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Inhibitory Learning for Anxiety-Related Disorders

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This article reviews the articles in this issue that describe the strategies derived from the inhibitory learning model as applied to exposure therapy for anxiety disorders. The major principles of inhibitory learning are to create and strengthen nonthreat associations in memory (largely by engaging prefrontal cortical regions), and to effectively retrieve those nonthreat associations in the long term. Several case vignettes are provided that demonstrate how the principles of inhibitory learning (which include maximizing expectancy violations, limiting distraction, fear antagonistic actions, deepened extinction, elimination of safety behaviors, occasional reinforced extinction, increasing variability of exposures and offsetting reinstatement and context renewal effects) can be applied in clinical practice.

This special issue of *Cognitive and Behavioral Practice* provides excellent examples of the evaluation and implementation of the principles of *inhibitory learning* (Craske et al., 2008; Craske, Treanor, Conway, Zbozinek, & Vervliet, 2014). First, Frank and McKay (2019) describe numerous elements of inhibitory learning in the context of misophonia treatment. Krompinger, van Kirk, Garner, Potluri, and Elias (2019) provide case examples of the inhibitory learning principles of *occasional reinforced extinction* and *expectancy violation* in a residential treatment program for obsessive-compulsive disorder (OCD). Knowles and Olatunji (2019) discuss how to *maximize variability* in exposure. Blakey and Abramowitz (2019) describe the *removal of safety behaviors* and the *optimization of post-exposure retrieval cues*. de Jong, Lommen, de Jong, and Nauta (2019) review the use of *multiple contexts* and *retrieval cues* in exposure therapy. Marks, Walker, Ojalehto, Bedard-Gilligan, and Zoellner (2019) describe the process of *affect labeling* in the context of posttraumatic stress disorder (PTSD) treatment. McGuire and Storch (2019) address the implementation of multiple inhibitory learning principles for child and adolescent patients with anxiety-related disorders. Finally, Hoffman and Chu (2019) provide a critical analysis of *safety vs. coping behaviors* and their beneficial vs. deleterious effects in exposure. The aim of this paper is to review how these excellent articles illustrate the principles of inhibitory learning, and to provide additional clinical ideas and vignettes for the practicing clinician.

Keywords: anxiety; OCD; PTSD; cognitive-behavioral therapy; exposure therapy

Inhibitory Learning as a Model for Maximizing Exposure Therapy

Exposure therapy is based on the principles of fear extinction. Learned fear, such as that seen in many anxiety-related disorders, is based on associations between a conditioned stimulus (CS) and an unconditioned stimulus (US). Over the course of exposure, the CS is presented without the US (a CS-noUS pairing) and the fear is thereby extinguished. It is well established that fear responses are largely mediated by activity in limbic and paralimbic structures such as amygdala (e.g., Dilger et al., 2003), and that prefrontal cortical (PFC) regions can serve to inhibit limbic responsiveness (Delgado, Nearing, Ledoux, & Phelps, 2008). During exposure therapy, limbic regions initially become active (Sehlmeyer et al., 2009; Sotres-Bayon, Cain, & LeDoux, 2006); over the course of exposure, PFC regions are also engaged, including lateral (LaBar, Gatenby, Gore, LeDoux, & Phelps, 1998; Molchan, Sunderland, McIntosh, Herscovitch, & Schreurs, 1994; Yaguez et al., 2005) and medial (Milad & Quirk, 2002; Phelps, Delgado, Nearing, & LeDoux, 2004; Quirk, Garcia, & Gonzalez-Lima, 2006; Quirk, Russo, Barron, & Lebron, 2000; Yaguez et al., 2005), structures, which likely play an inhibitory role (Delgado et al., 2008). In exposure therapy, our aim at a biological level is to maximize PFC activation in such a manner as to strengthen nonthreat associations and attenuate the limbic-mediated threat associations. Though the initial CS-US pairing is never eliminated from long-term memory, over time, these new PFC-mediated CS-NoUS associations become the dominant response—a process known as *inhibitory learning*. It is also critical to ensure that these new neural pathways remain the dominant response over time (i.e., to prevent return of fear). This requires that the inhibitory associations are not only learned, but that they are successfully *retrieved* from long-term memory storage.

The principles of the inhibitory learning model have been summarized elsewhere (Craske et al., 2008; Craske et al., 2014; Weisman & Rodebaugh, 2018). Offered as an alternative to the emotional processing model (Foa & Kozak, 1986), the inhibitory learning model suggests several modifications to exposure therapy, derived largely from animal models of fear extinction and tested (to varying degrees) in human laboratory settings (e.g., Bouton, 1993), that aim to maximize PFC engagement and thereby create new neural pathways that will successfully compete with those from limbic regions. Two major processes are suggested. First, several strategies are suggested that purport to *develop nonthreat associations*. In other words, these strategies are designed to help the patient learn that the feared situation, object, or activity (CS) does not necessarily predict an aversive outcome (US). Second, once new inhibitory learning has taken place, strategies are suggested that aim to *enhance retrieval* of these newly learned associations. In this article I will briefly review several of these inhibitory learning strategies, and present hypothetical case vignettes to illustrate how they might be employed in clinical practice.

Inhibitory Learning Strategies to Develop Nonthreat Associations

The first set of strategies from the inhibitory learning model seeks to maximize nonthreat associations. That is, the broad aim is to help the patient learn that the CS does not necessarily predict the US. In exposure therapy, this is done by creating CS-noUS pairings that, over time, override the CS-US association. In the case of a dog phobia, for example, the patient's initial expectancy might be that the dog (CS) will bite him/her (US). By repeatedly presenting a dog that does not bite (CS-noUS), a new lesson is learned that competes with the CS-US pairing in memory. Strategies to develop these nonthreat associations include *maximizing expectancy violations, limiting distraction, fear antagonistic actions, deepened extinction, elimination of safety behaviors,* and *occasional reinforced extinction.*

Maximizing Expectancy Violations

McGuire and Storch (2019) asked a child with OCD to estimate how long it would take him (2 minutes) to stab his mother if he held a sharp object in her presence. They then adjusted the exposure session to make sure that the exposure lasted long enough for the feared consequence to occur (according to the patient's expectations). This strategy is based on Rescorla and Wagner's (1972) learning theory, which posits that the success of extinction training is the result of a *mismatch* between expectations and experience. According to this model, it would be reasonable to predict that the success of exposure is directly proportional to the degree of expectancy violation (e.g., Deacon et al., 2013). The clinical aim, therefore, is to maximize the "surprise" experienced by the patient. One relatively straightforward way to do this is to ensure that exposures are long enough to violate the expectancy. Clinicians using the emotional processing model (Foa & Kozak, 1986) have recommended long exposures to allow sufficient time for within-session habituation. However, as noted by Craske et al. (2008), clinical research raises questions about the necessity of long exposures and within-session habituation for fear reduction. Some older research shows that long (e.g., 2 hours) exposures were more effective than briefer exposures for clients with agoraphobia (Stern & Marks, 1973) and OCD (Rabavilas, Boulougouris, & Stefanis, 1976). However, more recent research suggests that exposure therapy might be just as effective when exposures are short and there is not sufficient time for within-session habituation (e.g., Nacasch et al., 2015). In an analog sample, the length of exposure did not seem to matter, so long as there was sufficient time for expectancy violation—that is, as long as the exposure is long enough for the patient to be surprised (Baker et al., 2010).

Clinical Example

Phil, a patient (P) with dog phobia, fears that if he were to pet a dog, the dog would bite him. The therapist (T) has brought a dog in for today's session.

T: Let's just have you pet the dog for a while and then we'll see whether it turns out the way you fear it will.

P: OK. [*Josh pets the dog; the remaining discussion continues as he pets it*]

T: So what are you noticing as we do this?

P: I notice I'm feeling scared.

T: OK. What's your fear telling you about this?

P: It's telling me the dog is going to bite me.

T: OK. When is that bite likely to happen? Right now?

P: Well, maybe right now and maybe later.

T: Keep petting. How much later? Like an hour from now?

P: No, I think that if the dog is going to bite me, it'll happen within like the first ten minutes.

T: OK, then let's make a point of staying in contact with the dog for at least ten minutes to give it a really good test.

Limiting Distraction

Relatedly, inhibitory learning theory suggests that patients should limit the use of distraction as a coping

technique during exposure therapy. Research suggests that distraction is less effective during exposure than is focusing on the exercise, including the feared stimulus and the feeling of fear (Grayson, Foa, & Steketee, 1982; Kamphuis & Telch, 2000; Telch et al., 2004), though results have been mixed (e.g., Oliver & Page, 2008). From an inhibitory learning perspective, distraction has several adverse effects. First, it breaks up the exposure, so that instead of one long exposure session, the patient is actually experiencing several briefer exposure sessions (which are potentially not long enough to violate expectancies, as discussed above), punctuated by periods of distracted attention. Second, distraction reduces the patient's awareness of the CS, and the relationship between the CS and nonoccurrence of the US (Craske et al., 2014). In everyday language, distraction impairs the patient's ability to recognize that the disaster is not occurring in the presence of the feared situation or stimulus.

Clinical Example

Catherine, a patient with OCD, fears that she will be overcome with the urge to stab someone and will lose control of herself (despite the fact that she has no history of violence). For today's exposure, the therapist has brought a large kitchen knife into the session.

T: For this exercise, I'd like you to hold this knife and point it at me.

P: OK. [*points the knife at the therapist*]

T: Now, as you do this, I want you to think about stabbing me. Can you do that?

P: Yeah, I can imagine that.

T: Good. Imagine the knife going right into my belly and imagine that there's blood all over the place.

P: OK. [*a minute passes*] I'm still feeling nervous about it. Where do you think that comes from? I mean, why does this bother me so much?

T: There are some really good reasons which we can talk about later in our session. But right now what I'd like you to do is really focus on this exposure. Can you bring back the image of stabbing me in the belly, and keep feeling that fear?

Fear Antagonistic Actions

As proposed by Weisman and Rodebaugh (2018), it may be useful to encourage patients to engage in fear antagonistic actions: that is, behaving as if they are unafraid. Research with patients with specific phobia (heights) as well as students with public speaking fears demonstrates that exposure therapy is more effective when patients are instructed to engage in "brave" behaviors such as running toward the balcony (Wolitzky & Telch, 2009) or deliberately stuttering during a speech (Nelson, Deacon, Lickel, & Sy, 2010). These actions serve to maximize the mismatch between expectancies and outcomes.

Clinical Example

James, a patient with social phobia, is fearful that he will look foolish in public and that others will think badly of him if he does. For exposure, the therapist has brought James outside to a busy sidewalk. The aim in this exposure is not simply to expose James to the possibility of public scrutiny, but to encourage him to engage in a fear-antagonistic action of engaging in a "foolish" behavior.

T: You've done a great job with exposures so far, like striking up conversations with strangers.

P: Yeah, I feel like that's gotten a lot easier.

T: Right. And so far, all of those interactions have gone pretty well, haven't they?

P: Yes. I didn't screw up like I thought I was going to.

T: That's great. Now I want to see if we can get you more comfortable with the idea of looking foolish in front of people. Here's what I'm thinking: I want to have you deliberately look foolish so that you can learn that that's OK too.

P: That idea really makes me nervous.

T: Yes, I thought it would. And that's exactly why it's important. Your brain is learning that you're OK when the social interaction goes smoothly; but it hasn't learned yet that you're OK even when you look foolish. Does that make sense?

P: Yeah, I see what you mean.

T: So here's what I have in mind. You and I are going to stand here on the sidewalk and sing a song. How about *The Star Spangled Banner*? I'll do it with you, at first. Shall we begin?

P: OK. [*therapist and patient sing*]

T: Let's go a little louder. Let's act like we really don't care who's listening.

P: OK. This is really scary to me.

T: I know, and you're doing great. Let's do it together. [*therapist and patient sing loudly*] Terrific job. Now I'm going to stop singing and I just want you to solo. That way it's even weirder.

P: Yeah, it's definitely weirder if it's only one person.

T: So that's a really powerful exposure for you. Ready to start?

P: OK. [*sings alone*]

Deepened Extinction

The concept of "deepened extinction" (Rescorla, 2006), or "multiple conditioned excitors" (Craske et al., 2008), refers to the simultaneous presentation of multiple CSs, which have previously been extinguished in isolation. When multiple CSs are presented, the nonoccurrence of the US results in an even greater expectancy violation due to the combined associative strength of the CSs (Rescorla & Wagner, 1972). Put more plainly, when multiple feared stimuli are presented at the same time ("piled on"), we maximize the patient's ability to be surprised by the outcome.

Clinical Example

Fiona suffers from PTSD after a motor vehicle accident. In previous sessions, the therapist had worked with Fiona on two separate exposures. First, they practiced *in vivo* exposure in which Fiona returned to the site where her accident took place. Second, the therapist conducted imaginal exposure, in which Fiona vividly recalled the details of the accident. They also listened to audio clips online of car crash sounds. For today's exposure, the therapist has accompanied Fiona to the site of the accident.

T: You've done a great job so far with our exposures. I really get a sense that you're starting to overcome your fears.

P: Yeah, I think so too. They were really scary at first, but after a while they didn't seem so bad.

T: Right. That's you getting stronger, and your fear getting weaker. Now I want to try combining some of the exposures you've done. Did you download the car crash audio files to your phone like we discussed?

P: I did, and I have my phone right here.

T: OK, great. What I have in mind for today is for you to stand here at the scene of the accident, just like you've done before. But this time I want to have you listen to the car crash sounds too, and remember the accident itself. Feel up to it?

P: Sounds scary, but yeah, I think I can do it.

T: I bet you can. OK, when you feel ready, put your earbuds in and just play the sound over and over while you look at the spot where the accident took place.

P: OK [*plays the audio file*]. This feels really scary.

T: It's a lot more real this way, isn't it? You're doing fine.

Eliminating Safety Behaviors

Blakey and Abramowitz (2019) emphasize the importance of stopping safety behaviors, although Hoffman and Chu (2019) point out that safety and coping behaviors are not necessarily the same. Perhaps the most obvious example of safety behavior is the compulsions (e.g., hand washing, ordering, checking) exhibited by patients with OCD. Safety behaviors are not limited to OCD, however. Indeed, many anxiety-related disorders are associated with subtle behavioral adjustments that serve to make the person feel safer (Kamphuis & Telch, 2000; Wells et al., 1995). From a cognitive perspective, when safety behaviors are employed during exposure (for example, a patient with OCD washing his/her hands, or a patient with social phobia standing in an empty corner at a party), the nonoccurrence of the US is attributed not to the *unconditional safety* of the situation, but rather to the *conditional safety* of the behavior. In other words, safety behaviors contribute to learning things like "Yes, I used a public bathroom, but I only survived because I washed my hands."

Several studies demonstrate that exposure therapy is more effective when patients are encouraged not to engage in, or have access to, safety behaviors (Kim, 2005; Morgan & Raffle, 1999; Powers, Smits, & Telch, 2004; Salkovskis, 1999; Sloan & Telch, 2002; Wells et al., 1995); safety behaviors also appear to decrease objective performance during public speaking for socially anxious clients (Rowa et al., 2015). The deleterious effects of safety behavior during exposure have been demonstrated in children as well (Hedtke, Kendall, & Tiwari, 2009). It is noted that some (e.g., Rachman, Radomsky, & Shafran, 2008) have suggested that judicious application of safety behaviors might help, rather than detract from, exposure. To this point, some studies of fearful student samples have failed to show deleterious effects of safety behaviors (Deacon, Sy, Lickel, & Nelson, 2010; Hood, Antony, Koerner, & Monson, 2010; Milosevic & Radomsky, 2008; Rachman, Shafran, Radomsky, & Zysk, 2011; Sy, Dixon, Lickel, Nelson, & Deacon, 2011), and asymptomatic students report that they find exposure more acceptable when they are allowed to use safety behaviors (Levy & Radomsky, 2014), although students with claustrophobic

fears do not find exposure with safety behavior to be more acceptable than exposure alone (Deacon et al., 2010). To date, no studies have demonstrated an actual improvement in the efficacy of exposure therapy with the addition of safety behaviors (see Meulders, Van Daele, Volders, & Vlaeyen, 2016, for review).

Clinical Example

Eleanor, a patient with panic disorder and agoraphobia, has come to a shopping mall, accompanied by her therapist, where they plan to have Eleanor walk through a crowded space. Before entering the mall, they are sitting in Eleanor's car to discuss the plan.

T: One thing that's really important is to get rid of safety behaviors. As you might remember from our previous conversations, safety behaviors are all of those things, big or little, that you use to help you feel better, or that you think might be keeping you safe. What kinds of things can you envision having with you in the mall that would be safety behaviors?

P: Well, I have my bottle of Xanax here. I don't take it much, but just having it makes me feel better, like I can take one if I start to panic.

T: Yes, that's a good example of a safety behavior. We've talked a little about "yes-but's"—where your brain learns the wrong message and attributes your success to the wrong thing. So let's say you take your Xanax in with you. What will the "yes-but" be?

P: I guess it would be "Yes, I made it through the mall, but that's only because I had my pills?"

T: Exactly. And we really want to eliminate those "yes-but" explanations. So for today's exercise, I'm going to recommend that you leave the bottle in the car, instead of taking it into the mall. Do you get why I'm recommending that?

P: Yeah, I need to learn it's just safe and that it's not because of the pills.

T: Right. So let's leave the pills here in the car. What else?

P: Hmm, I'm not sure I have anything else with me that makes me feel safe.

T: How about your cell phone? Does having that with you make you feel safer, or make you feel like you could use it to stop something bad from happening?

P: Oh yeah, I feel like I'd be totally screwed without my cell phone. I mean, if I start freaking out I could call someone, or if I started having a heart attack I could call 911.

T: So what do you think I would recommend here?

P: You'd recommend I leave it behind. That's scary.

T: Yes, it's scary because you've come to rely on it so much. But through this exercise we really want your brain to see that it's not the cell phone that's keeping you safe. Can we leave it behind, even though that feels scary?

P: OK.

T: Now, I'm curious: Is having me there also a safety behavior? That is, is my presence in the mall going to make you feel safer?

P: Oh, definitely. I mean, if I started to have a panic attack you'd be able to talk me down. And you could help me get out of the mall if I needed to.

T: And so . . .

P: I should do it without you?

T: My thoughts exactly. How about this: I'll come in with you and we'll do the exercise together, but then after you start feeling a little stronger, at a time we agree on, I'll leave and have you stay in the mall without me there. Sound OK?

P: OK.

Occasional Reinforced Extinction

Krompinger et al. (2019) provide examples of *occasional reinforced exposure*, such as an OCD patient coming across seemingly fear-confirming evidence online. These reinforcements occurred accidentally; by contrast, McGuire and Storch (2019) describe the deliberate presentation of "disasters," such as having a parent report a stubbed toe while the child is refraining from checking behaviors. Occasional reinforced extinction refers to occasionally allowing the CS and US to be paired during extinction (Woods & Bouton, 2007). This is perhaps the most clinically counterintuitive aspect of inhibitory learning theory: traditionally, exposure is thought to be successful when the CS is repeatedly presented in the *absence* of the US (e.g., Foa & Kozak, 1986). The principle of occasional reinforced extinction, conversely, suggests that, when prudent to do so, we arrange for the "disaster" to occur occasionally throughout the process of exposure. The inhibitory learning model posits that occasional reinforced exposure heightens the expectancy violation effect because CS-US pairings (reinforced extinction) are associated, through repeated exposure exercises, with both further CS-US pairings and with CS-noUS pairings

(Craske et al., 2014). In other words, the patient learns that "disastrous" exposure may be followed by either another disaster or by no disaster, resulting in a decreased expectancy that all exposures will be disastrous. I would further suggest that exposure to the "disaster" serves to diminish the threat value of the US, thereby teaching the patient that even if the "disaster" occurs, the results are not necessarily catastrophic.

Clinical Example

James, the patient with social phobia, successfully completed the previous exposure to singing on a busy sidewalk. To his surprise (expectancy mismatch), no one ridiculed him. In fact, no one seemed to notice. That is, the CS (singing) did not result in the US (ridicule). Here, the therapist introduces the US into the exposure by bringing in two graduate students to serve as confederates (C1 and C2).

T: Great job with that last exposure, James. What surprised you about it?

P: I think the thing that surprised me most was that no one even paid that much attention to me.

T: Right. The thing your brain tells you is going to happen isn't really all that likely.

P: Yeah, my brain thought it was going to be a lot worse than it actually turned out.

T: I want to up the ante a little bit now. A big piece of your fear is that someone will ridicule you. We've seen that this isn't very likely, but I'd like to see if we can get you less afraid of ridicule too, just like we got you less afraid of singing.

P: So you think I should get ridiculed?

T: Yes, exactly—at least, in a controlled way. I want to do the same exercise again, but this time, while you're singing, I'm going to ask my students here to heckle you.

P: Wow, that's a lot scarier than the last one.

T: Yes, I'm sure it is—because now we're kind of making the fear come true, at least as an exercise. But can you understand why I'd want to do this?

P: Yeah, you want me to be less afraid of being ridiculed.

T: Right. I'd like to see if we can get you to the point where even if someone makes fun of you, it's not that big a deal to you. It can just roll right off you rather than stick to you. Are there some kinds of heckling that are worse than others?

P: Yeah. I think that if someone just didn't like my singing, that would be kind of bad—maybe a 70—but if someone actually said I looked stupid or foolish or something like that, that would be a lot worse, like a 90.

T: OK, so we can grade it accordingly. Can you sing *The Star Spangled Banner* again, and this time we'll have some heckling, starting with just not liking your singing?

P: OK. [*sings*]

C1: You sound awful!

C2: You stink!

T: Keep singing.

C1: Learn to sing!

C2: Ow, my ears!

T: OK, let's pause for a moment. What did you experience, James?

P: That was pretty scary.

T: It wasn't nice hearing them say those things.

P: No. But I guess I handled it.

T: Right, you kept on singing anyway. Let's try again but this time we'll have our helpers say that you look foolish, OK?

P: OK. [*sings*]

C1: What an idiot!

C2: Are you crazy or something?

T: Keep singing.

C1: You're making a fool out of yourself!

T: OK, let's pause again. James, what was that like for you?

P: [*chuckles*] I guess it wasn't so bad. I mean, at first I felt my fear rising up, but then it just started to seem a little silly.

T: Right, I get that. It is a little silly. And were you able to treat what they were saying as just some silly words, rather than something you need to take to heart?

P: I think I was.

Affect Labeling

As Marks, Walker, Ojalehto, and Zoellner (2019) suggest, verbally labeling emotions (e.g., "fear," "disgust") during exposure sessions may engage the PFC and allow for more in-depth processing. The process of affect labeling is thought to increase inhibitory control by the PFC over limbic regions. Difficulty labeling emotions (also termed *alexithymia)* is a phenomenon seen across diagnoses (Taylor, 1984), including anxiety disorders (de Berardis et al., 2008; Izci et al., 2014), OCD (de Berardis et al., 2005), and PTSD (Frewen, Dozois, Neufeld, & Lanius, 2008), and is associated with poorer decisions in a simulated gambling task (Aite et al., 2014; Kano, Ito, & Fukudo, 2011), greater impulsivity when experiencing negative emotions (Shishido, Gaher, & Simons, 2013), and impaired processing of traumatic experiences (Mazzeo & Espelage, 2002; Ogrodniczuk, Joyce, & Abbass, 2014), all potentially consistent with diminished regulatory capacity of the PFC. Affect labeling appears to generally decrease emotional experience (Frattaroli, 2006), and studies of exposure therapy suggest that affect labeling during exposure may facilitate the effects of exposure, at least in terms of psychophysiologic responding (Niles, Craske, Lieberman, & Hur, 2015), though it is not clear whether the results are specific to affect labeling or to verbal behavior in general during exposure.

Clinical Example

Fiona, the patient with PTSD, is engaging in imaginal exposure to her motor vehicle accident.

P: I'm sitting in the wreck of my car. There's blood gushing from my forehead. I'm trapped in the car and I can see there are people standing on the sidewalk looking at me.

T: OK, you're doing great. Can you give me a distress rating right now, from 0–100?

P: About an 85.

T: 85, OK. What emotion are you experiencing right now?

P: I just feel terrible.

T: Terrible in what way?

P: Just like I'm never going to get out of this car and it's going to explode.

T: Yes, you're thinking that. If you had to put a label on this feeling, what would it be?

P: I don't know; just awful. My heart's racing.

T: Your heart is racing and you're thinking about dying. Would "fear" be an appropriate word to use here?

P: Yes, I guess so.

T: Can you try that on? Let's see if it rings true for you. Try "I'm trapped in the car and I think it's going to explode and I feel afraid."

P: I'm trapped in the car and I think it's going to explode and I feel afraid. Maybe "terrified" is a better word. But what about those people standing there? Why aren't they helping?

T: Maybe you're feeling something else too, besides terrified?

P: Yeah, like what the heck is wrong with them?

T: Perhaps "angry" would be the right word here?

P: Yeah. Terrified and angry. That's what I'm feeling.

T: OK, let's stay with that.

Strategies to Enhance Retrieval of Newly Learned Associations

The second set of strategies seeks to maximize the retrieval of nonthreat associations from memory once they have been learned. Once a CS-noUS pairing has been created, the aim is to help the patient to retrieve this pairing from memory during fear-eliciting situations. In the case of dog phobia, for example, during exposure the patient has learned that a dog (CS) is unlikely to bite him/her (noUS). The aim now is to ensure that this CS-noUS pairing becomes the dominant pathway the next time he/she encounters a dog. Strategies to enhance CS-noUS retrieval include *increasing variability of exposures* and *offsetting reinstatement and context renewal effects*.

Increasing Variability of Exposures

In general, variability of training is thought to maximize generalization of learning (Schmidt & Bjork, 1992), and the inhibitory learning model suggests several ways to increase the variability of exposures. One such method is to space the scheduling of exposure trials. Retrieval of information from memory is enhanced when an *expanding spaced* schedule of training, rather than massed training, is used (Bjork & Bjork, 1992). That is, rather than conducting learning trials all at once, or adhering to a fixed interval between learning sessions, retrieval of the learned information is strongest when the interval

between sessions gradually increases. Results from exposure therapy have been mixed, though in one study of spider-fearful students, participants receiving an expanding spaced schedule of exposure over 1 week showed less return of fear (i.e., better extinction memory retrieval) at follow-up than did participants who received the same amount of exposure massed within 1 day (Rowe & Craske, 1998). Clinically, this could be accomplished by scheduling repeated exposure sessions with an increasing interval between sessions.

Another method of increasing variability, as described by Knowles and Olatunji (2019), is to mix up the order of task difficulty. Retention of learned material seems to be optimized when practice is variable, rather than adhering to a fixed order (Magill & Hall, 1990). In traditional exposure therapy, the therapist and patient construct an exposure hierarchy, assign a subjective units of discomfort (SUD) rating to each item, and then proceed in a linear fashion, starting with less distressing exposures and working their way up to the most distressing exposures. The inhibitory learning model, however, suggests that exposure might be more effective when stimuli are presented in a random or quasi-random order, rather than progressing in linear fashion (Kircanski et al., 2012; Lang & Craske, 2000). As Knowles and Olatunji (2019) point out, the patient's ability to engage in variable, rather than linear, exposures may depend on his/her capacity to tolerate distress.

Clinical Example

Catherine, the patient with OCD, is fearful that she will be seized with an uncontrollable urge to stab someone, and avoids sharp objects in response to this fear. The therapist and Catherine have developed an exposure hierarchy, ranking each item according to SUD rating. Rather than progress in a linear fashion, the therapist will vary the order of exposures.

T: We have a lot of good exposures on our list here. I see that we have some lower-level items, such as having a knife near you while you talk to someone, and some medium-level items like holding a knife around someone, and then some really high items like pointing a knife at someone. Now, we could just start with the easiest, and then work our way up, but we have some reason to believe that this process might be even more effective if we vary it up a little bit. So what would be the highest item you think you could do right now?

P: I think I could probably hold a knife near someone. That's still really scary but I think I could do it.

T: Great. So let's have you hold this knife in your hand while you sit near me.

P: OK [*the exposure proceeds for the duration previously determined to maximize expectancy violation*]

T: Great. You did a terrific job with that. Now let's back down a little bit. Let's put the knife over here on my desk, so that it's close to you but not in your hand.

P: That's going to be easier.

T: Yes, I expect so. So let's practice this easier one now. (the exposure proceeds)

P: That wasn't so bad.

T: Great. Now I'd like to go to the higher item, which is having you point the knife at me.

P: That's the scariest one.

T: I know; it's a real challenge. But let's see how you do with it. [*the exposure proceeds*]

Offset Reinstatement and Context Renewal Effects

In the specific case of fear extinction, fear can be reinstated after extinction by changing the context in which the feared stimulus is encountered (Mineka, Mystkowski, Hladek, & Rodriguez, 1999); this phenomenon can be mitigated by extinguishing the fear in multiple contexts (Bouton, 1993). Varying the kind of exposures conducted—for example, exposure to several different kinds of dogs, rather than one kind—is one straightforward way of increasing variability. Another is to change the conditions under which the stimulus is encountered. For example, we could vary the *external* contexts by conducting exposures in the therapist's office, outside, and in the patient's home or other location, during the day and at night. We could also vary the *internal* context by having the patient engage in exposures both when relatively calm and after fear has been aroused.

Bouton (1993) suggests creating a "bridge" between extinction and recall contexts. Tangible retrieval cues, such as a specific piece of jewelry worn during exposure sessions, is one theoretical option, though as many of the authors in this issue note, the potential for such retrieval cues to become maladaptive safety behaviors is high. Perhaps a more promising approach, as suggested by Blakey and Abramowitz (2019), is to cue the patient to remember the exposure session when entering new contexts.

Clinical Example

Catherine, the patient with OCD, has successfully completed an exposure of touching a toilet in the therapist's

office suite. The therapist now combines maximizing variability with offsetting reinstatement and context renewal effects.

T: Great job with that exposure. Now for our next step I'd like to go down the hall and we'll touch the toilet in another bathroom.

P: OK [*they walk to the next bathroom*]. Yeah, this feels scarier.

T: That's very understandable. You beat your fear back in my office, but your brain still hasn't fully embraced the safety of the activity. That's why we need to do it in a lot of places in a lot of different ways. Let's take a moment and remember the exercise back in my office. Can you tell me what happened?

P: I was really scared at first. And then once we started touching the toilet it was yucky, but I didn't feel as scared as I thought I would. I felt better after doing it.

T: That's right. It wasn't as terrible as your brain was telling you it would be. Let's take a minute just to reflect on that. Can you mentally picture yourself touching the toilet in my office—really see it in your mind?

P: Yeah.

T: OK, let's touch this toilet [*the exposure proceeds*]. Great job again. You're beating your fear once again. Now just to change it up a little bit, I'm going to step out of the bathroom and let you do this by yourself for a little bit, to really help your brain learn it's safe even without me there.

Conclusions

The articles presented in this issue provide a wealth of innovative examples of inhibitory learning principles in exposure therapy. As Weisman and Rodebaugh (2018) note, many of the specific strategies proposed by the inhibitory learning model are either untested, or have yielded mixed results, in anxiety-disordered human populations. Nevertheless, the principles derive from a strong model of extinction and renewal in fear conditioning (e.g., Hermans, Craske, Mineka, & Lovibond, 2006). Exposure therapy has two broad aims. In the short term, the aim is to reduce fearful emotion and behavior by engaging PFC regions that will develop nonthreat associations (CS-NoUS) which compete with the original fear learning (CS-US). The initial development of CS-NoUS associations is theoretically enhanced by maximizing the degree of mismatch with the patient's expectancies; strategies for increasing this mismatch include conducting exposures that are long enough to violate the expectancy, minimizing distraction which interrupts the exposure process, and encouraging patients to engage in fear-antagonistic actions (e.g., acts of "bravery"). Deepened extinction, in which multiple previously extinguished CSs are presented simultaneously; the reduction of safety behaviors, which serve to undermine the CS-NoUS pairing; occasional reinforced extinction, in which the "disaster" is allowed to occur when prudent to do so; and affect labeling, in which verbal labels are attached to emotional response, are additional strategies used to engage the PFC and develop non-threat associations.

In the long term, the aim of exposure is to reduce the degree of return of fear by enhancing the retrieval of learned CS-NoUS associations from long-term memory storage. That is, once the patient has learned that the feared object, activity, or situation is safe, it is critical to make sure that this safety learning remains the dominant response, effectively competing with the original CS-US association. Here, variability of exposure is thought to be important. This variability can include moving randomly or quasi-randomly around the exposure hierarchy rather than going in fixed order, varying (expanding) the time interval between exposure sessions, and conducting exposure in multiple settings with many different stimuli. Facilitated recall of exposure trials when encountering new contexts is also proposed to help improve memory retrieval.

Not discussed here, but previously reviewed within the context of inhibitory learning (Craske et al., 2008; Craske et al., 2014; Weisman & Rodebaugh, 2018), is the use of cognitive-enhancing medication that specifically targets PFC activation, critical to fear extinction (Milad & Quirk, 2002; Quirk et al., 2006; Quirk et al., 2000). Such medications include D-cycloserine (Walker, Ressler, Lu, & Davis, 2002), yohimbine (Cain, Blouin, & Barad, 2004; Morris & Bouton, 2007), and methylene blue (Gonzalez-Lima & Bruchey, 2004; Wrubel, Barrett, Shumake, Johnson, & Gonzalez-Lima, 2007) . Though research is still in the early stages, these compounds show some promise for augmenting exposure therapy (see Tolin, 2017, for review).

In this article, I have presented a number of case vignettes that demonstrate how the basic principles of inhibitory learning can be applied within the clinical context of exposure therapy. There is, of course, an infinite number of variations on these themes, and clinicians are encouraged to apply their creativity. From a research perspective, the inhibitory learning model posits several key hypotheses about adjustments to exposure that will better engage the primary mechanistic target (PFC inhibition of limbic activity) and result in better clinical outcomes; these hypotheses merit further study in clinical trials.

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