has been theorized to facilitate extinction learning by allowing an individual to engage in goal-directed behavior despite feelings of distress (Asnaani et al., 2016; Craske et al., 2008). It has been proposed that increasing distress tolerance is one of the mechanisms through which exposure therapy leads to symptom relief (Benito et al., 2024). Distress tolerance has been found to increase during IR-based exposure therapy for health anxiety (Sauer et al., 2023) and to predict symptom improvement

in exposure therapy for obsessive-compulsive disorder (Xu et al., 2024). However, no studies have yet tested whether distress tolerance increases during exposure therapy for PTSD.

The current study is a first attempt to examine a full treatment protocol following IR-based principles in a sample of patients with PTSD. We employed a single-case experimental design (SCED), closely following patients before, during and three months after IR-based exposure therapy for PTSD. Participants completed daily measures of PTSD symptoms, negative expectancies and distress tolerance during baseline, treatment and follow-up. These daily measures provided us with sufficient statistical power to test treatment effects even in a small sample. They also offered a more nuanced understanding of how treatment impacts individuals differently and ensured greater temporal precision in capturing the immediate effects of treatment on symptoms and proposed mechanisms. We hypothesized that IR-based exposure would lead to significant and clinically meaningful reductions in PTSD symptoms from baseline to post-treatment and follow-up. Additionally, we hypothesized that IR-based exposure would reduce negative expectancies and enhance distress tolerance. To explore the relationship between therapeutic procedures and change mechanisms, we carried out another SCED (c.f. Hollander et al., 2020) using an EPT-based approach (i.e., the PE manual; Foa et al., 2019), in which we investigated the same aims. Carrying out the additional SCED allowed us to gauge whether any of the established effects are specific to IR-based exposure or not.



## Methods

### Design

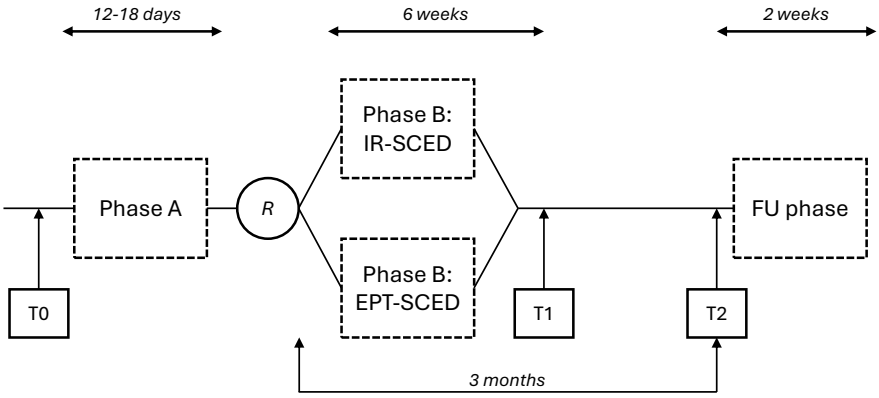
This study follows the Single-Case Reporting Guidelines in Behavioral Interventions (SCRIBE; Tate et al., 2016). This study uses a sequentially randomized replicated single-case AB with follow-up design: a baseline phase (A), intervention phase (B), and a follow-up phase (FU). A randomization list was generated by computer software and an independent researcher guarded the randomization. Each participant was randomly allocated to 1) length of baseline phase (varying between 12 and 18 days) and 2) SCED study (IR vs EPT). Both SCEDs included exposure therapy, comprising twelve 90-minute exposure sessions delivered over four weeks.

Primary outcomes were collected with daily measures via an app (m-Path; Mestdagh et al., 2023). Participants completed daily measures for 12-18 days during the baseline phase (phase A), 56 days (four weeks of treatment and two weeks immediately after) during the treatment phase (phase B), and for 14 days three months after the start of the intervention (follow-up, FU, see Figure 1). In addition to the daily measures, three assessments took place, carried out by a member of the

research team. The baseline assessment (T0) was scheduled approximately three to two weeks before the start of the intervention. The posttreatment assessment (T1) took place in the week after the final session of the intervention. The follow-up assessment (T2) took place at three-month follow-up.

Data for this study was collected between October 2023 and September 2024. The study was approved by the Medical Ethics Committee of Leiden the Hague Delft (NL83302.058.22) and the study was registered in the International Clinical Trial Registry Platform (https://trialsearch.who.int/; NL-OMON53620).

**Figure 1.** Overview of the study design




*Note.* T0 = Baseline assessment; T1 = posttreatment assessment; T2 = three-month follow-up assessment; Phase A = baseline phase; Phase B = intervention phase; FU phase = follow-up phase; R = randomization; IR-SCED = SCED with inhibitory retrieval-adapted exposure intervention; PE-SCED = SCED with Prolonged Exposure intervention based on Emotional Processing Theory.

### Participants

We included participants from two Dutch outpatient mental health services specializing in the treatment of PTSD, with at least eight participants per SCED study (IR-SCED and EPT-SCED). Enrollment was continuous and ceased when the eighth participant in each SCED met criteria for inclusion in the analysis (i.c., > 5 assessments in each phase).

Participants were included if they (1) satisfied DSM-5 defined criteria for chronic PTSD as established by CAPS-5 interview (primary diagnosis), following repeated trauma; (2) had at least three distinct memories associated with the index trauma;

(3) had self-reported PTSD symptoms above the clinical cut-off (i.e., PCL-5 score > 31; Meer et al., 2017); (4) had at least three trauma-related negative expectancies (VAS > 70); (5) owned a smartphone to be able to complete the daily measures; (6) aged between 18 and 70 years. Participants were excluded if they: (1) were currently undergoing trauma-focused treatment (e.g., prolonged exposure, EMDR), (2) had received prolonged exposure treatment for PTSD in the past (> three sessions), (3) were experiencing ongoing traumatization, (4) had significant suicidal ideations or serious self-injurious behavior, or had enacted suicidal behaviors or serious self-injurious behavior within three months prior to intake, (5) had a diagnosis of autism spectrum disorder (established by the referring institution), (6) had an intellectual disability (estimated IQ < 80), (7) had a severe substance use disorder, (8) had a somatic illness that interfered with exposure interventions, (9) were pregnant, (10) could not commit to refraining from using sedative medication or alcohol on the days of the intervention and testing, (11) or had insufficient ability to speak and write Dutch.



**Measures**

*Daily measures*

Participants received one questionnaire (13 items) on their smartphone each day during the phases (total amount of questionnaires ranging from 68 to 74, depending on baseline length). The notification was sent at 9AM. Participants were able to fill out the questionnaire until 12AM (midnight), with reminders sent every two hours.

**PTSD symptomatology** was measured with the 8-item version of the PCL-5 (Price et al., 2016), hereafter referred to as PCL-5*. Items referred to the past 24 hours. Items are scored on a 5-point Likert scale, ranging from 0 (not at all) to 4 (extremely). The total score ranges from 0 to 32. Previous research has successfully used this abbreviated version for the daily tracking of PTSD symptoms (Brier et al., 2020; Contractor et al., 2024), and the scale has shown to have good psychometric properties (Geier et al., 2020; Price et al., 2016).

**Negative expectancies** were measured with two idiosyncratic items ("*In the past 24 hours, when you were confronted with something that reminded you of the trauma, how concerned were you that…*?") rated on a 0-100 VAS scale. Rating idiosyncratic exposure-related expectancies this way is common practice (de Jong et al., 2024; de Kleine et al., 2017; Pittig et al., 2022). To guide participants in choosing their idiosyncratic expectancies, they first rated a questionnaire with prespecified negative outcomes on how concerned they were that might happen to them. Within the IR framework, exposure exercises are aimed at testing whether the expected negative outcome actually occurs, making it crucial that the expectancies are clearly defined to allow for effective testing (Craske et al., 2022). Together with the

researcher, the participants discussed which concrete and testable expectancies represented their most feared outcome (i.e., the US). If the US was not concrete (e.g., 'losing control'), participants chose a behavioral response associated with this outcome (e.g., 'not being able to talk'). Negative expectancies could not be about the fear response (e.g., 'I will panic'). Throughout the study participants rated the same two expectancies, and these scores were averaged per day, with ranges from 0 ('not concerned at all') to 100 ('extremely concerned').

**Distress tolerance** was measured through the 3-item 'tolerance' subscale of the Distress Tolerance Scale (DTS; Simons & Gaher, 2005), which measures the perceived ability of someone to tolerate emotional distress (the specific items were: 'feeling distressed or upset is unbearable to me', I can't handle feeling distressed or upset', and 'there's nothing worse than feeling distressed or upset'). All items asked about the past 24 hours. Items are scored on a 5-point Likert ranging from 1 ('strongly disagree') to 5 ('strongly agree'). The total score ranges from 5 to 15, where higher scores indicate more distress tolerance. The psychometric properties of the DTS are considered to be good (Galiano et al., 2024; Simons & Gaher, 2005).

**Assessment measures**

To assess PTSD symptomatology, the Clinician-Administered PTSD Scale (CAPS-5; Boeschoten et al., 2018; Weathers et al., 2018) and the PTSD Checklist for DSM-5 (PCL-5; Blevins et al., 2015; Weathers et al., 2013) were used. The CAPS-5 is a 20-item clinical interview that assesses both DSM-5 PTSD diagnostic criteria and PTSD symptom severity. Total scores range from 0 to 80, where higher scores indicate higher symptom severity. The PCL-5 is a 20-item self-report questionnaire which assesses PTSD symptoms. Total PCL-5 score ranges between 0-80 with higher scores indicating higher symptom severity. Both of these measures have good psychometric properties.

The Posttraumatic Cognitions Inventory (PTCI; Foa et al., 1999) was administered to asses negative posttraumatic cognitions. The PTCI is a 36-item questionnaire, scored on a 7-point Likert scale. The total PTCI score ranges from 33 to 231. Its psychometric properties are good.

**Exposure approaches**

All participants received twelve 90-minute sessions of exposure therapy, with homework assignments between sessions. Before the start of therapy, all participants had one preparatory session with their therapist. In this session, exposure therapy was introduced (without reference to its specific mechanisms of action). Moreover, topics such as substance use/abuse, suicidal ideation, and social support were discussed. Importantly, these sessions identified the index

trauma, determining which traumatic experience was most related to the current PTSD symptoms and functional interference. Participants started with exposure therapy approximately the week after.

The EPT-approach to exposure (EPT-SCED) followed the treatment manual by Foa et al. (2019). It included psycho-education, in vivo exposure, and imaginal exposure and processing. During psycho-education, emotional processing, signaled by distress reduction, was emphasized as exposure's mechanism of action. One distinct memory related to the index trauma was the primary focus of treatment. Exposure was gradual, with participants beginning in session five to focus on the most distressing parts of the trauma memory, known as hotspots. A hierarchy was also used for in vivo exercises. Ratings of subjective units of distress (SUDs) were used to monitor distress levels throughout exposure. The protocol also included breathing retraining to help the patient reduce general tension and anxiety that might disrupt daily functioning. All sessions were carried out by the same therapist with a similar room set-up each session. Although the presentation of new and corrective information is a central aspect of PE, specific and concrete expectancies were not identified prior to exposure, and their non-occurrence was not specifically emphasized after exposure during processing.



The IR approach to exposure (IR-SCED) was an adaptation of the PE protocol, following recommendations by (Craske et al., 2014, 2022). During psycho-education, inhibitory learning and retrieval was emphasized as exposure's mechanism of action. Exposure exercises were designed as 'hypothesis-testing mini-experiments', in which patients tested their most feared outcome (US). Using the OptEx Nexus (a map of associations, see Craske et al., 2022), therapists were instructed to identify the 'principal CS' (the stimulus that is most predictive of the US occurring) as main target. Furthermore, therapists identified and removed safety signals (i.e., conditional inhibitors and negative occasion setters) during the exposure. In vivo exercises were introduced in the first session and tailored to optimally test the most important feared outcome. Participants were encouraged to tolerate the distress that might arise from the exposure exercises and to direct their attention toward the disconfirmation of expectancies related to their distress or external danger. Throughout exposure treatment, variability was increased. Three distinct memories associated with the index trauma were selected and were the focus of treatment. Since variability should not come at the expense of extinction to the primary CS (Craske et al., 2022), half of the imaginal exposure sessions were focused on the most distressing memory related to the index trauma. The first two imaginal exposure sessions focused on this memory. From the third session onwards, the patient and therapist randomly drew a card from an envelope containing nine folded cards, each specifying one of the predetermined distinct memories, to

determine the focus of the session. Moreover, participants were immediately encouraged to focus on 'hotspots' during imaginal exposure. Thus, exposure was not gradual. Expectancy ratings were used to monitor expectancy violation and change in expectancies (see 'exposure plan' and 'exposure log' in (Craske et al., 2022). Per session, two imaginal exposure exercises were conducted. After each exposure exercise, attention was paid to the recognition and non-occurrence of the feared outcome, thereby promoting the consolidation of new learning (i.e., CS-noUS association). If, throughout treatment, other/new USs were identified, a new OptEx nexus was generated for this specific US. Contextual variability was maximized by changing the room in which the exposure took place (i.e., different furniture and odor). Furthermore, three sessions were provided via video-conferencing. Variability was further increased by alternating between two therapists who conducted the exposure. A brief overview of the differences between treatment approaches is presented in Table 1.

Therapists' adherence to the protocols was ensured through training and weekly group supervision (supervisor RAdK). We further assessed protocol adherence through checklists filled out by the therapists (see Foa et al., 2019). All participants received twelve treatment sessions. In IR-SCED, at least one OptEx Nexus for in vivo and one for imaginal exposure was drafted for all participants. All participants had two therapists, except one who had three due to the original therapist's illness-related absence. Half of the sessions for all participants focused on the index trauma, and half on related traumatic events. Most participants had some sessions online (typically three out of twelve, with one participant having two due to technical issues). Hotspots were introduced immediately for all. Imaginal exposure was provided in all but one session, where in vivo exposure was used. For the majority of sessions (79.8%) it was reported to consist of two imaginal exposure exercises, lasting about 40 minutes. In EPT-SCED, all patients had one therapist, all sessions were on site, and hotspots were introduced gradually. For most participants, all sessions focused on the index trauma. For two participants, the index trauma was changed during therapy, as another traumatic event became more prominent, with no further changes made thereafter. Imaginal exposure was provided in all sessions where planned, and in the majority of sessions (93.3%), it was reported to last at least 40 minutes.

**Table 1.** Overview of exposure approaches

| | IR-exposure | EPT-exposure |
|---|---|---|
| Rationale | Inhibitory learning and retrieval | Emotional processing |
| View on distress | Tolerance (distress can be experienced and withstood) | Reduction (distress diminishes over time) |
| Stimulus variability | High | Low |
| | - 50% index; 50% related events | - 100% index |
| Fear variability | High | Low |
| | - Random | - Gradual |
| | - Focus on hotspots: session 2 | - Focus on hotspots: session 4 |
| Context variability | High | Low |
| | - Two alternating therapists | - One therapist |
| | - 25% of the sessions online | - All sessions on-site |
| | - Different office set-up | - Same office |
| Process variable | Threat expectancies | SUDs |



**Data analysis**

Data were analyzed in Rstudio (version 2024.9.0.375). Descriptive information was provided on the individual level. We visually inspected the diary data (i.e., PCL-5 short version, PCL-5*; negative expectancies, N-exp; and tolerance subscale of the distress tolerance scale, DT-T) on the individual level across the different phases (A, B and follow-up). Furthermore, for all three diary measures, we calculated the pooled standardized mean difference (pSMD), which is recommended as a possible quantification for the effect size of levels across phases (Tanious et al., 2019).

To evaluate the effects of the exposure intervention on the diary measures (PCL-5*, N-exp and DT-T) across cases within each SCED (IR vs EPT), we ran separate hierarchical linear models for single case analyses (e.g., Manolov & Moeyaert, 2017; Moeyaert et al., 2014), using the nlme package in R (Pinheiro et al., 1999). Our data analytic plan was informed by Sauer et al. (2023; IR-based exposure using a single-case series). Compared to the baseline (phase A), we assessed the effect of the intervention (phase B) on both the intercept and slope, and the effect of the follow-up (phase FU) on the intercept only, as we had no hypotheses regarding slope during follow-up. Two dummy variables were created for Phase to contrast the level of the intervention and the follow-up phases with the baseline. The first dummy variable, Phase1, was coded 1 for the intervention, and 0 for the baseline and follow-up.

The second dummy variable, Phase2, was coded 1 for follow-up and 0 for baseline and intervention. We also created dummy variables for Time (i.e., daily repeated measures) to investigate slopes during phases (see also Moeyaert et al., 2014; Sauer et al., 2023). The first dummy coded time variable, Time1, equaled 0 at the start of the baseline (A) and remained constant after the start of the intervention (B). The second time variable, Time2, was centered around the start of the intervention (B), e.g., the first measurement of the intervention is indicated as 0. We used the following regression equation for the level 1 data:

$$Y_{ij} = \beta_{0j} + \beta_{1j}Time1 + \beta_{2j}Phase1 + \beta_{3j}Phase2 + \beta_{4j}Time2Phase1$$

Here, $\beta_{0j}$ , reflects the baseline intercept, $\beta_{1j}$ reflects the slope within the baseline, $\beta_{2j}$ reflects the immediate effect of the intervention relative to the end point of the baseline, $\beta_{3j}$ reflects the averaged effect of the follow-up relative to the baseline (intercept), and $\beta_{4j}$ reflects the change in slope due to the onset of the intervention. Random effects of intercept and slopes were entered in all multilevel models. We also incorporated a parameter typically applied in first-order autoregressive models (i.e., AR(1)) to account for autocorrelation (see also Hoeboer et al., 2024; Maric et al., 2015). Missing data was handled with maximum likelihood estimation. Following recommendations (McNeish & Stapleton, 2016), all models were calculated using Restricted Maximum Likelihood Estimation (REML).

Secondly, we assessed PTSD symptomatology (CAPS-5, PCL-5) for each participant at each assessment timepoint. We used the Leeds Reliable Change Index (RCI) to evaluate whether an individual's change on PCL-5 and CAPS-5 score was reliable (Morley & Dowzer, 2014), which is commonly used to determine whether an individual's change in a particular measure over time is reliable and beyond what would be expected due to chance alone. To calculate the Leeds RCI, the test-retest correlation and standard deviation of this measure are needed. For the CAPS-5, we used .78 for test-retest correlation (Weathers et al., 2018) and 9.54 for the SD (derived from a large RCT we conducted in a similar population, Oprel et al., 2021). For the PCL-5, we used .82 for test-retest correlation (Blevins et al., 2015) and 13.64 for the SD (derived from a large RCT we conducted, Oprel et al., 2021). Participants with an RCI >1.96 or <-1.96 were classified as having experienced a reliable increase or decrease, respectively, in PTSD symptoms.

This study was preregistered at the open science framework (OSF; osf.io/3dn7w) and adaptations in our data-analytic strategy (i.e., a switch from randomization tests to multilevel analyses) were logged here.

## Results

The attrition diagram is presented in Figure 2. In the IR-SCED, ten patients were included and started the intervention. All participants had sufficient datapoints (>5) per phase. For one participant, treatment and assessments were discontinued due to ongoing traumatization, a predefined exclusion criterion, requiring different therapeutic intervention. We classified this as a late exclusion. This led to a final sample of nine participants (*N* = 9). All participants completed the assessment timepoints. In the EPT-exposure SCED, ten patients were included and started the intervention. All participants had sufficient datapoints (>5) per phase. This led to a final sample of ten participants (*N* = 10). One participant (P4) discontinued the intervention. This participant did complete the post-intervention assessment (T2), but not follow-up (T3). Two participants (P12 and P18) missed T1 questionnaires, and P18 also missed follow-up diary data. Compliance with the diary measure was good. Across SCEDs, a total of 1,472 questionnaires were sent out, of which 1,209 (82.1%) were completed. The percentage of missed questionnaires per participant ranged from 0% (P9, P14, and P17) to 59% (P4, who dropped out).



See Table 2 for characteristics on the individual level. In IR-SCED, the mean age was 31.6 (*SD* = 12.8), the majority were women (*n* = 6, 66.7%), most had a western cultural background (*n* = 6, 66.7%), and the majority was a student or employed (*n* = 7, 77.8%) with two people being unemployed or unable to work. In EPT-SCED, the mean age was 34.0 (*SD* = 12.1), the majority were women (*n* = 9; 90%), most had a western cultural background (*n* = 8, 80%) and the majority was a student or employed (*n* = 6, 60%) with four people being unemployed or unable to work. In both SCEDs, the participant's index trauma was either related to sexual or physical abuse, mostly experienced during childhood.

**Figure 2.** Attrition diagram

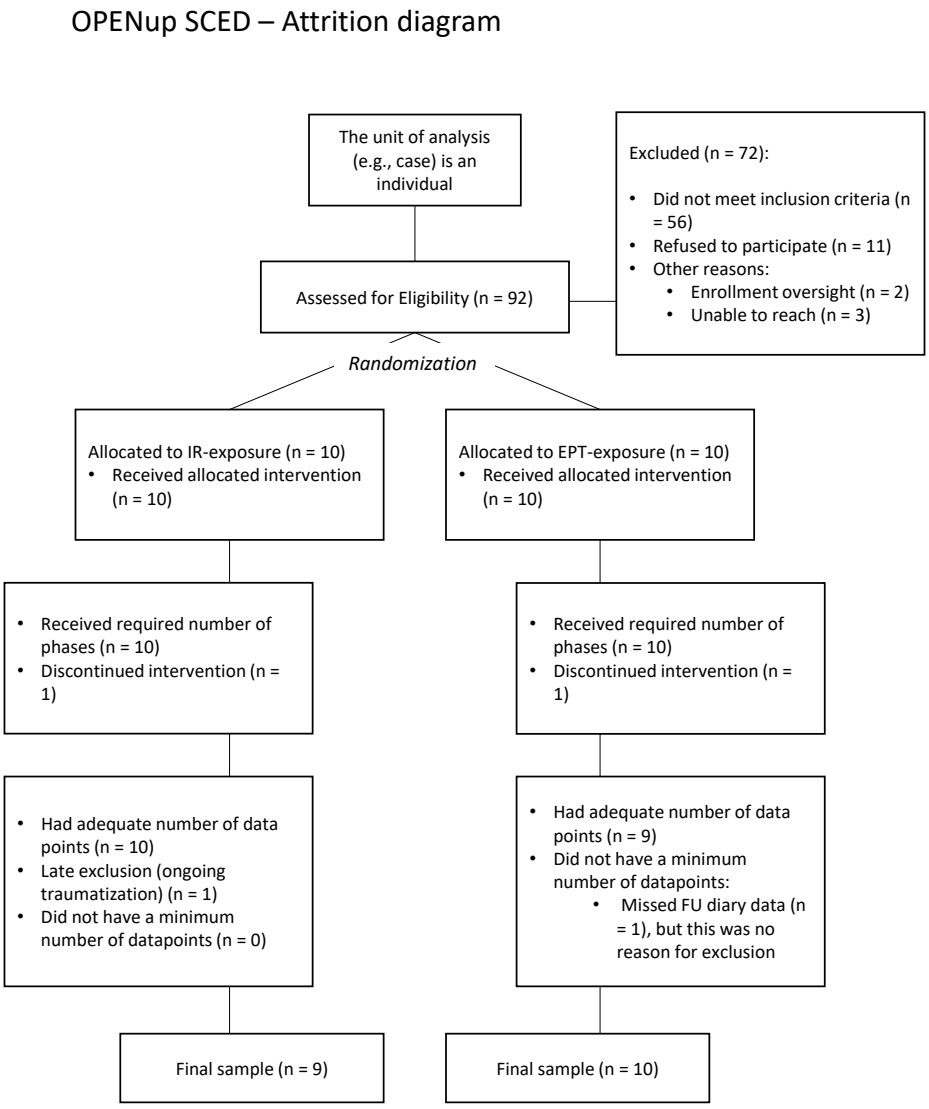


**Table 2.** Baseline characteristics of participants including their idiosyncratic negative expectancies

| Study | ID | Baseline days | Gender | Age | CAPS-5 at T0 | Index trauma | Childhood | Negative expectancy 1 | Negative expectancy 2 |
|---|---|---|---|---|---|---|---|---|---|
| IR | P2 | 18 | W | 21 | 36 | Physical abuse | N | Becoming a victim again/ being in danger | Choking |
| | P3 | 12 | W | 43 | 30 | Sexual abuse | Y | Unable to think (having a blackout) | Unable to stop crying |
| | P7 | 18 | W | 23 | 33 | Sexual abuse | Y | Vomiting | Being rejected |
| | P9 | 13 | M | 23 | 39 | Sexual abuse | Y | Walking away or running away | Unable to function |
| | P10 | 18 | M | 61 | 48 | Physical abuse | Y | Becoming a victim again/ being in danger | Hitting or kicking |
| | P11 | 18 | M | 30 | 41 | Physical abuse | Y | Being rejected | Unable to stop crying |
| | P14 | 18 | W | 26 | 32 | Sexual abuse | Y | Dying | Unable to stop crying |
| | P15 | 14 | W | 31 | 34 | Sexual abuse | N | Becoming a victim again/ being in danger | Unable to feel anything |
| | P16 | 14 | W | 26 | 40 | Physical abuse | Y | Unable to think (having a blackout) | Unable to stop crying |
| EPT | P1 | 13 | W | 24 | 55 | Sexual abuse | Y | Swearing or cursing | Throwing things |
| | P4 | 12 | W | 27 | 38 | Physical abuse | Y | Becoming a victim again/ being in danger | Hurting someone else |
| | P5 | 14 | M | 29 | 24 | Physical abuse | Y | Becoming a victim again/ being in danger | Unable to feel anything |
| | P6 | 13 | W | 54 | 48 | Sexual abuse | Y | Becoming a victim again/ being in danger | Unable to talk |

**Table 2.** Baseline characteristics of participants including their idiosyncratic negative expectancies *Continued.*

| Study | ID | Baseline days | Gender | Age | CAPS-5 at T0 | Index trauma | Childhood | Negative expectancy 1 | Negative expectancy 2 |
|---|---|---|---|---|---|---|---|---|---|
| | P8 | 15 | W | 29 | 63 | Physical abuse | Y | Speaking gibberish | Becoming a victim again/ being in danger |
| | P12 | 17 | W | 39 | 38 | Sexual abuse | Y | Becoming a victim again/ being in danger | Being rejected |
| | P13 | 14 | W | 24 | 25 | Sexual abuse | Y | Being ignored | Unable to move |
| | P17* | 16 | W | 22 | 40 | Physical abuse | Y | Unable to stop crying | Unable to function |
| | P18 | 13 | W | 55 | 44 | Physical abuse | N | Becoming a victim again/ being in danger | Unable to function |
| | P19 | 14 | W | 37 | 46 | Sexual abuse | Y | Hurting myself | Unable to function |

*Note.* IR = Inhibitory retrieval; EPT = Emotional processing theory; ID = participant; W = woman; M = man; CAPS-5 at T0 = baseline score of the Clinician-Administered PTSD Scale for DSM-5; Childhood = whether the index trauma happened during childhood.
* This participant was mistakenly included with minimum baseline expectancies of 60 rather than 70. Given that thresholds of 60 are also used in exposure (e.g., Craske et al., 2022) and treatment and assessments were already completed, we decided to retain them.

**Daily measures**

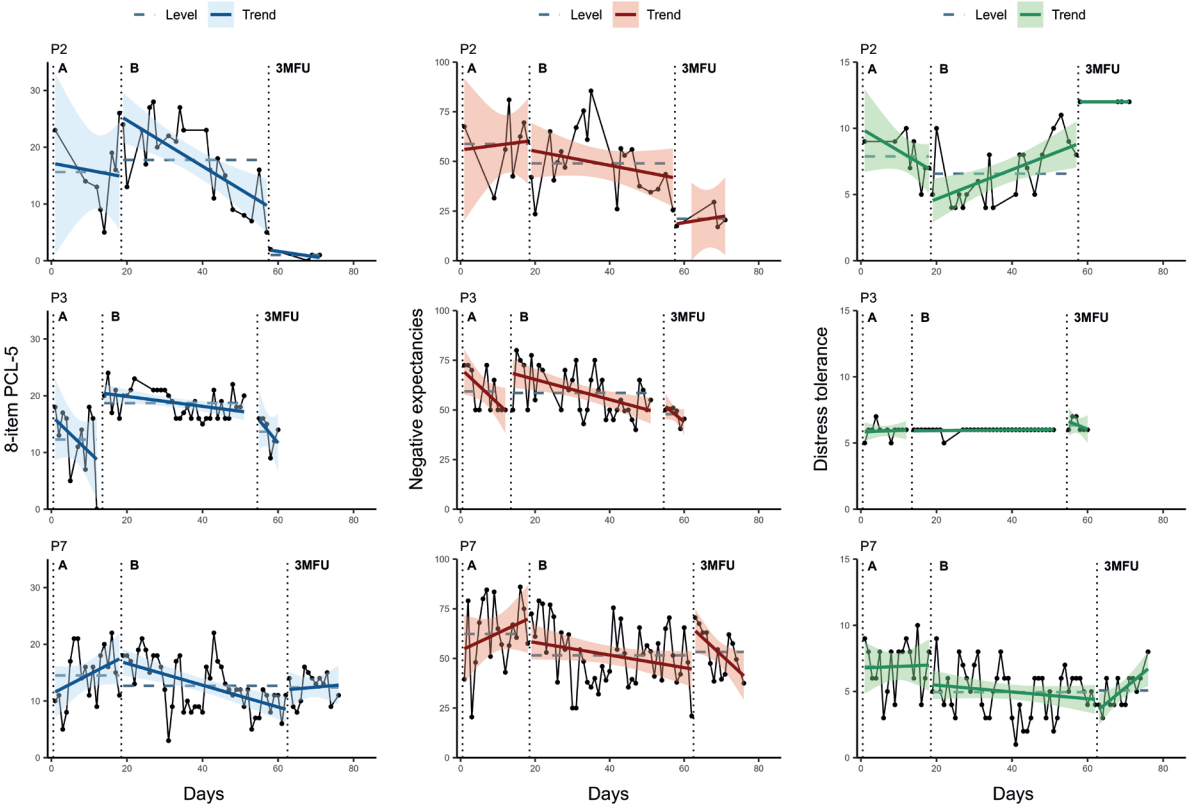
*Individual level*

The individual graphs on the PCL-5*, N-exp, and DT-T across phases (A, B, FU) are shown in Figure 3. For the sake of manuscript conciseness, the appendix contains the individual graphs of the EPT-SCED (Appendix A) and the raw scores of the individual data of both SCEDs (Appendix B). Through visual inspection of the IR-SCED figures we observed that PCL-5* and N-exp scores exhibit considerable day-to-day fluctuations, both during baseline (PCL-5* range *SD* = 1.54-6.97, N-exp range *SD* = 4.27-17.79) and treatment (PCL-5* range *SD* = 1.16-7.77, N-exp range *SD* = 2.65-30.41), with some exceptions (P9 and P11). During FU, there appears to be less fluctuation in these measures (PCL-5* range *SD* = 0.74-2.74, N-exp range *SD* = 0.00-11.60). DT-T scores were generally more stable, with several participants showing very minimal to no variation in responses (see, for instance, P14). During baseline, no clear up-or downward trends are observed in any of the measures. Additionally, there is no immediate decrease in any of the measures with the onset of treatment. Similar observations were made through the visual inspection of EPT-SCED.



The pSMD values (i.e., effect size for level) for PCL-5*, N-exp, and DT-T are shown in Table 3. In IR-SCED, for the A-B comparison, the majority of participants showed small to large negative effect sizes for PCL-5* (*n* = 7, 77.8%) and N-exp (*n* = 8, 88.9%), indicating reductions in PTSD symptoms and negative expectancies, while DT showed small to large positive effect sizes for most participants (*n* = 6, 66.7%), suggesting an improvement in distress tolerance. In the A-FU comparison, most participants showed negative effect sizes for PCL-5* (*n* = 7, 77.8%, including *n* = 6 with a large effect) and N-exp (*n* = 6, 66.7%, including *n* = 5 with a large effect). DT showed large positive effect sizes for the majority (*n* = 7, 77.8%). Overall, although the majority seemed to improve over treatment, the range of pSMD values demonstrate substantial variability in individual responses across both phase comparisons on all measures. Again, similar observations were made for EPT-SCED.

**Figure 3 (cont. 1 of 3).** Individual graphs of daily measures



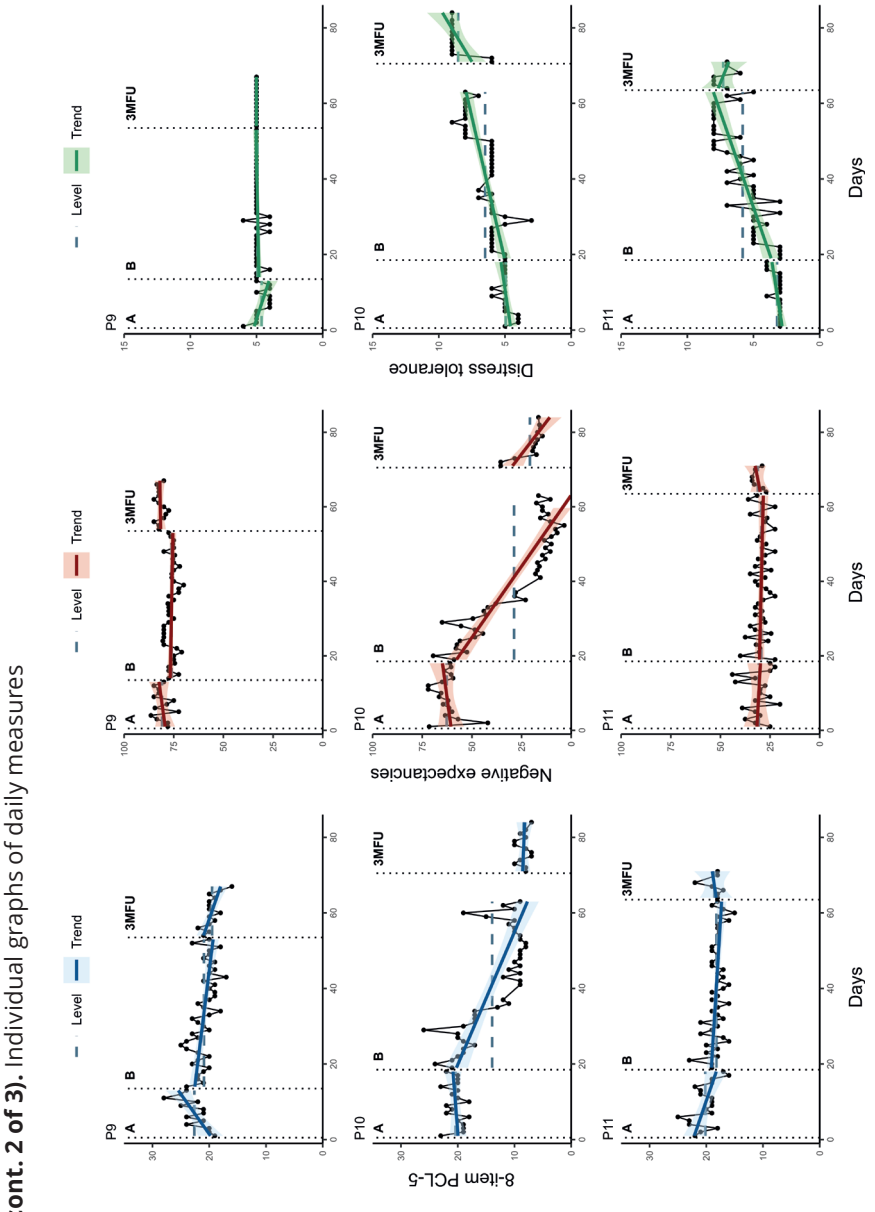



**Figure 3 (cont. 2 of 3).** Individual graphs of daily measures

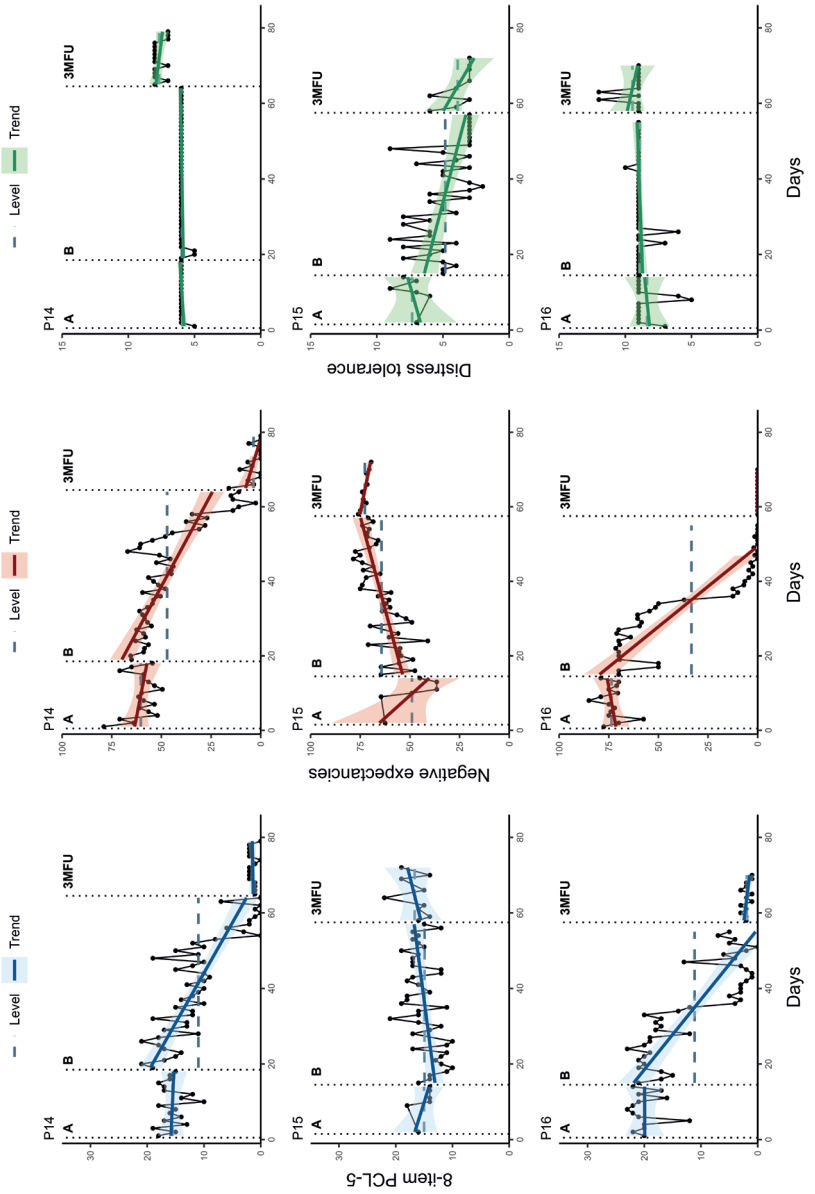



**Figure 3 (cont. 3 of 3).** Individual graphs of daily measures

**Table 3.** Level change effect size (pSMD) across phases

| | | pSMD of PCL-5* | | pSMD of N-exp | | pSMD of DT-T | |
|---|---|---|---|---|---|---|---|
| | | A-B | A-FU | A-B | A-FU | A-B | A-FU |
| IR- | P2 | 0.31 | -2.95 | -0.62 | -3.19 | -0.65 | 3.55 |
| SCED | P3 | 1.42 | 0.30 | -0.07 | -1.39 | 0.15 | 0.80 |
| | P7 | -0.38 | -0.53 | -0.65 | -0.60 | -1.02 | -1.07 |
| | P9 | -0.75 | -1.48 | -1.35 | 0.27 | 0.59 | 0.84 |
| | P10 | -1.72 | -8.92 | -2.31 | -5.93 | 1.68 | 4.07 |
| | P11 | -1.03 | -0.81 | -0.24 | 0.08 | 2.12 | 6.62 |
| | P14 | -0.99 | -8.19 | -1.01 | -8.98 | 0.05 | 4.49 |
| | P15 | -0.03 | 0.73 | 1.41 | 2.69 | -1.63 | -2.98 |
| | P16 | -1.50 | -8.23 | -1.83 | -16.56 | 0.53 | 0.89 |
| EPT- | P1 | -2.40 | -2.08 | -1.42 | -0.62 | 2.55 | 2.80 |
| SCED | P4 | -0.02 | . | -0.57 | . | -3.65 | . |
| | P5 | -0.96 | -2.55 | -1.18 | -2.37 | 0.81 | 2.61 |
| | P6 | -0.21 | -1.16 | -1.14 | -1.20 | -0.38 | 0.09 |
| | P8 | -0.61 | -0.41 | -0.14 | -0.20 | -0.51 | -1.63 |
| | P12 | -0.48 | 1.54 | 1.22 | 4.49 | -0.08 | -2.70 |
| | P13 | -1.94 | -3.94 | -1.48 | -3.30 | 0.98 | 2.79 |
| | P17 | -0.12 | -3.16 | -1.62 | -2.45 | . | . |
| | P18 | -1.49 | . | -1.45 | . | 1.67 | . |
| | P19 | 1.70 | 0.02 | 1.11 | 0.59 | -2.01 | -1.62 |

*Note.* pSMD = pooled standardized mean difference; IR = inhibitory retrieval; EPT = emotional processing theory; P = participant; PCL-5* = 8-item version of the PTSD Checklist for DSM-5; N-exp = idiosyncratic negative expectancies, DT-T; tolerance subscale of distress tolerance scale; A = baseline phase; B = intervention phase; FU = three-month follow-up phase.

*Across case analyses*

The outcomes of the hierarchical linear models can be found in Table 4. We first present outcomes of IR-SCED. For PCL-5*, no significant trend was observed during baseline, but the intervention onset led to a significant immediate increase in scores, relative to the end point of the baseline phase, $b = 2.80$, $SE = 0.88$, $t = 3.17$, $p = .002$, while follow-up was associated with a significant lower average of scores compared to the baseline (intercept), $b = -6.24$, $SE = 2.34$, $t = -2.67$, $p = .008$. A significant negative trend in scores was observed during intervention compared with baseline, $b = -0.22$, $SE = 0.05$, $t = -4.43$, $p < .001$. For N-Exp, again, no significant trend was observed during baseline. Follow-up was associated with a significant lower average of scores compared to the baseline, $b = -18.22$, $SE = 8.77$, $t = -2.08$, $p = .038$, and a

significant negative trend in scores was observed during intervention compared with baseline, $b$ = -0.60, $SE$ = 0.18, $t$ = -3.29, $p$ = .001. For DT, no significant trends or treatment effects were observed.

The outcomes for EPT-SCED can also be found in Table 4. No significant trends during baseline or immediate effects of the intervention were observed for any of the outcomes measures. For PCL-5*, follow-up was associated with a significant lower average of scores compared to the baseline, $b$ = -10.16, $SE$ = 2.27, $t$ = -4.48, $p$ < .001, and a significant negative trend in scores was observed during intervention, $b$ = -0.31, $SE$ = 0.05, $t$ = -6.61, $p$ < .001. For N-Exp, follow-up was also associated a significant lower average of scores compared to the baseline, $b$ = -15.84, $SE$ = 6.87, $t$ = -2.31, $p$ = .022, and a significant negative trend was observed during intervention compared to baseline, $b$ = -0.71, $SE$ = 0.14, $t$ = -5.06, $p$ < .001. For DT, follow-up was associated with a significant higher average of scores compared to the baseline, $b$ = 2.57, $SE$ = 1.16, $t$ = 2.22, $p$ = .027, and a significant positive trend was observed during intervention compared to baseline, $b$ = 0.09, $SE$ = 0.02, $t$ = 3.92, $p$ < .001.

**Assessment data**

See Table 5 for the outcomes of the Leeds RCI analysis. In the IR-SCED, using the CAPS-5, 55.6% ($n$ = 5) of participants demonstrated a reliable decrease in PTSD symptoms from baseline (T0) to post-treatment (T1), and 66.7% ($n$ = 6) from baseline to follow-up (T2). The remaining participants showed no reliable change at either time point. Using the PCL-5, 88.9% ($n$ = 8) demonstrated a reliable decrease in symptoms across both T0–T1 and T0–T2, with 11.1% ($n$ = 1) showing no reliable change.

In the EPT-SCED, 80.0% ($n$ = 8) of participants demonstrated a reliable decrease in symptoms on the PCL-5 from T0 to T1, and 70.0% ($n$ = 7) from T0 to T2, with the remaining participants showing no reliable change. On the PCL-5, reliable decreases were observed in 75.0% ($n$ = 6) of participants from T0 to T1 and in 77.7% ($n$ = 7) from T0 to T2.

**Adverse outcomes**

Across all measures and time points, no participants showed a reliable increase in symptoms. No adverse events occurred during either intervention. One participant, who was randomized in the EPT-SCED, decided to stop the treatment and was considered a drop-out.

**Table 4.** Outcomes fixed effects of hierarchical linear models

| | IR-SCED | | | EPT-SCED | | |
|---|---|---|---|---|---|---|
| Parameter | Est. (SE) | *t* | *p* | Est. (SE) | *t* | *p* |
| **PCL-5*** | | | | | | |
| Baseline intercept ($b_0$) | 18.21 (1.44) | 12.61 | <.001 | 16.28 (1.80) | 9.06 | <.001 |
| Trend during baseline ($b_1$) | -0.08 (0.10) | -0.81 | .417 | 0.08 (0.14) | 0.55 | .582 |
| Treatment effect ($b_2$) | 2.80 (0.88) | 3.17 | .002 | -0.15 (1.21) | -0.13 | .900 |
| Follow-up effect ($b_3$) | -6.24 (2.34) | -2.67 | .008 | -10.16 (2.27) | -4.48 | <.001 |
| Treatment slope effect ($b_4$) | -0.22 (0.05) | -4.43 | <.001 | -0.31 (0.05) | -6.61 | <.001 |
| **N-Exp** | | | | | | |
| Baseline intercept ($b_0$) | 61.29 (5.84) | 10.49 | <.001 | 49.54 (6.24) | 7.95 | <.001 |
| Trend during baseline ($b_1$) | -0.15 (0.33) | -0.44 | .658 | -0.44 (0.43) | -1.02 | .309 |
| Treatment effect ($b_2$) | 2.66 (2.86) | 0.93 | .353 | 1.60 (3.76) | 0.42 | .672 |
| Follow-up effect ($b_3$) | -18.22 (8.77) | -2.08 | .038 | -15.84 (6.87) | -2.31 | .022 |
| Treatment slope effect ($b_4$) | -0.60 (0.18) | -3.29 | .001 | -0.71 (0.14) | -5.06 | <.001 |
| **DT** | | | | | | |
| Baseline intercept ($b_0$) | 6.08 (0.59) | 10.33 | <.001 | 5.97 (1.15) | 5.21 | <.001 |
| Trend during baseline ($b_1$) | 0.00 (0.02) | 0.01 | .989 | 0.04 (0.05) | 0.91 | .364 |
| Treatment effect ($b_2$) | -0.45 (0.27) | -1.66 | .097 | -0.60 (0.40) | -1.50 | .135 |
| Follow-up effect ($b_3$) | 0.94 (0.75) | 1.26 | .208 | 2.57 (1.16) | 2.22 | .027 |
| Treatment slope effect ($b_4$) | 0.02 (0.02) | 1.22 | .223 | 0.09 (0.02) | 3.92 | <.001 |

*Note*. IR-SCED = study with inhibitory retrieval based exposure; EPT-SCED = study with emotional processing based exposure.

**Table 5.** Outcome variables per assessment timepoint

| | | CAPS-5 | | | | | PCL-5 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | T0 | T1 | T2 | RCI T0-T1 | RCI T0-T2 | T0 | T1 | T2 | RCI T0-T1 | RCI T0-T2 |
| IR-SCED | P2 | 36 | 31 | 3 | -1.12 | -7.37 | 67 | 23 | 2 | -7.60 | -11.23 |
| | P3 | 30 | 29 | 31 | -0.22 | 0.22 | 57 | 39 | 39 | -3.11 | -3.11 |
| | P7 | 33 | 22 | 24 | -2.46 | -2.01 | 47 | 28 | 31 | -10.02 | -8.64 |
| | P9 | 39 | 38 | 33 | -0.22 | -1.34 | 59 | 52 | 52 | -1.21 | -1.21 |
| | P10 | 48 | 11 | 8 | -8.27 | -8.94 | 54 | 15 | 18 | -6.74 | -6.22 |
| | P11 | 41 | 31 | 26 | -2.23 | -3.35 | 57 | 39 | 42 | -3.11 | -2.59 |
| | P14 | 32 | 6 | 4 | -5.81 | -6.26 | 58 | 6 | 4 | -8.99 | -9.33 |
| | P15 | 34 | 36 | 37 | 0.45 | 0.67 | 52 | 40 | 37 | -2.07 | -2.59 |
| | P16 | 40 | 9 | 1 | -6.93 | -8.72 | 58 | 12 | 10 | -7.94 | -8.29 |
| EPT-SCED | P1 | 55 | 3 | 28 | -11.62 | -6.03 | 60 | 6 | 26 | -9.33 | -5.88 |
| | P4 | 38 | 45 | . | 1.56 | . | 70 | 56 | . | -2.42 | . |
| | P5 | 24 | 3 | 1 | -4.69 | -5.14 | 59 | 1 | 9 | -10.02 | -8.64 |
| | P6 | 48 | 38 | 40 | -2.23 | -1.79 | 46 | 40 | 32 | -1.04 | -2.42 |
| | P8 | 63 | 27 | 16 | -8.05 | -10.50 | 67 | 23 | 40 | -7.60 | -4.67 |
| | P12 | 38 | 17 | 19 | -4.69 | -4.26 | 60 | . | 63 | . | 0.52 |
| | P13 | 25 | 1 | 0 | -5.36 | -5.59 | 33 | 5 | 2 | -4.84 | -5.36 |
| | P17 | 40 | 16 | 0 | -5.36 | -8.94 | 48 | 14 | 0 | -5.88 | -8.29 |

**Table 5.** Outcome variables per assessment timepoint *Continued.*

| | CAPS-5 | | | | | PCL-5 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **T0** | **T1** | **T2** | **RCI T0-T1** | **RCI T0-T2** | **T0** | **T1** | **T2** | **RCI T0-T1** | **RCI T0-T2** |
| P18 | 44 | 5 | 5 | -8.72 | -8.72 | 58 | . | 10 | . | -8.29 |
| P19 | 46 | 46 | 38 | 0.00 | -1.79 | 51 | 46 | 36 | 0.86 | -0.86 |

*Note.* IR = inhibitory retrieval; EPT = emotional processing theory; P = participant; CAPS-5 = Clinician-Administered PTSD Scale for DSM-5; PCL-5 = PTSD Checklist for DSM-5; T0 = baseline assessment; T1 = posttreatment assessment; T2 = three month follow-up assessment; RCI = reliable change index.

## Discussion

Our findings indicate that implementing IR principles (e.g., increasing variability and emphasizing expectancy violation) in exposure treatment for PTSD is feasible and leads to marked improvements of PTSD symptoms and negative expectancies. However, similar effects were found in exposure-based treatment following EPT principles, suggesting that these effects were not specific to IR-based exposure.

IR-exposure was effective in reducing PTSD symptoms, as evidenced by the across-patient effects in the diary data and reliable improvements in assessment measures (i.e., CAPS-5 and PCL-5) for the majority of patients. A comprehensive IR adapted exposure protocol has also shown promise in earlier single-case studies involving adults with pathological health anxiety and children with anxiety disorders. (Kennedy & Hawks, 2021; Sauer et al., 2023). Applying IR principles to exposure introduces more unpredictability during sessions compared to EPT-based exposure. This includes greater variation in the exposure target, a lack of gradual progression, and random selection of the exposure focus. Our findings suggest that implementing IR principles in exposure therapy for PTSD is feasible, as demonstrated by high adherence to the IR-exposure protocol, no reported adverse events, and no participant dropouts. Notably, it has been suggested that applying the IR principles might *enhance* exposure effects, although not all studies directly testing this hypothesis have found clear evidence to support this (de Jong et al., 2019; Jong et al., 2023; Kooistra, Schoorl, et al., 2025; Krause et al., 2022). In the current study, significant and clinically meaningful changes in PTSD symptoms were also observed in the EPT-SCED. That EPT-based exposure would lead to a reduction of PTSD symptoms was unsurprising, as the effectiveness of this manualized protocol has been well-established (McLean et al., 2022). The current study was not set-up as a head-to-head comparison between IR- based and EPT-based exposure, but interpreting the outcome of both SCEDs, we found no indication that IR-exposure is more effective than EPT-exposure at post-treatment or the long-term.

The second study aim was to assess whether IR-exposure changed the proposed mechanisms, namely reducing negative expectancies and increasing distress tolerance. With respect to expectancy changes, we found a significant trend effect during intervention, indicating that, in line with other studies, negative expectancies decreased over exposure therapy (de Kleine et al., 2017; Kooistra, Schoorl, et al., 2025; Pittig et al., 2022). Extending earlier work, the current study design allowed us to test whether change in expectancies was specific to exposure, as we could compare slopes during the baseline and treatment phase. Granted that we found no significant trend in negative expectancies during baseline, and a significant decrease during the intervention phase, we conclude that it is not merely measuring

expectancies (i.e., increased awareness), but the actual testing of expectancies (either explicit or implicit) during exposure that is necessary to elicit change. A recent study found that expectancies decreased immediately following exposure and that this decrease remained relatively stable over the following days (Losiewicz et al., 2025), whereas we found no immediate effects of exposure onset and found day-to-day fluctuations in expectancies over treatment. One key difference between the two studies lies in the focus of expectancy assessment: Losiewicz and colleagues evaluated expectancies tied to specific exposure exercises, while we assessed expectancies related to exposure to trauma-related stimuli or situations more broadly. Future research should investigate the relationship between expectancy violation during specific exposure exercises and the extent to which these violations generalize to related feared stimuli, situations, or across varying contexts. Changes in expectancies are a suggested mechanism of change of exposure therapy (Pittig et al., 2022). We found no immediate effects of intervention onset on negative expectancies, suggesting that it is not an activating mechanism (i.e., a mechanism that is directly activated by the intervention), but rather a downstream mechanism (i.e., any mechanism that is part of a dynamic cascade of effects (Cohen, 2023)) or a proxy of treatment response. Interestingly, we showed that negative expectancies also decreased over treatment in EPT-SCED, where no emphasis was placed on concrete expectancies prior to exposure. However, as EPT-based exposure posits that patients receive disconfirming information during exposure, and process their experiences with the therapist (e.g., 'nothing bad happened') after exposure, change in expectancies may still occur even without specific focus on expectancy violation by targeted intervention. Together with the finding of our earlier study (Kooistra, Schoorl, et al., 2025), this suggests that negative expectancies decrease following exposure, whether they are explicitly targeted or not.

Contrary to what we expected, across participants, distress tolerance did not significantly increase after IR-exposure. Distress tolerance is often conceptualized as a trait-like construct that is relatively stable over time, but amenable to change, for instance due to treatment (Leyro et al., 2010; Veilleux, 2023). Using the tolerance subscale of the DTS, we found that day-to-day levels of distress tolerance were quite stable for the majority of patients. Interestingly, distress tolerance significantly increased following EPT-based exposure. This was surprising, as strategies designed to maximize inhibitory retrieval are thought to promote distress tolerance, and emphasizing distress reduction (following EPT principles) is believed to be at odds with fostering distress tolerance (Craske et al., 2008). However, it can be argued that by emphasizing short-term increases in distress to achieve long-term reduction, as in EPT-exposure, distress tolerance may also be facilitated. Our findings support

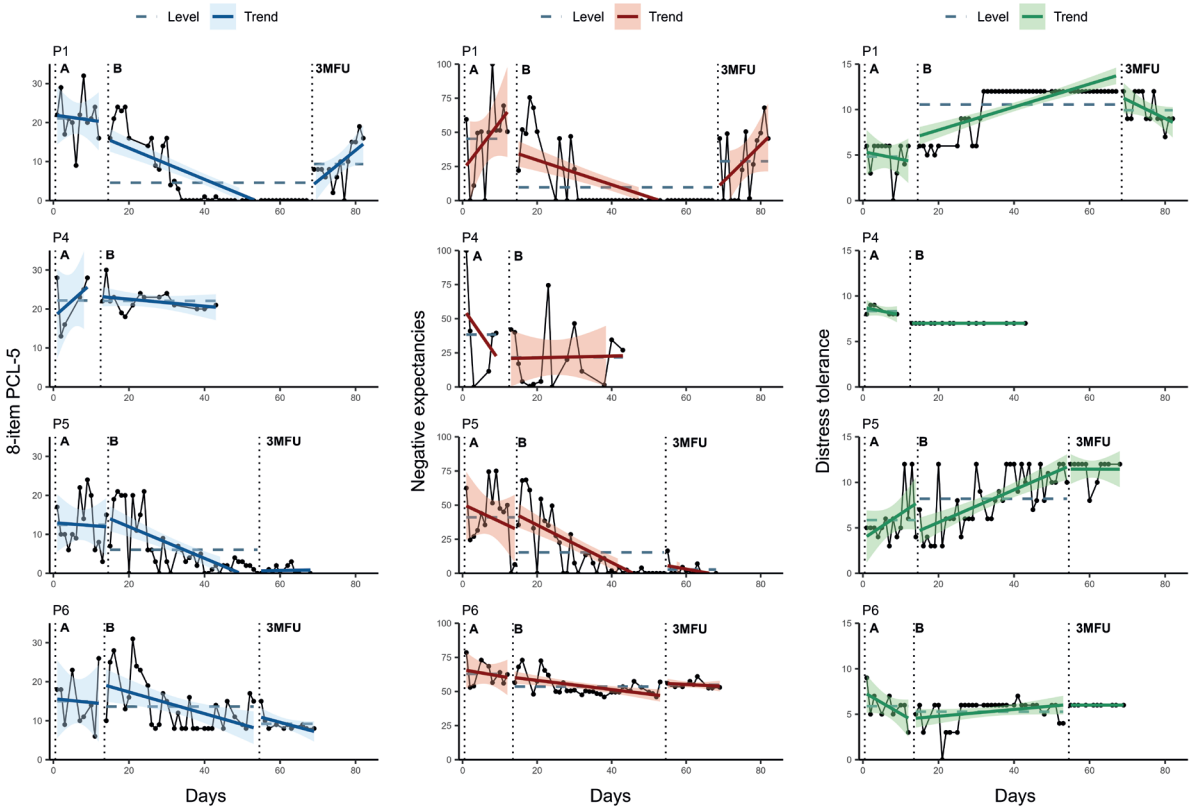
this, suggesting that focusing on distress reduction does not prevent patients from learning to better tolerate distress.

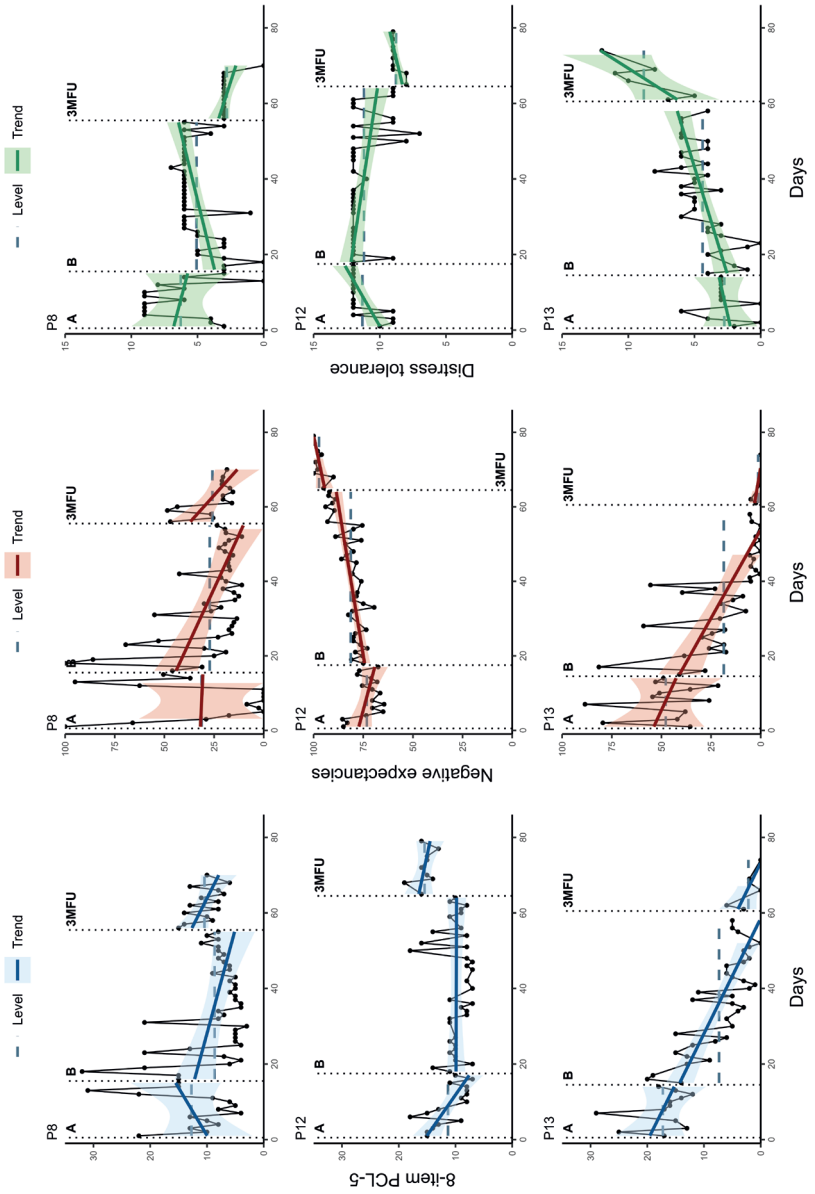
This study has several limitations. This is a single-case design with a limited number of patients, which limits generalizability of the results. Related, with this design we could not compare whether one exposure approach was significantly more effective than the other. Second, we were underpowered to assess whether changes in negative expectancies or distress tolerance would mediate the effect between intervention and PTSD symptoms. To do so, more within-person repeated measures are needed. For assessing changes in distress tolerance over treatment, other measures of distress tolerance might be more suitable as they appear more sensitive to daily fluctuations (e.g., Momentary Distress Intolerance Scale (Veilleux, 2023; Veilleux et al., 2018)). This study also has several strengths. As far as we know, we are the first to test a full IR-based protocol in a clinical sample of patients with PTSD. Moreover, measuring PTSD symptoms daily over the course of exposure treatment increased insight into symptom fluctuations over treatment and individual response patterns. Unlike a previous study reporting increased PTSD severity with daily symptom monitoring in trauma-exposed female college students (Pedersen et al., 2014), we found no evidence that daily measurements exacerbated PTSD symptoms in a treatment-seeking sample. Consistent with previous studies (Biggs et al., 2019; Black et al., 2016; Schuler et al., 2021), we observed substantial day-to-day fluctuations in PTSD symptoms for most participants. Building on these findings, our results demonstrate that fluctuations also occur during treatment and are observable in both treatment responders and non-responders, suggesting that they are independent of treatment response. Compliance of the daily measures was very high, with some participants having no missing data. The three-month follow-up phase allowed us to evaluate longer-term effects of the exposure intervention, and showed that effects remained. The use of multiple baselines lengths increased the internal validity of our study.

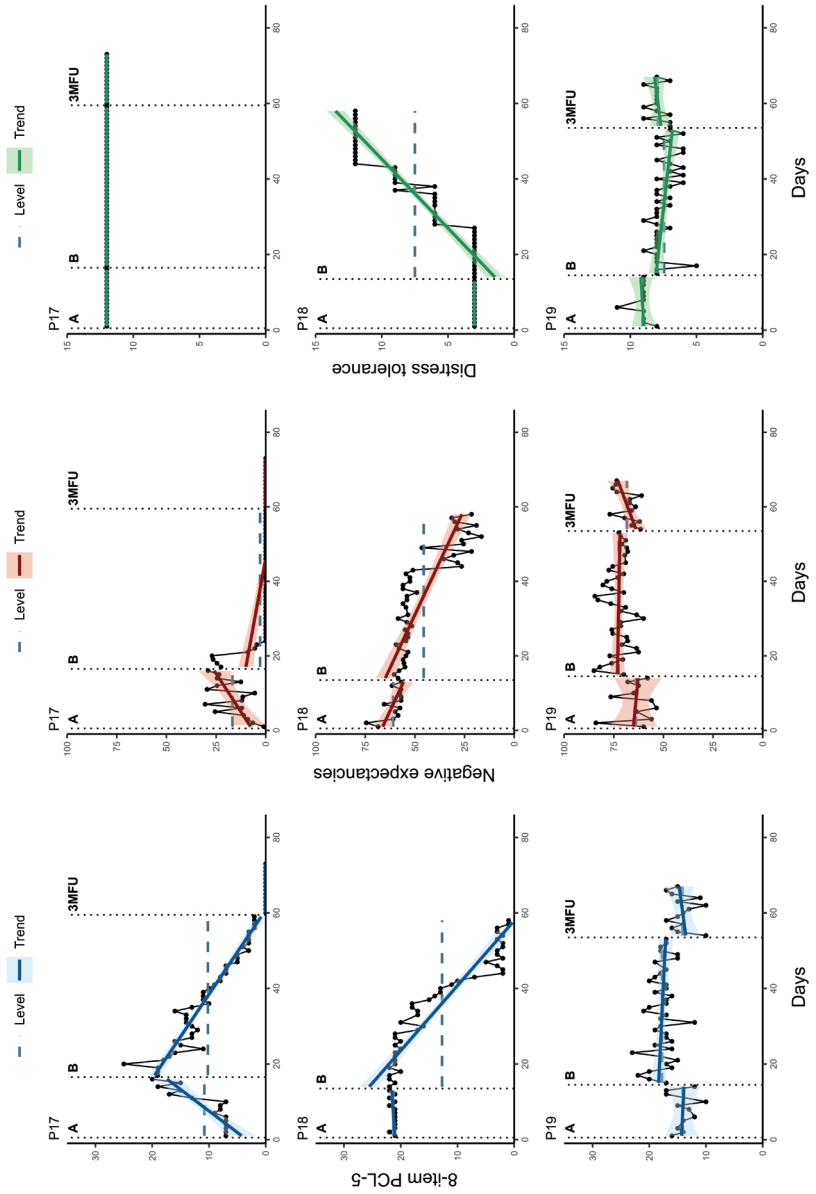
This study offers a proof-of-concept that exposure therapy adapted to IR principles is a feasible and effective intervention for patients with PTSD. Our findings give no indication that it would be more effective than the PE protocol for exposure for PTSD. The value of conducting a large-scale randomized clinical trial (RCT) to determine whether IR-exposure enhances exposure outcomes is uncertain and warrants careful consideration. However, the results highlight that exposure for PTSD can be delivered effectively in various ways.

# Appendix A

## Individual graphs of EPT-SCED




Level
Trend
P8
P12
P13
A
B
3MFU
8-item PCL-5
Negative expectancies
Distress tolerance
Days


8-item PCL-5
Negative expectancies
Distress tolerance
Days
Level
Trend
P17
P18
P19
A
B
3MFU

# Appendix B

## Raw data of diary measures

| | | PhaseA | | | | PhaseB | | | | FU | | | | A-B | A-FU |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | M | SD | range | Trend | M | SD | range | Trend | M | SD | range | Trend | pSMD | pSMD |
| PCL | | | | | | | | | | | | | | | |
| IR | P2 | 15.62 | 6.97 | 5-26 | Down | 17.76 | 6.94 | 5-28 | Down | 1.00 | 0.82 | 0-2 | Down | 0.31 | -2.95 |
| | P3 | 12.27 | 5.93 | 0-18 | Down | 18.71 | 2.44 | 15-24 | Down | 13.67 | 2.73 | 9-16 | Down | 1.42 | 0.30 |
| | P7 | 14.50 | 4.95 | 5-22 | Up | 12.68 | 4.58 | 3-22 | Down | 12.38 | 2.66 | 8-16 | Up | -0.38 | -0.53 |
| | P9 | 22.62 | 2.60 | 19-28 | Up | 20.92 | 1.83 | 17-25 | Down | 19.50 | 1.45 | 16-22 | Down | -0.75 | -1.48 |
| | P10 | 20.39 | 1.54 | 18-23 | Up | 13.93 | 5.09 | 8-26 | Down | 8.38 | 1.12 | 7-10 | No | -1.72 | -8.92 |
| | P11 | 20.17 | 2.28 | 16-25 | Down | 18.20 | 1.46 | 15-23 | Down | 18.57 | 1.62 | 17-22 | Up | -1.03 | -0.81 |
| | P14 | 15.56 | 2.33 | 10-19 | Down | 10.98 | 6.09 | 0-21 | Down | 1.40 | 0.74 | 0-2 | No | -0.99 | -8.19 |
| | P15 | 15.00 | 1.67 | 14-18 | Down | 14.93 | 2.79 | 10-21 | Up | 16.67 | 2.74 | 14-22 | Up | -0.03 | 0.73 |
| | P16 | 19.93 | 3.00 | 12-23 | No | 11.12 | 7.77 | 0-23 | Down | 1.92 | 0.76 | 1-3 | Down | -1.50 | -8.23 |
| EPT | P1 | 21.08 | 5.90 | 9-32 | Down | 4.57 | 7.73 | 0-24 | Down | 9.36 | 5.36 | 0-19 | Up | -2.40 | -2.08 |
| | P4 | 22.17 | 6.31 | 13-28 | Up | 22.07 | 2.81 | 18-30 | Down | . | . | . | . | -0.02 | . |
| | P5 | 12.43 | 6.41 | 3-24 | Down | 6.05 | 6.89 | 0-21 | Down | 0.73 | 1.10 | 0-3 | No | -0.96 | -2.55 |
| | P6 | 15.00 | 6.73 | 6-26 | Down | 13.62 | 6.57 | 8-31 | Down | 9.20 | 2.15 | 8-15 | Down | -0.21 | -1.16 |
| | P8 | 12.73 | 7.42 | 4-31 | Up | 8.65 | 5.99 | 3-32 | Down | 10.43 | 2.93 | 6-15 | Down | -0.61 | -0.41 |
| | P12 | 11.31 | 3.40 | 7-18 | Down | 9.86 | 2.55 | 7-18 | No | 15.44 | 1.67 | 13-19 | Down | -0.48 | 1.54 |
| | P13 | 17.25 | 4.94 | 12-29 | Down | 7.33 | 5.30 | 0-20 | Down | 2.17 | 2.23 | 0-6 | Down | -1.94 | -3.94 |

| | | PhaseA | | | | PhaseB | | | | FU | | | | A-B | A-FU |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | M | SD | range | Trend | M | SD | range | Trend | M | SD | range | Trend | pSMD | pSMD |
| | P17 | 10.81 | 4.83 | 7-20 | Up | 10.19 | 5.88 | 2-25 | Down | 0.00 | 0.00 | 0-0 | No | -0.12 | -3.16 |
| | P18 | 21.31 | 0.48 | 21-22 | No | 12.70 | 8.17 | 1-22 | Down | . | . | . | . | -1.49 | . |
| | P19 | 14.09 | 2.21 | 10-17 | Down | 17.74 | 2.08 | 12-23 | Down | 14.14 | 2.35 | 10-17 | Up | 1.70 | 0.02 |
| Exp | | | | | | | | | | | | | | | |
| IR | P2 | 58.81 | 15.66 | 31.5-81 | Up | 48.98 | 16.30 | 23.5-85.5 | Down | 21.12 | 5.79 | 17-29.5 | Up | -0.62 | -3.19 |
| | P3 | 59.32 | 10.90 | 50-72.5 | Down | 58.53 | 11.51 | 40-80 | Down | 47.83 | 4.09 | 40.5-51 | Down | -0.07 | -1.39 |
| | P7 | 62.31 | 17.79 | 20.5-86 | Up | 51.52 | 15.30 | 21-79 | Down | 53.27 | 11.60 | 37.5-70.5 | Down | -0.65 | -0.60 |
| | P9 | 80.88 | 4.27 | 72.5-86.5 | Up | 76.09 | 2.65 | 70-80.5 | No | 81.79 | 2.19 | 77.5-85 | No | -1.35 | 0.27 |
| | P10 | 62.69 | 6.76 | 42-72 | Up | 28.76 | 19.66 | 3.5-69.5 | Down | 20.77 | 7.38 | 14.5-35.5 | Down | -2.31 | -5.93 |
| | P11 | 30.72 | 6.72 | 20-44 | Down | 29.38 | 4.16 | 22.5-40 | No | 31.14 | 2.90 | 27-34 | No | -0.24 | 0.08 |
| | P14 | 60.36 | 7.52 | 49.5-79 | Down | 47.12 | 16.95 | 2.5-67 | Down | 3.57 | 4.84 | 0-16 | Down | -1.01 | -8.98 |
| | P15 | 49.00 | 12.26 | 36.5-64.5 | Down | 64.32 | 9.20 | 41-78.5 | Up | 72.67 | 2.12 | 69.5-76 | Down | 1.41 | 2.69 |
| | P16 | 73.61 | 6.29 | 57.5-85 | Up | 33.38 | 30.41 | 0-71.5 | Down | 0.00 | 0.00 | 0-0 | No | -1.83 | -16.56 |
| EPT | P1 | 45.29 | 28.97 | 0-100 | Up | 9.70 | 20.54 | 0-75.5 | Down | 28.75 | 24.40 | 0-68 | Up | -1.42 | -0.62 |
| | P4 | 38.33 | 34.64 | 0-100 | Down | 21.67 | 22.06 | 0-74.5 | No | . | . | . | . | -0.57 | . |
| | P5 | 41.07 | 22.29 | 0-75 | Down | 15.37 | 21.25 | 0-68.5 | Down | 2.77 | 5.11 | 0-16.5 | Down | -1.18 | -2.37 |
| | P6 | 62.89 | 8.97 | 5-78.5 | Down | 53.61 | 7.29 | 46-73 | No | 54.95 | 2.67 | 52.5-61 | Down | -1.14 | -1.20 |
| | P8 | 31.23 | 35.66 | 0-100 | Down | 27.19 | 19.93 | 11-100 | Down | 25.82 | 11.58 | 15.5-48.5 | Down | -0.14 | -0.20 |
| | P12 | 73.22 | 6.85 | 64.5-85.5 | Down | 81.31 | 6.38 | 69.5-94 | Up | 97.28 | 3.23 | 90-100 | Up | 1.22 | 4.49 |
| | P13 | 47.83 | 19.87 | 21.5-88.5 | Down | 18.62 | 19.58 | 0-81.5 | Down | 1.25 | 2.09 | 0-5 | Down | -1.48 | -3.30 |
| | P17 | 16.75 | 9.69 | 1-30.5 | Up | 2.78 | 7.46 | 0-27 | Down | 0.00 | 0.00 | 0-0 | None | -1.62 | -2.45 |

| | | PhaseA | | | | PhaseB | | | | FU | | | | A-B | A-FU |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | M | SD | range | Trend | M | SD | range | Trend | M | SD | range | Trend | pSMD | pSMD |
| | P18 | 60.96 | 5.44 | 57-74.5 | Down | 45.55 | 14.00 | 16.5-6.5 | Down | . | . | . | . | -1.45 | . |
| | P19 | 63.91 | 9.31 | 53.5-84 | Down | 72.54 | 5.89 | 60-85 | No | 68.39 | 5.46 | 61-77 | Up | 1.11 | 0.59 |
| DT | | | | | | | | | | | | | | | |
| IR | P2 | 7.88 | 1.64 | 5-10 | Down | 6.57 | 2.29 | 4-11 | Up | 12.00 | 0.00 | 12-12 | No | -0.65 | 3.55 |
| | P3 | 5.91 | 0.54 | 5-7 | No | 5.97 | 0.17 | 5-6 | No | 6.33 | 0.52 | 6-7 | Down | 0.15 | 0.80 |
| | P7 | 6.89 | 1.97 | 3-10 | No | 4.95 | 1.83 | 1-9 | Down | 5.08 | 1.38 | 3-8 | Up | -1.02 | -1.07 |
| | P9 | 4.62 | 0.65 | 4-6 | Down | 4.92 | 0.35 | 4-6 | No | 5.00 | 0.00 | 5-5 | No | 0.59 | 0.84 |
| | P10 | 4.94 | 0.54 | 4-6 | Up | 6.50 | 1.19 | 3-9 | Up | 8.54 | 1.13 | 6-9 | Up | 1.68 | 4.07 |
| | P11 | 3.22 | 0.43 | 3-4 | Up | 5.82 | 1.67 | 3-8 | Up | 7.29 | 0.76 | 6-8 | Down | 2.12 | 6.62 |
| | P14 | 5.94 | 0.24 | 5-6 | No | 5.96 | 0.21 | 5-6 | No | 7.67 | 0.49 | 7-8 | Down | 0.05 | 4.49 |
| | P15 | 7.33 | 1.03 | 6-9 | Up | 4.83 | 1.91 | 2-9 | Down | 3.89 | 1.27 | 3-6 | Down | -1.63 | -2.98 |
| | P16 | 8.36 | 1.34 | 5-9 | No | 8.90 | 0.58 | 6-10 | No | 9.46 | 1.13 | 9-12 | Down | 0.53 | 0.89 |
| EPT | P1 | 4.83 | 1.95 | 0-6 | Down | 10.55 | 2.50 | 5-12 | Up | 9.93 | 1.69 | 7-12 | Down | 2.55 | 2.80 |
| | P4 | 8.33 | 0.52 | 8-9 | Down | 7.00 | 0.00 | 7-7 | No | . | . | . | . | -3.65 | . |
| | P5 | 5.86 | 2.74 | 3-12 | Up | 8.21 | 3.05 | 3-12 | Up | 11.45 | 1.29 | 8-12 | No | 0.81 | 2.61 |
| | P6 | 5.89 | 1.69 | 3-9 | Down | 5.28 | 1.46 | 0-7 | Up | 6.00 | 0.00 | 6-6 | No | -0.38 | 0.09 |
| | P8 | 6.27 | 2.91 | 0-9 | Down | 5.08 | 1.59 | 0-7 | Up | 2.79 | 0.80 | 0-3 | Down | -0.51 | -1.63 |
| | P12 | 11.31 | 1.25 | 9-12 | Up | 11.20 | 1.47 | 7-12 | Down | 8.78 | 0.44 | 8-9 | Up | -0.08 | -2.70 |
| | P13 | 2.75 | 1.60 | 0-6 | Up | 4.39 | 1.75 | 0-8 | Up | 8.83 | 2.64 | 5-12 | Up | 0.98 | 2.79 |
| | P17 | 12.00 | 0.00 | 12-12 | No | 12.00 | 0.00 | 12-12 | No | 12.00 | 0.00 | 12-2 | No | . | . |

| | PhaseA | | | | PhaseB | | | | FU | | | | A-B | A-FU |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | M | SD | range | Trend | M | SD | range | Trend | M | SD | range | Trend | pSMD | pSMD |
| P18 | 3.00 | 0.00 | 3-3 | No | 7.50 | 3.80 | 3-12 | Up | . | . | . | . | 1.67 | . |
| P19 | 9.09 | 0.70 | 8-11 | No | 7.45 | 0.92 | 5-9 | Down | 7.93 | 0.73 | 7-9 | Up | -2.01 | -1.62 |

# Chapter 6

# ‘If I am reminded of my trauma, I will …’: Assessing threat expectancies for being confronted with trauma reminders

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## Abstract

*Purpose:* Dysfunctional threat appraisal plays a key role in both the development and treatment of PTSD. It is unclear how these appraisals can best be measured. This study aimed to explore the specific negative outcome predictions held by patients with PTSD and to develop and validate the Threat Appraisal in PTSD Scale (TAPS).
*Methods:* We used data from a non-clinical (*N* = 309) and clinical sample (*N* = 125) to assess the psychometric properties of the TAPS.
*Results:* The TAPS had excellent internal consistency and test-retest reliability, and convergent and discriminative validity were adequate. The TAPS showed to be sensitive to change following treatment. The TAPS demonstrated incremental validity beyond general cognitions in predicting PTSD symptoms in the combined sample, but not in the patient sample. An exploratory factor analysis suggested three factors: 'losing control', 'externalizing reactions', and 'physical reactions', and patients seemed most concerned about outcomes related to 'losing control'.
*Conclusions:* These findings imply that the TAPS could be clinically beneficial, enabling patients and therapists to recognize dysfunctional expectancies and tailor therapeutic interventions accordingly.


*Keywords*: Posttraumatic stress disorder, threat appraisal, posttraumatic cognitions, assessment, validation.

## Introduction

People who suffer from posttraumatic stress disorder (PTSD) tend to hold negative beliefs about themselves, others, and the world. In different theoretical models of PTSD, negative trauma-related cognitions about the trauma and its sequala have been suggested to be central in PTSD symptom development and maintenance (Ehlers & Clark, 2000; Rauch & Foa, 2006; Resick & Schnicke, 1992). Indeed, many empirical studies have underscored the centrality of negative cognitions and its relationship with the onset, maintenance, and recovery from PTSD (Brown, Belli, et al., 2019; Gómez de La Cuesta et al., 2019). With regard to PTSD treatment, changes in negative cognitions predict subsequent changes in other PTSD symptoms, and changing negative cognitions have therefore been proposed as one of the mechanisms of change during treatment (Alpert, Shotwell Tabke, et al., 2023; Cooper, Clifton, et al., 2017).

To underscore its importance, persistent negative alterations in cognitions were added to the diagnostic criteria of PTSD in the DSM-5 (American Psychiatric Association, 2013). Expectancies are considered a subgroup of cognition and include specific predictions about the likelihood of future events or experiences (Herzog et al., 2023; Rief et al., 2015). Dysfunctional expectancies are presumed to be closely related to more general negative beliefs. For instance, someone may hold the negative belief that the world is dangerous and may therefore wrongfully expect to be attacked when going out. Negative expectancies are theorized to be overestimated in both likelihood and cost by individuals with PTSD (Ehlers & Clark, 2000; Rauch & Foa, 2006). Moreover, experimental psychopathology studies have shown that negative threat expectancies are related to the development and severity of PTSD symptoms (Engelhard et al., 2009; Herzog et al., 2022; Kimble et al., 2018). For instance, negative expectancies about the intensity and uncontrollability of intrusions following a trauma-film paradigm were predictive of PTSD intrusion symptom development one week later (Herzog et al., 2022). As expectancies are generally formulated in 'if-then' statements, they are suitable targets for therapeutic interventions such as behavioral experiments and exposure exercises.

Given that elevated threat expectancies appear to be an important feature of PTSD and a treatment target, it would be useful to have a measure that specifically gauges these cognitions. Several instruments that measure (trauma-related) cognitions already exist, such as the Posttraumatic Cognitions Inventory (PTCI; Foa et al., 1999), the Posttraumatic Growth Inventory (PTGI; Tedeschi & Calhoun, 1996), the Posttraumatic Maladaptive Beliefs Scale (PMBS; (Vogt et al., 2012), the Dissociation-Related Beliefs about Memory Questionnaire (DBMQ; Huntjens et al., 2023) and the Metacognitions Questionnaire (MCQ-30; Wells & Cartwright-Hatton,

2004). However, these questionnaires seem to primarily measure general or meta cognitions rather than specific expected negative outcomes. The PTCI, the most commonly used instrument to assess negative trauma-related cognitions, includes only a few future-oriented items with just one framed as an if-then statement ("If I think about the event, I will not be able to handle it"). Specific predictions about negative outcomes in relation to future trauma-related events or experiences are therefore barely covered.

For social anxiety disorder, a measure does exist that assesses expected negative outcomes in social events (the Appraisal of Social Concerns scale; ASC; Schultz et al., 2006; Telch et al., 2004). More specifically, this 20-item questionnaire measures the concern for concrete negative outcomes (e.g., 'people laughing at you' and 'appearing weird') in future challenging social situations. This measure proved valid and has been used to tailor treatment sessions and evaluate treatment effects (Krafft et al., 2020; Laposa & Rector, 2023; Winkler et al., 2022). Based on this instrument, we developed a scale that assesses threat expectancies for trauma-related events or experiences for those suffering from PTSD. Recently, a similar measure has been developed, the Posttraumatic Expectations Scale (PTES; Herzog et al., 2023), which covers a broad range of PTSD and treatment related expectancies. In a sample of 70 treatment-seeking patients suffering from PTSD, the authors found that expectancies explained additional variance in predicting PTSD symptom severity over the effect of more general negative trauma-related cognitions (as assessed with the PTCI). The full version of the PTES contains 81 items and is thereby quite lengthy. Furthermore, not all subscales of the measure appeared to be reliable. The authors also developed a short version (13 items), but this version only has one item that assesses an expectation related to confrontation with a trauma-reminder ('When I am reminded of the traumatic event, I will feel that the world around me is not real'). Our measure specifically focuses on concerns about concrete and testable negative outcomes in response to trauma reminders. The assessment of negative expectations related to confrontation with trauma-reminders may have great clinical utility, as (imaginal) exposure to trauma-reminders is a common and critical element of empirically supported psychotherapeutic treatments for PTSD (Schnyder et al., 2015). Patients often struggle to identify concrete negative expectancies, and having a valid instrument may increase awareness while helping therapists design interventions that target dysfunctional predictions and optimize treatment outcomes.

The aim of the current study is to advance the assessment of commonly perceived threats in response to confrontation with trauma-related stimuli or situations in patients with PTSD. We created a 24-item self-report measure called the Threat Appraisal in PTSD Scale (TAPS). Individuals are asked to rate their level

of concern about anticipated specific negative outcomes of confrontation with trauma reminders (e.g., 'not being able to talk' or 'fainting'). Using a nonclinical and a patient sample, we report on the development of the measure and its psychometric properties: internal consistency, factor structure, discriminative, convergent and incremental validity, and sensitivity to change over the course of treatment.

## Methods

### Scale and item development

The instructions and scoring of the TAPS were based on the ASC (Schultz et al., 2006; Telch et al., 2004). Multiple sources were used to create items for the current measure. First, items were generated by reviewing data from the IMPACT study, a large randomized controlled trial on the effectiveness of three variants of exposure therapy (Oprel et al., 2021). In the IMPACT study, 149 patients reported idiosyncratic concrete outcomes they feared when confronted with a trauma-reminder (in total, this dataset contained 1385 idiosyncratic feared outcomes). These outcomes were reviewed and clustered, and formed the basis for the TAPS. We also examined similar, previously developed, scales (i.e., scales that assess cognitions in the context of PTSD and anxiety disorders). Finally, we let three international experts in the field of PTSD and exposure therapy review all generated items, which led to the addition and reformulation of several items. We ended up with 24 items for the questionnaire. Similar to the ASC, we chose to ask participants to rate their degree of concern about a negative anticipated outcome, aiming to capture its perceived likelihood and cost, whilst keeping the measure concise and easy to administer. Participants are asked to rate their level of concern for a negative outcome when confronted with a trauma reminder, ranging from 0 ('not at all concerned') to 100 ('extremely concerned'), where a score of 50 represents moderate concern. The TAPS total score is calculated by taking the individual's mean on all items.



### Participants

A nonclinical sample ($N$ = 309) was recruited via university campus advertisements. Individuals from this nonclinical sample were excluded if they had not experienced a traumatic or severely stressful event in the past, as defined by the Life Events Checklist for the DSM-5 (LEC-5). Furthermore, potential participants were excluded if they reported a current diagnosis of a mental disorder and/or were receiving professional help for a mental disorder or psychological problems at the time of the study. A clinical sample of adult patients with PTSD ($N$ = 125) was recruited via two out-patient clinics specializing in the treatment of PTSD. Individuals from this clinical sample were included if they satisfied DSM-5 criteria for PTSD assessed by clinical

interview (SCID-S or CAPS-5). Patients were excluded if they had insufficient ability to speak and read Dutch and/or if their estimated IQ was below 70. Data from the non-clinical sample was collected from January 2021 to April 2022. Data from the patient sample was collected from November 2020 to September 2024.

### Measures

**Negative life events.** The Life Events Checklist for the DSM-5 (LEC-5; Weathers et al., 2013) was used to identify the traumatic events participants had experienced. The self-report questionnaire contains 16 items on distressing events where participants can respond with 'happened to me', 'witnessed it', 'learned about it', 'part of my job', 'not sure', or 'does not apply'. One item (item 17) is open-ended where participants can identify a severely stressful event that was not listed before.

**Childhood trauma.** The short version of the Childhood Trauma Questionnaire (CTQ-SF; Bernstein et al., 2003) was used to assess the extent of childhood trauma in the samples. The CTQ-SF is a 28-item self-report questionnaire. Each item is rated on a 5-point Likert scale, ranging from 'never true' (1) to 'very often true' (5). The total score ranges from 25 to 125, where higher scores reflect more childhood trauma. The measure contains five subscales: emotional abuse, physical abuse, sexual abuse, emotional neglect and physical neglect.

**PTSD symptomatology.** The PTSD checklist for DSM-5 (PCL-5; Blevins et al., 2015; Hoeboer et al., 2024) was used to assess PTSD symptoms. The PCL-5 is a 20-item self-report questionnaire. Each item is rated on a 4-point Likert scale, ranging from 'not at all' (0) to 'extremely' (4). The total score is calculated by summing all items and ranges from 0 to 80, where higher scores reflect higher symptom severity. The PCL-5 has good psychometric properties, with a high internal consistency (including in the present non-clinical and patient samples, Cronbach's $\alpha$ = .91 and .89 respectively) and good validity (Hoeboer et al., 2024).

**Posttraumatic cognitions.** The Posttraumatic Cognitions Inventory (PTCI; Foa et al., 1999; van Emmerik et al., 2006) was used to assess trauma-related cognitions. The PTCI is a 33-item self-report questionnaire. Each item is rated on a 7-point Likert scale, ranging from 'totally disagree' (1) to 'totally agree' (7). The total score is calculated by summing all items and ranges from 33 to 231, where higher scores reflect more trauma-related cognitions. The PTCI total score has adequate psychometric properties. Internal consistency is high (including in the present non-clinical and patient samples, Cronbach's $\alpha$ = .94 and .95 respectively).

**Intolerance of uncertainty.** The Intolerance of Uncertainty Scale-Short Form (IUS-12; Carleton et al., 2007; Helsen et al., 2013) was used to assess the tendency to find a potential negative event unacceptable, regardless of how likely it is to happen. The IUS-12 is a 12-item self-report questionnaire where each item is rated

on a 5-point Likert scale, ranging from 'not at all characteristic of me' (1) to 'entirely characteristic of me' (5). The total score ranges from 5 to 60, where higher scores reflect more intolerance of uncertainty. The psychometric properties have been shown to be strong (Boelen et al., 2010; Carleton et al., 2007), with high internal consistency (including in the present non-clinical and patient samples, Cronbach's α = .90 and .87 respectively).

**Procedures**

The study was approved by the Leiden University Psychology Ethics Committee (#2022-11-23-R.A.de Kleine-V1-4357). All participants provided informed consent before participating in the study. In the non-clinical sample, eligible and interested participants received a link to online questionnaires. Before starting the questionnaires, participants were asked whether they had experienced a very stressful or traumatic event (yes/no). Only those who answered 'yes' were redirected to complete the questionnaires. Nine participants did not finish the entire set of questionnaires, leading to missing data on questionnaires that followed the TAPS. The total sample (*N* = 309) completed the TAPS, 307 participants completed the PCL-5, 304 completed the PTCI, 303 completed the CTQ, and 300 completed the IUS-12. A number of participants in the non-clinical sample (*n* = 158, 51.1%) was asked to fill out the TAPS again one week later, in order to assess test-retest reliability. The patient sample had to fill out the questionnaires within the first two months of treatment. Questionnaires were completed online, but patients who were unable to do so were given the option to complete them on paper. Again, not all participants completed the full set of questionnaires. The total sample (*N* = 125) completed the TAPS, of which 123 participants completed the PCL-5, 124 completed the PTCI, 123 completed the CTQ, and 101 completed the IUS-12. A number of participants in the patient sample (*n* = 80, 64.0%) completed the questionnaires as part of their participation in other treatment studies (Kooistra, Oprel, et al., 2025; Kooistra, Schoorl, et al., 2025).

Additionally, to test sensitivity to change, a number of participants in the patient sample (*n* = 41, 32.8%) was asked to fill out the questionnaires pre and post PTSD treatment. Participants all received intensified Prolonged Exposure therapy for PTSD (iPE; Foa et al., 2019; Oprel et al., 2021), which was delivered in 12 to 14 face-to-face sessions of 90-minutes of PE, with 3 sessions per week for 4 weeks. Treatment included psycho-education, imaginal exposure, and exposure in vivo. Between sessions, patients were instructed to do homework assignments (e.g., listening to audiotaped exposure sessions and exposure in vivo exercises). Participants completed the PCL-5, PTCI and TAPS for the second time three months after starting treatment.

**Statistical analyses**

We provide descriptive information on the TAPS items in the non-clinical and patient sample, such as item mean and standard deviation. We also assessed which items were, on average, rated as most concerning by making a ranked list of items (from most to least concerning). To examine the underlying factors in the TAPS, we conducted an exploratory factor analysis (EFA) using Principal Axis Factoring (PAF) as extraction method on the combined sample (nonclinical and patient samples). PAF was chosen as the TAPS items were not normally distributed. When developing the scale, we did not have a priori hypotheses about its potential underlying factors. As the TAPS is primarily intended for clinical populations, analyzing the patient sample alone would have been ideal, but this sample was relatively small. We used oblimin rotations as the factors were expected to correlate. Eigenvalues, the scree method, factor loadings and fit statistics were assessed to derive the underlying factor structure of the scale. Discriminative validity was assessed by testing whether the TAPS was significantly higher in the patient sample through an independent sample t-test. Internal consistency was assessed in the combined and patient sample through Cronbach's α and McDonald's ω, with a value of ≥ 0.7 indicating sufficient reliability. The 'Cronbach's α if Item Deleted' was assessed to identify items that lower the overall internal consistency of the scale. The test-retest reliability of the TAPS was assessed using the subsample of the non-clinical individuals by calculating the Spearman correlation between the first time it was administered and the second time it was administered (a week later). Spearman was chosen as the TAPS was not normally distributed. Convergent validity was examined by calculating Spearman correlations between the TAPS, the PCL-5, the PTCI, and the IUS-12. Incremental validity of the TAPS was assessed via a multiple hierarchical regression analysis, with the PCL-5 as dependent variable and the PTCI and the TAPS as independent variables (added in separate steps). Finally, to assess whether the TAPS was sensitive to change due to Prolonged Exposure therapy, we conducted a multilevel analysis with random intercept, where Time (pre- and posttreatment) was entered as the independent variable and TAPS as dependent variable. We explored whether potential TAPS subscales were also sensitive to treatment. We carried out the same analysis for the PCL-5 to gauge whether treatment was effective. Finally, we assessed the relationship between change in TAPS ($TAPS_{pre}$ – $TAPS_{post}$) and change in PCL-5 ($PCL\text{-}5_{pre}$ – $PCL\text{-}5_{post}$) by calculating a Pearson correlation. Analyses were carried out in SPSS version 29, except for the multilevel analyses. Multilevel analyses were tested in R (Version 4.0.1) with maximum likelihood estimation using the lme4 package (v1.1-28; Bates et al., 2015). Alpha level for all analyses was set at .05. This study was preregistered at the open science framework (OSF; osf.io/av8e9).

## Results

### Sample characteristics

The sample characteristics are shown in Table 1. Between the groups, there were significant differences in age (the non-clinical sample was younger), $t(432) = -11.67$, $p < .001$, but not in gender, $\chi 2(2, N = 434) = 5.27$, $p = .072$. The patient group reported greater severity of childhood trauma (CTQ; $t(424) = -18.08$, $p < .001$), more PTSD symptoms (PCL-5, $t(428) = -25.34$, $p < .001$), higher levels of negative trauma-related cognitions (PTCI, $t(426) = -20.10$, $p < .001$), and higher intolerance of uncertainty (IUS-12, $t(399) = -9.98$, $p < .001$).

As assessed with the LEC-5, in the nonclinical sample, the most frequently endorsed concrete negative life event that was directly experienced or witnessed was an unwanted or uncomfortable sexual experience ($n = 123$, 39.8%), followed by physical assault ($n = 113$, 36.6%), and a life-threatening illness or injury ($n = 115$, 37.2%). In the patient sample, the most experienced or witnessed was physical assault ($n = 116$, 92.8%), followed by an unwanted or uncomfortable sexual experience ($n = 97$, 77.6%), and sexual assault ($n = 93$, 74.4%). Additionally, 47.2% ($n = 146$) of the non-clinical sample and 80.8% ($n = 101$) of the patient sample reported to have experienced or witnessed another negative life event, such as being bullied or a divorce. Patients reported to have experienced on average 7.3 types of potentially traumatic events ($SD = 2.8$), and non-clinical participants on average 3.2 ($SD = 1.9$).



**Table 1.** Baseline characteristics of participants

| | Non-clinical ($N = 309$) | Patient ($N = 125$) |
|---|---|---|
| Age in years, mean (SD) | 23.8 (9.8) | 36.9 (12.2) |
| Gender, *n* (%) | | |
| Male | 49 (15.9) | 31 (24.8) |
| Female | 259 (83.8) | 93 (74.4) |
| Non-binary | 1 (0.3) | 1 (0.8) |
| Number of negative LEs | 3.2 (1.9) | 7.3 (2.8) |
| PCL-5, mean (SD) | 19.8 (14.1) | 55.7 (11.0) |
| PTCI, mean (SD) | 80.7 (32.0) | 151.5 (35.4) |
| CTQ | 37.3 (13.2) | 69.7 (23.3) |
| Emotional abuse | 8.4 (4.4) | 16.7 (6.3) |
| Physical abuse | 6.1 (3.0) | 12.5 (6.4) |

**Table 1.** Baseline characteristics of participants *Continued.*

| | Non-clinical (*N* = 309) | Patient (*N* = 125) |
|---|---|---|
| Sexual abuse | 6.0 (2.7) | 12.3 (6.6) |
| Emotional neglect | 9.8 (4.2) | 17.5 (5.3) |
| Physical neglect | 7.0 (2.8) | 11.0 (4.5) |
| IUS-12 | 34.1 (9.4) | 44.7 (8.7) |

*Note.* SD = standard deviation; LEs= life events; PCL-5 = PTSD Checklist for DSM-5; PTCI = Posttraumatic Cognitions Inventory; CTQ = Childhood Trauma Questionnaire; IUS-12 = Intolerance of uncertainty scale, short form.

**TAPS item analysis**

Per TAPS item, the mean score and standard deviation are shown in Table 2 for both samples. In the non-clinical sample, the mean rate of concern per item ranged from 4.1 (item 16 'Wetting or soiling my pants') to 32.6 (item 5 'Becoming a victim again/being in danger'). In the patient sample, the mean rate of concern per item ranged from 7.3 (item 16 'Wetting or soiling my pants') to 65.8 (item 12 'Unable to think, having a black out'). The ranking of items, based on their mean scores (with the highest mean score assigned the highest rank), was consistent across samples, with the same items appearing in the top five positions. Clinically, it is especially relevant to identify anticipated negative outcomes for which patients have a high level of concern (Craske et al., 2022). Therefore, we counted how many concerns about negative outcomes were rated 60 or higher (see also, Craske et al., 2022). In the non-clinical sample, participants had on average 2.3 items above 60 (*SD* = 3.7; range: 0–22) and, 135 participants (43.7%) had no concern rated over 60. In the patient sample, participants had on average 8.1 items above 60 (*SD* = 5.0; range: 0–23), and seven participants (5.6%) had no concern rated over 60.

**Exploratory factor analysis**

All items were entered in an EFA with oblimin rotation. Kaiser's criterion (i.e., eigenvalues > 1) favored a four-factor solution, while the Scree method favored a two-factor solution. We therefore explored a two, three and four factor structure. The three-factor structure proved to be the best fit, based on the assessment of cross-loading items, non-loading items, communalities of items and interpretability (see the appendix of this chapter for the other factor solutions). The three-factor model explained 50.4% of the variance. We used a cutoff of 0.40 for factor loadings to determine the items that meaningfully contributed to the factor in the analysis. Table 3 provides an overview of the factors, and the factor loading and communality of each item. We labelled the first factor, consisting of 11 items, 'losing control', the

second factor, 5 items, 'externalizing reactions' and the third factor, 5 items, 'physical reactions'. Three items did not appear to load on any factor (item 23 'Moving uncontrollably', item 17 'Collapsing', and item 3 'Vomiting'), and were therefore removed from the final scale. The correlation between the factors were moderate, ranging from $r$ =.38 to $r$ =.55.

The final scale thus consisted of 21 items. The patient sample had a significantly higher total score ($M$ = 38.0, $SD$ = 18.6) than the non-clinical sample ($M$ = 14.8, $SD$ = 14.0), $t(432)$ = -14.17, $p$ < .001. The subscales 'losing control' ($M$ = 49.6, $SD$ = 22.9 vs. $M$ = 19.2, $SD$ = 17.7), 'externalizing reactions' ($M$ = 30.3, $SD$ = 26.1 vs. $M$ = 11.4, $SD$ = 15.5), and 'physical reactions' ($M$ = 20.1, $SD$ = 19.9 vs. $M$ = 8.3, $SD$ = 14.7) were also significantly higher in the patient sample, $t(432)$ = -14.81, -9.29, and -6.78, respectively, all $p$ < .001.

**Reliability**

The internal consistency of the TAPS was excellent in both the combined sample (Cronbach's α = 0.93, McDonald's ω = 0.94) and the patient sample (Cronbach's α = 0.89, McDonald's ω = 0.89). Internal consistency would not improve by deleting any item, suggesting that all items contribute to internal consistency. Internal consistency was also good for all subscales; 'losing control' (combined sample: Cronbach's α = 0.91, McDonald's ω = 0.91; patient sample: Cronbach's α = 0.86, McDonald's ω = 0.86), 'externalizing reactions' (combined sample: Cronbach's α = 0.85, McDonald's ω = 0.85; patient sample: Cronbach's α = 0.83, McDonald's ω = 0.83), and 'physical reactions' (combined sample: Cronbach's α =.80, McDonald's ω =.81; patient sample: Cronbach's α =.73, McDonald's ω =.74).

We also assessed the temporal stability of the TAPS in the non-clinical sample. Out of the 158 participants in the non-clinical sample who were asked to fill out the TAPS questionnaire one to two weeks later, 127 participants did so. The Spearman showed a strong positive correlation between the TAPS at both timepoints, $r$ =.77, $p$ <.001, indicating good test-retest reliability (i.e., temporal stability).

**Table 2.** Overview of TAPS items, including their mean, ordered by rank in the patient sample

| | | Non-clinical sample | | | Patient sample | | |
|---|---|---|---|---|---|---|---|
| Item | | *M* (*SD*) | Rank | >60, *n* (%) | M (SD) | Rank | >60, *n* (%) |
| 12 | Unable to think (having a blackout) | 27.0 (30.1) | 3 | 57 (18.4) | 65.8 (31.6) | 1 | 88 (70.4) |
| 5 | Becoming a victim again/being in danger | 32.5 (32.7) | 1 | 88 (28.5) | 60.3 (35.6) | 2 | 76 (60.8) |
| 24 | Unable to function | 21.9 (29.6) | 5 | 50 (16.2) | 58.5 (33.1) | 3 | 71 (56.8) |
| 14 | Unable to feel anything | 22.1 (29.8) | 4 | 50 (16.2) | 57.3 (34.8) | 4 | 72 (57.6) |
| 19 | Unable to stop crying | 30.0 (31.6) | 2 | 70 (22.7) | 52.8 (37.1) | 5 | 64 (51.2) |
| 21 | Walking away or running away | 16.4 (23.8) | 7 | 21 (6.8) | 49.5 (36.5) | 6 | 60 (48.0) |
| 11 | Unable to talk | 18.4 (27.1) | 6 | 40 (12.9) | 47.6 (35.2) | 7 | 55 (44.0) |
| 7 | Unable to move | 16.1 (27.2) | 9 | 34 (11.0) | 42.7 (37.2) | 8 | 51 (40.8) |
| 15 | Hurting myself | 10.7 (22.5) | 15 | 24 (7.8) | 41.1 (36.7) | 9 | 49 (39.2) |
| 13 | Swearing or cursing | 16.4 (24.9) | 7 | 27 (8.7) | 41.0 (37.6) | 10 | 50 (40.0) |
| 9 | Not knowing where I am | 8.7 (19.9) | 17 | 17 (5.5) | 38.8 (34.4) | 11 | 44 (35.2) |
| 1 | Screaming | 16.0 (23.0) | 10 | 30 (9.7) | 34.2 (35.3) | 12 | 38 (30.4) |
| 17 | Collapsing | 13.5 (24.6) | 12 | 31 (10.0) | 31.5 (32.6) | 13 | 33 (26.4) |
| 20 | Speaking gibberish | 8.0 (17.2) | 20 | 13 (4.2) | 31.4 (34.4) | 14 | 34 (27.2) |
| 8 | Fainting | 13.8 (24.4) | 11 | 24 (7.8) | 30.8 (30.5) | 15 | 30 (24.0) |
| 23 | Moving uncontrollably | 7.4 (16.8) | 21 | 12 (3.9) | 29.9 (33.5) | 16 | 31 (24.8) |
| 3 | Vomiting | 13.1 (23.7) | 13 | 25 (8.1) | 28.5 (30.7) | 17 | 27 (21.6) |
| 2 | Throwing things | 10.9 (18.7) | 14 | 14 (4.5) | 28.5 (32.4) | 18 | 29 (23.2) |
| 10 | Hitting or kicking | 8.6 (18.9) | 18 | 14 (4.5) | 28.4 (34.4) | 19 | 32 (25.6) |
| 6 | Choking | 6.2 (15.3) | 22 | 9 (2.9) | 25.3 (33.2) | 20 | 24 (19.2) |

**Table 2.** Overview of TAPS items, including their mean, ordered by rank in the patient sample *Continued.*

| | | Non-clinical sample | | | Patient sample | | |
|---|---|---|---|---|---|---|---|
| Item | | *M* (*SD*) | Rank | >60, *n* (%) | M (SD) | Rank | >60, *n* (%) |
| 18 | Dying | 9.0 (21.9) | 16 | 21 (6.8) | 20.1 (32.6) | 21 | 23 (18.4) |
| 22 | Hurting someone else | 5.1 (15.4) | 23 | 10 (3.2) | 19.1 (29.4) | 22 | 15 (12.0) |
| 4 | Having a heart attack | 8.4 (19.9) | 19 | 17 (5.5) | 16.9 (25.9) | 23 | 14 (11.2) |
| 16 | Wetting or soiling my pants | 4.1 (13.5) | 24 | 6 (1.9) | 7.3 (18.4) | 24 | 5 (4.0) |

*Note. M* = mean; *SD* = standard deviation; Rank = relative standing of the item based on highest mean; >60 = number of participants who rated that item as higher than 60.

**Table 3.** 3-factor pattern loadings and communalities

| Items | | Factor 1<br>Losing control | Factor 2<br>Externalizing reactions | Factor 3<br>Physical reactions | $h^2$ |
|---|---|---|---|---|---|
| 12. | Unable to think (having a blackout) | **.913** | -.139 | -.008 | **.71** |
| 11. | Unable to talk | **.816** | .007 | -.068 | **.62** |
| 24. | Unable to function | **.781** | -.037 | .083 | **.65** |
| 14. | Unable to feel anything | **.702** | .013 | .017 | **.52** |
| 7. | Unable to move | **.668** | -.015 | .066 | **.49** |
| 9. | Not knowing where I am | **.623** | .025 | .196 | **.58** |
| 5. | Becoming a victim again/being in danger | **.569** | .044 | .034 | .38 |
| 20. | Speaking gibberish | **.559** | .116 | .078 | **.46** |
| 19. | Unable to stop crying | **.531** | .128 | -.089 | .32 |
| 21. | Walking away or running away | **.493** | .294 | -.117 | **.42** |
| 15. | Hurting myself | **.486** | .211 | .094 | **.46** |
| 17. | Collapsing | .388 | .082 | .387 | **.52** |
| 23. | Moving uncontrollably | .387 | .106 | .274 | **.42** |
| 2. | Throwing things | -.013 | **.742** | .129 | **.63** |
| 1. | Screaming | .021 | **.740** | -.024 | **.55** |
| 10. | Hitting or kicking | .079 | **.724** | .057 | **.63** |
| 13. | Swearing or cursing | .158 | **.654** | -.130 | **.50** |
| 22. | Hurting someone else | -.085 | **.581** | .322 | **.50** |
| 4. | Having a heart attack | -.059 | .045 | **.821** | **.65** |
| 18. | Dying | .020 | .031 | **.676** | **.49** |

**Table 3.** 3-factor pattern loadings and communalities *Continued.*

| Items | Factor 1 Losing control | Factor 2 Externalizing reactions | Factor 3 Physical reactions | $h^2$ |
|---|---|---|---|---|
| 16. Wetting or soiling my pants | .019 | .099 | **.530** | .34 |
| 8. Fainting | .365 | -.109 | **.481** | **.48** |
| 6. Choking | .212 | .162 | **.450** | **.47** |
| 3. Vomiting | .272 | -.006 | .378 | .32 |
| Eigenvalue | 8.40 | 5.71 | 5.57 | |
| (Additional) % of variance | 39.44 | 5.78 | 5.15 | |

*Note.* $h^2$ = communalities; Factor loadings in bold indicate that the item loads on a factor (with a cutoff of .40).

**Convergent and incremental validity**

To assess convergent validity, we calculated Spearman correlations between the TAPS and measures that it should theoretically be related to, see Table 4. In the combined sample, the TAPS and its subscales were significantly and positively correlated with all other measures (PCL-5, PTCI, and IUS-12). In the patient sample, the TAPS and its subscales 'losing control' and 'physical reactions' significantly and positively correlated with the other measures. Externalizing reactions did not correlate significantly with the other measures.

In the combined sample, the hierarchical multiple regression analysis showed that the TAPS provided additional predictive power beyond the PTCI (i.e., incremental validity). In Block 1, PTCI was a significant predictor, $R^2 = 0.70$, $F(1, 425) = 990.87$, $p < .001$. Adding TAPS in Block 2 resulted in a significant increase in explained variance, $\Delta R^2 = 0.03$, $F(1, 424) = 46.86$, $p < .001$, with the final model being significant, $R^2 = 0.73$, $F(2, 424) = 572.33$, $p < .001$. Both PTCI ($\beta = .31$, $p < .001$) and TAPS ($\beta = .27$, $p < .001$) significantly predicted PCL-5 scores. This was not true for the patient sample, where in Block 1, $R^2 = 0.36$, $F(1, 121) = 67.25$, $p < .001$, PTCI was a significant predictor ($\beta = .19$, $p < .001$). Adding TAPS in Block 2 resulted in no significant increase in explained variance, $\Delta R^2 = 0.01$, $F(1, 120) = 1.48$, $p = .227$.

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**Sensitivity to treatment**

Out of the 41 participants in the patient sample who were asked to fill out the TAPS after treatment, 32 participants did so. In this sample, the PCL-5 significantly decreased from pre-treatment ($M = 56.5$; $SD = 10.2$) to post-treatment ($M = 28.3$; $SD = 18.5$), $b = -28.37$, $SE = 1.16$, $t = -12.42$, $p < .001$, showing that the treatment was effective in reducing PTSD symptoms. The TAPS total score also significantly decreased from pre-treatment ($M = 37.5$; $SD = 14.4$) to post-treatment ($M = 17.9$; $SD = 18.4$), $b = -19.80$, $SE = 2.81$, $t = -7.04$, $p < .001$, indicating that it is sensitive to treatment-related changes. Moreover, all subscales (losing control, externalizing reactions, and physical reactions) significantly decreased from pre to post-

treatment, $b = -26.51$, $SE = 3.37$, $t = -7.87$, $p < .001$, $b = -13.87$, $SE = 3.63$, $t = -3.82$, $p < .001$, $b = -13.89$, $SE = 3.64$, $t = -3.81$, $p = .001$, respectively. Change in the TAPS (i.e., pre-treatment minus post-treatment) was positively, strongly and significantly related with change in PTSD symptoms (i.e., pre-treatment minus post-treatment), $r = .58$, $p < .001$.

**Table 4.** Correlations of TAPS and theoretically related measures

| Combined sample | 1. | 2. | 3. | 4. | 5. | 6. | 7. |
|---|---|---|---|---|---|---|---|
| 1. TAPS | - | - | - | - | - | - | - |
| 2. TAPS-LC | .96*** | - | - | - | - | - | - |
| 3. TAPS-ER | .72*** | .58*** | - | - | - | - | - |
| 4. TAPS-PR | .68*** | .59*** | .45*** | - | - | - | - |
| 5. PCL-5 | .70*** | .70*** | .43*** | .44*** | - | - | - |
| 6. PTCI | .67*** | .68*** | .43*** | .41*** | .82*** | - | - |
| 7. IUS-12 | .52*** | .53*** | .36*** | .30*** | .59*** | .63*** | - |
| Patient sample | | | | | | | |
| 1. TAPS | - | - | - | - | - | - | - |
| 2. TAPS-LC | .92*** | - | - | - | - | - | - |
| 3. TAPS-ER | .65*** | .38*** | - | - | - | - | - |
| 4. TAPS-PR | .67*** | .51*** | .29** | - | - | - | - |
| 5. PCL-5 | .32*** | .32*** | .09 | .19* | - | - | - |
| 6. PTCI | .38*** | .40*** | .17 | .20* | .57*** | - | - |
| 7. IUS-12 | .36*** | .38*** | .14 | .22* | .59*** | .63*** | - |

*Note*. TAPS = Threat Appraisal in PTSD Scale; TAPS-LC = Losing control TAPS subscale; TAPS-ER = Externalizing reactions TAPS subscale; TAPS-PR = Physical reactions TAPS subscale; PCL-5 = PTSD Checklist for DSM-5; PTCI = Posttraumatic Cognitions Inventory; IUS-12 = Intolerance of uncertainty scale, short form; *$p < .05$; ** = $p < .01$; ***$p < .001$.

## Discussion

The current study presents the initial reliability and validity of a newly developed measure, called TAPS (threat appraisal for PTSD scale), using combined data from a non-clinical and treatment seeking patient sample. Testable and concrete dysfunctional expectancies are considered an important subcategory of negative cognitions, as they can be directly targeted in psychological interventions (e.g., 'if I recount the traumatic event, I will be unable to stop crying'). Negative cognitions are commonly more generally assessed as beliefs about the self, others and the world (e.g., 'I am weak' and 'The world is a dangerous place'), as in the DSM-5 and the PTCI

(American Psychiatric Association, 2013; Foa et al., 1999). We developed the TAPS to capture concrete and testable trauma-related expectancies. The psychometric properties of the TAPS indicate it is a valuable addition to the field. On average, patients recognized to have high concerns for multiple negative outcomes, with considerable variation between participants (e.g., ranging from high concerns for zero items to as many as 23). An exploratory factor analysis reduced the scale from 24 to 21 items with three factors. The TAPS was internally consistent, temporally stable, and correlated to theoretically related constructs. The weak to moderate correlation with the PTCI suggest that the TAPS aligns with this established measure while also potentially capturing unique aspects of trauma-related cognition, reflecting its refined scope. The TAPS was able to distinguish between patients and controls and was sensitive to treatment. In the combined sample, the TAPS also demonstrated incremental validity beyond more general cognitions (PTCI) in predicting PTSD symptoms, although this was not true in the patient sample only.

The first factor of the factor analysis was labeled 'losing control'. The idea that one is losing mental control is theoretically presumed to maintain a sense of current threat in those suffering from PTSD (Ehlers & Clark, 2000), and trauma-focused treatments, such as Prolonged Exposure, target the erroneous beliefs of 'loss of control' and 'going crazy' (Foa et al., 2019). Our data shows more concretely what this losing control may look like. Interestingly, a majority of patients (>50%) rated items relating to dissociative symptoms as highly concerning (e.g., having a black out or being unable to talk or feel anything). This aligns with findings that individuals diagnosed with PTSD and dissociative disorders often hold meta-memory beliefs, perceiving that retrieving and processing traumatic memories may result in negative consequences (e.g., 'I believe that if I would allow myself to remember, my memories would overwhelm me'; Huntjens et al., 2023). Interestingly, the only item about trauma-reminder confrontation that was retained in the short version of the PTES was also related to dissociation ('When I am reminded of the traumatic event, I will feel that the world around me is not real'; Herzog et al., 2023), further emphasizing the importance of negative expectancies associated with dissociative responses to trauma reminders. With the TAPS, we present a list that more thoroughly captures such expectations. This factor, 'losing control', was most strongly related to PTSD symptoms and general posttraumatic cognitions, in both the combined (strong correlations) and patient sample (moderate correlations).

The second factor comprised items referring to concerns about externalizing reactions, and was labeled as such. Externalizing reactions are included in the arousal symptom cluster of PTSD (i.e., 'irritable behavior and angry outburst'), and anger difficulties seem more pronounced in PTSD compared to other anxiety-based disorders (American Psychiatric Association, 2013; Olatunji et al., 2010).

Surprisingly, concerns about externalizing reactions did not relate to more severe PTSD symptoms in the patient sample, although it was significantly higher in this sample compared to healthy controls. Previous research has suggested that the link between anger and PTSD is more pronounced in men (Taft et al., 2017). It would be interesting to explore the relation between concerns about externalizing reactions and PTSD symptomatology in a more gender-balanced sample, as our sample had a relatively high proportion of women. A substantial proportion of patients expressed high concern for outcomes related to externalizing reactions, for instance 12% was concerned about 'hurting someone else' and over 25% about 'hitting or kicking'. Addressing these concrete concerns can therefore also be of relevance in PTSD treatment.

The third factor comprised items referring to concerns about physical reactions. Patients with PTSD often experience (intense) bodily sensations, either in response to trauma-related stimuli or due to heightened physical arousal (American Psychiatric Association, 2013). A catastrophic misinterpretation of these symptoms, as is also seen in panic disorder (Austin & Richards, 2001), may lead to high concern for these negative outcomes. Panic symptoms, including panic attacks, are frequently reported by patients with PTSD (Teng et al., 2013). However, although significant, this factor showed a weak association with PTSD symptoms. Concerns about concrete physical reactions (such as dying of a heart-attack) upon exposure to trauma-reminders may especially resonate with a subgroup of patients with PTSD.



We found that threat expectancies assessed with the TAPS strongly diminished following intensified PE, in the full measure and its three subscales. Furthermore, a reduction of threat expectancies was related to a reduction of PTSD symptoms. Specifically for exposure therapy, the interest in negative threat expectancies has increased under the influence of the inhibitory learning approach to exposure therapy (Craske et al., 2008, 2014, 2022). This approach emphasizes expectancy violation as a crucial mechanism of inhibitory learning during exposure therapy. Identifying negative expectancies is thereby an important aspect. In clinical practice, patients with PTSD often find it difficult to identify concrete and testable negative outcomes they are (most) worried about. Although items in the TAPS do not necessarily refer to a biologically significant event or unconditioned stimulus (as is highlighted in the inhibitory learning approach), it may be a useful tool to initiate the conversation on threat expectancies before starting imaginal or in-vivo exercises, which can then by refined and specified to fit with the inhibitory learning approach (filling out the OptEx Nexus, see Craske et al., 2022, e.g., further concretizing what 'unable to function' may look like). Beyond exposure therapy, the reduction of elevated threat expectancies upon exposure to trauma reminders may represent a common underlying mechanism shared across various

psychotherapeutic treatment approaches for PTSD. Administering the TAPS during other evidence-based treatments for PTSD, such as Eye Movement Desensitization and Reprocessing (EMDR) therapy or Cognitive Processing Therapy (CPT) would be valuable.

This study has several limitations and strengths. A first limitation is the relatively small size of the patient sample, which prevented us from analyzing the factor structure of the TAPS in this sample only. Second, the questionnaire was developed in the Dutch language. Third, the scale could benefit from further refinement. Our first factor ('losing control') contains one item that does not refer to internal threat (one's own reactions) but rather to an external threat ('becoming a victim again/ being in danger again'). Outcomes related to external threat are underrepresented in this list, although it is an important domain of posttraumatic cognitions (e.g., 'the world is a dangerous place'). Other future-oriented threat measures in anxiety-based disorders also seem to identify factors related to both individuals' own reactions and external influences (Hicks et al., 2005; Scheveneels & Carpentier, 2024; Schultz et al., 2006). The addition of concerns for external threats may be clinically useful (e.g., getting physically/sexually attacked; socially rejected). In the current measure, it was difficult to add standardized expectancies related to external threat, as these depend on the type of traumatic exposure. Further research is needed to confirm the factor structure of the TAPS via confirmatory factor analysis in an independent sample. Furthermore, future work should assess whether the TAPS demonstrates incremental validity beyond a more global measure of pessimism, such as the Life Orientation Test-Revised (LOT-R; Hinz et al., 2017). A strength is that we introduce a novel measure to refine the assessment of trauma-related cognition, and show that it appears reliable, valid and relevant in the context of treatment. Additionally, the development of the items was largely data-driven, using patient responses from a large previously collected dataset, ensuring their clinical relevance. The development of this scale contributes to our understanding of negative expectancies in relation to trauma reminders in patients with PTSD.

The TAPS is a promising measure to assess trauma-related, concrete and negative expectancies, an important subcategory of posttraumatic cognitions. Outcomes showed that most patients with PTSD have multiple high concerns about negative outcomes when being confronted with trauma reminders. A three-factor solution best fitted the TAPS, where the factors 'losing control', 'externalizing reactions', and 'physical reactions' were identified. The TAPS, and its subscales strongly decreased following treatment and this decrease was related to a decrease in PTSD symptomatology, highlighting the relevance of the measure in a treatment context.

The current findings need to be replicated, ideally in larger and more diverse patient samples. The TAPS may serve as a helpful clinical tool to identify specific threat expectancies and tailor therapeutic interventions.

# Appendix A

## EFA in the combined sample

Based on eigenvalues and the scree method, we explored a two, three and four-factor structure. The three-factor structure, which we deemed to provide the best fit, is described in the main manuscript of our paper. In this supplement, we provide a summary table of the factor solutions (see Table A1) and we provide the outcomes of the two and four-factor structure.

**Table A1.** Summary of factor solutions of combined sample

| Factors | 2 | 3 | 4 |
|---|---|---|---|
| Cross-loading items | 0 | 0 | 2 |
| Non-loading items | 1 | 3 | 3 |
| Low communality items | 7 | 4 | 0 |
| Factors well-defined | 2 of 2 | 3 of 3 | 3 of 4 |
| Variance explained | 44.92% | 50.38% | 52.83% |

*Note.* Cross-loading items are items with factor loadings >.40 on two or more factors. Non-loading items are items that have no factor loading >.40 on any factor. Low communality are items with communality <.40. Factors that are well defined are factors with a minimum of three items.

**Table A2.** Two-factor structure in combined sample

| Items | | Factor 1 | Factor 2 | Communalities |
|---|---|---|---|---|
| 12. | Unable to think (having a black-out) | **.885** | -.163 | **.63** |
| 24. | Unable to function | **.831** | -.067 | **.63** |
| 9. | Not knowing where I am | **.763** | -.005 | **.58** |
| 11. | Unable to talk | **.739** | -.013 | **.53** |
| 8. | Fainting | **.723** | -.131 | **.42** |
| 7. | Unable to move | **.708** | -.042 | **.46** |
| 14. | Unable to feel anything | **.700** | -.012 | **.48** |
| 17. | Collapsing | **.669** | .061 | **.50** |
| 20. | Speaking gibberish | **.603** | .095 | **.44** |
| 23. | Moving uncontrollably | **.585** | .087 | **.41** |
| 5. | Becoming a victim again/being in danger | **.582** | .024 | .36 |

**Table A2.** Two-factor structure in combined sample *Continued.*

| Items | | Factor 1 | Factor 2 | Communalities |
|---|---|---|---|---|
| 3. | Vomiting | **.553** | -.025 | .29 |
| 15. | Hurting myself | **.537** | .196 | **.46** |
| 6. | Choking | **.536** | .149 | **.41** |
| 4. | Having a heart attack | **.529** | .046 | .31 |
| 18. | Dying | **.511** | .027 | .28 |
| 19. | Unable to stop crying | **.444** | .115 | .27 |
| 16. | Wetting or soiling my pants | **.408** | .090 | .22 |
| 21. | Walking away or running away | .377 | .284 | .36 |
| 2. | Throwing things | .031 | **.773** | **.63** |
| 1. | Screaming | -.051 | **.773** | **.55** |
| 10. | Hitting or kicking | .069 | **.753** | **.64** |
| 13. | Swearing or cursing | .017 | **.667** | **.46** |
| 22. | Hurting someone else | .130 | **.584** | **.45** |
| Eigenvalue | | 9.07 | 6.15 | |
| (Additional) % of variance | | 39.24 | 5.68 | |

*Note.* $h^2$ = communalities; Factor loadings in bold indicate that the item loads on a factor (with a cutoff of .40).

**Table A3.** Four-factor structure in combined sample

| Items | | Factor 1 | Factor 2 | Factor 3 | Factor 4 | $h^2$ |
|---|---|---|---|---|---|---|
| 11. | Unable to talk | **.886** | -.003 | -.097 | -.085 | **.66** |
| 12. | Unable to think (having a blackout) | **.840** | -.101 | .000 | .134 | **.70** |
| 7. | Unable to move | **.745** | -.038 | .046 | -.105 | **.53** |
| 24. | Unable to function | **.734** | -.012 | .086 | .086 | **.65** |
| 14. | Unable to feel anything | **.715** | .017 | .009 | -.015 | **.53** |
| 9. | Not knowing where I am | **.636** | .022 | .192 | -.017 | **.59** |
| 5. | Becoming a victim again/being in danger | **.566** | .051 | .031 | .009 | **.38** |
| 20. | Speaking gibberish | **.472** | .150 | .094 | .144 | **.46** |
| 15. | Hurting myself | **.467** | .220 | .098 | .025 | **.46** |
| 23. | Moving uncontrollably | .394 | .101 | .274 | -.014 | **.42** |
| 21. | Walking away or running away | .376 | .346 | -.098 | .188 | **.44** |
| 19. | Unable to stop crying | .346 | .208 | -.068 | .336 | **.41** |

**Table A3.** Four-factor structure in combined sample *Continued.*

| Items | | Factor 1 | Factor 2 | Factor 3 | Factor 4 | $h^2$ |
|---|---|---|---|---|---|---|
| 1. | Screaming | -.115 | **.807** | .006 | .162 | **.62** |
| 2. | Throwing things | -.016 | **.732** | .142 | -.033 | **.62** |
| 10. | Hitting or kicking | .174 | **.699** | .046 | -.217 | **.67** |
| 13. | Swearing or cursing | .102 | **.675** | -.110 | .052 | **.50** |
| 22. | Hurting someone else | .023 | **.541** | .316 | -.240 | **.56** |
| 4. | Having a heart attack | -.056 | .021 | **.821** | .009 | **.64** |
| 18. | Dying | .075 | -.010 | **.673** | -.088 | **.50** |
| 8. | Fainting | .167 | -.069 | **.547** | .350 | **.58** |
| 16. | Wetting or soiling my pants | .040 | .077 | **.528** | -.034 | **.34** |
| 6. | Choking | .251 | .137 | **.447** | -.070 | **.47** |
| 3. | Vomiting | .055 | .048 | **.444** | .369 | **.43** |
| 17. | Collapsing | .285 | .110 | **.410** | .177 | **.54** |
| Eigenvalue | | 8.30 | 5.86 | 5.74 | 1.48 | |
| (Additional) % of variance | | 39.53 | 5.91 | 5.22 | 2.17 | |

*Note.* $h^2$ = communalities; Factor loadings in bold indicate that the item loads on a factor (with a cutoff of .40).

# Chapter 7

# General discussion

In the previous chapters, we aimed to elucidate the mechanisms of change in exposure therapy for PTSD and to translate ILR principles into clinical practice. To this end, we analyzed data from treatment studies to establish a temporal link between proposed mechanisms and treatment outcomes, and we conducted experimental studies, designed to manipulate the proposed mechanisms through variations in therapeutic delivery. In the current chapter, I summarize the main findings, provide a critical discussion, examine limitations, and reflect on the implications for future research and clinical practice.

**Summary of main findings**

In **Chapter 2** we examined whether changes in posttraumatic cognitions temporally preceded changes in PTSD symptoms during PE in adult patients with PTSD following childhood abuse. Change in posttraumatic cognitions is a proposed mechanism through which exposure therapy leads to a reduction in PTSD symptoms. We found a bi-directional relationship between cognitions and symptoms, meaning that reductions in posttraumatic cognitions predicted decreases in PTSD symptoms, and vice versa. However, the effect of cognitions on symptoms was almost twice as great as the reverse effect. Our findings indicate that cognitive change (operationalized as general negative cognitions about the self, about the world and self-blame) precedes PTSD symptom reduction, although cognitive change and PTSD symptom change are not entirely distinct processes. Greater precision in measuring the specific cognitions that are targeted in treatment may help to elucidate which cognitive changes precede symptom reduction.

In **Chapter 3** we used the same dataset to examine whether in-session distress variability temporally precedes changes in PTSD symptoms during PE. According to ILR principles, variation in distress levels during exposure may facilitate extinction learning, thereby enhancing the effectiveness of exposure therapy. Capturing in-session distress variability in a way that aligned with its theoretical conceptualization (i.e., an up-and-down pattern of in-session distress levels) proved difficult, as existing metrics did not fully reflect this definition. Using several operationalizations of in-session distress variability, we found that none predicted subsequent PTSD symptom improvement during PE. In other words, greater distress variability within a given session was not associated with greater symptom reduction at the next session (i.e., no temporal or within-person effect). However, we did find that average distress variability across sessions (i.e., the between-person effect) was associated with greater overall symptom improvement. This suggests that distress variability may be a marker of who responds well to PE in general, rather than reflecting a mechanism of change of PE. A clinical implication is that distress variability may

not require explicit emphasis during sessions. Optimization efforts may be better directed at other proposed mechanisms, such as expectancy violation.

In **Chapter 4,** we took a closer look at the effect of expectancy violation on treatment outcomes. Using a one-session treatment paradigm, we assessed whether exposure with an explicit focus on expectancy violation resulted in better exposure outcomes compared to exposure without an expectancy focus, in a clinical sample of treatment-seeking patients with PTSD. Whether emphasizing expectancy violation leads to enhanced outcomes has not yet been studied in PTSD. We assessed exposure outcomes through fear-related responses to a personalized imagery task and a PTSD symptom questionnaire (PCL-5). On average, fear responses to the imagery and PTSD symptoms decreased from pre to post exposure session. We found no significant differences between conditions, indicating that the identification of negative expectancies and emphasizing their non-occurrence during exposure did not lead to enhanced immediate treatment outcomes. As we used a single-session paradigm, we were unable to assess potential effects over an extended period. This study revealed that emphasizing expectancy violation during (imaginal) exposure did not immediately affect outcomes. This does not rule out beneficial effects beyond the first session, however.

**In Chapter 5**, we evaluated the applicability and effects of a comprehensive ILR-adapted exposure therapy in PTSD patients using a single-case experimental (SCED) design. Although the ILR approach has been proposed as an improvement to exposure therapy, it is crucial to first determine whether a full ILR-based exposure can produce meaningful therapeutic effects. Participants in this study tracked negative expectancies, distress tolerance, and PTSD symptoms daily throughout baseline, treatment, and follow-up. We found that ILR-based exposure led to significant reductions in negative expectancies and PTSD symptoms. However, we found similar results for EPT-based exposure. Our findings indicate that ILR-based principles can be effectively applied to exposure therapy for PTSD, but there is no indication that these principles increase the efficacy of the treatment or uniquely affect its theorized change mechanisms.

Finally, in **Chapter 6**, we assessed the psychometric properties of the Threat Appraisal in PTSD Scale (TAPS), a measure we developed to evaluate concerns about concrete trauma-related negative outcomes. Although negative expectancies have been increasingly emphasized as playing a crucial role in the maintenance and recovery of PTSD, there was no valid measure to assess these. We found that the TAPS was a reliable and valid measure, making it a valuable contribution to the field. Patients seemed most concerned about items related to the factor 'losing control'.

The TAPS moderately correlated with more general posttraumatic cognitions, suggesting that they are related but different constructs.

**Exposure therapy is not so easily optimized**

Our findings consistently demonstrate the effectiveness of exposure therapy for PTSD (**Chapters 2, 3, 4**, and **5**), which is in line with a multitude of studies (see for meta-analyses: (Mavranezouli et al., 2020; McLean et al., 2022). The ILR approach to exposure was introduced with the idea that the implementation of its proposed strategies (e.g., maximizing expectancy violation, incorporating variability) would lead to enhanced treatment efficacy and less relapse (return of fear). Although we find that ILR principles can be effectively applied to exposure therapy for PTSD, we found no optimized exposure outcomes in this population and within the time frame investigated (**Chapters 3, 4,** and **5**).

*Applying ILR principles to exposure for PTSD*

The ILR approach is a clinical theory on the application of exposure therapy, grounded in findings from experimental fear conditioning studies, most of which have been conducted with healthy participants. We were the first to test ILR principles in PTSD treatment and translating these principles to the delivery of exposure therapy presented several challenges.

In Pavlovian fear conditioning research, the US is typically an external threat, such as an electric shock, that naturally elicits a fear response (Craske et al., 2014; Hermans et al., 2006; Pittig et al., 2018). In other words, the ILR principles are grounded in experimental paradigms where the feared outcome is concrete, and occurs (fairly) immediate. However, in PTSD the feared outcomes are not always concrete and immediate. For example, patients with PTSD frequently report relatively abstract expectancies, related to distress or internal threats, such as 'losing control' or 'going crazy' (de Kleine et al., 2017; Foa & McLean, 2016; Rothbaum et al., 2019; and also **Chapter 6**). Some patients are unable to articulate a feared outcome at all, beyond expressing that the exposure will be aversive, despite adequate inquiry by the therapist. Moreover, feared outcomes are sometimes long-term or unknowable (e.g., 'my body will eventually stop functioning'), which is also seen in patients with obsessive-compulsive disorder (Jacoby & Abramowitz, 2016). According to the ILR framework, such expectancies should be reframed into concrete and immediately testable outcomes. However, this is difficult when patients do not endorse fears that qualify as a US, a challenge also reported in two empirical studies with other (clinical) populations (Kennedy & Hawks, 2021; Scheveneels & Carpentier, 2025). There is considerable variation in the types of expectancies that are targeted in empirical studies on expectancy violation (e.g., concrete, abstract, internal, external,

idiographic, and predetermined/fixed). It remains unclear whether the application of the ILR approach to exposure therapy for PTSD is only meaningful for patients who report a clear US expectancy and whether this US needs to be biologically significant (e.g., impending death) or whether more vague expectancies (e.g., long-term damage) can also be targeted.

Another challenge in translating the ILR approach to PTSD is that the guidance provided by Craske and colleagues (2014, 2022) focuses solely on in vivo exposure, while imaginal exposure is a core component of exposure therapy for PTSD. Empirical studies on expectancy violation have similarly focused on in vivo procedures (Baker et al., 2010; De Jong et al., 2023; Deacon et al., 2013; Krause et al., 2022). Expectancies related to external threat (e.g., 'the perpetrator will attack me again') may be best tested in vivo, whereas expectancies related to internal threat (e.g., 'I will lose my mind') can be tested during imaginal exposure. As mentioned above, expectancies related to this internal threat can also be less concrete and immediate. Interestingly, two studies on virtual reality exposure therapy tested which expectancies showed greatest reductions: expectancies about external threat (e.g., 'the spider will bite me', 'people will criticize me') which were not directly testable in a virtual reality environment, or expectancies about internal threat (e.g., 'I will die of fear'), which could be tested and falsified in this context (Scheveneels, Boddez, Van Daele, et al., 2019; Scheveneels & Carpentier, 2025). Following ILR principles, it was hypothesized that testable expectancies (i.e., related to internal threat) would diminish most following exposure. However, the findings in these studies were mixed: internal threat expectations appeared more testable in public speaking anxiety (Scheveneels, Boddez, Van Daele, et al., 2019), whereas external threat expectations appeared more testable in spider fear (Scheveneels & Carpentier, 2025). The questions of which types of expectancies are best testable in which exposure forms and how this relates to symptom change still warrant further investigation.

Finally, the ILR approach to exposure primarily targets fear reduction through extinction learning. However, whether PTSD is best conceptualized as a fear-based disorder has been a matter of debate (Resick & Miller, 2009; Schnyder et al., 2015; Yehuda et al., 2016; Zoellner et al., 2014). Fear plays an important role in PTSD, but it is neither the sole nor necessarily the dominant emotional response involved in its development and maintenance. Emotions such as shame, guilt, and anger are also frequently implicated (McLean & Foa, 2017; Resick & Miller, 2009). By focusing primarily on fear-related expectancies, the ILR approach may overlook clinically relevant processes involving other important emotions. Notably, the original Prolonged Exposure (PE) manual (Foa et al., 2019) includes postexposure processing that explicitly addresses emotions beyond fear, including shame, guilt, and anger.

*A broader perspective on ILR principles in clinical practice*

Although there are many reviews describing the application of ILR principles in clinical practice (see, for instance: Arch & Abramowitz, 2015; Blakey & Abramowitz, 2016; De Jong et al., 2019; Gropalis et al., 2018; Jacoby & Abramowitz, 2016; Knowles & Olatunji, 2019; Pittig et al., 2016; Tolin, 2019; Weisman & Rodebaugh, 2018), empirical studies testing these principles are still scarce. Since Craske's seminal paper in 2014, several empirical studies have been conducted in non-treatment-seeking individuals with elevated clinical symptoms or specific phobias, recruited from community or university settings, to test whether incorporating ILR strategies into exposure improves treatment outcomes (Blakey et al., 2019; Buchholz et al., 2022; De Jong et al., 2023; Jacoby et al., 2019; Jessup et al., 2025; Johnco et al., 2025; Sauer & Witthöft, 2022; Schyns et al., 2018; Shiban et al., 2015). These studies have used widely varying methods to manipulate different ILR strategies in varying samples. However, none of these studies find evidence that the use of ILR strategies led to improved symptom reduction. See Table 1 for an overview of the studies.

It is striking how few empirical studies testing ILR principles to *improve* treatment outcomes have been conducted in treatment-seeking clinical populations. So far, we have identified only one other study that did so, namely in a sample of youths with an anxiety disorder (Kennedy & Hawks, 2021). In this pilot randomized controlled trial ($N$ = 13), the authors found that ILR-based exposure was effective and feasible. Like us, they encountered methodological challenges, such as delineating ILR exposure from 'standard', EPT-based exposure, and operationalizing 'maximum' violation of expectancies. It is noteworthy that the scarcity of empirical studies in treatment-seeking samples was identified as a critical concern nearly a decade ago (Jacoby & Abramowitz, 2016; Pittig et al., 2016), yet little progress appears to have been made since.

**Table 1.** Overview of studies manipulating exposure procedures to enhance inhibitory learning since Craske et al., 2014.

| Study | Sample | ILR strategy manipulation | Conditions | Outcome | |
|---|---|---|---|---|---|
| Blakey et al., 2019 | Adults with spider phobia (*N* = 60) | Reduction of safety behaviors | 1) Exposure with the elimination of safety behaviors (E/ESB)<br>2) Exposure with judicious use of safety behaviors (E/JU) | No significant group differences in treatment outcome (fear of spiders and behavioral approach task) or acceptability. | - |
| Buchholz et al., 2022 | Adults with spider phobia (*N* = 45) | Expectancy violation | 1) CR before exposure (CR-exp)<br>2) Exposure before CR (exp-CR)<br>3) Stress management (CTL) | CR-exp and exp-CR led to greater reductions in spider phobia than CTL, with no differences between the two on fear, avoidance, or cognitions. | - |
| De Jong et al., 2023 | Youths with specific phobia (*N* = 50) | Expectancy violation | 1) Exposure conducted in large steps (LSE)<br>2) Exposure in small steps (SSE) | SSE resulted in less expectancy violation but in a larger decline of specific phobia symptoms compared to LSE. | < |
| Jacoby et al., 2019 | Adults with an obsessional thought (*N* = 40) | Stimulus variability | 1) Gradual exposure (EXP-G)<br>2) Variable exposure (EXP-V) | There were no significant differences in pre to post changes in OCD symptoms between EXP-G and EXP-V. | - |
| Jessup et al., 2025 | Community adults with snake phobia (*N* = 134) | Context and stimulus variability | 1) Exposure in multiple contexts (MC)<br>2) Exposure to multiple stimuli (MS)<br>3) Exposure to multiple C and S (MCS) | MC resulted in lower threat expectancy than MS and MCS. No effects on symptoms were reported. | < |

**Table 1.** Overview of studies manipulating exposure procedures to enhance inhibitory learning since Craske et al., 2014. *Continued.*

| Study | Sample | ILR strategy manipulation | Conditions | Outcome | |
|---|---|---|---|---|---|
| Johnco et al., 2025 | Adults with elevated public speaking anxiety (*N* = 249) | Expectancy violation | 1) Behavioral experiments based exposure (BE)<br>2) CR before exposure (CR-exp)<br>3) Exposure without processing of expectancies (CTL) | BE and CR-exp reduced anxiety more than CTL; BE led to more expectancy change. More expectancy change was associated with more anxiety reduction | -/> |
| Sauer & Witthöft, 2022 | Adults with heightened health anxiety (*N* = 54) | Multiple strategies | 1) ILR based exposure (ILR)<br>2) Habituation based exp (HA) | There were no significant differences in pre- to post changes on health anxiety between conditions. | - |
| Schyns et al., 2018 | Obese females (*N* = 52) | Expectancy violation | 1) Exposure aimed at habituation (HA)<br>2) Aimed at expectancy violation (EV)<br>3) No exposure control (CTL) | There were no significant differences between HA and EV on eating the exposed foods. | - |
| Shiban et al., 2015 | Adults with spider phobia (*N* = 58) | Context and stimulus variability | 1) Single stimulus and context (SSSC)<br>2) Multiple stimulus single context (MSSC)<br>3) Single stimulus multiple context (SSMC)<br>4) Multiple stimulus and context (MSMC) | Multiple stimulus but not multiple context exposure led to less return of fear at follow-up test. | -/> |

*Note.* CR = cognitive restructuring; ILR = Inhibitory learning and retrieval; < = significant in favor of non-ILR (control) condition; - = non-significant finding; > = significant finding in favor of ILR condition.

**Identifying and targeting mechanisms is difficult**

The scarcity of empirical studies testing ILR-enhanced exposure may reflect a gap in the field, but it may also indicate the inherent difficulty of conducting mechanism research. Research aimed at optimizing exposure by actively targeting its mechanisms of change poses several challenges.

First, there is a lack of conceptual clarity in mechanism research (Benito et al., 2024; Cohen et al., 2023). For instance, studies fail to clearly distinguish between active elements (i.e., treatment procedures), proposed mechanisms, and outcomes. These are related, but distinct, concepts: therapeutic elements activate mechanisms which subsequently drive therapeutic outcomes. In the studies included in this dissertation, we aimed to clearly describe and distinguish these processes to gain a more precise understanding of how exposure brings about change. In **Chapter 2**, we controlled for potential conceptual overlap between the mechanism (posttraumatic cognitions) and the outcome (PTSD symptoms) by conducting sensitivity analyses that excluded symptom items reflecting negative cognitions. In **Chapter 4**, we explicitly separated the therapeutic procedure (exposure with a focus on expectancy violation) from the proposed mechanism of change (expectancy change). Despite these efforts, conceptual ambiguity remains, in part due to theoretical overlap. Theories, such as EPT and ILR, often overlap or emphasize different parts of the same process (e.g., distress reduction also violates the expectancy that fear will never subside). This makes it difficult to identify and disentangle mechanisms, and to summarize findings across studies.



Second, mechanism research is challenging due to measurement issues (Benito et al., 2024). Instruments to assess change mechanisms, such as expectancy violation, often lack psychometric validation and empirical studies use different measures or definitions for similar constructs. We have tried to further the field in regard of measurement by providing and testing alternative operationalizations of distress variability (**Chapter 3**), using a combination of objective and subjective measures for fear reduction (**Chapter 4**), and by introducing a new measure that can be used to assess threat appraisal in PTSD (**Chapter 6**). Even so, operational challenges remain. A fundamental issue may lie in the lack of clear operationalization of expectancy violation. There is no standard for how expectancy violation should be defined or measured, and the ILR approach lacks specificity in this regard (see also: Stemerding et al., 2023). Empirical studies have used divergent approaches, such as comparing exposure with and without cognitive restructuring (based on the assumption that restructuring reduces expectancy violation; Buchholz et al., 2022; Johnco et al., 2025), emphasizing expectancies and their non-occurrence (**Chapter 4**), or focusing on the degree to which expectancies are testable (Scheveneels, Boddez, Van Daele,

et al., 2019). A more unified and precise understanding of what constitutes optimal expectancy violation is needed.

Third, individual and contextual differences may affect mechanisms. We often think of mechanisms as competing with one another, but it is likely that multiple mechanisms are simultaneously at play in each individual, interacting in complex ways to produce treatment effects (Benito et al., 2024; Knowles & Tolin, 2022; Scheveneels et al., 2024). For instance, several studies have shown that both expectancy change and distress reduction (i.e., habituation) contribute to symptom improvement (De Jong et al., 2024; Elsner et al., 2022; Scheveneels & Carpentier, 2025). In our studies, although we aimed for precision in measuring individual mechanisms, a limitation is that we did not examine multiple mechanisms concurrently. Additionally, mechanisms may differ across individuals, what works for one person may not work for another (Cooper, Clifton, et al., 2017). Context (e.g., setting, therapist behavior, etc.) also plays a role. For instance, clinicians often tailor exposure procedures to the individual patient (e.g., more gradual exposure when a patient disengages during exposure), a flexibility that is difficult to capture in standardized research designs.

Finally, demonstrating the added value of targeting specific mechanisms is challenging, in part because exposure therapy is already highly effective. Even when a mechanism has been clearly identified and targeted, the added clinical benefit may be small and difficult to detect. Null results do not necessarily indicate that the effect is absent. This issue has also emerged in other enhancement approaches, such as pharmacological augmentation, where null findings are common (McLean & Foa, 2024; Metcalf et al., 2020). Moreover, full-package interventions can introduce considerable noise, making it hard to isolate the impact of individual components and mechanisms. In our work, we have attempted to address this issue using more targeted designs, such as a one-session experimental design (**Chapter 4**) and single-case experimental designs (**Chapter 5**).

**Tracking versus manipulating**

While the extent to which ILR principles *optimize* exposure outcomes is questioned in this dissertation, this is not to suggest that they are inconsequential within the context of exposure therapy. Although there is a lack of studies in clinical samples investigating the added benefit of these specific exposure strategies, multiple treatment studies have established a (temporal) link between expectancy change and symptom improvement, in a variety of clinical samples, including patients with OCD and anxiety disorders (De Jong et al., 2024; Elsner et al., 2022; Pittig et al., 2022). More specifically, these studies found that more expectancy change was related to more symptom improvement. In non-clinical samples, expectancy change during

exposure has also been linked to subsequent symptom improvement (Johnco et al., 2025; Scheveneels & Carpentier, 2025). We have also found that more general posttraumatic cognitions drive symptom improvement in PTSD during PE (**Chapter 2**), which is in line with reviews on mechanisms of PTSD treatment (Alpert, Shotwell Tabke, et al., 2023; Cooper, Clifton, et al., 2017). How changes in expectancies relate to these more general posttraumatic cognitions requires further investigation. It has been suggested that repeated expectancy violations may subsequently lead to changes in posttraumatic cognitions (Knowles & Tolin, 2022). For instance, repeatedly experiencing that you will not be attacked when going out in the dark may change the more general belief that the world is a dangerous place. We found that concerns about specific outcomes (expectancies) moderately correlated with more general posttraumatic cognitions (measured with the PTCI), suggesting that they indeed capture related but unique aspects of trauma-related cognitions (**Chapter 6**).

Cognitive change, including general posttraumatic cognitions and specific expectancies, is important for symptom reduction. This is evident both in treatments that do not explicitly target cognitions, such as PE, and in those that do, such as Cognitive Processing Therapy (CPT, Asmundson et al., 2019; Holliday et al., 2018). Interestingly, CPT does not seem to be associated with greater (general) cognitive change than PE (Brown, Belli, et al., 2019), even though cognitions are targeted more directly. Furthermore, adding cognitive restructuring to PE (PE+CR) has not led to greater cognitive change or PTSD symptom reduction compared to PE only (Foa et al., 2005; Foa & Rauch, 2004; McLean & Foa, 2024). Thus, even though cognitive change appears to drive symptom improvement, explicitly targeting cognitions has not been shown to improve treatment effects. This may be because different therapeutic procedures engage similar mechanisms through direct or downstream pathways, or because promoting one procedure may positively affect some mechanisms but negatively affect others. For instance, cognitive restructuring may promote cognitive change, but at the same time may diminish threat expectancies before exposure, leaving less room for expectancy violation to occur. Although cognitive change seems an important change process during treatment, there is limited understanding of how to effectively promote it through targeted therapeutic procedures. This question extends beyond exposure therapy for PTSD. In mechanism research on cognitive therapy for depression, it also remains unclear whether cognitive change results directly from procedures designed to target it, as cognitive change has also been observed following interventions that do not explicitly aim to produce it (Lorenzo-Luaces et al., 2015). Nonetheless, tracking cognitive change throughout treatment can provide earlier insight into treatment effectiveness and help tailor interventions, for example by discussing an individual's strongly held cognitions.

**Future research agenda**

Despite the clear challenges of conducting mechanism research, this type of research remains essential for advancing theoretical frameworks that guide clinical decision-making. Importantly, mechanism research should not only clarify which procedures are effective, but also address other clinically relevant outcomes, such as willingness to engage in exposure and treatment dropout. This interplay is clearly illustrated in the literature on safety behavior. While safety behaviors were initially viewed as counterproductive, which is also posited by the ILR approach, this view has been increasingly challenged by empirical findings (Blakey & Abramowitz, 2016). Some empirical findings suggest that, when used judiciously, safety behavior may enhance the acceptability and tolerability of exposure, and promote approach behavior, self-efficacy, and even inhibitory learning (Blakey & Abramowitz, 2016). This line of research thus helps guide a more nuanced and evidence-informed use of safety behavior in clinical practice. More work is needed, including on other strategies such as expectancy violation, as it is conceivable that exposure sessions in which the patient first tests their most feared outcome could have detrimental effects on willingness to engage or increase the risk of dropout.

The ILR approach to exposure has achieved broad dissemination and is now widely implemented in clinical settings. Its influence is evident in the high citation counts of Craske et al.'s review articles on the clinical application of ILR: 1,047 (2008), 1,392 (2014), and 108 (2022). However, there is still uncertainty about the extent to which ILR strategies should be applied and under what conditions they are most likely to enhance treatment outcomes. While this type of research is methodologically challenging, it remains essential for advancing exposure therapy's theoretical frameworks that inform clinical decision-making. There is a need for consensus on how inhibitory learning strategies should be compared and tested. At present, the variability in methods makes it difficult to synthesize findings or draw conclusions, for example, through meta-analytic approaches. A crucial first step is to establish clear operationalizations of core constructs (such as expectancy violation), supported by validated measurement instruments.

In addition, future (mechanism) research may look into the extent to which active elements of therapy are received by patients (i.e., what the patient understands from the therapist during the session) and applied (i.e., the patient's active implementation of the active elements in daily situations outside the therapy context), as outlined in the framework introduced by Cohen et al., 2023. To date, mechanism research, including our own, has primarily focused on the delivery of specific active elements by the therapist, presumed to activate underlying change processes. However, little attention has been paid to whether these strategies actually reach the patient in a meaningful way. To address this, it is essential to assess, both within and outside

the session, whether patients understand and implement the rationale behind the active elements. With the increasing use of ecological momentary assessment (EMA), also in patient samples (Wrzus & Neubauer, 2023), studies involving such repeated assessments during and between sessions are becoming more feasible.

**Clinical implications and recommendations**

The ILR approach to exposure has already been implemented in clinical practice. In training settings, there is often strong emphasis on ILR as the correct way to deliver exposure therapy. However, evidence for the clinical superiority of ILR-based exposure over traditional approaches, such as EPT-based exposure, is still lacking. There is currently also no evidence that indicates that ILR-based exposure leads to poorer outcomes. It is therefore one possible way of delivering exposure, but not the only way.

Exposure therapy operates through multiple pathways, some at different or parallel levels, including expectancy violation and change, distress reduction (i.e., habituation), cognitive shifts such as US devaluation, increased self-efficacy, and behavioral activation (Cooper, Clifton, et al., 2017; Scheveneels et al., 2024; Vervliet et al., 2024). It is likely that different exposure exercises engage different processes. For example, the in vivo exercise to repeatedly visit the same local park may no longer elicit strong expectancy violation, but could still promote habituation or behavioral activation. It is important that therapists are aware of the various mechanisms through which exposure can exert its effects, as well as of the different therapeutic procedures and strategies that may activate these mechanisms. This awareness enables therapists to flexibly draw on a range of techniques to facilitate therapeutic change. The ILR strategies are a valuable addition to the exposure therapist's toolkit, but this toolkit may become rather empty if these strategies are treated as the only valid tools.

Exposure therapy for PTSD is effective, this cannot be emphasized enough. At the same time, it remains underused in clinical practice. A recent study from the Netherlands found that two out of three patients with probable PTSD did not receive first-line treatments, including exposure therapy (Hoeboer et al., 2025). Therapist-related factors play a role in this underutilization (Langthorne et al., 2023). Mechanism research has the potential to positively influence the use of exposure therapy in at least two ways: it can help refine treatments or protocols by identifying which elements to in- or exclude, and it can provide therapists with concrete guidance on how to implement interventions. The latter helps therapists build competence and confidence, allowing them to deliver more targeted treatment and make informed decisions during treatment. However, one potential drawback is that such research may inadvertently be interpreted in overly rigid ways, creating

confusion about what is or is not 'allowed' during sessions. This could raise the threshold for using exposure, even when clearly indicated. Rather than policing *how* exposure *should* be delivered, we may lower the threshold for using exposure therapy by encouraging *that* it *is* delivered.

**Conclusion**

The primary objective of this dissertation was to identify potential avenues for enhancing the efficacy of exposure therapy for PTSD through inhibitory learning and retrieval processes. The ILR approach engendered great expectations, as it promised to optimize exposure therapy. However, we did not find evidence that ILR principles are associated with better treatment outcomes for patients with PTSD. The promise of optimization has not yet been fulfilled, but this does not mean that ILR principles are unimportant. Cognitive change, including expectancy change, has emerged as an important predictor of treatment outcome. However, facilitating these processes through therapeutic procedures remains elusive. A shift in how exposure therapy for PTSD is delivered, based solely on ILR principles, does not seem warranted. Nonetheless, ILR offers a valuable addition to existing approaches.

# Chapter 8

# Appendices

# Nederlandse samenvatting

# Hoge verwachtingen: inhibitoir leren en veranderprocessen tijdens exposuretherapie voor PTSS

**Exposuretherapie voor PTSS**

Mensen die een zeer ingrijpende gebeurtenis meemaken kunnen een posttraumatische stress stoornis (PTSS) ontwikkelen. Kenmerkend voor PTSS zijn herbelevingen van de traumatische gebeurtenis, het vermijden van prikkels die aan de gebeurtenis doen denken, negatieve veranderingen in gedachten en gevoelens, en een aanhoudende verhoogde prikkelbaarheid of alertheid. Deze klachten kunnen het dagelijks functioneren aanzienlijk belemmeren en leiden tot problemen in sociale contacten, beroepsmatig functioneren en emotioneel welzijn. Exposuretherapie is een effectieve behandeling voor PTSS. Tijdens exposuretherapie worden patiënten blootgesteld aan de herinnering aan de traumatische gebeurtenis en aan situaties, mensen of plekken die hen aan het trauma doen denken, maar die in werkelijkheid geen gevaar vormen. Hoewel de behandeling effectief is, is er een aanzienlijk deel van de patiënten die er onvoldoende van profiteert. Een beter begrip van hoe exposuretherapie werkt kan helpen om de behandeling gerichter toe te passen en effectiever te maken.

**Theorieën over de uitvoering van exposure**

Exposuretherapie voor PTSS is van oorsprong gebaseerd op de 'Emotional Processing Theory' (EPT). Kort gezegd stelt deze theorie dat langdurige blootstelling aan trauma-gerelateerde stimuli leidt tot emotionele verwerking, wat op zijn beurt leidt tot vermindering van klachten. Die verwerking is niet direct zichtbaar, maar wordt afgeleid uit angstdalingen tijdens en tussen de sessies, en uit veranderingen in negatieve gedachten over jezelf en de wereld, zogenaamde negatieve trauma-gerelateerde gedachtes (bijv. 'ik ben zwak', of 'de wereld is door en door gevaarlijk'). Volgens deze theorie is het belangrijk dat angst tijdens en tussen sessies afneemt, wat wordt gestimuleerd door herhaalde en langdurige blootstelling in de sessies. Echter, onderzoek laat geen eenduidig verband zien tussen de mate van angstdaling tijdens exposure en vermindering van PTSS klachten. In combinatie met het feit dat een deel van de patiënten onvoldoende opknapt, heeft dit geleid tot nieuwe theoretische inzichten over hoe exposuretherapie werkt.

Een nieuwer model, het *inhibitoire model*, stelt dat exposure niet werkt door een afname van angst (angstdaling), maar door het aanleren van nieuwe, niet-bedreigende associaties die de oorspronkelijke gevaar-associaties onderdrukken (inhiberen). In de context van PTSS betekent dit dat iemand moet leren en onthouden dat confrontatie met trauma-gerelateerde stimuli niet leidt tot de verwachte negatieve gevolgen (zoals controleverlies of opnieuw in gevaar zijn). Dit model is

gebaseerd op klassieke leertheorie en doet verschillende concrete aanbevelingen om exposuretherapie te verbeteren. Bevindingen uit preklinische studies, met gezonde proefpersonen of mensen met verhoogde angstklachten, suggereren dat deze inhibitoire strategieën exposure kunnen optimaliseren. Aan het begin van dit promotietraject werden het maximaliseren van verwachtingsfalsificatie en het toevoegen van variatie tijdens exposure gezien als de twee belangrijkste strategieën om effectiviteit te vergroten. Met verwachtingsfalsificatie wordt bedoeld dat tijdens exposure wordt getoetst of angstige verwachtingen kloppen, bijvoorbeeld "als ik eraan denk, verlies ik de controle". Het niet uitkomen van deze verwachtingen tijdens exposure wordt gezien als een krachtig leerproces dat het vormen van nieuwe, niet-bedreigende associaties bevordert. Het toevoegen van variatie (in stimuli en contexten) zou vervolgens helpen om deze nieuwe associatie makkelijker op te roepen in verschillende situaties. Hierdoor zou exposure effectiever worden: het nieuw-geleerde wordt sterker opgeslagen en het wordt makkelijker onthouden.

**Doel van dit proefschrift**

Er is nog weinig onderzoek gedaan naar de toepassing van de aanbevelingen van het inhibitoire model in de klinische praktijk, en nog helemaal niet bij patiënten met PTSS. Het doel van dit proefschrift was om beter te begrijpen hoe exposuretherapie werkt bij PTSS en te onderzoeken of we de effectiviteit kunnen verbeteren door strategieën uit het inhibitoire model toe te passen.

**Resultaten van dit proefschrift**

*Het belang van posttraumatische cognities*

In **hoofdstuk 2** hebben we onderzocht of veranderingen in negatieve trauma-gerelateerde gedachtes voorafgaan aan vermindering van PTSS-klachten tijdens exposuretherapie voor PTSS. We hebben dit onderzocht in 83 volwassenen met PTSS ten gevolge van kindermishandeling die 14 tot 16 sessies exposuretherapie kregen. We vonden dat veranderingen in trauma-gerelateerde gedachtes en PTSS klachten elkaar wederzijds beïnvloedden, maar veranderingen in gedachtes voorspelden klachten sterker dan andersom. Dit suggereert dat veranderingen in negatieve trauma-gerelateerde gedachtes een belangrijke rol spelen in klachtvermindering. Therapeuten doen er daarom goed aan om deze gedachtes tijdens de behandeling te volgen en uit te dagen.

*Een variabel angstniveau hoeft therapeutisch niet bevorderd te worden*

In **hoofdstuk 3** hebben we in dezelfde groep patiënten onderzocht of meer variatie in angstniveau tijdens de exposuresessies voorafgaat aan vermindering van PTSS-klachten in de volgende sessie. Een meer variabel angstniveau zou namelijk volgens

het inhibitoire model de effectiviteit van de behandeling bevorderen. Hoeveel iemands angst varieerde tijdens de sessies ging niet vooraf aan klachtvermindering. We weten nog te weinig over het optimale verloop van angstniveaus om klinische aanbevelingen te doen.

*Focus op verwachtingsfalsificatie maakt exposure niet direct effectiever*

In **hoofdstuk 4** onderzochten we of exposuretherapie beter werkt als de therapeut extra nadruk legt op het falsificeren van angstige verwachtingen. Zestig mensen met PTSS kregen één exposuresessie, met of zonder deze expliciete nadruk op verwachtingen. Angstreacties en klachten namen in beide groepen af, maar er was geen verschil tussen de twee vormen van exposure. Dit betekent dat het benadrukken van verwachtingsfalsificatie niet direct tot betere effecten leidde, al is niet uitgesloten dat dit op langere termijn wel effect kan hebben.

*Inhibitoir-gebaseerde exposure behandeling voor PTSS is effectief*

**Hoofdstuk 5** richtte zich op de vraag of een volledig inhibitoir-gebaseerde vorm van exposuretherapie toepasbaar en effectief is bij PTSS. Hoewel deze vorm van exposure veelbelovend lijkt, moet eerst blijken of zij uitvoerbaar en effectief is. Negen patiënten met PTSS volgden twaalf sessies exposuretherapie. Deelnemers registreerden dagelijks hun PTSS-klachten, angstige verwachtingen en hun vermogen om angst te verdragen, zowel voor en tijdens de behandeling als drie maanden later. PTSS klachten en verwachtingen namen significant af tijdens de behandeling. Dit gold ook voor een vergelijkbare groep van 10 patiënten die traditionele (EPT-) exposure kreeg. De inhibitoire uitvoer van exposure is dus uitvoerbaar en effectief. We vonden echter geen aanwijzingen dat het beter zou werken dan traditionele (EPT-)exposure.



*Het meten van negatieve verwachtingen*

In **hoofdstuk 6** onderzochten we een nieuwe, zelf-ontwikkelde vragenlijst: de '*Threat Appraisal in PTSD Scale*' (TAPS). Deze vragenlijst brengt concrete angstige verwachtingen in kaart bij PTSS. We vonden dat de TAPS betrouwbaar, valide en gevoelig voor verandering was. Patiënten maakten zich vooral zorgen over verwachtingen die te maken hadden met het verliezen van controle. De TAPS kan klinisch waardevol zijn om negatieve verwachtingen te identificeren en interventies gerichter vorm te geven.

**Discussie**

Onze bevindingen laten consistent zien dat exposuretherapie voor PTSS werkt. We vinden echter geen aanwijzingen dat exposure voor PTSS effectiever wordt door het toevoegen van inhibitoire strategieën. Dit suggereert dat inhibitoire exposure niet *beter* werkt dan traditionele vormen van exposure. Het is ook mogelijk dat het inhibitoire model niet altijd even toepasbaar is in exposure voor PTSS. Het inhibitoire model is namelijk gebaseerd op situaties waarin angstige verwachtingen duidelijk en onmiddellijk toetsbaar zijn, zoals angst voor een directe bedreiging van buitenaf. Bij PTSS zijn de gerapporteerde angstige verwachtingen vaak minder concreet (bijvoorbeeld gerelateerd aan een intern gevaar zoals 'gek worden van angst'). We weten nog weinig over welk type verwachtingen gefalsificeerd moeten worden om exposuretherapie te bevorderen. Daarnaast richt het inhibitoire model zich vooral op het verminderen van angst, terwijl andere negatieve emoties, zoals schaamte en boosheid, ook een belangrijke rol spelen bij PTSS.

Tegelijkertijd is er ook in onderzoek met andere populaties geen overtuigend bewijs dat exposure effectiever wordt door het toepassen van inhibitoire strategieën. Opvallend daarbij is dat de meerwaarde van deze strategieën nauwelijks is onderzocht bij patiënten die behandeling zoeken, terwijl ze in de klinische praktijk al regelmatig worden toegepast. Een mogelijke verklaring voor het beperkte aantal studies in patiënten is dat onderzoek naar de werkingsmechanismen van behandelingen complex is. De theoretische begrippen zijn niet altijd scherp afgebakend, bestaande meetmethoden zijn vaak ontoereikend, en ook zijn er individuele en contextuele verschillen die de effecten beïnvloeden (wat voor de één werkt, werkt misschien niet voor de ander). Desondanks blijft het belangrijk om de theoretische basis van exposuretherapie verder te ontwikkelen om zo klinische besluitvorming te ondersteunen.

Hoewel het nog onduidelijk is of de toepassing van inhibitoire strategieën exposuretherapie optimaliseert, komt uit onderzoek wel naar voren dat verandering in verwachtingen, evenals verandering in cognities in bredere zin, samenhangt met symptoomverbetering, ook bij PTSS. Dit suggereert dat deze processen relevant zijn voor klachtvermindering. Het blijft nog onduidelijk hoe deze processen kunnen worden beïnvloed om exposure te optimaliseren. Daarnaast zijn dit niet de enige veranderprocessen tijdens exposure die leiden tot klachtenvermindering. Zelfvertrouwen en angstdaling lijken ook voorspellers van klachtvermindering. Therapeuten dienen zich te realiseren dat inhibitoir leren slechts één werkingsmechanisme is, en dat maatwerk per patiënt essentieel blijft.

**Conclusie**

In dit proefschrift is onderzocht of exposuretherapie voor PTSS verbeterd kan worden met inzichten uit het inhibitoir leren. Hoewel op basis van preklinische studies de verwachtingen hoog waren, vonden we geen bewijs dat deze aanpak tot betere resultaten leidt. Veranderingen in cognities en verwachtingen lijken voorspellend aan symptoomvermindering, maar we weten nog niet hoe we dit proces therapeutisch kunnen bevorderen. Het toetsen van verwachtingen over de werking van exposuretherapie is essentieel om de klinische praktijk te blijven verfijnen.

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# Curriculum Vitae

Marike Jolien Kooistra was born on the 6th of January 1994 in Amsterdam. She completed her secondary school education at the Berger Scholengemeenschap (BSG) in Bergen (Noord-Holland) in 2012. Marike obtained her Bachelor's degree in Psychology at Leiden University in 2016 (cum laude), combining it with the Honours Programme of the Faculty of Social and Behavioural Sciences. She obtained her Research Master's degree in Clinical and Health Psychology at Leiden University in 2020 (cum laude), during which she conducted a research internship at the Affect Regulation and Cognition Lab at Yale University and a clinical internship at PsyQ The Hague 'Angststoornissen'.

In January 2020, Marike started as a PhD candidate at the Department of Clinical Psychology, Leiden University, with an affiliation to PsyQ The Hague 'Psychotrauma', under the supervision of dr. Rianne de Kleine, prof. Maartje Schoorl, and prof. Willem van der Does. Her research focused on investigating mechanisms of change in exposure therapy for PTSD and on optimizing its effectiveness. Marike received training from the Dutch-Flemish postgraduate school for Experimental Psychopathology (EPP) and the Graduate School of Social and Behavioral Sciences of Leiden University. As part of her PhD trajectory, she was involved in teaching activities, including supervising Master thesis students and giving lectures in the in Clinical Psychology Master.

Marike currently works at Leiden University, combining research and clinical work at the Leids Universitair Behandel- en Expertise Centrum (LUBEC), where she started her postmaster training (GZ-opleiding) in January 2025.

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