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The Efficacy of Exposure Therapy for Anxiety-Related Disorders and Its Underlying Mechanisms: The Case of OCD and PTSD

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posttraumatic stress disorder, obsessive-compulsive disorder, prolonged exposure, exposure and response (ritual) prevention, exposure therapy

Abstract

In this review we describe the intricate interrelationship among basic research, conceptualization of psychopathology, treatment development, treatment outcome research, and treatment mechanism research and how the interactions among these areas of study further our knowledge about psychopathology and its treatment. In describing the work of Edna Foa and her colleagues in anxiety disorders, we demonstrate how emotional processing theory of anxiety-related disorders and their treatment using exposure therapy have generated hypotheses about the psychopathology of posttraumatic stress disorder and obsessive-compulsive anxiety disorder that have informed the development and refinement of specific treatment protocols for these disorders: prolonged exposure and exposure and response (ritual) prevention. Further, we have shown that the next step after the development of theoretically driven treatment protocols is to evaluate their efficacy. Once evidence for a treatment's efficacy has accumulated, studies of the mechanisms involved in the reduction of the targeted psychopathology are conducted, which in turn inform the theory and further refine the treatments. We conclude our review with a discussion of how the knowledge derived from Foa and colleagues' programmatic research together with knowledge emerging from basic research on extinction learning can inform future research on the psychopathology of anxiety disorders and their treatments.

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INTRODUCTION

Exposure therapy greatly impacted the prognosis of patients suffering from anxiety-related disorders. Emanating from theory-driven research on learning and behavior, exposure therapy was the first psychosocial treatment whose procedures were described in detail, which allowed researchers to replicate the procedures in their studies and clinicians to follow them with their patients. Beginning in the 1960s and continuing to date, exposure procedures have been developed, studied, and refined, such that relief from anxiety-related disorders has become much more likely than it was several decades ago. Disorders that were once considered refractory, such as obsessive-compulsive disorder (OCD), are now considered highly treatable. This significant progress notwithstanding, some patients still do not benefit from exposure therapy, and many remain symptomatic. In order to further refine existing protocols and develop new, more efficacious treatments for pathological anxiety, researchers have sought to elucidate the mechanisms of exposure therapy for anxiety-related disorders as well as the psychopathology underlying these disorders.

In this review, we describe more than three decades of research conducted by Edna Foa and colleagues on the clinical psychology science of anxiety-related disorders, including (*a*) the development of emotion processing theory (EPT), a framework for understanding the psychopathology and treatment of anxiety-related disorders, as well as studies testing the hypotheses emanating from the theory; (*b*) studies evaluating the efficacy and effectiveness of exposure therapy; (*c*) research aimed at elucidating mechanisms underlying exposure therapy; (*d*) studies focusing on understanding the psychopathology involved in anxiety-related disorders; (*e*) assessment methods; and (*f*) treatment dissemination. In this review, we focus on describing EPT, treatment outcome research, and treatment mechanism research as they relate to posttraumatic stress disorder (PTSD) and OCD, the two disorders that have been a major focus of Foa's research.

OCD: obsessive-compulsive disorder

EPT: emotion processing theory

PTSD: posttraumatic stress disorder

EXPOSURE THERAPY AND ITS THEORETICAL FOUNDATION

Exposure therapy is a set of treatment approaches that are frequently used to reduce the pathological fear and related emotions, such as guilt, that are common in anxiety-related disorders. During exposure, patients are encouraged to approach feared, but safe, objects, situations, thoughts, sensations, and memories, with the ultimate goal of reducing fear reactions to those stimuli. Exposure procedures are divided into three primary types: in vivo (real-life) exposure, imaginal exposure (revisiting the distressing traumatic memory in imagination), and interoceptive exposure. The selection of the type of exposure is determined by the pathological characteristics of a given disorder. Often, several types of exposure are used concurrently in exposure therapy programs.

Early Conceptualization of Anxiety Disorders

The conceptualization of anxiety disorders was greatly influenced by Mowrer's two-factor theory (Mowrer 1960, Mowrer & Suter 1950) and by Dollard & Miller's (1950) application of this theory to the treatment of pathological anxiety. The two-factor theory posits the acquisition of fear as involving classical conditioning and the maintenance of the conditioned fear as involving operant conditioning. Specifically, avoidance prevents extinction learning, which is learning that the conditioned stimulus no longer signals harm, and exposure to the conditioned stimulus in the absence of avoidance or escape alleviates the fear response. A further conceptual development of exposure therapy was advanced by Foa & Kozak (1985, 1986), who expanded on the early learning accounts by generating EPT, a comprehensive theory for understanding pathological anxiety and the mechanisms involved in exposure therapy for anxiety.

Emotional Processing Theory

Inspired by Lang (1977, 1979), a basic supposition of EPT (Foa & Kozak 1986) is that emotions such as fear are represented in memory as a cognitive structure that includes information about the fear stimuli, the fear responses, and the meaning of the stimuli and responses. The stimuli, responses, and their meaning are interrelated within the fear structure such that inputs matching any one part of the structure will activate the entire structure.

EPT distinguishes between normal and pathological fear structures, emphasizing the role of meaning representations in this distinction. When a person is faced with a realistically dangerous situation, the activation of the fear structure elicits adaptive behavior (e.g., muscle tension, increased sympathetic activation). A fear structure becomes pathological when the associations among stimulus, response, and meaning representations do not accurately reflect reality and the fear structure becomes activated by harmless stimuli or responses that are erroneously viewed as dangerous. Foa & Kozak (1986) proposed that anxiety disorders represent specific underlying pathological structures. In the next section, we describe the pathological fear structures of PTSD and OCD.

EPT proposes that the psychological interventions that reduce pathological fear, such as exposure therapy, achieve their effects through emotional processing, the process by which corrective, realistic information is incorporated into the fear structure and modifies the pathological elements in the structure. Influenced by modern learning theories that view extinction as generating new associations rather than modifying old ones (e.g., Bouton & Swartzentruber 1991), Foa & McNally (1996) proposed that exposure therapy does not alter the existing pathological structure, but rather forms a competing structure that does not include pathological associations among stimulus, response, and meaning representations. The pathological and the normal, realistic structures

contain overlapping elements, so they can be activated by the same stimuli and responses. When therapy is successful, the new structure is more easily retrieved when shared elements are present; conversely, when the old, pathological structure is activated, relapse occurs.

EPT further posits that two conditions are necessary for emotional processing, which is manifested by reduction of pathological anxiety, to occur. First, the fear structure must be activated (i.e., retrieved) so that it can be available for modification. Second, new information that is incompatible with the pathological elements of the fear structure must be available so that it can be incorporated into the pathological structure.

Exposure therapy is an efficient way to achieve these two conditions: Approaching feared but safe stimuli is likely to activate the fear structure and at the same time provide corrective information about the probability and cost of feared consequences. EPT's emphasis on the integration of disconfirming information as the mechanism of change is consistent with Rescorla & Wagner's (1972) mathematical model of classical conditioning in which learning results from the discrepancy between what is expected to occur and what actually occurs. This learning then modifies future expectations according to the Rescorla-Wagner model, or meaning elements according to EPT.

Although it is not possible to directly observe fear structures and emotional processing, Foa & Kozak (1986) postulated three indicators of successful emotional processing: (*a*) activation of the fear structure, as indicated by both subjective and objective measures of fear; (*b*) within-session habituation, or the reduction of anxiety within the course of a treatment session; and (*c*) between-session habituation, that is, lower peak anxiety to fear-related stimuli during successive treatment sessions.[1] As Foa & Kozak (1986) suggested, many sources of data can be brought to bear when testing the prediction that these three indicators of emotional processing are associated with the reduction of pathological fear. In the following sections, we describe studies examining the validity of these proposed indicators and other hypotheses derived from emotional processing theory. Many of these studies, but certainly not all, were conducted within the context of exposure therapy for PTSD and OCD.

Emotional processing conceptualization of PTSD. Most individuals exposed to a traumatic event experience fear-related symptoms that overlap with those of PTSD, including reexperiencing the event in response to trauma reminders, hyperarousal, and avoidance of trauma-related stimuli (e.g., Breslau et al. 2005). For most trauma survivors, these symptoms ameliorate over time. When symptom reduction does not occur, PTSD develops. Applying EPT to PTSD, Foa & Cahill (2001) suggested that natural recovery following a trauma occurs when the fear structure is repeatedly activated in the absence of feared consequences. Thus, individuals who think and talk about the traumatic event, engage with trauma-related feelings, and approach reminders of the trauma in daily life would be expected to recover from a traumatic event (see also Foa et al. 2006). In contrast, individuals who avoid the traumatic memory and trauma-related stimuli may develop PTSD.

How does EPT conceptualize the fear structure of PTSD? Foa & Rothbaum (1989) proposed that the traumatic memory associated with PTSD can be conceived as a specific pathological fear structure that includes erroneous associations among stimuli and responses that were present at the time of the trauma and their meaning. For example, the fear structure of an individual with combat-related PTSD may include representations of stimuli such as roadside garbage (by association with improvised explosive devices), representations of responses such as increased

[1]Although the term extinction is now more commonly used than habituation, we use these terms interchangeably throughout this review, given that habituation was the term favored at the time that EPT was proposed.

respiration and sweating while exposed to roadside garbage, and representations of the meaning assigned to the stimuli, such as "Roadside garbage is dangerous," and "Increased respiration means I am afraid." Foa and Rothbaum further proposed that (*a*) the fear structure underlying PTSD is characterized by a large number of stimulus representations that are erroneously associated with danger and (*b*) representations of the responses during the trauma and of PTSD symptoms are associated with the meaning of self-incompetence (e.g., "My reaction during the trauma and my PTSD symptoms mean that I am a weak person"). These erroneous perceptions—"The world is entirely dangerous" and "I am completely incompetent"—promote avoidance of trauma-related thoughts, images, and situations, which in turn prevent emotional processing and serve to maintain PTSD symptoms.

Emotional processing conceptualization of OCD. Individuals with anxiety-related disorders attempt to reduce the anxiety elicited by situations, objects, and people that they erroneously perceive as harmful by avoiding or escaping them. In addition to avoidance, people who suffer from OCD also engage repeatedly in certain behavioral or mental acts, called compulsions or rituals, that are designed to reduce anxiety or to prevent the feared consequences from occurring. Foa & Kozak (1985, 1986) proposed that several erroneous cognitions are represented in the OCD fear structure. First, OCD sufferers assign a high probability of danger to situations that are relatively safe. For example, an individual with OCD may believe that if he touches the floor without washing his hands thoroughly, he will get a deadly disease and will also cause illness and death in other people whom he touched with his dirty hands. Second, individuals with OCD overestimate the cost of their feared consequences. For example, not washing one's hand and getting a minor infection on the finger may be viewed as a disaster. In addition, Foa and Kozak suggested that individuals with OCD often conclude that a situation is dangerous based on lack of evidence for its safety. Because the null hypothesis cannot be proven, individuals with OCD require constant proof of safety and thus engage repeatedly with rituals to prevent harm. According to EPT, the fear structure of an individual with OCD includes representations of stimuli such as doorknobs or public handrails, representations of responses such ritualistic behavior (e.g., washing, checking), and representations of the meaning of the stimuli as "contamination," "illness," or "death," and the meaning of responses such as rituals as "protection from harm."

TREATMENT FOR POSTTRAUMATIC STRESS DISORDER: PROLONGED EXPOSURE THERAPY

The story of how prolonged exposure (PE) therapy was developed begins in 1980 with the addition of PTSD into the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) (Am. Psychiatr. Assoc. 1994). Prior to this date, PTSD was not formally recognized and there was little empirical knowledge of how to best treat the disorder. Notably, by that time the efficacy of exposure therapy for anxiety-related conditions was well documented. Moreover, viewing PTSD patients as suffering from extensive phobias, some clinicians were already treating trauma survivors successfully with exposure therapy. Indeed, the two principal components of prolonged exposure (PE) therapy, developed by Foa and colleagues to treat PTSD, are in vivo exposure to trauma reminders designed to help patients overcome avoidance of safe situations and objects, and imaginal exposure designed to help patients process and digest the traumatic event. In this context, Foa and colleagues applied for a National Institute of Mental Health (NIMH) grant in 1982 to develop PE for PTSD and to examine the efficacy of this treatment with rape survivors suffering from PTSD. Since the time of this first PE grant, Foa and colleagues have received continuous funding from the NIMH, the National Institute of Alcohol Abuse and Alcoholism,

PE: prolonged exposure

NIMH: National Institute of Mental Health

and more recently the Department of Defense to conduct randomized controlled trials (RCTs) to study the efficacy and effectiveness of PE with different patient populations.

RCT: randomized controlled trial

Theoretical Underpinnings of Prolonged Exposure

As noted above, EPT conceptualizes PTSD as a failure to adequately process the trauma memory due to avoidance of thoughts and situations related to the trauma. These behaviors maintain individuals' erroneous negative perceptions about themselves and the world and prevent emotional processing from occurring. Accordingly, the goal of PE is to promote emotional processing through deliberate, systematic confrontation with trauma-related stimuli. In vivo exposure to trauma reminders and imaginal exposure (repeated revisiting and recounting the trauma aloud) followed by discussion of the revisiting experience (processing) are used concurrently in order to disconfirm the erroneous perceptions that underlie PTSD.

In vivo exposures are designed to target PTSD patients' erroneous perceptions that safe stimuli are harmful and therefore should be avoided, that their anxiety will last forever if they remain in trauma-related situations rather than escape them, and that they are incapable of coping with stress and distress. Consequently, in vivo exposure exercises involve approaching safe situations that patients perceive to be dangerous (e.g., driving on highways for fear of an improvised explosive device) as well as situations that they avoid because the situations are trauma reminders and cause high distress that patients believe they would not be able to tolerate (e.g., watching news coverage about the war). Thus, in vivo exposures are designed to achieve the two necessary conditions for emotional processing: activation of the trauma cognitive structure and disconfirmation of the expected disasters.

Imaginal exposure comprises a large part of the PE session. Individuals with PTSD frequently hold the erroneous belief that recalling the trauma memory is dangerous or harmful (e.g., will cause them to go crazy or lose control) and that anxiety will last forever when thinking about the trauma. Revisiting and recounting the most distressing traumatic memory in imagination is designed to help patients organize the memory, reexamine negative perceptions about themselves and others, distinguish between thinking about the trauma and reexperiencing the trauma, remember the trauma without causing undue anxiety through extinction, and foster the realization that engaging in the trauma memory does not result in harm.

Imaginal exposure creates a powerful opportunity for new learning by activating the trauma fear structure and bringing to the surface unhelpful or unrealistic beliefs that maintain the symptoms of PTSD as well as new insights about evidence that contradicts erroneous beliefs. However, patients may have difficulty identifying and integrating disconfirming information that emerges from imaginal exposure on their own. Processing is conducted immediately after imaginal exposure in order to explore contradictions between the patients' erroneous perceptions and what they had recounted during the imaginal exposure. Encouraging patients to elaborate on new insights and making insights explicit is likely to facilitate emotional processing and modification of the pathological fear structure underlying PTSD.

Description of Prolonged Exposure

PE is a manualized exposure therapy program for PTSD that typically consists of 8 to 15 individual 90-minute sessions that are implemented once or twice weekly (Foa et al. 2007). As noted previously, the two main components in PE are in vivo exposure to trauma reminders, which are completed as between-session assignments, and imaginal exposure, which is conducted during sessions followed by processing of the revisiting experience.

In the first session, the therapist provides a rationale for how PE is likely to ameliorate PTSD symptoms by presenting a basic and succinct summary of emotional processing theory and of the treatment mechanisms involved in exposure therapy. Accordingly, the patient learns that PTSD symptoms are maintained by two key factors. The first factor is avoidance of thoughts, images, situations, and objects that are trauma reminders. The second factor is unhelpful, negative perceptions that the world is extremely dangerous and that the patient is completely incompetent. Next, the therapist and patient determine which trauma to focus on during imaginal exposure. For patients with a history of multiple traumas, the index trauma is selected by determining which event is currently causing the most distress (i.e., associated with the most frequent and upsetting reexperiencing symptoms).

SIT: stress inoculation training

SC: supportive counseling

The second session involves a discussion of common reactions to trauma, which provides patients with a framework for understanding their PTSD symptoms. The therapist then introduces in vivo exposure and, together with the patient, develops a list of safe or low-risk situations that the patient has been avoiding. In vivo exposure is conducted outside of therapy sessions (i.e., homework) in a stepwise fashion, beginning with situations that provoke moderate anxiety and gradually progressing to more challenging situations.

In the third session, the therapist presents a rationale for imaginal exposure and then spends the majority of the session conducting imaginal exposure (~40 min). Imaginal exposure is followed by 15 to 20 minutes of processing, which involves discussing the patient's thoughts and feelings about the imaginal exposure experience. Imaginal exposure is conducted in each subsequent session. Patients are also asked to listen to an audio recording of the imaginal exposure daily as part of their weekly homework.

The remainder of treatment (sessions 4 to 10[2]) begins with a review of the preceding week's homework, followed by imaginal exposure and processing, and concluding with assigning homework exercises for the coming week. During the final session, the therapist and patient review progress, discuss lessons learned, and develop a plan for relapse prevention. The goal is for patients to shift their way of managing PTSD symptoms from avoiding trauma reminders, which maintains symptoms, to approaching trauma reminders, which promotes recovery and mastery (for details, see Foa et al. 2007).

Prolonged Exposure Outcome Research

The first RCT (Foa et al. 1991) compared nine sessions of PE, stress inoculation training (SIT), supportive counseling (SC), and waitlist among 45 women with PTSD related to sexual assault. Therapy was delivered in twice-weekly 90-minute sessions. The results showed that those who received PE, SIT, and to a lesser extent, SC, significantly improved from pretreatment to posttreatment, whereas those on the waitlist did not. One year after treatment, those who received PE showed continued improvement, whereas the other groups maintained their gains. Although this study included a small sample size, the results were promising.

In the second RCT (Foa et al. 1999b), 97 women with PTSD related to sexual or nonsexual assault were randomized to nine twice-weekly, 90-minute sessions of PE, SIT, their combination (PE/SIT), or waitlist. All active treatments significantly reduced PTSD severity and depression compared to waitlist. At posttreatment, 32% of those who received PE, 40% of those who received SIT, and 41% of those who received PE/SIT retained a diagnosis of PTSD. Although the effect sizes for PE were considerably larger than for SIT and PE/SIT in terms of PTSD severity, general

[2]The PE manual describes a 10-session program. In practice, however, PE is typically delivered in 8 to 15 sessions.

anxiety, and depression, contrary to the study hypothesis, PE/SIT was not more efficacious than PE or SIT alone at posttreatment and at a one-year follow-up. In fact, PE alone was superior to SIT and PE/SIT on several outcome indices, such as effect size. The fact that the combined treatment was no more efficacious than either treatment alone was surprising; it was hypothesized that adding SIT components to PE components might have overloaded the patient.

CR: cognitive restructuring

CBT: cognitive behavioral therapy

CPT: cognitive processing therapy

In light of these findings, the third RCT (Foa et al. 2005a) was designed to examine whether adding one additional component to PE, cognitive restructuring (CR), would enhance PE-alone outcome. Given that cognitive therapy was beneficial for other anxiety disorders, it was hypothesized that adding CR to PE would boost outcomes. This hypothesis was tested in 171 women with PTSD resulting from sexual or nonsexual assault and/or childhood sexual abuse. Participants received nine to twelve 90-minute sessions of therapy provided at a community rape treatment center by a counselor with no prior training or experience with cognitive behavioral therapy (CBT), including PE. All study therapists received training in PE and trauma-focused CR prior to beginning the study. Two main findings emerged from this study. First, no site differences in treatment outcomes emerged, indicating that counselors with no prior CBT experience could be trained to deliver CBT with high fidelity and could achieve outcomes comparable to those of CBT experts. Second, contrary to expectation, PE alone was as effective as PE plus CR in reducing symptoms of PTSD, general anxiety, and depression at posttreatment and at one-year follow-up. Both active treatments were superior to waitlist, although effect sizes were larger in PE alone than in PE combined with CR.

A persistent and common view among clinical researchers has been that treatment programs for PTSD that include multiple components will have superior outcomes to those with fewer components (e.g., Kilpatrick et al. 1982). However, both studies described above (Foa et al. 1999b, 2005a) found that combining PE with additional techniques (SIT and CR, respectively) did not yield any improvement in outcomes. Other researchers examining whether adding CR to PE enhances outcomes have also concluded that more isn't necessarily better (Marks et al. 1998, Paunovic & Ost 2001). This pattern does not appear to be unique to PE. A dismantling study by Resick et al. (2008) found no significant differences between the full cognitive processing therapy (CPT; a form of cognitive therapy that sometimes includes some exposure in the form of writing and reading the trauma narrative) program and its constituent components, cognitive therapy only, and written accounts. Taken together, these findings suggest that combining separately efficacious treatments does not enhance treatment outcome for PTSD. An exception to this conclusion is Bryant et al.'s (2008) finding that adding CR to exposure therapy for PTSD did lead to improved outcomes. However, the exposure therapy condition (which included both in vivo and imaginal exposure) intentionally excluded processing. As previously noted, processing is considered a key component of PE; therefore, the design of this study precludes conclusions about the benefit of adding CR to standard PE. Another possible exception is Cloitre et al.'s (2010) finding that adding eight sessions of skills training to address mood regulation prior to beginning PE yielded a marginally significant improvement in outcomes among women with PTSD related to childhood abuse. On the whole, the evidence to date does not strongly support the notion that additional treatment components can improve PTSD outcomes.

In summary, PE has compared favorably to waitlist (Foa et al. 1991, 1999b; Keane et al. 1989; Resick et al. 2002), supportive counseling (Bryant et al. 2003, Schnurr et al. 2007), relaxation training (Marks et al. 1998, Taylor et al. 2003, Vaughan et al. 1994), and treatment as usual (Asukai et al. 2010, Nacasch et al. 2011). A meta-analysis pooling the findings across these numerous studies found that PE was associated with large effect sizes relative to comparison conditions at posttreatment and at follow-up (Powers et al. 2010).

PE has also been evaluated in several comparative RCTs with other evidence-based interventions. Resick et al. (2002) compared nine 90-minute sessions of PE with twelve 60-minute sessions of CPT among women with PTSD related to sexual assault. Both treatments showed significant reductions in symptoms of PTSD and depression compared to waitlist, and these improvements were maintained through the nine-month follow-up period. Overall, there were no significant differences between PE and CPT on the primary outcomes. Gains made during PE and CPT were maintained 5 to 10 years posttreatment (Resick et al. 2012).

Rothbaum et al. (2005) compared PE with eye movement desensitization and reprocessing (Shapiro 1989, 1995), another evidence-based treatment for PTSD that involves asking the patient to generate images, thoughts, and feelings about the trauma to evaluate and reappraise cognitions related to the trauma while rapid saccadic movements are elicited. At posttreatment, both treatments produced significant improvement in PTSD, depression, and anxiety compared to waitlist, but the two active treatments did not differ. At the six-month follow-up assessment, a larger percent of PE participants achieved good end-state functioning, defined as a 50% or more decrease in PTSD symptoms and low scores on measures of depression and state anxiety.

Many other researchers in the United States and abroad have used imaginal and in vivo exposure with and without other CBT components in comparative RCTs. The results of these studies indicate that exposure-based treatments including PE are effective in reducing symptoms of PTSD, depression, and anxiety, and when compared to other forms of CBT (e.g., eye movement desensitization reprocessing), achieve similar outcomes. Although most studies comparing PE with other evidence-based treatments have not found significant differences in outcomes, it is important to note that most of the RCTs do not have sufficient power to detect the small differences in effect size that would be expected when comparing two efficacious treatments (Schnurr et al. 2007).

Over the past 30 years, a large number of RCTs by Foa and colleagues as well as by independent research centers around the world have investigated the efficacy and effectiveness of PE (for a review, see McLean & Foa 2011). This body of research indicates that PE generally leads to rapid improvement and maintenance of gains over time, up to five years posttreatment (Foa et al. 2005a, Powers et al. 2010, Resick et al. 2012, Taylor et al. 2003). PE has been found to be effective with PTSD sufferers across a wide variety of trauma types, and it has demonstrated efficacy with PTSD sufferers with a number of common comorbid disorders (cf. McLean & Foa 2014), including alcohol dependence (Foa et al. 2013b, Harned et al. 2012), psychosis (van den Berg et al. 2015), and mild to moderate traumatic brain injury (Sripada et al. 2013). In addition to reducing PTSD symptom severity, PE has also been found to improve symptoms associated with PTSD, including depression, general anxiety, guilt, anger, anxiety sensitivity, impaired social functioning and health.

In light of this large body of evidence for its efficacy, PE was identified in the joint Veterans Affairs/Department of Defense Clinical Practice Guideline for PTSD (VA/DoD Guidel. Work. Group 2010) as "strongly recommended" for use with veterans with PTSD. An Institute of Medicine (Inst. Med. 2008) report concluded that exposure therapy was the only treatment for PTSD with sufficient evidence for its efficacy. This conclusion has led to PE being included in several practice guidelines from the American Psychiatric Association (Ursano et al. 2004), the Department of Veterans Affairs and Defense (Dep. Veterans Aff. Def. 2004), and the International Society for Traumatic Stress (Cahill et al. 2009).

A logical extension of the treatment outcome research described above is to focus on the dissemination and implementation of PE. Foa and colleagues have long been involved in efforts to train mental health professionals in PE and to empirically evaluate these efforts. Foa and colleagues have conducted PE workshops around the world and have facilitated systematic dissemination programs throughout treatment centers in Israel and Japan as well as in the US Veterans Health

Administration system (for a review, see McLean & Foa 2013). In addition, two studies (Foa et al. 2013a, Gilboa-Schechtman et al. 2010) have evaluated PE delivered at a community mental health clinic by counselors who had no prior experience with manualized therapy or CBT, and results indicated that PE can be implemented effectively by non-CBT experts in a community setting.

Prolonged Exposure Treatment Mechanisms Research

Another major focus of Foa's research has been to examine the processes underlying the efficacy of treatments for pathological anxiety. She and her colleagues have conducted numerous studies to better understand how treatments such as PE work, with the aims of further refining and improving the efficacy and efficiency of the treatment and of better understanding the psychopathology of anxiety disorders. As discussed previously, EPT posits three indicators of emotional processing (i.e., that the pathological elements of the fear structure were modified): activation of the fear and within-session and between-session habituation to fear-related stimuli. The hypotheses that are generated by the proposed indicators can be tested by examining anxiety or distress responses during PE. Accordingly, EPT hypothesizes that the degree of fear activation, the degree of fear reduction within sessions, and the lower peak responses in successive exposure sessions will all be positively associated with improvement in PTSD symptom severity. As previously noted, the adaptation of EPT to PTSD (Foa & Cahill 2001, Foa & Rothbaum 1998) emphasizes that negative cognitions impede recovery after a traumatic experience, and reduction of these cognitions is viewed as a key mechanism of emotional processing and recovery. Below we consider these hypotheses, beginning with the role of negative cognitions.

Negative trauma-related cognitions. According to EPT, erroneous cognitions that "The world is extremely dangerous" and "I am extremely weak and incompetent" mediate the development and maintenance of PTSD by promoting avoidance that prevents disconfirmation. Accordingly, treatment that aims to ameliorate PTSD symptoms should correct these erroneous associations by introducing new information that is incompatible with the erroneous cognitions (Foa et al. 2006). Several lines of research support the hypothesis that negative trauma-related cognitions (most often measured via patient self-report inventories) are a key mechanism of recovery from PTSD.

Several studies have found that negative trauma-related cognitions are associated with PTSD symptom severity (e.g., Foa et al. 1999c, Moser et al. 2007) and that decreases in negative cognitions are highly correlated with reductions in PTSD symptoms during PE as well as with other forms of CBT (e.g., Kleim et al. 2007, Smith et al. 2007). For example, Foa & Rauch (2004) found that following 9 to 12 weekly sessions of PE, female assault survivors showed a significant reduction in negative cognitions about the self and world, as measured by the Posttraumatic Cognitions Inventory (Foa et al. 1999c). Importantly, the reduction in negative cognitions was associated with lower PTSD symptoms.

Most compelling is research showing that reductions in negative trauma-related cognitions temporally precede decreases in PTSD symptoms during PE among women with assault-related PTSD (Zalta et al. 2014), individuals with comorbid PTSD and alcohol dependence (McLean et al. 2015), and adolescents with PTSD related to sexual abuse (McLean et al. 2015), whereas PTSD symptom reduction did not precede reduction in negative cognitions. In the adolescent study, the pattern of findings was similar for PE and the comparison condition, client-centered therapy, indicating that reductions in negative cognitions may be an important mechanism of therapeutic recovery in a variety of interventions that ameliorate PTSD. These findings are consistent with the EPT supposition that change in negative cognitions is involved in PTSD recovery, whether

it be natural recovery or therapeutic recovery, and whether it is due to PE or to another PTSD treatment (Foa et al. 2006).

Fear activation (emotional engagement). Foa and colleagues have used several methods to examine the role of emotional engagement in PTSD treatment. One study that operationalized emotional engagement as facial fear expression during the first session of imaginal exposure found that higher fear expression was associated with superior treatment outcome after PE (Foa et al. 1995b). In an examination of several physiological indicators of emotional engagement, Pitman et al. (1996) found that peak heart rate during the first imaginal exposure session predicted a decrease on the intrusion subscale of the impact of events scale. However, subjective reports of peak anxiety during the first imaginal exposure have not always been associated with PE outcome (Rauch et al. 2004, van Minnen & Hagenaars 2002). Taken together, however, studies do provide support for the EPT hypothesis that emotional engagement would be associated with therapeutic recovery.

Research findings from extinction learning paradigms (often conceptualized as an analogue to exposure therapy) in animals lend support to the hypothesis that greater fear activation during exposure therapy is associated with greater reductions in anxiety. Animals who were administered chemicals that reduce fear activation, such as barbiturates (Barry et al. 1965) and benzodiazepines (Bouton et al. 1990), showed greater fear responses to later presentations of the conditioned stimuli compared to animals that did not receive the drugs. Similarly, animals administered with yohimbine (which increases anxiety) showed enhanced fear extinction results, whereas animals administered propranolol (which decreases anxiety) exhibited impaired extinction (Cain et al. 2004).

Within- and between-session extinction (habituation). As noted previously, EPT originally proposed that the gradual reduction of anxiety within a session is an indicator of emotional processing, which is the process by which pathological anxiety is reduced. To explain the role of within-session reduction of anxiety, Foa & Jaycox (1999) proposed that anxiety reduction constitutes information that disconfirms patients' feared expectation that anxiety during exposure will persist indefinitely and lead to harmful consequences such as loss of control. Thus, when PE was first developed, the rationale for establishing long imaginal exposure (45–60 minutes) was derived from the supposition that within-session reduction of distress is required for emotional processing to occur and thus would be associated with PTSD symptom reduction. Although anxiety does typically decline from the beginning to the end of an exposure session, the role of within-session extinction in treatment outcomes has not received strong support (Jaycox et al. 1998, van Minnen & Hagenaars 2002; for a review, see Craske et al. 2008). Indeed, since PE was first developed, a robust literature related to extinction learning in animals and humans has indicated that within-session fear reduction is not related to fear extinction (i.e., long-term fear reduction). These findings have clinical implications, as they suggest that shortening exposure sessions may be feasible without reducing treatment efficacy. Indeed, although longer exposures have been shown to promote greater within-session extinction than shorter exposures (e.g., van Minnen & Foa 2006), the fact that within-session fear reduction does not predict treatment outcome suggests that the length of PE sessions can be shortened without compromising efficacy. Two studies to date have examined this issue within the context of PTSD in humans.

In a nonrandomized study, van Minnen & Foa (2006; $N = 92$) found that 60-minute imaginal exposures within 90-minute sessions did not produce superior outcomes to 30-minute imaginal exposures within 60-minute sessions, despite greater within-session extinction in the longer exposures. Weaknesses of this study include the lack of random assignment and the reliance on self-report data. To address some of these limitations, Nacasch et al. (2015) conducted a small pilot RCT ($N = 39$) comparing 20-minute imaginal exposures (during 60-minute sessions) with

40-minute imaginal exposures (during 90-minute sessions). The results replicated the van Minnen & Foa (2006) study finding no differences in outcome between the two groups. Ninety-minute sessions constitute a barrier to PE implementation in many mental health systems; thus, although these studies were small, their results have important theoretical and practical implications.

In contrast to within-session extinction, an association of between-session extinction with therapeutic recovery has been found in many (e.g., Rauch et al. 2004, Sripada et al. 2013, van Minnen & Foa 2006) but not all (Pitman et al. 1996) studies. Using cluster analysis, Jaycox et al. (1998) found three distinct patterns of change among female assault victims during PE: (*a*) high distress in the first session followed by a gradual decline in distress over subsequent sessions, (*b*) high distress in the first session and no decline across sessions, and (*c*) moderate distress in the first session and no change across sessions. At posttreatment, participants in the first group showed superior improvement compared to participants in either of the other groups. These findings are consistent with the proposition that emotional engagement and habituation are involved in recovery. Thus, although within-session reductions in fear are no longer considered critical for improvement (Foa et al. 2006), extinction across therapy sessions appears to be important for treatment success. Consequently, EPT has shifted away from a focus on within-session extinction toward a model emphasizing emotional engagement, disconfirmation (i.e., change in negative cognitions), and between-session extinction. It remains to be tested, however, whether within-session reductions in fear are important for a subset of patients who strongly believe that distress during exposure will be intolerable or will last forever. Within-session fear reduction would constitute disconfirming information and may be helpful for these patients.

Foa (1979) posited that different brain mechanisms are involved in within- and between-session habituation in exposure therapy. Building on findings by Groves & Lynch (1972), she argued that a low-level brain structure (i.e., reticular formation) is involved in within-session habituation, whereas between-session habituation relies on forebrain structures. Foa further argued that if forebrain structures are necessary for retention of habituation across time, then higher-level cognitive processes seem to be necessary for consolidation of extinction learning.

Gillihan & Foa (2011) summarized a large number of animal studies indicating that distinct neural regions underlie the retention of fear extinction (analogous to between-session habituation) versus the acquisition of fear extinction (analogous to within-session habituation). The vast majority of these studies have implicated the medial prefrontal cortex in the retention of extinguished fear in animals (for a review, see Quirk et al. 2006). Similar studies in humans have corroborated the results from animal work (e.g., Kalisch et al. 2006, Milad et al. 2007). It seems that between-session habituation relies on higher cognitive processes more so than within-session habituation. Consistent with this conclusion are the findings that different brain structures are involved in each, suggesting a distinction between extinction learning and extinction retention. These laboratory findings that extinction retention and extinction learning comprise different processes may explain why between-session habituation, which may be viewed as akin to extinction retention, is related to treatment outcome (e.g., Kozak et al. 1988, Lang et al. 1970, Rauch et al. 2004), whereas within-session habituation generally is not.

TREATMENT OF OBSESSIVE-COMPULSIVE DISORDER: EXPOSURE AND RESPONSE (RITUAL) PREVENTION

Until the mid-1960s, OCD was considered to be an untreatable condition. Psychodynamic psychotherapy and a wide variety of medications had been unsuccessful in significantly reducing OCD symptoms. Exposure procedures (e.g., systematic desensitization, paradoxical intention, satiation) and operant-conditioning procedures (e.g., punishing obsessions and compulsions via thought

stopping, aversion therapy, covert sensitization) proved to be ineffective in ameliorating OCD symptoms. The first breakthrough came in 1966, when Victor Meyer described two patients who had been successfully treated with a behavioral therapy program that included exposure to distressing objects and situations combined with strict prevention of rituals [exposure and response (ritual) prevention (EX/RP)] (Meyer 1966). Meyer and his colleagues continued to implement EX/RP with additional OCD patients and found that the treatment program was highly successful in 10 of 15 cases, and partially effective in the remaining patients. Moreover, five years later, only two of the patients in the case series had relapsed (Meyer & Levy 1973, Meyer et al. 1974). All patients were hospitalized during their EX/RP treatment. Excitement about the efficacy of EX/RP prompted several clinical researchers to conduct controlled studies, which indeed gave empirical support to Meyer's findings (e.g., Marks et al. 1975, Rachman et al. 1971). All treatments in these studies were conducted in inpatient wards.

EX/RP: exposure and response (ritual) prevention

In 1971, Foa began a postdoctoral fellowship with Joseph Wolpe at Temple University; her first patient presented with severe OCD and had failed to benefit from numerous systematic desensitization sessions. The challenge presented by the patient marked the beginning of Foa and colleagues' research on OCD that continues to date. This research began with dismantling studies of EX/RP and continued with exploring how best to combine EX/RP with medication.

Theoretical Underpinnings of Exposure and Response (Ritual) Prevention

As noted previously, in addition to avoiding safe but feared situations, individuals with OCD develop compulsions or rituals that are designed to reduce anxiety or prevent expected harm from occurring. Like avoidance, the performance of rituals prevents individuals from disconfirming their belief that contact with feared but safe situations will be harmful, thus impeding emotional processing. Therefore, exposure and ritual prevention need to be implemented in concert. Interestingly, the idea that EX/RP works through disconfirming erroneous cognitions was implied by Meyer in 1966 when he titled his paper, "Modification of expectations in cases with obsessional rituals."

In vivo exposure (e.g., asking a patient with harm obsessions to hold a knife) facilitates modification of the OCD fear structure in three ways. First, exposure disconfirms the patient's erroneous beliefs, including that anxiety/distress will last forever and that a nervous breakdown will occur. Second, if the patient anticipates that exposure to the feared situation in the absence of ritualistic behavior will result in disastrous consequences such as dying from illness or causing a fire or a flood, in vivo exposure disconfirms these erroneous expectations. Third, via repeated in vivo exposure, patients who fear disastrous consequences in the remote future or fear harm that is vague or not easily subject to disconfirmation learn to tolerate uncertainty.

Imaginal exposure is used when in vivo exposure cannot be utilized because of real danger or legal or ethical considerations. Imaginal exposure often includes the patient's most feared disastrous consequences. For example, imaginal exposure may be used to help patients confront the feared scenario that if rituals are not completed, harm will come to their family. Imaginal exposure helps modify the fear structure in several ways. First, repeatedly imagining the feared disasters results in fear reduction, disconfirming the belief that anxiety will remain forever and cause patients to fall apart. Second, patients learn that even though their anxiety to the feared disasters decreases when thinking about the disasters, they are not likely to engage in the fear-evoking behaviors. For example, not being anxious while imagining themselves physically harming their child does not result in harming their child. Third, imaginal exposure helps sharpen the distinction between thinking and doing and therefore disconfirms the belief that imagining horrible consequences will make them come true.

Processing involves discussing the patient's experiences during or after the in vivo or imaginal exposure. Processing helps the patient modify erroneous cognitions in light of the disconfirming information that was imbedded in these exposures.

Description of EX/RP. During the first EX/RP session, the therapist collects information about the patient's general history, OCD symptoms, and previous treatment. The therapist presents a rationale for EX/RP and a description of the treatment, and introduces the patient to the practice of daily self-monitoring of obsessions and compulsions. The rationale is a summary of the EPT conceptualization (presented above) of how EX/RP reduces OCD symptom severity. It is important that the patient has a clear understanding of how and why EX/RP works to reduce OCD symptom severity and related symptoms. Understanding the rationale for EX/RP will increase patient motivation to approach the stimuli that trigger obsessions and to resist the urges to engage in compulsions, as well as to complete homework assignments, which are typically done without supervision. In vivo exposure is initiated in the second session. The therapist and the patient collaboratively create a list of situations and objects that the patient will be asked to gradually confront during treatment. In the third session, the therapist and the patient choose an in vivo exposure and ritual prevention to practice during the session. Patients are also asked to practice the exposures and ritual prevention at home and to monitor their distress during the exposures. This helps patients realize that their anxiety or distress diminishes even without ritualizing and that the negative consequences of exposure without ritualizing do not actually occur. If needed, imaginal exposure is introduced in the fourth session.

Intermediate sessions follow a similar format, focusing on increasingly more challenging in vivo situations or objects that are avoided or trigger ritualistic behavior. At approximately the eighth session, the patient confronts the most distressing item on the hierarchy. During sessions 9 to 16, the patient repeats previous exposures and adds any new ones that may have been overlooked in the original list. If practical and necessary, the therapist visits the patient's home once or twice to coach him or her with exposures and to help implement EX/RP at home.

During the final sessions, the therapist evaluates the patient's progress and helps prepare him or her for a return to regular behavior. This includes a discussion of strategies that can maximize the maintenance of the patient's gains and prevent relapse. Part of the final session is devoted to discussing follow-up phone calls or booster sessions and to saying goodbye.

Exposure and Response (Ritual) Prevention Treatment Outcome Research

EX/RP is a manualized exposure therapy program for OCD that typically consists of 17 to 20 individual 90-minute sessions. The program can be implemented once weekly, twice weekly, or daily depending on symptom severity and logistical considerations. It includes four components: response or ritual abstinence (prevention), in vivo exposure to distress-evoking stimuli, imaginal exposure to feared consequences of the exposure or to situations that cannot be approached in reality, and processing of the exposure experiences (for more details, see Foa et al. 2012).

In the first RCT of EX/RP (Rachman et al. 1971), 10 patients with OCD received relaxation therapy followed by either EX/RP in which increasingly difficult exposures were approached after being modeled by the therapist, or EX/RP in which the most distressing situation was approached from the start without therapist modeling. Both conditions led to significantly more improvement than did relaxation treatment, and gains were maintained at three-month and two-year follow-ups (Marks et al. 1975). Although there were no significant differences in outcome between conditions, patients preferred the gradual EX/RP condition.

Building on these promising initial findings, Foa & Goldstein (1978) conducted a quasi-experimental study of EX/RP with a series of 21 patients with OCD. In addition to being the

first study of EX/RP with outpatients, treatment comprised 10 rather than 15 daily sessions and, on the basis of promising findings of imaginal exposure with phobias (Mathews 1978), included both imaginal exposure and in vivo exposure. This EX/RP program was associated with very large improvements in OCD symptoms overall, and two-thirds of patients achieved minimal symptoms. As the evidence supporting EX/RP continued to accumulate, Foa and her colleagues began to examine the relative contribution of the different components of the treatment program.

SSRI: selective serotonin reuptake inhibitor

CMI: clomipramine

In the first of a series of dismantling studies, Foa et al. (1980) examined the utility of adding imaginal exposure to EX/RP with patients whose primary ritual was checking. Specifically, ten sessions of a 90-minute imaginal exposure plus 30 minutes of in vivo exposure were compared to ten 120-minute sessions of in vivo exposure with no imaginal exposure. Both groups were asked to refrain from performing rituals. The results showed that both groups improved equally at posttreatment, but the group with in vivo exposure only had a higher rate of relapse at follow-up compared to the group with imaginal and in vivo exposure, suggesting that imaginal exposure is important in helping patients maintain their treatment gains.

The next study examined the relative effects of exposure and ritual prevention. Foa et al. (1984) randomly assigned patients with contamination-related OCD to exposure only (EX), response (ritual) prevention only (RP), or their combination (EX/RP). Treatment was conducted daily for fifteen 120-minute sessions followed by one home visit. Patients in all conditions improved significantly at both posttreatment and follow-up, but those who received EX/RP showed significantly greater improvement at both time points on almost every outcome in comparison with EX-only or RP-only treatments. Moreover, the EX-only group reported lower anxiety when confronting feared situations than did the RP-only group, whereas the RP-only group reported lower urges to ritualize than did the EX-only group, indicating that EX and RP affected OCD symptoms differently. The implications of this study were clear: Exposure and response (ritual) prevention should be implemented concurrently in order to maximize outcomes.

Following these early investigations, numerous studies of EX/RP showed that it compared favorably to placebo medication (Marks et al. 1980), relaxation (Fals-Stewart et al. 1993, Marks 1981), and anxiety management training (Lindsay et al. 1997). At the same time, studies examining the use of certain medications to treat OCD either alone (e.g., Greist et al. 1995) or in combination with EX/RP showed that serotonin reuptake inhibitors (SRIs) were effective for OCD and that combining EX/RP with SRIs led to better outcomes at posttreatment but not at follow-up (Marks et al. 1980, 1988). A similar pattern was observed in studies examining the use of selective serotonin reuptake inhibitors (SSRIs) and EX/RP alone and in combination; an advantage of combined treatment was observed at posttreatment (Hohagen et al. 1998), but this effect disappeared by the follow-up (Cottraux et al. 1990).

The first study to evaluate the relative and combined efficacy of the SSRI clomipramine (CMI), intensive EX/RP, their combination (EX/RP + CMI), and placebo marked the start of an ongoing, 30-year collaboration between Foa and colleagues at the University of Pennsylvania and Leibowitz, Simpson, and colleagues at Columbia University. In the first collaborative study, EX/RP was composed of an intensive phase (15 two-hour sessions conducted over four weeks) and a follow-up phase (6 one-hour sessions delivered over eight weeks). EX/RP was compared to 12 weeks of CMI, EX/RP + CMI, and placebo. All active treatments were superior to placebo at posttreatment, and EX/RP was superior to CMI. The combined treatment was superior to CMI but not to EX/RP, indicating that CMI did not enhance EX/RP outcomes (Foa et al. 2005b). It should be noted, however, that the three-week intensive phase of EX/RP was completed before patients reached their maximum CMI dose, which may have obscured an additive effect of CMI.

In practice, most patients with OCD who seek treatment are already taking medication, typically an SSRI. Although SSRIs are the most common treatment for OCD (Blanco et al. 2006,

SMT: stress management training

Mancebo et al. 2006), patients on an adequate dose of an SSRI typically continue to have clinically significant OCD symptoms that affect their health, functioning, and quality of life (Blanco et al. 2006, Mancebo et al. 2006). Thus, an important question is how best to augment medication for OCD patients who have significant residual symptoms despite an adequate dose of medication. By the early 2000s, several uncontrolled, open studies had found that adding or augmenting medication for OCD with EX/RP seemed to be effective (Franklin et al. 2002, Kampman et al. 2002, Tolin et al. 2004).

The second collaborative RCT examined whether EX/RP significantly augmented the effects of medication (Simpson et al. 2008). Patients with OCD who were on a stable, therapeutic dose of SRI medication and continued to experience clinically significant OCD symptoms were randomized to either EX/RP or stress management training (SMT) while continuing their medication. EX/RP and SMT were both delivered in 17 twice-weekly, 90- to 120-minute sessions. SMT included deep breathing, progressive muscle relaxation, positive imagery, assertiveness training, and problem-solving techniques. Compared to SMT, EX/RP was associated with significantly lower OCD symptoms (Simpson et al. 2008) and improved functioning and quality of life (Huppert et al. 2009).

Another SRI augmentation strategy for OCD that had been supported in previous studies, and was widely used, was antipsychotic medication such as risperidone. Having determined that EX/RP was an effective SRI augmentation strategy that was superior to SMT, a logical next step was to compare EX/RP with risperidone. In a third collaborative RCT with Columbia University, Foa and colleagues and Simpson and colleagues compared the effectiveness of SRI augmentation with EX/RP, risperidone, or placebo among OCD patients with significant residual symptoms. The results showed that EX/RP led to significantly greater reductions in OCD symptoms and improvements in insight, functioning, and quality of life compared to risperidone and placebo (which were not significantly different from each other) at posttreatment (Simpson et al. 2013) and six-month follow-up (Foa et al. 2015). Taken together, these augmentation studies indicate that patients with OCD who are receiving an SRI but who continue to have clinically significant symptoms can benefit from EX/RP, which is superior to both SMT and risperidone as an augmentation strategy.

Although many patients experience significant reductions in their OCD symptoms following medication augmentation with EX/RP, most continue with their medication regimen. However, SRIs have many side effects that interfere with patients' quality of life. Thus, the next important question is whether patients who greatly benefited from augmentation with EX/RP can taper off their medication and maintain their gains. The fourth ongoing collaborative study seeks to determine whether people with OCD who are taking an SRI and attain wellness after EX/RP, as defined by a Yale Brown Obsessive-Compulsive Scale score $\leq$14, can then discontinue the SRI and maintain wellness over the following six months. Participants are patients who have clinically significant OCD despite receiving an adequate SRI trial (i.e., at least 12 weeks on a stable therapeutic dose). All participants receive up to 25 sessions of twice-weekly EX/RP, and those who achieve a Yale Brown Obsessive-Compulsive Scale $\leq$14 for two weeks are then randomized to either continue their SRI or taper to pill placebo over the course of four to eight weeks. Participants are followed up for six months and assessed for OCD severity, depression severity, quality of life, functioning, and medication side effects. Psychological, biological, and behavioral factors are expected to moderate the effects of SRI discontinuation on these outcomes.

Results of numerous other studies of EX/RP by Foa and colleagues have helped to refine our understanding of the efficacy of EX/RP. For example, Abramowitz and colleagues (2003) found that twice-weekly EX/RP was as effective as daily EX/RP sessions in reducing OCD symptoms at both posttreatment and follow-up. This finding has important practical implications, given that intensive treatment schedules are often difficult to implement in many mental health settings.

Another study found that EX/RP was effective with 110 clinic outpatients with OCD who were not excluded from studies for reasons of age, comorbidity, previous treatment failure, or medical problems. On average, patients in this study showed a 60% reduction in OCD symptoms, providing compelling evidence that the effects of EX/RP are not confined to the often highly selected patient samples that are treated in RCTs (Franklin et al. 2000).

In light of the large body of research on OCD treatment that has accumulated over the past 30 years, several expert consensus guidelines have been put forth and revised over the years to best reflect our current knowledge. By the mid-1990s, both EX/RP and SRIs were recognized as efficacious treatments, and many expert clinicians used EX/RP with the addition of medication only when OCD symptoms were severe (March et al. 1997). Later guidelines continued to recommend CBT (including EX/RP) and medication, alone or in combination, depending on the degree of functional impairment (Natl. Inst. Health Clin. Excell. 2006). It was concluded that "based on current evidence, ensuring access to adequate cognitive and/or behavioural therapies would currently appear to provide people with OCD with the best chance of improvement through psychological therapies" (Natl. Inst. Health Clin. Excell. 2006, p. 108).

Exposure and Response (Ritual) Prevention Mechanisms Research

In addition to EX/RP outcome research, Foa and colleagues have conducted studies aiming to improve our understanding of how EX/RP works. The application of EPT to OCD emphasizes the role of disconfirmation of feared consequences. Along with disconfirmation, the relationship between all three indicators of emotional processing (fear activation, within-session extinction, and between-session extinction) and EX/RP outcome has been examined. The interplay between OCD and depressive symptoms over the course of EX/RP is another area that has been examined by Foa and colleagues that helps shed light on our understanding of the processes of recovery from OCD.

Disconfirmation. Many OCD patients will either articulate a specific feared consequence (e.g., patients with contamination OCD may fear contracting a venereal disease after using a public bathroom) or report that they fear that they will not be able to tolerate the distress associated with exposure in the absence of rituals. Although disconfirmation of feared consequences is considered an important mechanism of EX/RP, not all OCD patients can articulate a feared consequence. For example, some patients say that "something bad will happen" if they do not ritualize but are unable to specify what they fear will happen. Still others say that their rituals are driven by the feeling that things are "just not right." This variability in individuals' ability to articulate a feared consequence as well as great variability in the types of feared consequences that patients report renders it difficult to study the role of disconfirmation in EX/RP. Moreover, although many OCD patients acknowledge that their obsessions and rituals are senseless and/or excessive, some patients firmly believe that their rituals function to prevent their feared consequences from occurring (i.e., they have "poor insight"). In a study of 20 OCD patients receiving EX/RP, Foa et al. (1999a) examined the degree to which the presence of feared consequences and poor insight impacted treatment efficacy. They found that patients who articulated feared consequences showed more improvement following EX/RP than those who did not articulate feared consequences. Additionally, patients with good insight had better outcomes than patients with poor insight. The finding that patients who articulated feared consequences showed better outcomes was consistent with previous findings in OCD patients with contamination obsessions and washing rituals (Steketee et al. 1982).

Taken together, these findings can be interpreted as supporting the disconfirmation hypothesis. First, the inability to articulate feared consequences of exposure decreases the therapist's ability

to contrive exposure exercises that provide disconfirming information, and this in turn might hinder treatment with EX/RP. Second, patients with poor insight may have particular difficulty in modifying their strong erroneous beliefs in light of the disconfirming information that presented during EX/RP. Studies that directly examine the role of disconfirmation in EX/RP are needed.

In the previously mentioned paper on failures in treating obsessive compulsives, Foa (1979) observed that patients with poor insight displayed within-session habituation but not between-session habituation, and she argued that different brain structures are involved in these two types of habituation. Given the findings from extinction studies (discussed above) suggesting that between-session habituation involves higher cognitive functioning, it may be that OCD patients with poor insight have worse EX/RP outcomes due to impaired higher cognitive processes that make it difficult to incorporate disconfirming information. Future studies should pursue this line of research with OCD.

As noted, variability in the types of feared consequences that OCD patients report makes it difficult to directly study the role of disconfirmation in EX/RP. Another approach that emerged from cognitive theories of OCD emphasizes a related but distinct set of erroneous OCD beliefs including inflated responsibility, overestimation of threat, overimportance of thoughts, importance of controlling one's thoughts, intolerance of uncertainty, and perfectionism (Obsessive Compuls. Cogn. Work. Group 1997, 2001). From a cognitive perspective, modification of these beliefs is a key mechanism of recovery from OCD (Wilhelm & Steketee 2006). Using the self-report Obsessive Beliefs Questionnaire (OBQ; Obsessive Compuls. Cogn. Work. Group 2005), Su and colleagues (Y. Su, J.K. Carpenter, L.J. Zandberg, H.B. Simpson, & E.B. Foa, manuscript under review) examined whether changes in these dysfunctional obsessive beliefs mediated symptom reduction during EX/RP. Contrary to the cognitive hypothesis, cross-lagged multilevel modeling showed that reductions in obsessive beliefs did not mediate subsequent OCD symptom reduction. In addition, reduction in OCD symptoms did not significantly mediate subsequent change in obsessive beliefs. Thus, the results suggest that changes in these beliefs are not responsible for OCD symptom improvement during EX/RP. Importantly, the erroneous beliefs assessed by the OBQ are distinct from those emphasized in EPT. Thus, the results of this study do not shed light on the role of the pathological, erroneous perceptions of individuals with OCD emphasized in EPT (the exaggerated probability and cost of harm, and the likelihood of distress and the urge to ritualize persisting indefinitely), which remains a fruitful area for future research.

Fear activation and within- and between-session extinction. To evaluate whether the proposed indicators of emotional processing are related to EX/RP outcome, Kozak et al. (1988) measured fear levels during session 6 and session 14 of EX/RP, using both self-report and physiological assessments, in a study of 14 OCD patients. Consistent with EPT, fear activation during in vivo exposure (self-report and physiologic) and between-session extinction (self-report only) was associated with superior posttreatment OCD symptoms. Although significant within-session extinction was evident, this reduction in fear was not correlated with outcome. These findings are consistent with the findings of mechanisms during PE described previously.

The important role of between-session extinction was demonstrated in an experiment designed to examine the impact of distraction versus attention focusing during exposure to contamination in a sample of 16 OCD patients with washing rituals (Grayson et al. 1982). Using a crossover design, some patients received exposure with instructions to focus their attention on the contaminated object they touched on the first day followed by exposure with instructions to engage in a distraction activity (video game) on the second day; the remaining patients were instructed to distract themselves on the first day and to focus on the second day. Within-session extinction of heart rate and subjective anxiety was observed under both conditions. However,

return of subjective fear at the beginning of the next session was significantly lower for patients who received the attention condition first than for those who received the distraction condition first, indicating that attending to the feared obsessional stimuli was associated with greater between-session but not within-session extinction.

In an attempt to develop a model that could predict which patients would do well in EX/RP, Foa et al. (1983) examined the relationships between several pretreatment variables, therapy process variables, and OCD outcomes among 50 patients who received EX/RP. Consistent with EPT, greater within- and between-session extinction was associated with superior outcomes at posttreatment. Pretreatment depression and fear activation during the first exposure sessions were both negatively related to outcome. Path analysis indicated that the relationship between depression and OCD outcomes was mediated by fear activation during the first exposure. Fear activation, in turn, was negatively related to within-session extinction. And finally, within-session extinction was associated with outcome via between-session extinction. These findings are partly consistent with those reported previously for PE in that between-session extinction was associated with better outcomes, whereas within-session extinction was not. The finding that depression impedes the efficacy of exposure therapy by interfering with extinction learning was consistent with the results of a previous study by Foa et al. (1982).

Comorbid depression. Numerous studies have found that EX/RP leads to a significant improvement in both OCD and comorbid depression (e.g., Abramowitz et al. 2002), even without the addition of adjunctive depressive treatment such as medication or cognitive therapy. For example, Foa et al. (1992) found that contrary to expectation, treating OCD patients with imipramine prior to initiating EX/RP did not enhance OCD outcomes. Both OCD and depressive symptoms were significantly reduced in participants following EX/RP, regardless of whether they received imipramine or placebo. Although fewer studies have examined how changes in OCD and depressive symptoms are related to each other during treatment, the research to date suggests that reductions in OCD symptoms account for a greater proportion of reductions in depressive symptoms than the reverse. In a recent study of 40 OCD patients receiving EX/RP, Zandberg et al. (2015) used lagged multilevel mediational analysis to examine the temporal relationship between changes in OCD symptoms and changes in depressive symptoms. The findings indicated that reductions in OCD symptoms fully mediated the subsequent change in depressive symptoms, accounting for 65% of the variance in depressive symptoms. In contrast, changes in depressive symptoms only partially mediated subsequent change in OCD symptoms, accounting for 20% of the variance in outcome. Thus, it seems that there is a reciprocal relationship between OCD and depressive symptoms, with changes in OCD symptoms driving changes in depressive symptoms more than changes in depression drive changes in OCD symptoms.

THE INTERRELATIONSHIPS AMONG THEORY, RESEARCH ON TREATMENT EFFICACY, AND RESEARCH ON TREATMENT MECHANISM

In this review we have attempted to demonstrate the intricate interrelationships among basic research, conceptualization of psychopathology, treatment development, treatment outcome research, and treatment mechanism research; the interactions among these areas of study further enrich our knowledge about psychopathology and treatment. See **Figure 1** for a schematic model of the reciprocal relationships among these areas of investigation. By describing the work of Foa and her colleagues in anxiety disorders, we have demonstrated how EPT has generated hypotheses about the psychopathology of PTSD and OCD that have informed the

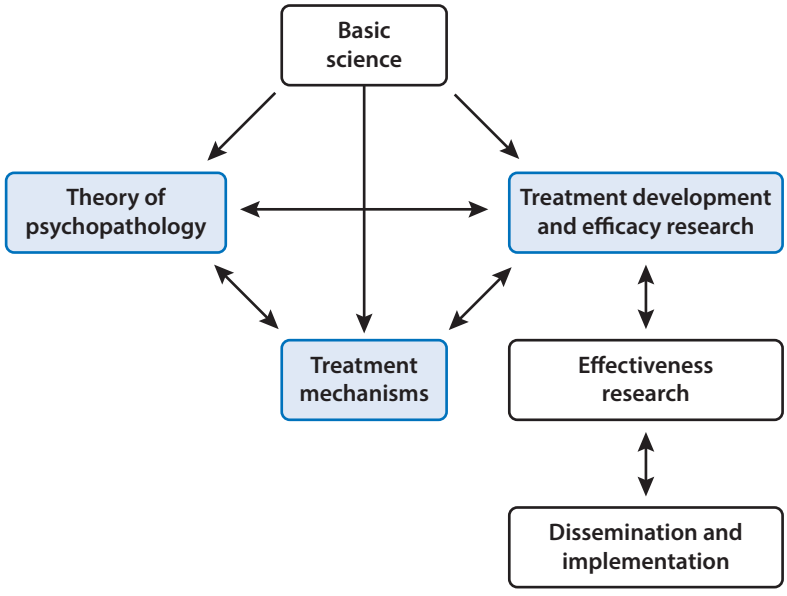

Figure 1

Schematic model of the interrelationships among developments in research, theory, and the application of exposure treatment. Shaded components in the model are the focus of the current review.

development and refinement of specific treatment protocols for these disorders: PE and EX/RP. After theoretically driven treatment protocols are developed, the next step is to evaluate their efficacy. Once evidence for a treatment's efficacy has accumulated, studies of the mechanisms involved in the reduction of the targeted psychopathology can be conducted and in turn inform the theory and further refine the treatments. An example of this process is the study of within- and between-session extinction during PE. The finding that within-session extinction is unnecessary for recovery from PTSD has led to studies examining the efficacy of shorter exposure sessions and to studies focusing on the critical role of cognitive changes during treatment.

FUTURE DIRECTIONS

Although exposure therapy has been studied extensively in the treatment of anxiety disorders including PTSD and OCD, important areas are under ongoing investigation. One pressing question is how to increase the immediate and long-term efficacy of treatment. As noted previously, despite its success, some patients who receive exposure therapy do not improve, and even among patients who do improve, many remain symptomatic. Findings from the fear extinction literature may have important implications for the practice of exposure therapy. In noting that some patients fail to benefit from exposure therapy and many remain symptomatic, Foa & Kozak (1997) argued that the apparent "efficacy ceiling," the leveling off of response rates to empirically tested cognitive and behavioral treatments, may be due to "an alienation from psychopathology and experimental psychology" (p. 606). They suggest that researchers have not exploited findings from basic research in psychopathology.

Motivated by Foa & Kozak's (1997) plea to increase communication between basic researchers and clinical researchers, Gillihan & Foa (2011) integrated knowledge derived from the experimental literature on extinction learning and knowledge of mechanisms emerging for exposure

therapy. In their review, Gillian & Foa reexamined EPT by considering three core suppositions of the theory—activation, within-session habituation, and between-session habituation—in light of results from experimental extinction-learning and extinction-retention paradigms. They concluded that initial fear activation is an important factor in achieving extinction of conditioned fear as well as reducing pathological anxiety after exposure therapy. Indeed, behavioral, neural, and pharmacological data converge to indicate that the fear structure must be activated in order for the conditioned fear to be extinguished. These consistent findings from diverse domains can serve as a foundation for further research that will enhance our understanding of the basic mechanisms underlying fear extinction and exposure therapy. Of particular interest is the finding that activity in specific neural regions, namely the medial prefrontal cortex, is necessary for the maintenance of extinction learning across extinction-training sessions. These results highlight how basic research and treatment research can increase our knowledge in both domains.

As noted previously, not all patients complete exposure therapy, and not all patients respond to treatment sufficiently. Thus, there is room for improvement in terms of treatment efficiency and efficacy. Basic research suggests that certain pharmacologic agents may enhance the extinction of conditioned fear, which suggests that they may help augment exposure therapy. Specifically, cognitive enhancers hypothesized to boost extinction learning (e.g., D-cycloserine) have now been examined in many studies and hold promise as a means of improving treatment response and shortening treatment duration. There is evidence that D-cycloserine can augment the efficacy of exposure therapy with various anxiety disorders (see Bontempo et al. 2012, Norberg et al. 2008, Rodrigues et al. 2014). However, the results of clinical studies have been mixed, particularly in PTSD, where some studies have failed to show D-cycloserine effects (e.g., de Kleine et al. 2012, Litz et al. 2012, Rothbaum et al. 2014). Other agents thought to enhance extinction learning that have now been examined in human studies include yohimbine (Smits et al. 2014), methylene blue (Telch et al. 2014), and estrogen (Milad et al. 2010). Much additional research is needed to better understand the effects of these agents on exposure therapy and the mechanisms involved in these effects. The clinical implications of positive results are profound: Patients with anxiety-related disorders may experience more relief and/or they may experience relief more quickly. Of particular importance is the possibility that people who might otherwise drop out before experiencing the effectiveness of the treatment might have faster gains that encourage them to complete the treatment and reach full remittance of symptoms when using these agents.

Relapse following exposure therapy—or the laboratory analogue, return of fear after extinction training (i.e., reinstatement, renewal, and spontaneous recovery)—suggests that exposure does not eliminate or modify pathological fear responses but rather creates new learning that inhibits activation of pathological fear structures. However, evidence now suggests that pathological fear responses may be changed if corrective information is presented during the reconsolidation period when the retrieved information is labile (see Schiller et al. 2010). These important findings suggest that new information can be incorporated into old memory structures when the memory is malleable during the reconsolidation window. Although this hypothesis requires further investigation, an important challenge for researchers is to explore whether these results from basic research can be translated to enhance exposure therapy for anxiety disorders.

Another exciting area of research is examining the breadth of exposure therapy efficacy. In a variant of PE that was found to be helpful with complicated grief, individuals recount the story of the death using imaginal exposure and conduct grief-related in vivo exposures in a fashion similar to that of PE. Exposure therapy is more effective than interpersonal therapy (Shear et al. 2005), cognitive therapy (Boelen et al. 2007), and cognitive-behavioral therapy without exposure (Bryant et al. 1999) in the reduction of grief-related symptoms. Exposure has also been used in the treatment of depression to target experiential avoidance. In Adele Hayes's exposure-based cognitive

therapy for depression, patients are encouraged to approach negative thoughts and emotions associated with their depression through activities such as writing essays about their depression and recounting these essays in therapy sessions. In a preliminary open treatment trial, exposure-based cognitive therapy effectively reduced depressive symptoms, and symptom reduction was negatively associated with avoidance (Hayes et al. 2005). Exposure therapy has even been successfully applied to the treatment of problem gambling by helping patients confront external and internal gambling triggers and implement response prevention to reduce the urge to gamble (Smith et al. 2015). Taken together, these studies illustrate that exposure techniques can have therapeutic applications beyond the reduction of pathological anxiety. These studies suggest that exposure therapy may be an effective treatment when pathological emotions that arise from erroneous perceptions are maintained through cognitive and behavioral avoidance because avoidance prevents access to, and integration of, disconfirming information.

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Errata

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