Attenuating Fearful Memories Through Modulation of Learning: Effects of Modified Consolidation and Cued Extinction on Intrusions

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A thesis

submitted in partial fulfillment of the

requirements for the degree of

Master of Science

University of Washington

2013

Committee:

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Program Authorized to Offer Degree:

Psychology

University of Washington

Abstract

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Exposure-based therapies for PTSD are thought to reduce intrusive memories through extinction processes. Methods that enhance extinction may translate to improved treatment. Rat research suggests cueing a memory with a conditioned stimulus (CS) cue and then modifying the retrieved memory within a specific reconsolidation window, enhances extinction. In humans, two studies (Schiller et al., 2010; Kindt & Soeter, 2013) using basic learning paradigms show discrepant findings. Using a distressing film paradigm, participants (N = 148) completed fear acquisition and extinction. At extinction, they were randomized to: CS cue within reconsolidation window; CS cue outside window, or non-CS cue within window. Intrusions were assessed 24 hr after extinction. Participants receiving the CS cue and completing extinction within the reconsolidation window had more intrusions (M = 2.40, SD = 2.54) than those cued outside (M = 1.65, SD = 1.70) or those receiving a non-CS cue (M = 1.24, SD = 1.26), $F(2,145)$ = 4.52, p = .01, d = 0.55. Consistent with the reconsolidation hypothesis, presenting a CS cue does appear to activate a specific period of time during which a memory can be updated. However, the CS cue caused increased rather than decreased frequency of intrusions. Understanding parameters of pre-extinction cueing may help us better understand reconsolidation as a potential memory updating mechanism.

Following a trauma experience, individuals often experience intrusive memories of the event (APA, 1994). Such memories include vivid thoughts and images of the event and are often categorized as either image-based or conceptual. Image-based intrusions are sensory-perceptual impressions of the trauma, while conceptual intrusions are more analytical, organized thoughts related to the event (e.g., Brewin, Gregory, Lipton, & Burgess, 2010). Intrusions can be cued by some type of trauma-related cue in the environment or can arise unexpectedly in situations completely unrelated to the trauma. These emotional memories typically diminish over time. However, in individuals who develop posttraumatic stress disorder (PTSD), such distressing memories from the traumatic experience persist and are considered one of the hallmark symptoms of the disorder, associated with significant distress and functional impairment (APA, 1994; Hackmann, Ehlers, Speckens, & Clark, 2004).

Exposure-based therapies aim to decrease the fear associated with the traumatic event using extinction-like processes (e.g., Foa & Rothbaum, 1998). Exposure therapy is an effective treatment for many anxiety disorders, and is one of the most empirically supported interventions for chronic adult PTSD (Foa, Keane, Friedman, & Cohen, 2009). Through exposure therapies, patients learn to approach previously avoided thoughts, feelings, and situations associated with the trauma. Gradually, patients learn that such internal states and external cues are safe, and fear responses to trauma-related memories and reminders diminish. Similarly, in fear extinction training, a conditioned stimulus (CS) previously associated with a fear-eliciting stimulus (US) is presented repeatedly. Through repeated trials, it is learned that the CS is safe, and fear associated with the CS decreases (e.g., Davis, 1986). Thus, if we are able to improve our understanding of mechanisms underlying fear extinction, we may enhance exposure-based treatments for psychological disorders. Extinction is a form of new learning, as novel

information is added to previously learned information (Bouton & Bolles, 1979). As part of this process, it is thought that extinction may involve memory-updating mechanisms. One potential updating mechanism that has received attention over the past decade is the reconsolidation process. The reconsolidation hypothesis states that, upon retrieval through an environmental cue, a consolidated memory becomes labile and available for update (e.g., Sara, 2000; Nader, Schafe, & LeDoux, 2000; Eisenberg, Kobilo, Berman, & Dudai, 2003; Duvarci & Nader, 2004). It is thought that there exists a specific window of time, known as the reconsolidation window, during which the memory is labile (thought to last for about six hours post-retrieval (Duvarci & Nader, 2004; Walker, Brakefield, Hobson, & Stickgold, 2003). In order for the window to be effectively opened via memory retrieval, it is also thought that the retrieval cue must terminate (Holmes, James, Coode-Bate, & Deeprose, 2009; Pedreira, Perez-Cuesta, & Maldonado, 2004). Reconsolidation is posited to be a protein synthesis-dependent process, wherein specific molecular changes must occur in the lateral and basal amygdala in order for the retrieved memory to be restored to long-term memory (e.g., Nader et al., 2000). If new information is added to the retrieved memory within the reconsolidation window, the updated memory is likely then stabilized as a long-term memory.

Evidence for the lability of retrieved fear memories comes from a body of animal research using pharmacological agents to induce post-retrieval interruptions in rats. Protein synthesis inhibitors such as anisomycin and beta blockers such as propranolol appear to block the reconsolidation of retrieved fear memories in rats after the presentation of an isolated memory retrieval cue, but not when administered six hours post-retrieval (e.g., Nader et al., 2000; Schafe & LeDoux, 2000; Debiec & LeDoux, 2004; Milekic & Alberini, 2002). Findings from these studies suggest that pharmacological disruption of reconsolidation can produce amnestic effects

by acting on specific, time-sensitive molecular mechanisms and preventing the retrieved memories from being updated and restored to long-term memory. Given the toxic effects of anisomycin and other protein synthesis-inhibitors in humans, recent research has shifted to examine fear extinction as a behavioral alternative to pharmacological disruption of memory updating (Monfils, Cowansage, Klann, & LeDoux, 2009). When fear extinction took place after an isolated CS cue presentation (i.e., within the reconsolidation window) rats showed an enhanced effect of extinction compared to rats not cued with an isolated CS and rats cued after extinction was completed. These findings suggest that there is indeed a period of time post-retrieval during which fear memories are particularly malleable and available for update.

Only two studies to date have examined the effects of within-window extinction on reconsolidation in humans, paralleling Monfils et al.'s (2009) study design. Schiller et al. (2010) used a classical fear-conditioning paradigm with two colored squares as conditioned stimuli and shock as the US. To investigate the effects of a CS cue presentation on fear extinction, Schiller et al. compared a CS cue presented 10 minutes prior to extinction (i.e., within-window extinction) with a CS cue presented 6 hours prior to extinction (i.e., out-of-window extinction) and extinction with no CS cue presentation. Consistent with the animal literature, fear extinction completed after a CS cue and within the reconsolidation window enhanced extinction outcomes, as evidenced by decreased return of fear compared to those undergoing extinction outside of the reconsolidation window and those undergoing extinction without a CS cue. At one year follow-up, these gains were maintained, with participants in the cued extinction condition slower to reinstate fear. Kindt and Soeter (2013) used more fear-relevant stimuli (e.g., photos of spiders) as their CS cues and shock as the US in a fear-conditioning paradigm similar to that of Schiller et al. (2010). No significant differences were found in the return of fear between participants

undergoing extinction 10 minutes after CS cue presentation and participants undergoing extinction with no CS cue presentation. Contrary to Monfils et al. (2009) and Schiller et al. (2010), these findings suggest that an isolated cue followed by within-window extinction does not attenuate fear memories. In addition to the different stimuli used in the two studies, other methodological differences may explain the discrepant findings.

Animal research examining fear extinction and memory reconsolidation, as well as Schiller et al. (2010) and Kindt and Soeter (2013) have examined the return of fear using physiological measures (e.g., skin conductance). Given that reconsolidation may be a memory updating mechanism that could be applied to PTSD treatments, an important next step in better understanding the reconsolidation hypothesis in humans is to examine the return of fear using more real-world stimuli. The use of more real-world stimuli allows for a more complex measure of fear, namely, intrusive memories. Just as fear extinction depends on conditioning processes (e.g., Bouton, 1984; Bouton & Peck, 1989), the way in which individuals process a traumatic event can predict the presence of intrusive memories post-trauma (e.g., Ehlers & Clark, 2000). More specifically, it has been suggested that there exist two distinct types of processing that occur during memory encoding: data-driven processing and conceptual processing (Roediger, 1990). Data-driven processing focuses predominantly on the sensory-perceptual components of a traumatic event, and encoding occurs in a disorganized manner without contextual or chronological meaning. Conceptual processing focuses primarily on putting the event into meaningful context, and encoding of the event occurs in a chronological, organized manner (Ehlers & Clark, 2000). Consistent with this theory, predominant theories of PTSD cite a lack of conceptual trauma processing as a key contributor to the development of chronic PTSD (e.g., Foa, Steketee, & Rothbaum, 1989; Brewin, Dalgleish, & Joseph, 1996; Ehlers & Clark, 2000).

Importantly, the ability to engage in conceptual processing during a distressing event may be inhibited by high levels of negative emotions (e.g., fear) experienced during the event (Ozer, Best, Lipsey, & Weiss, 2003). In a prospective study after trauma exposure, Halligan, Clark, and Ehlers (2002) found that higher data-driven processing was associated with higher re-experiencing symptoms 1 week later. Given the proposed relationship between processing of a distressing event and the development of intrusions, combined with the need to better understand reconsolidation using real-world stimuli, it is important to consider the role of processing variables in the return of fear.

To our knowledge, our study is the first to examine intrusions as related to the reconsolidation hypothesis. Given the lack of research and mixed findings regarding the return of fear in humans, the present study examined the effects of retrieval cue presentation followed by fear extinction on later memory intrusions. We sought to increase the ecological validity by using a distressing film paradigm within a fear conditioning design in order to mirror a traumatic event and exposure therapy for PTSD. We showed a distressing film segment as fear acquisition while monitoring distress levels, and assessed frequency and intensity of intrusions 24 hours later. For fear extinction, we showed a longer version of the acquisition segment, designed to parallel exposure therapy. To examine the effects of a CS cue on extinction, we had three cue conditions: Pre CS, with a CS cue presented 10 minutes prior to fear extinction, Delayed CS, with a CS cue presented 10 minutes after fear extinction, and Scrambled CS, a non-retrieval cue presented 10 minutes prior to fear extinction. We were most interested in frequency and intensity of intrusions assessed 24 hours after fear extinction. We hypothesized that participants presented with a retrieval cue followed by extinction within the reconsolidation window would experience fewer and less distressing intrusions after extinction compared to those who

completed extinction prior to cue presentation and those presented with a non-retrieval cue prior to extinction. We also hypothesized that higher baseline psychopathology, particularly anxiety and traumatic stress-related psychopathology, would predict more frequent and distressing intrusions after extinction, and that more intense negative emotions and data-driven processing during acquisition would predict more frequent and distressing intrusions following extinction.

Method

Participants

Two hundred-sixteen undergraduate psychology students at a large, metropolitan university participated in this study. Participants enrolled in introductory-level psychology classes accessed a psychology subject pool website to read the study description, view participant inclusion/exclusion criteria, and sign up for time slots if interested. Eligible participants were between the ages of 18 and 65 years old and fluent in English.

Of the 216 participants who consented, 163 participants completed all phases of study. Forty participants failed to attend the final session of procedures, including two participants who discontinued after the first session due to distress, and an additional 13 who failed to complete the final assessment. Fifteen additional participants failed to adhere to study procedures (e.g., fell asleep, on telephone, etc.) and were excluded from the analysis, resulting in 148 participants for data analysis (N = 148). Those who failed to attend the final session did not significantly differ from those who completed all phases of the study on any measures of baseline psychopathology. See Table 1 for participant demographics.

Materials

Distressing film paradigm. A 10-min segment from *The Last King of Scotland* (Steel,

Bryer, Calderwood, & MacDonald, 2006) was used for both acquisition and extinction phases. The segment includes graphic images of mutilation and death and was piloted to ensure its effectiveness in eliciting intrusions. The film was projected (6’ x 6’) onto a white wall.

The film segment was shown one time during fear acquisition. During the extinction phase, the 10-min segment was shown in its entirety, then a 6-min segment, and then a 3-min segment repeated five times, mirroring exposure therapies for PTSD (i.e., recounting of the trauma memory and then shifting to the most distressing part of the memory in subsequent recountings) (e.g., Keane, Marshall, & Taft, 2006; Foa, Hembree, & Dancu, 2002). The total extinction segment lasted 30 min.

CS cuing stimuli. The conditioned stimulus (CS) was a 6' x 6' image of a mutilated woman taken directly from the film segment, projected onto the same white wall used for film presentation. Based on piloting procedures, this image was determined to appropriately cue the film’s key thematic content. The image was used as a cue during the extinction phase for Pre CS and Delayed CS conditions. For the Scrambled CS condition, a pixilated version of the CS image was used. This scrambled CS image controlled for the effects of viewing an image prior to extinction, matching hue, saturation, brightness, and gloss.

Computer task. A visual-spatial game, Tetris, was used as a stimulus offset technique following activation of film-related memories via CS cue. Tetris is a video game in which players manipulate falling shapes in order to form horizontal lines. Tetris has been shown to actively compete with cognitive resources associated with intrusive images (Holmes et al., 2009). The ability of Tetris to stop film-related thoughts and images was assessed via a single question: “Using the scale below, how effective was the computer game task in distracting you from your

thoughts related to the film previously viewed?" Responses were rated on a 9-point scale from 0 (*not at all effective or no film-related thoughts*) to 8 (*extremely effective*).

Intrusions. Intrusions, defined as unwanted distressing thoughts or images related to the film, were assessed via telephone assessment. Although previous studies used intrusion diary assessment procedures (e.g., Holmes et al., 2004), recording in a diary can serve as a memory cue, potentially altering the experience of future intrusions. Clear and concise definitions of imagery-based (intense, vivid snapshot-like) and cognitive-based (narrative, chronological) intrusions preceded assessment items (Bernstein, 2009). Frequency of intrusions was assessed separately for each of the two intrusion types for the preceding 24 hr. To obtain intensity ratings, memory distress was rated on a scale from 0 (*not at all distressing*) to 8 (*extremely distressing*). For instances when more than one memory was reported, intensity ratings for the most distressing memory were recorded. A description of the content of each intrusion was also included in the assessment. The intrusions assessment was scored by summing the total number of intrusions, with subscores for total number of imagery-based and total number of cognitive-based intrusions. Maximum distress was calculated as the highest distress rating across all intrusions reported.

Fear renewal task. Fear renewal was assessed using a 25-s audio clip taken from the acquisition segment in order to test the return of fear 24 hr after extinction. The audio clip consisted of footsteps and a woman screaming (an uninterrupted excerpt from the film), and was intended to serve as a clear reminder of the film's content. Participants were instructed to close their eyes and focus on the sounds being played. The number of intrusions, if any, they experienced during or immediately after the clip was assessed via an abbreviated intrusion

assessment. State emotions were assessed via the Post-Film Questionnaire (PFQ; Rottenberg, Ray, & Gross, 2007), described below.

Measures

Demographics questionnaire. This brief questionnaire includes basic questions about participant sex, age, race, and education level.

Posttraumatic Diagnostic Scale (PDS; Foa, Cashman, Jaycox, & Perry, 1997). The PDS is a 49-item self-report measure used to assess prior trauma exposure and subsequent PTSD symptoms. The PDS includes a checklist of 12 traumatic experiences, followed by 4 yes-no questions regarding physical injury and emotions the individual felt during the experience (e.g., helpless) to assess DSM-IV Criterion A status. The next 17 questions correspond to DSM-IV PTSD symptoms and were rated on a scale from 0 (*not at all or only one time*) to 3 (*5 or more times/week or almost always*). Nine additional yes-no questions assess functional impairment as a result of the trauma. Symptom severity scores are calculated by totaling the 17 symptom frequency items, with higher scores indicating more severe symptoms. PDS severity scores are correlated with the Beck Depression Inventory (r = .79, Foa et al., 1997) and State-Trait Anxiety Inventory—State version (r = .73, Foa et al., 1997) and State-Trait Anxiety Inventory—Trait version (r = .74, Foa et al., 1997). The scale also demonstrates good internal consistency (α = .92) and diagnostic test-retest reliability of .87 (Foa et al., 1997).

State-Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983). The STAI is a 40-item self-report measure assessing domains of both current and trait anxiety. Items are statements about current feelings related to self, contentedness, and anxious thoughts, (e.g., “I feel frightened,” “I feel worried”). The STAI-T allows for the assessment of baseline anxiety prior to beginning study procedures (i.e., “how you generally

feel.") Items are statements about typical feelings related to those same domains (e.g., "I feel like a failure," "I am a steady person.") All items are rated on a 4-point scale from 1 (*not at all*) to 4 (*very much so*). State and trait scales are independently scored by summing the 20 associated items, with higher totals indicating more anxiety. The STAI-T has demonstrated good convergent validity, positively correlating with other measures of trait anxiety (r = .52 - .80, Spielberger et al., 1983). The STAI-T also demonstrates good test-retest reliability (r = .73 - .86, Spielberger et al., 1983).

Anxiety Sensitivity Questionnaire- Revised (ASI-R; Peterson & Reiss, 1992). The ASI is a 36-item self-report measure fear of anxiety-related symptoms. Items on the ASI-R are statements such as, "It scares me when I feel faint," and responses are answered on a Likert scale from 0 (*very little*) to 4 (*very much*). Total ASI-R scores are calculated by summing responses to all 36 items, with higher scores indicating heightened anxiety sensitivity. The ASI-R shows satisfactory convergent validity with the Beck Anxiety Inventory (r = .60) and the Beck Depression Inventory (r = .53) and demonstrates good internal consistency (α = .95; Taylor & Cox, 1998).

Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996). The BDI is a 21-item self-report measure of the presence and severity of depressive symptoms. BDI-II questions address various domains of depression such as mood, self-perception, interest, motivation, suicidality, appetite, and sleep. Responses are answered on a 0 to 3 scale, with each item addressing a specific domain (e.g., 0 = "I do not feel sad," and 3 = "I am so sad or unhappy that I can't stand it"). BDI-II scores are calculated by totaling responses to all 21 items, with higher scores indicative of more severe depression. The BDI-II has high levels of internal consistency (α = .91, Beck et al., 1996) and demonstrates good convergent validity with the

Hamilton Psychiatric Rating Scale for Depression (r = .71, Beck et al., 1996) and the Beck Anxiety Inventory (r = .66, Beck et al., 1996).

Emotion Regulation Questionnaire (ERQ; Gross & John, 2003). The ERQ is a 10-item self-report measure of two distinct styles of emotional regulation: cognitive reappraisal (e.g., "When I want to feel more positive emotion, I change the way I'm thinking about the situation;" 6 items) and expressive suppression (e.g., "I keep my emotions to myself;" 4 items). Responses to each of the ten statements are rated on a scale from 1 (*strongly disagree*) to 7 (*strongly agree*). Scoring is calculated for each subscale by computing the mean item score for each subscale; the reappraisal and suppression subscales measure independent constructs (r = -0.01) and thus a total score is not meaningful. Both scales demonstrate good internal consistency (reappraisal α = .79; suppression α = .73, Gross & John, 2003). Reappraisal correlates with positive emotion experiences while suppression correlates with negative emotion experiences on the Positive and Negative Affect Scale (r = .42 and r = .39 respectively, Gross & John, 2003).

Subjective Units of Distress (SUDs; Wolpe, 1969). This 0 to 100 scale is used to measure state subjective discomfort, with 0 representing a completely calm and relaxed state, and 100 representing the most distress ever felt or imagined. Peak SUDs was defined as the highest SUDs rating reported during the film paradigm. SUDs ratings are correlated with measures of physiological arousal (heart rate, r = .39; peripheral vasoconstriction, r = .84; Thyer, Papsdorf, Davis, & Vallecorsa, 1984).

Post-Film Questionnaire (Rottenberg, Ray, & Gross, 2007). The PFQ is a brief questionnaire used in conjunction with film paradigms that are designed to elicit emotion, in order to measure the intensity and range of emotions experienced during viewing. Given previous associations between peritraumatic negative emotional experiences and later

symptomatology (e.g., Bernat, Ronfeldt, Calhoun, & Arias, 1998), this measure allows for assessing emotional reactions immediately following film viewing. The intensity of emotions experienced during film viewing is rated on a scale from 0 (*not at all/none*) to 8 (*extremely/a great deal*). Each item is considered individually (Rottenberg et al., 2007). Though the PFQ assesses 18 different emotions, for this study, we examined a priori anxiety, disgust, and fear. In the present study, each item demonstrated good test-retest reliability, despite differing versions of the film segment (anxiety r = .46; disgust, r = .59; fear, r = .59).

Thoughts and Feelings Questionnaire (TFQ; Halligan, Clark, & Ehlers, 2002). The TFQ is a 14-item questionnaire used to assess perceptual, data-driven processing and conceptual processing of emotionally evocative stimuli. TFQ items are assessed via a 0 (*not at all*) to 4 (*very strongly*) scale. The TFQ subscales of data-driven and conceptual processing are scored separately by summing responses associated with the subscale. The data-driven processing subscale demonstrates good internal consistency (α = .70, Ehlers, 1998). In the present sample, the conceptual processing subscale demonstrated adequate internal consistency (α = .70) while the data-driven subscale demonstrated good internal consistency (α = .88).

Study Design

The overall study design is a mixed design, with a between-subjects factor of cue condition (3: Pre CS, Delayed CS, Scrambled CS) and a within-subjects factor of study phase (2: Acquisition, Extinction). The primary dependent variables were frequency and intensity of intrusions, assessed via a phone assessment 24 hr following extinction.

Procedure

Upon arrival, written informed consent was obtained and participants were given the opportunity to ask questions individually.

Day 1: Acquisition. After consenting, participants completed the in-person phases of the study in groups, with group size ranging from five to 11 participants. Participants completed the baseline questionnaires (Demographics, PDS, BDI, ASI, ERQ, STAI-S, STAI-T). Participants then received instructions for viewing the film and were specifically asked to "pay careful attention to what is happening." Participants were then instructed how to rate their distress (SUDs) throughout the film. They then viewed the 10-min film segment for fear acquisition. SUDs were recorded pre-viewing, every 2 min during viewing, and at post-viewing, prompted by a research assistant announcing "SUDs 1," "SUDs 2," etc.

Participants completed state questionnaires (PFQ, TFQ) after viewing the acquisition segment. Prior to leaving, participants scheduled a phone assessment with a research assistant for 24 hr later. Participants were told that during the phone call they would be asked questions about memories of the film and how they remembered the film's content.

24-hr Initial Phone Assessment. Approximately 24 hr after completing the fear acquisition phase, participants completed the intrusions questionnaire via telephone at their predetermined time.

Day 2: Extinction. Two days after fear acquisition, participants returned for the extinction phase. Participants were block randomized (as a group) into one of three conditions (Pre CS, Delayed CS, or Scrambled CS) using a computerized randomization program, counterbalanced based on size of the Day 1 group. Participants completed the STAI-S upon arrival for Day 2 procedures.

Pre CS cue. Participants viewed the projected CS cue for 8 s. Participants were instructed to focus on the image until it disappeared. Participants were then instructed to play

Tetris on their individual computers for 10 min and rated the effectiveness of the game on effectiveness of stopping images/thoughts.

Scrambled CS cue. In the Scrambled CS condition, participants completed the same procedures as those in the Pre CS condition, with the exception of viewing the Scrambled CS instead of CS.

Delayed CS Cue. No cueing of the film occurred prior to extinction procedures.

Participants were given the same film-viewing instructions as Day 1 and then watched the 30-min extinction film segment. During the film segment, SUDs were recorded pre-viewing, every 5 min during viewing, and at post-viewing, prompted by a research assistant announcing "SUDs 1," "SUDs 2," etc. Participants then completed the PFQ and TFQ.

For participants in the Delayed CS Cue condition only, they then viewed the CS cue for 8 s and then played Tetris for 10 min. Participants were then scheduled for their second phone assessment.

24 hr Final Phone Assessment. The intrusions questionnaire was administered via phone 24 hr after extinction at a predetermined time. After assessing intrusions, participants then heard a brief 25 s audio clip from the film segment. Participants then completed the PFQ to assess emotional reactions elicited by the clip. They were additionally asked if they experienced any intrusive memories during or immediately following the clip.

Participants were then debriefed about the study. Upon study completion, participants received course credit for their participation.

Results

Manipulation Check

In order to ensure that our acquisition phase was effective, we ran preliminary analyses examining distress and negative emotions elicited during acquisition, as well as intrusions following acquisition. Distress (SUDs) significantly increased from pre- (M = 5.72, SD = 10.32) to post-film (M = 35.52, SD = 25.52) acquisition, $t(1,144) = -14.47$, $p < .001$, $d = 1.69$. The acquisition film segment evoked anxiety (M = 3.65, SD = 2.11), disgust (M = 5.23, SD = 2.19), and fear (M = 2.84, SD = 2.32), as rated on the PFQ. The vast majority (80.0%) of participants experienced at least one intrusion (M = 3.15, SD = 3.01) 24 hr after acquisition, and 64.2% reported at least some distress associated with that intrusion (M = 1.89, SD = 1.86). Overall, the acquisition phase elicited distress, negative emotions, and intrusions. On average, Tetris was effective at stopping film-related thoughts and images (M = 5.72, SD = 2.62). As expected, there were no significant differences between experimental conditions in intensity of emotions evoked, frequency or intensity of intrusions during acquisition, or Tetris effectiveness at blocking film-related thoughts before or after extinction.

Effect of Condition on Intrusions and Distress After Extinction

24 hr intrusions after extinction. To test our primary hypothesis of cued extinction, we examined between-condition differences in intrusions using an ANOVA. Conditions significantly differed on frequency of intrusions 24 hr after extinction, $F(2, 145) = 4.51$, $p = .01$, $d = 0.55$. As seen in Figure 1, the Pre CS condition experienced more intrusions (M = 2.40, SD = 2.54) than the Scrambled CS condition (M = 1.24, SD = 1.26), $t(1, 145) = 2.98$, $p = .003$, instead of fewer intrusions as we hypothesized. Though only a trend, the frequency of intrusions in the Delayed CS (M = 1.65, SD = 1.70) was also lower than the Pre CS condition, $t(1,145) = 1.95$, $p = .05$. These findings held when controlling for distress (SUDs) during Day 1 acquisition.

To better understand the nature of these intrusions, total intrusions were separated into image-based and conceptual intrusions. Image-based intrusions differed by condition ($F(2, 145) = 3.90$, $p = .02$) but conceptual intrusions did not ($F(2, 145) = 1.49$, $p = .23$. Again, as seen in Figure 2, the Pre CS condition experienced more image-based intrusions ($M = 1.67$, $SD = 2.04$) than the Scrambled CS condition ($M = 0.84$, $SD = 1.08$), $t(1,145) = 2.74$, $p = .01$. Though only a trend, frequency of image-based intrusions was again higher in the Pre CS than in the Delayed CS condition ($M = 1.09$, $SD = 1.21$), $t(1, 145) = 1.96$, $p = .05$. The frequency of conceptual intrusions following extinction did not differ between conditions, $F(2, 145) = 1.49$, $p = .23$. These findings also held when controlling for distress during Day 1 acquisition.

24 hr intrusion distress and return of fear. In order to better understand the intensity of these intrusions and the duration of extinction, we examined both intrusion distress and fear renewal 24 hr after extinction. With respect to intrusion distress, maximum intrusion distress did not differ by condition, $F(2, 145) = 0.39$, $p = .68$. Similarly, when examining anxiety, disgust, and fear from fear renewal 24 hr after extinction, intensity of emotions did not differ significantly by condition (anxiety: $F(2, 145) = 1.54$, $p = .22$; disgust, $F(2, 145) = 0.19$, $p = .83$; fear: $F(2, 145) = 1.85$, $p = .16$.

Presentation of a CS cue before extinction caused an increase in frequency of intrusions, specific to image-based intrusions, but did not affect intrusion distress or the return of fear.

Effect of Condition on Extinction Process

To examine whether the CS cue administered prior to extinction affected the way in which participants experienced extinction, we next examined patterns of distress (SUDs) at three key times during extinction (pre, mid, and post). As can be seen in Figure 3, the Pre CS cue condition began extinction with significantly higher SUDs ratings ($M = 8.60$, $SD = 12. 65$) than

the Delayed CS condition (M = 1.82, SD = 5.13, $t(96) = 3.16$, $p = .002$, $d = 0.64$). Further, the Pre CS condition remained significantly more distressed (M = 26.98, SD = 21.99) than the Delayed CS condition (M = 17.64, SD = 15.63) at mid extinction ($t(96) = 2.24$, $p = .03$, $d = 0.45$). However, at the end of extinction, there was no difference by condition ($p = .45$). The Pre CS condition entered extinction more distressed, continued to be more distressed midway through extinction, but ended extinction at a distress level comparable to the Delayed CS condition.

Examining the relationship between extinction distress and later intrusions, higher peak distress (SUDs) during extinction predicted higher intrusion frequency ($r = .35$, $p < .001$) and higher intrusion distress ($r = .62$, $p < .001$) 24 hr after extinction.

Baseline Predictors of Intrusions 24 hr After Extinction

To examine our secondary hypotheses that baseline psychopathology would predict later intrusions, we ran zero-order correlations between baseline characteristics (demographics, baseline psychopathology) and intrusion frequency and distress 24 hr after extinction, using a Bonferroni-Holm correction to control for multiple correlations; see Table 2. Higher levels of baseline psychopathology did not predict more frequent intrusions in the 24 hr after Day 2. Higher levels of baseline psychopathology, specifically trait anxiety (STAI-T), depression (BDI-II), and anxiety sensitivity (ASI-R) predicted more distressing intrusions. Neither expressive suppression (ERQ) nor cognitive reappraisal (ERQ) was strongly correlated with intrusions or intrusion distress after extinction. Though no measures of baseline psychopathology were associated with intrusion frequency, several measures were associated with intrusion distress.

Fear Acquisition Processing Predictors of Intrusions 24 hr After Extinction

To examine the relationship between acquisition processing factors and later intrusion frequency and distress, we ran zero-order correlations between various processing factors

(intensity of emotion, processing style), again using a Bonferroni-Holm correction to control for multiple correlations; see Table 3. Higher anxiety, disgust, and fear, as reported on the PFQ, all predicted both higher intrusion frequency and distress. Higher data-driven processing, but not conceptual processing (TFQ), also predicted higher intrusion frequency and intensity. Acquisition processing factors including intensity of negative emotions and data-driven processing were predictive of intrusion frequency and distress 24 hr after extinction.

Discussion

We examined the effect of cued memory retrieval followed by fear extinction on later memory intrusions. As predicted, individuals who were cued with an isolated CS presentation and then underwent extinction (Pre CS condition) significantly differed in frequency of intrusions after extinction compared to participants who were cued with a non-retrieval cue (Scrambled CS condition). This finding is consistent with the reconsolidation hypothesis (e.g., Nader et al., 2000) and previous findings (Monfils et al., 2009; Schiller et al., 2010), in that there is specific period of time following a memory cue during which the retrieved memory is available for modification. However, individuals who underwent extinction within the reconsolidation window experienced *more intrusions* 24 hr after extinction as compared to those who completed extinction outside of the reconsolidation window. These results held even after controlling for peak distress during fear acquisition, further suggesting the role of specific memory cueing effects in opening a reconsolidation window. Despite the increased intrusions, the idea that something as simple as a retrieval cue can activate a specific period of time during which memories can be modified has clear clinical implications for exposure-based therapies for psychological disorders such as PTSD.

Consistent with Kindt and Soeter (2013), a cue to open the reconsolidation window did not reduce intrusion distress or return of fear after extinction. Kindt and Soeter posit that methodological differences between the two studies, including their use of fear-relevant stimuli in place of geometric shapes, their use of a startle probe, and online expectancy ratings, may explain the discrepant findings. The authors also note that the number of extinction trials used in their study may not have been sufficient to fully extinguish the fear memory associated with their negatively-valenced stimuli. With more complex and real-world stimuli, perhaps it is the way in which individuals process a distressing event as it happens, that is, during conditioning, that is most critical to the return of negative emotions following extinction. Individuals who were higher in sensory-perceptual processing during acquisition reported more frequent and distressing intrusions after extinction. This is consistent with previous research linking data-driven processing with later distress (e.g., Halligan et al., 2002; Murray, Ehlers, & Mayou, 2002) and with several theories related to intrusive memories and distress (Brewin & Holmes, 2003; Ehlers & Clark, 2000; Brewin et al., 1996). These theories suggest that cognitive processing at the time of the trauma influences the later development of PTSD symptoms including intrusive memories.

It is possible that the nature of our retrieval cue contributed to an increase in post-extinction intrusion frequency. Increasing stress levels prior to memory modification may impair the reconsolidation process (Akirav & Maroun, 2013). More specifically, exposure to an out-of-context stressor facilitates consolidation but impairs reconsolidation in rats (Maroun & Akirav, 2008). In the present study, the retrieval cue was both unexpected and distressing; participants were told immediately before the cue appeared that a still image was going to be presented and were not given any information regarding its content. However, in our study, fear

extinction was meant to modify the content of the retrieved memory (i.e., decreased fear associated with film memory). In addition, we did not see enhanced extinction in the condition cued prior to extinction. Thus, if the cue presentation served as a stressor that in turn impaired reconsolidation, effects of enhanced extinction should have been counteracted for the Pre CS condition. Notably, the same cue presented after extinction (Delayed CS condition) did not increase later intrusion frequency. Future studies could use a more neutral retrieval cue that would still need to clearly signal the US in order to decrease distress associated with the cue presentation prior to extinction.

It is interesting to further consider the nature of the CS and US. The US was the graphic mutilation and murder of a central character in a distressing film paradigm. The image of the mutilated woman (CS), presented by itself as a still image, was used to evoke the US, with key aspects of the US (e.g., the murder, emotional reactions of characters, screams, etc.) missing in the still image. Perhaps a more neutral image of the same woman, given that she was shown in several other scenes, would not necessarily directly cue the US for participants. With exposure therapies for PTSD, the event itself is considered the US, and the most distressing memory associated with the event is considered the CS (Foa et al., 2002; Rothbaum & Davis, 2003). The difference between the event actually occurring (imminent danger) and a memory of the event (safe) separate the CS from the US. The same could be said in distressing film paradigms; a still image and the film segment are different, with the image of the mutilated woman representative of the most distressing moment in the film. Notably, the image of the mutilated woman when presented on its own would still be somewhat aversive. In this way, the cue we used cannot be considered a previously neutral cue, because of its negative valence. As was suggested by Kindt and Soeter's (2013) findings, negatively valenced and fear-relevant stimuli are especially

resistant to conditioning (see also Mineka & Ohman, 2002). Thus, the nature of our CS cue may have led to an association that was more difficult to extinguish.

Research examining mechanisms of extinction enhancement suggests that any emotional learning that takes place in during extinction is enhanced, not just successful fear extinction (Smits et al., 2013). In other words, it is not just the result of extinction that is being consolidated but the entire process. In the present study, the Pre CS condition experienced an altered extinction process; these participants entered extinction more distressed and remained more distressed halfway through extinction. If it is the extinction process, and not just the end extinction state, being consolidated, then heightened distress during the extinction process may be contributing to later intrusions seen in the Pre CS condition.

Several limitations should be noted. First, in terms of emotional reactions, our film elicited more disgust than either fear or anxiety. Though disgust, fear, and anxiety are closely related (e.g., Shin & Liberzon, 2010; Watson, 2005), and were strongly correlated in our sample, we do not yet have an understanding of reconsolidation as it relates to disgust. Our film also evoked moderate, but not high, levels of fear in participants. However, given both our goal of using more real-world stimuli and the ethical constraints involved in evoking analogue PTSD symptoms, it would be challenging to select a film that specifically evokes high levels of fear *and* mirrors a trauma memory. We also had a fairly high dropout rate across study phases. Our attrition rate was typical of an undergraduate student sample, and importantly there were no differences in characteristics in those who dropped out compared to those who completed the study. In addition, it would not make sense to analyze data from Day 1 for participants who later discontinued, given that the primary aim of our study was to examine extinction processes and later intrusions.

If we are better able to understand the reconsolidation hypothesis and its boundary conditions, there are clear and exciting clinical applications. As suggested in this study and previous work, there appears to exist a finite period of time following memory retrieval during which the memory is available for update. Translating animal research designs to human research is an ongoing challenge of PTSD research given the ethical dilemmas of inducing post-trauma symptoms in participants. Our study introduced an exciting next step in this translation process by increasing the ecological validity of a paradigm designed to examine reconsolidation as a possible memory updating mechanism. If something as simple as presenting a retrieval cue to open the reconsolidation window proves effective, it may be possible in the future to cue a client's trauma memory prior to an exposure session as a way to enhance their in-session learning.

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Table 1

Demographics & Baseline Psychopathology

Variable	*M (SD)* or Percentage (%)	Range
Age (years)	18.93 (*1.04*)	18 - 23
Gender (% female)	60.1	
Ethnicity (% Caucasian)	49.3	
Criterion A exposure (PDS) (%)	52.7	
PTSD severity (PDS) (*n* = 78)	6.29 (*7.20*)	0 - 27
Depression (BDI-II)	8.16 (*7.54*)	0 - 41
Trait anxiety (STAI-T)	41.18 (*11.35*)	20 - 72
Anxiety sensitivity (ASI-R)	28.78 (*19.32*)	0 - 96
Cognitive reappraisal (ERQ)	5.04 (*1.06*)	2.00 – 7.00
Expressive suppression (ERQ)	3.86 (*1.22*)	1.25 – 6.75

Table 2

Demographic and psychopathological predictors of intrusion frequency and distress (N = 148)

	Age	STAI-T	BDI-II	ASI-R	ERQ Reap	ERQ Supp	Intrusion Freq
Anxiety (STAI-T)	-.05						
Depression (BDI-II)	-.06	.75*					
Anxiety Sensitivity (ASI-R)	-.10	.51*	.41*				
Reappraisal (ERQ)	.04	-.24	-.24	.00			
Suppression (ERQ)	.06	.30*	.22	.15	.05		
Intrusion Frequency	-.07	.12	.10	.24	.03	-.02	
Intrusion Distress	-.01	.26*	.23	.32*	-.05	.05	.59*

Note. * $p < .05$, with Bonferroni-Holm correction.

Table 3

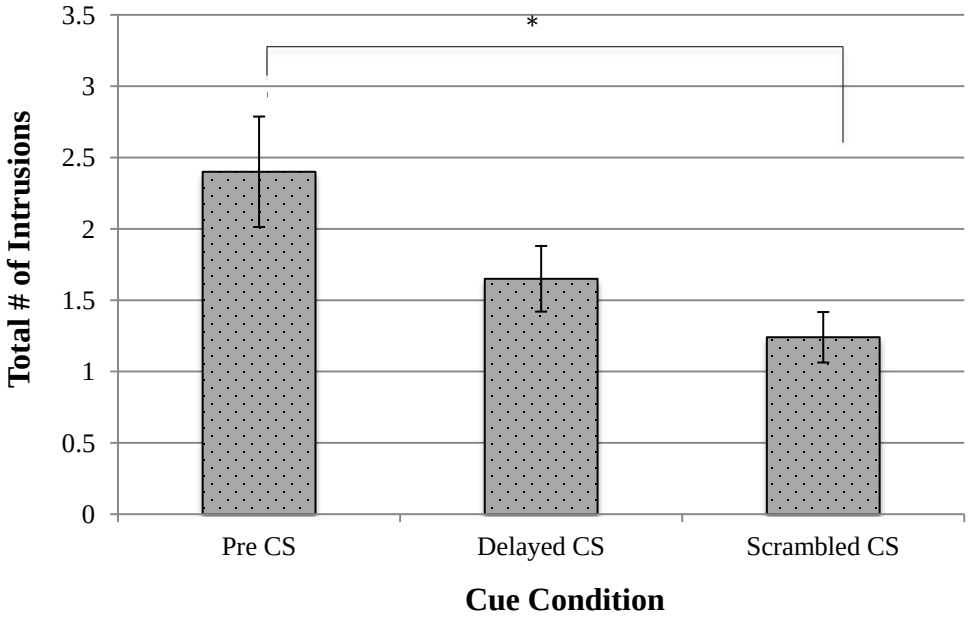
Acquisition processing predictors of intrusion frequency and distress

	Anxiety (PFQ)	Disgust (PFQ)	Fear (PFQ)	Data-Driven (TFQ)	Conceptual (TFQ)	Intrusion Freq
Disgust (PFQ)	.44*					
Fear (PFQ)	.65*	.54*				
Data-Driven Processing (TFQ)	.41*	.39*	.48*			
Conceptual Processing (TFQ)	-.03	-.25	-.11	-.29*		
Intrusion Frequency	.25*	.26*	.25	.25*	-.07	
Intrusion Distress	.31*	.33*	.37*	.35*	-.02	.59*

Note. * $p < .05$, with Bonferroni-Holm correction.

Figure 1

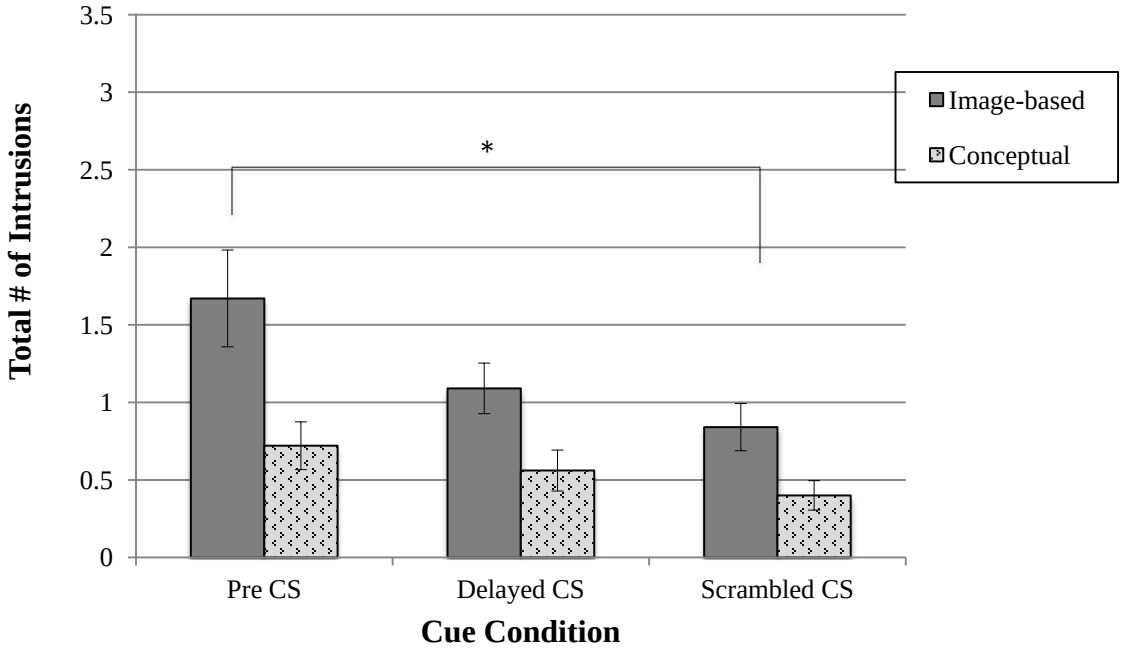
Frequency of Intrusions 24 h After Extinction



Note. * $p < .05$

Figure 2

Frequency of Intrusions by Intrusion Type 24 h After Extinction



Note. * $p < .05$

Figure 3

Effect of Condition on Extinction Distress