



# Between-session and within-session habituation in Prolonged Exposure Therapy for posttraumatic stress disorder: A hierarchical linear modeling approach



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## ABSTRACT

Prolonged Exposure Therapy is a frontline intervention for posttraumatic stress disorder, but the mechanisms underlying its efficacy are not fully understood. Previous research demonstrates that between- and within-session habituation of fear during exposure is associated with treatment outcome, but these calculations are historically performed with summary statistics such as mean subjective units of distress (SUDS). This question could be better assessed with an analytic technique that uses all SUDS measurements available within sessions. Hierarchical linear modeling was used to investigate the impact of treatment response on SUDS nested within therapy sessions nested within 14 patients. Symptom change ( $t = -2.43$ ,  $p = .03$ ) and responder status ( $t = -2.68$ ,  $p = .02$ ) predicted slope of SUDS across sessions, but did not reliably predict slope of SUDS within-session, indicating that high responders demonstrated differential between- but not within-session habituation. Thus, individuals who show greater habituation between treatment sessions may be more likely to respond to treatment.

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## 1. Introduction

Prolonged Exposure is a frontline intervention for posttraumatic stress disorder (PTSD) with substantial evidence supporting its efficacy for a variety of patient populations (Powers, Halpern, Ferenschak, Gillihan, & Foa, 2010; Rauch et al., 2009; Schnurr et al., 2007; Tuerk et al., 2011). The factors associated with treatment efficacy are of considerable interest and debate (e.g. Bluett, Zoellner, & Feeny, 2014). Previous research demonstrates that habituation<sup>1</sup> of fear is a key process in exposure and is associated with PE treatment outcome. In particular, previous findings have demonstrated that between-session habituation, or a decrease in patient-reported subjective units of distress (SUDS) between sessions, is an important contributor to symptom reduction. In several PE studies, greater reductions in mean and peak SUDS between the first and

last imaginal exposure session of PE were associated with greater PTSD symptom reduction (Bluett et al., 2014; Gallagher & Resick, 2012; Rauch, Foa, Furr, & Filip, 2004). Greater habituation between imaginal sessions one and two has also been shown to be a marker of treatment response (van Minnen & Hageraars, 2002). Another study demonstrated that between-session habituation was associated with reduced PTSD symptoms both at treatment endpoint and at one-month follow-up (van Minnen & Foa, 2006). Additionally, a hierarchical clustering analysis revealed that the best treatment outcomes were associated with “high engagers/habitators” – individuals who showed high SUDS during the first imaginal exposure session and gradually declining SUDS over the course of the next six sessions (Jaycox, Foa, & Morral, 1998). Outcomes in this group were superior to the outcomes of the two other classes of response: high engagers/non-habitators and low engagers/non-habitators. These studies provide promising preliminary evidence that differences in SUDS between sessions are associated with positive treatment response. However, several studies of individuals with PTSD (Bluett et al., 2014; Pitman, Orr Altman, Longpre, Poiré, et al., 1996; Pitman, Orr Altman, Longpre, Poire, et al., 1996), and other disorders (Kozak, Foa, & Steketee, 1988; Lang & Craske, 2000; Meuret, Seidel, Rosenfield, Hofmann, & Rosenfield, 2012; Rowe & Craske, 1998; Tsao & Craske, 2000) demonstrate positive treatment

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<sup>1</sup> We use the term habituation in this paper to indicate anxiety reduction during exposure, while recognizing that both extinction and habituation processes are active during exposure therapy.

outcomes in the absence of between-session habituation. Thus, further research is needed to determine the relationship between treatment response and between-session habituation.

Another habituation pattern that may be a beneficial component of PE is within-session habituation, or decline in SUDS over the course of an individual session. One PE study demonstrated that treatment responders showed greater within-session habituation than non-responders while listening to imaginal exposure at home, though not during the therapy session itself (van Minnen & Hagenaars, 2002). Another study found that amongst 106 individuals with various anxiety disorders, greater within-session habituation during the first exposure session was associated with lower risk for treatment dropout (Norton, Hayes-Skelton, & Klencz, 2011). Similarly, during the third exposure session, greater within-session habituation was associated with lower anxiety symptomatology at therapy endpoint (Norton et al., 2011). Thus, there is some evidence to suggest that a pattern of decreasing anxiety during a session of exposure is predictive of good treatment outcome. However, several studies show no evidence for the necessity of within-session habituation (Baker et al., 2010; Bluett et al., 2014; Culver, Stoyanova, & Craske, 2012; Jaycox et al., 1998; Kozak et al., 1988; Meuret et al., 2012; Pitman, Orr Altman, Longpre, Poiré, et al., 1996; Pitman, Orr Altman, Longpre, Poiré, et al., 1996; Riley et al., 1995; van Minnen & Foa, 2006; van Minnen & Hagenaars, 2002). Thus, there is mixed support for the association between within-session habituation and positive treatment response.

In addition to habituation, several other markers of PE efficacy have been proposed. A recent investigation demonstrated that the perceived helpfulness of imaginal exposure homework had an indirect effect on the relationship between distress reduction and clinical outcome such that individuals with modest reductions in peak distress still experienced clinical improvement if they perceived homework to be helpful (Bluett et al., 2014). Reduced negative cognitions about the world and the self may also mediate treatment response (Foa & Rauch, 2004). Finally, distress tolerance has recently emerged as an important potential mechanism of change in exposure therapy (Craske et al., 2008; Meuret et al., 2012). Fostering distress tolerance during exposure promotes the acquisition of inhibitory learning that weakens or negates the original conditioned stimulus-unconditioned stimulus expectancies (see Myers & Davis, 2002). While all these factors may contribute to successful treatment response, habituation remains the most consistent theoretical construct related to response in exposure therapy.

Though several theories have been proposed, the question of what predicts success in PE could be better assessed by using analytic techniques that capitalize on the wealth of data that is available from standard PE treatment. During imaginal exposure in the standard PE protocol, SUDS is collected every five minutes. Given such a large number of data points, past studies (Bluett et al., 2014; Jaycox et al., 1998; Rauch et al., 2004; van Minnen & Hagenaars, 2002) have used peak SUDS, mean SUDS, or another summary measure to estimate habituation, but no study to date has used the full extent of available data to model all of the variability in SUDS during imaginal exposure. The current analyses utilized all the SUDS data available in PE sessions from a small mechanistic study of PE to examine habituation both within and between sessions. Hierarchical linear modeling (HLM) is a multilevel modeling technique that accounts for the inherent nested nature of data generated by treatment studies. Unlike repeated measures ANOVA, HLM allows for different numbers of sessions between patients. In the current study, we modeled SUDS data points (level-one) nested within session (level-two), nested within patient (level-three). We then tested the effects of symptom change and treatment responder status at each level. We hypothesized that high responders

would show greater reduction in SUDS than low responders both within session and between sessions.

## 2. Material and methods

### 2.1. Sample and treatment setting

The following analyses were conducted as a post-hoc examination of data collected in a translational treatment mechanisms study. For a full description of study procedures and the sample, see (Rauch et al., in press). All Veterans participated in the treatment study between January 2008 and July 2010 ( $N = 14$ ; 9% Female, 23% African American, 73% White, 5% Asian). Mean age was 32.7 years ( $SD = 6.9$ ). With regard to combat location, 81% served in Iraq and 33% served in Afghanistan, with some Veterans reporting deployments to both locations. As reported in the primary outcome paper, comorbidity was representative of the OEF/OIF/OND population: 57% had depression or dysthymia, 10% had alcohol abuse, and 29% met criteria for another anxiety disorder at intake. All treatment was conducted by an experienced PE provider (author SAMR) with over 15 years of experience using the protocol. To enhance generalizability, exclusion criteria were minimized and included only contraindications for PTSD treatment and factors that would interfere with the biological mechanisms investigated in the parent study. Exclusion criteria were: (1) level of self-harm risk that requires immediate, focused intervention, (2) unmanaged psychosis or bipolar disorder, (3) alcohol or substance dependence in the past 3 months, (4) working night-shifts, (5) changes to psychoactive medications in the past 4 weeks, or (6) taking medication that makes hypothalamic-pituitary-adrenal axis measures difficult to interpret. Eligible Veterans reviewed consent with author SAMR. Those who were interested signed consent and were randomly assigned to receive 10–12, 80-min sessions of PE or Present Centered therapy, an active control condition. Data were collected with approval from the Institutional Review Board (IRB) for the VA Ann Arbor Healthcare System.

### 2.2. Measures

*Clinician Administered PTSD Scale (CAPS; Blake, Weathers, Nagy, & Kaloupek, 1995).* The CAPS is an interview measure of PTSD severity with excellent psychometric properties (Blake et al., 1995). Cronbach's alpha for this sample was .95. We used a stringent classification of responders, such that patients were characterized as high responders only if they experienced a 50% or greater reduction in CAPS over the course of therapy. CAPS was administered at pre-, mid-, and post-treatment. All treatment completers presented for the post-assessment, with the exception of early terminators, who were assessed only at pre- and mid-treatment. Early terminators were assessed via the last-visit carried forward technique.

*Subjective Units of Distress (SUDS)* are self-ratings of distress ranging from 0 (complete relaxation) to 100 (maximum distress) (Wolpe & Lazarus, 1966). SUDS were collected every 5 min during the imaginal exposure portion of the session. Imaginal exposure began at session three and occurred at every session thereafter, with the exception of sessions that included therapist-assisted in vivo exposure. Within-session habituation was operationalized as a drop in SUDS over the course of a session, and between-session habituation was operationalized as a drop in SUDS across sessions.

### 2.3. Intervention

Each patient underwent at least two and up to ten imaginal exposure sessions, and each imaginal exposure session assessed SUDS between two and ten times. Treatment completers were defined as any patient attending at least seven sessions of PE and at

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