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

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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

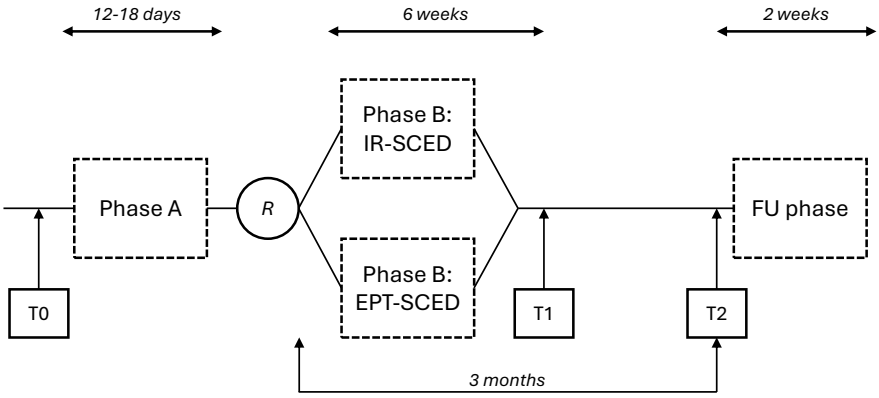
This study follows the Single-Case Reporting Guidelines in Behavioral Interventions (SCRIBE; Tate et al., 2016). This study uses a sequentially randomized replicated single-case AB with follow-up design: a baseline phase (A), intervention phase (B), and a follow-up phase (FU). A randomization list was 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, β_{0j} , reflects the baseline intercept, β_{1j} reflects the slope within the baseline, β_{2j} reflects the immediate effect of the intervention relative to the end point of the baseline, β_{3j} reflects the averaged effect of the follow-up relative to the baseline (intercept), and β_{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

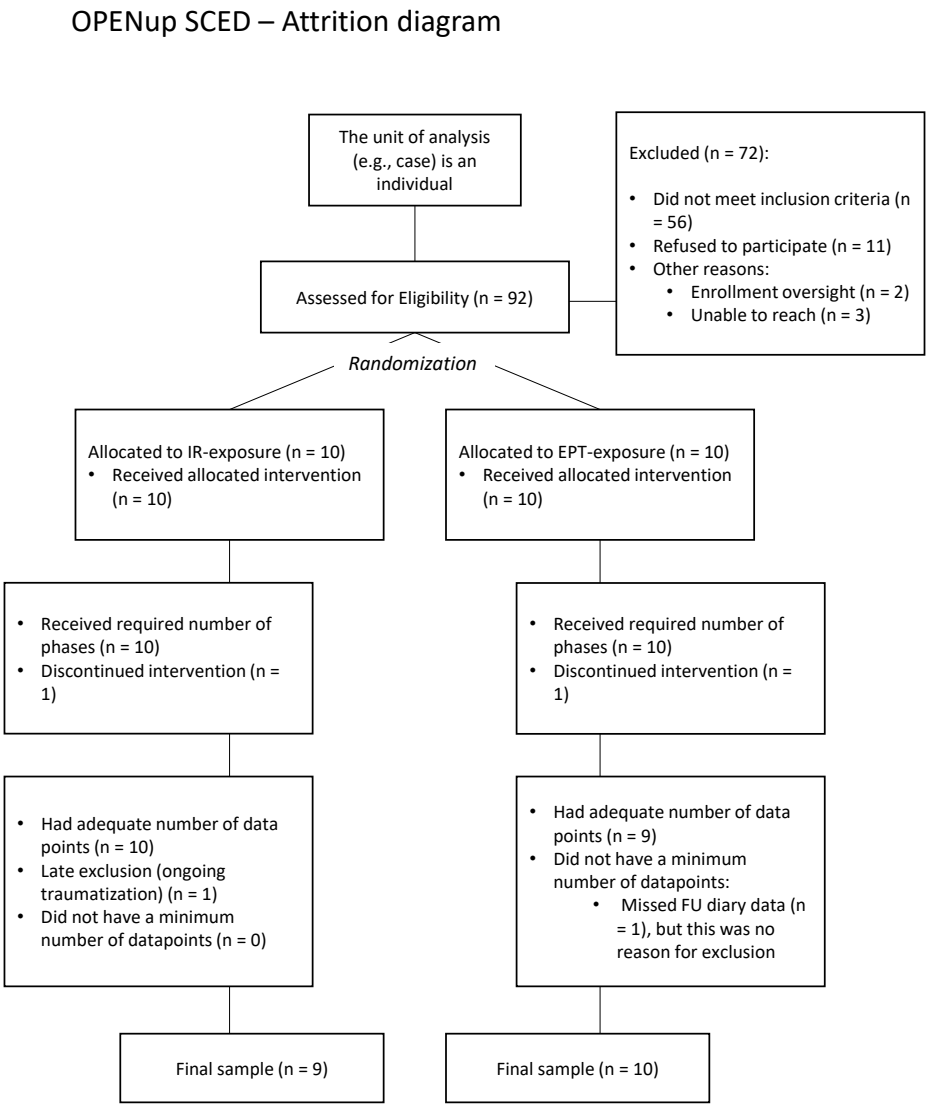


Table 2. Baseline characteristics of participants including their idiosyncratic negative expectancies

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.

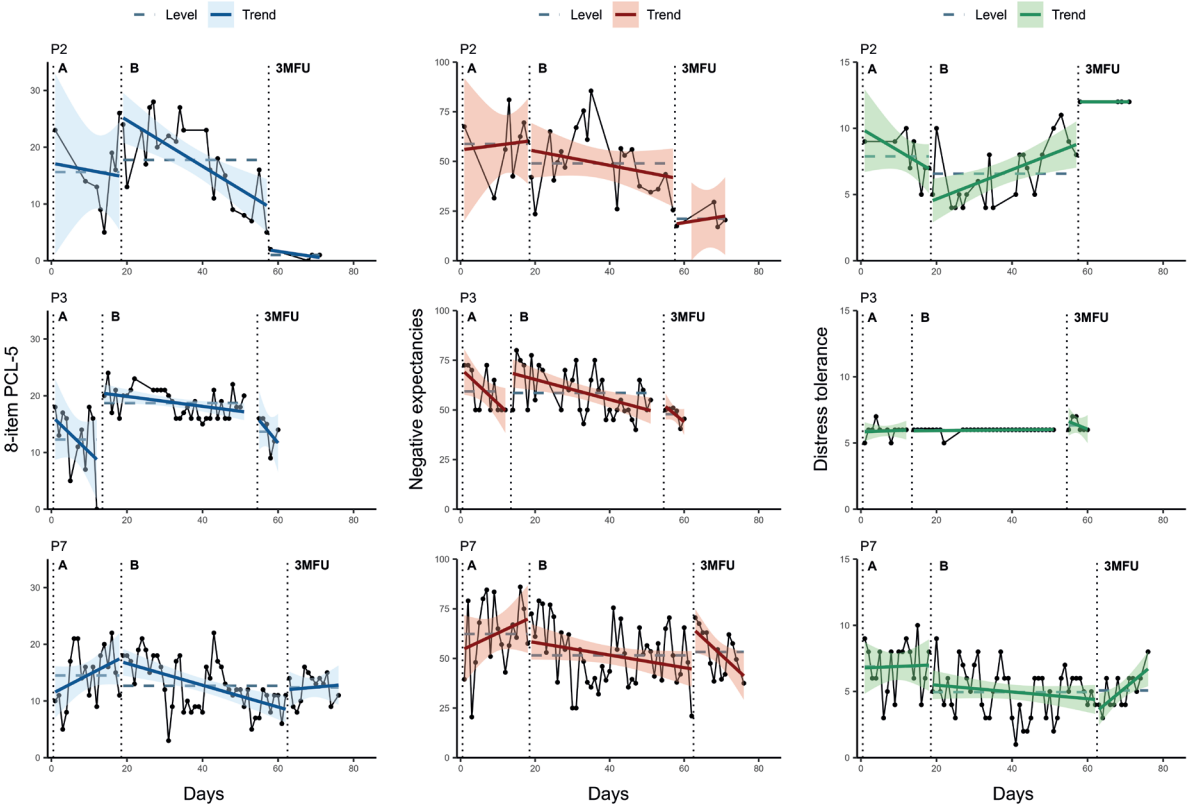
Daily measures

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



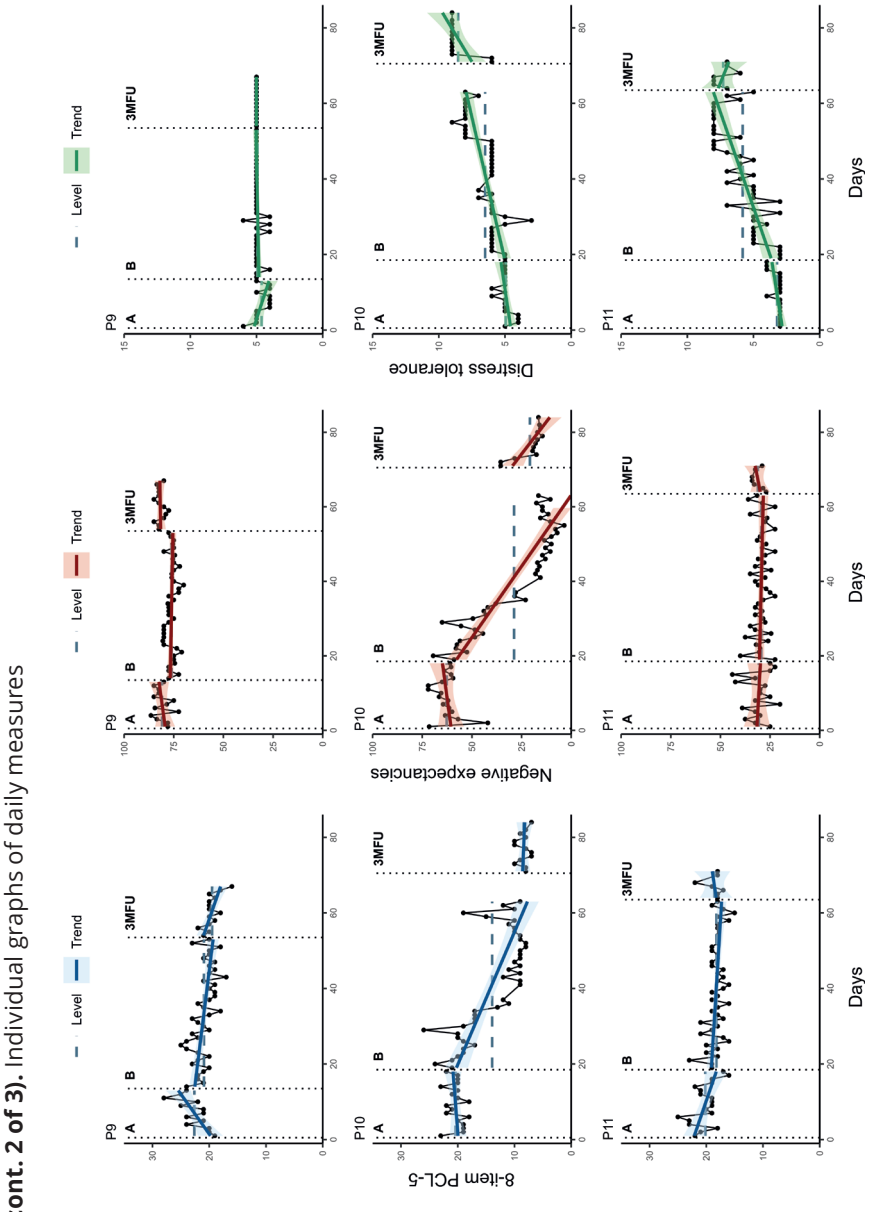


Figure 3 (cont. 2 of 3). Individual graphs of daily measures

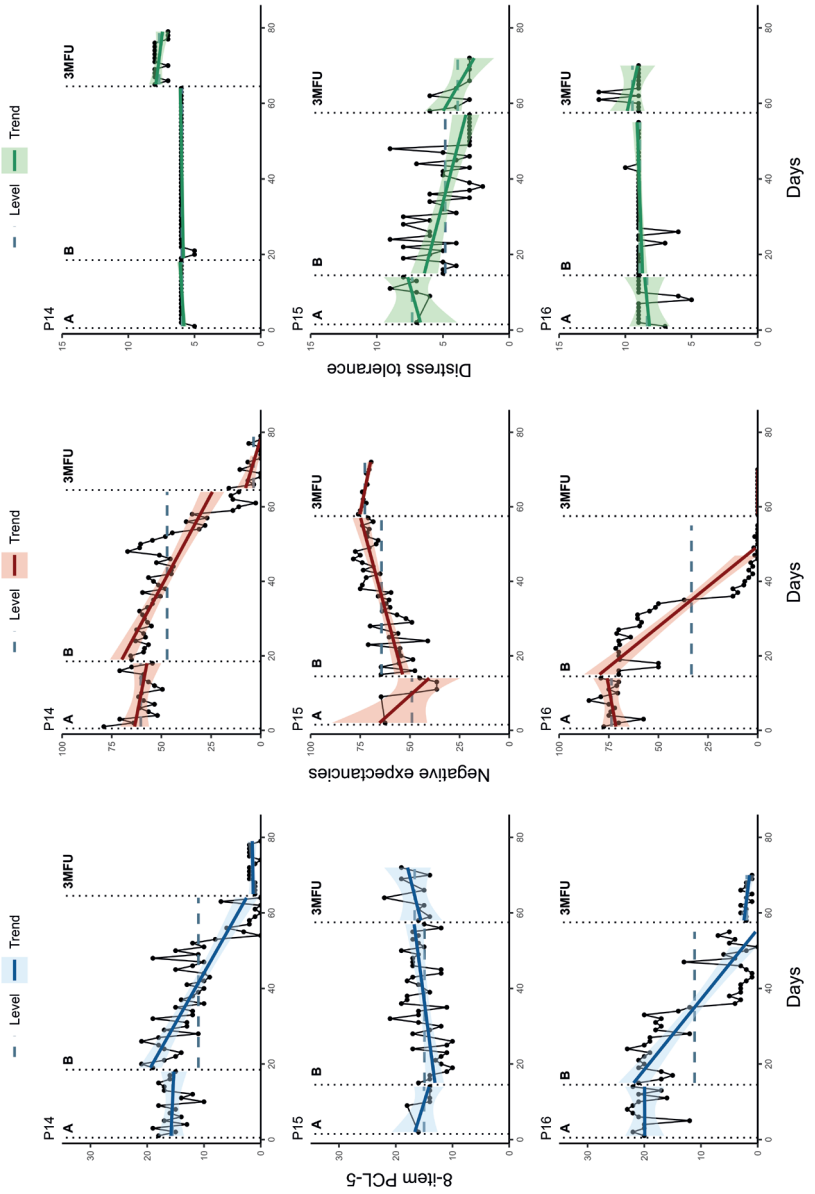


Figure 3 (cont. 3 of 3). Individual graphs of daily measures

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

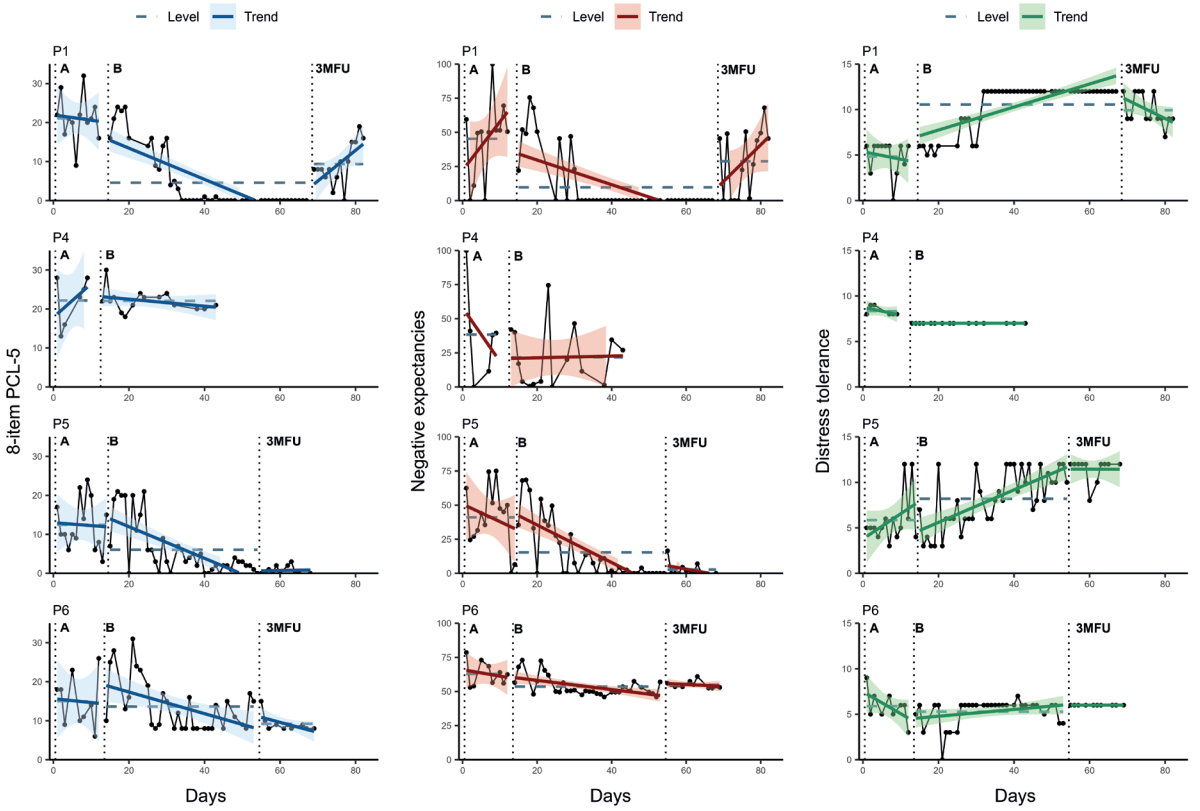
this, suggesting that focusing on distress reduction does not prevent patients from learning to better tolerate distress.

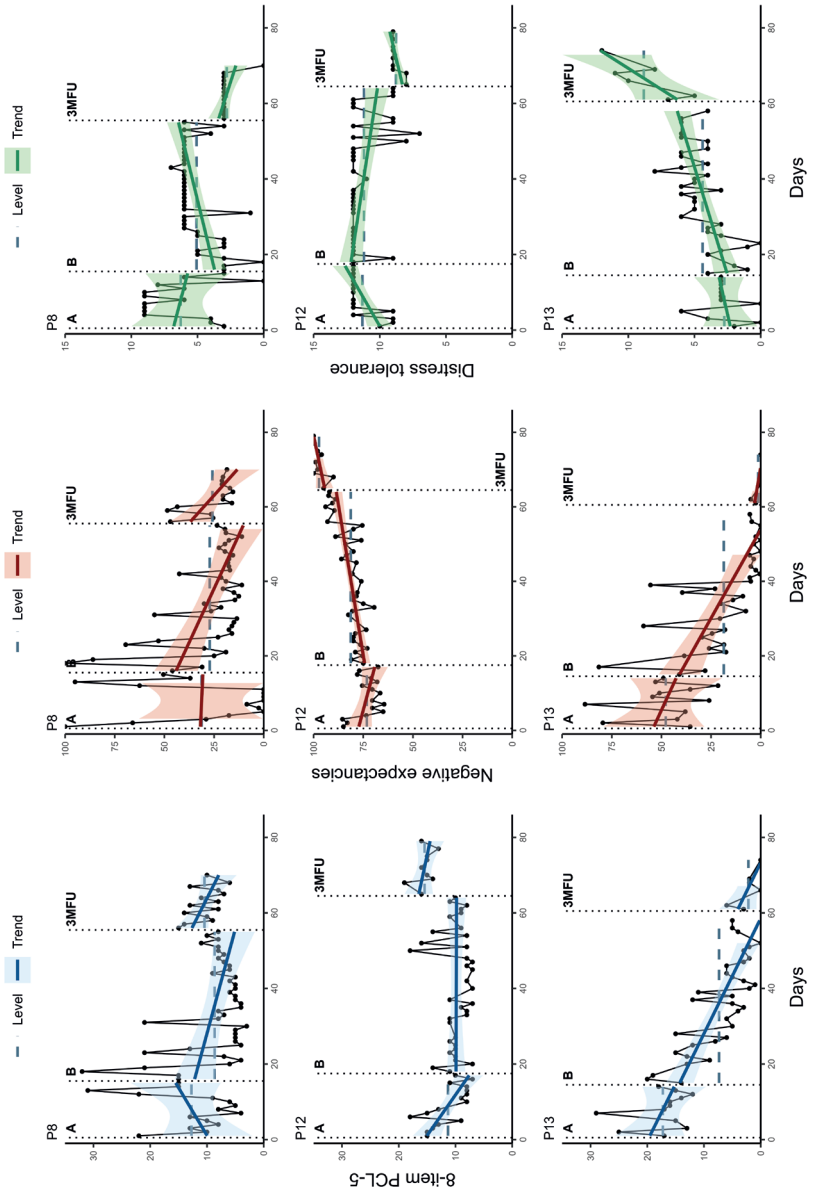
This study has several limitations. This is a single-case design with a limited number of patients, which limits generalizability of the results. Related, with this design we could not compare whether one exposure approach was significantly more effective than the other. Second, we were underpowered 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.

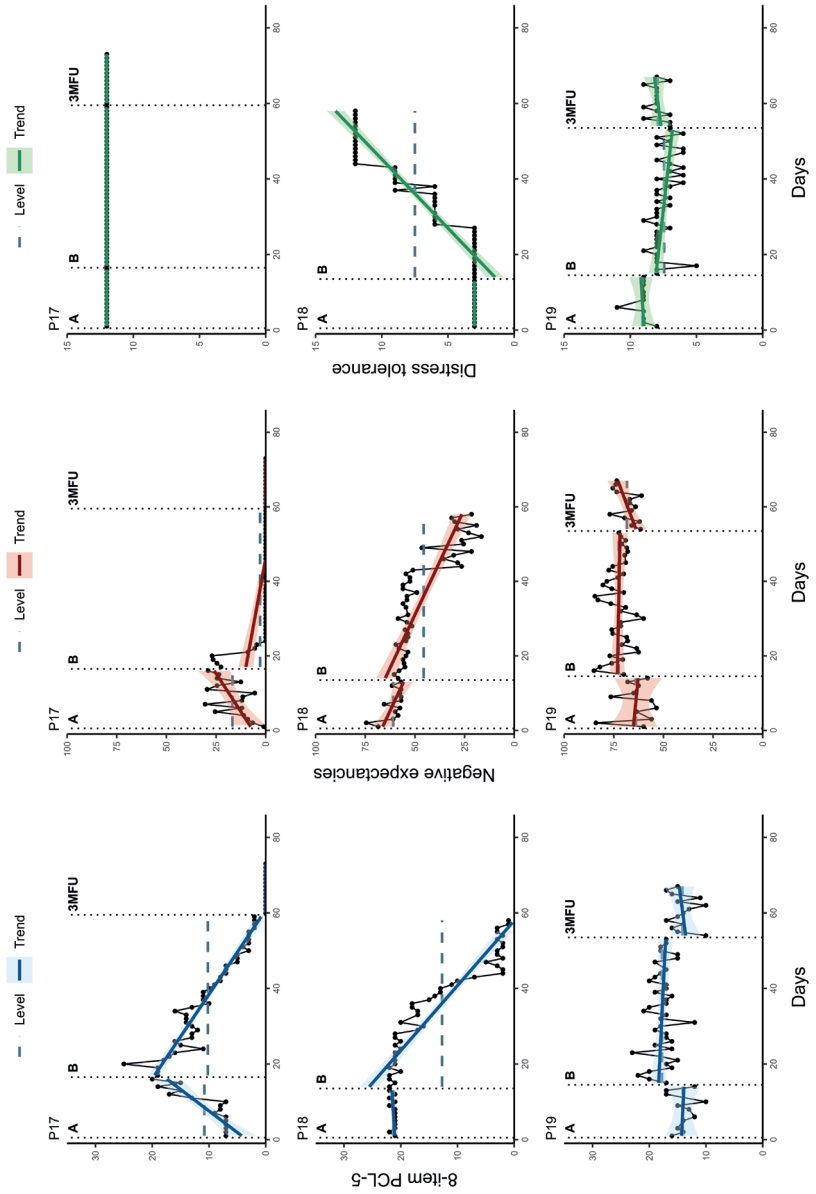
This study offers a proof-of-concept that exposure therapy adapted to IR principles is a feasible and effective intervention for patients with PTSD. Our findings give no indication that it would be more effective than the PE protocol for exposure for PTSD. The value of conducting a large-scale randomized 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