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Mechanisms of exposure therapy: How neuroscience can improve psychological treatments for anxiety disorders

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Abstract

Exposure therapy for anxiety disorders has been one of success stories of clinical psychology and psychiatry. Nevertheless, a significant minority of patients fail to benefit from extant treatments. This clinical impasse is prompting renewed attempts to understand fear and its reduction at neural, cellular, and molecular as well as behavioral levels of analysis. The purpose of this article is to provide a review of theories of exposure therapy, including recent developments in emotional processing theory, and to discuss insights from neuroscience that promise to improve psychological treatments for reducing pathological fears.

Cognitive-behavior therapy (CBT) for anxiety disorders is among the indisputable success stories of our field (Barlow, 2002; Craske, 1999). Syndromes once deemed nearly intractable during the heyday of psychoanalysis have yielded to science-based efforts to overcome them. Individuals suffering from an anxiety disorder today have far better prospects for relief than did their counterparts several decades ago. Embodying the principle of exposure, today's treatments affirm that the conquest of our fears requires confrontation with the things we fear the most.

These notable achievements notwithstanding, many patients fail to benefit fully from extant CBT interventions (Barlow, Allen, & Choate, 2004), and many who do benefit fail to maintain their gains (Brown & Barlow, 1995). We have now reached a therapeutic impasse, and further advances will require a deeper understanding of the mechanisms of fear and its reduction. The purpose of this article is to review insights emerging from the field of neuroscience that promise to improve our psychological treatments for anxiety disorders. Prior to addressing these breakthroughs, I review theories of exposure therapy.

1. Historical background

Contemporary exposure treatments for anxiety disorders have their roots in Wolpe's (1958) systematic desensitization. Unusual among the founders of behavior therapy, Wolpe was a physician (but not a psychiatrist) who had done experimental research on the learning and unlearning of fears in cats. Although he did very little laboratory work thereafter, his seminal experiments provided the conceptual and procedural foundations for his revolutionary clinical work. In the canonical version of desensitization, the patient was first taught progressive, deep

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muscle relaxation. The therapist then had the patient imagine a hierarchy of brief, anxiety-provoking scenes. Each imagined scene was designed to provoke a dose of anxiety that could be overridden by the competing state of relaxation. Viewing neurotic fears as akin to Pavlovian conditioned responses (CRs), Wolpe conceptualized the imagined scene as the functional equivalent of a conditioned stimulus (CS). He believed that the competing relaxation response reciprocally inhibited the weaker anxiety response, thereby replacing the associative bond between stimulus (imagined fear scene) and response (neurotic anxiety) with one between the stimulus and relaxation response.

In retrospect, it is odd that Wolpe described his method as *behavior* therapy. After all, desensitization did not require much behavior of the patient, other than to become profoundly relaxed before generating a series of mental images. Indeed, for a therapy inspired by neo-Hullian S-R learning theory, a naive observer would have been at a loss to identify any stimuli or any responses. The stimuli were imaginary, and the responses were covert and unobservable.

Nevertheless, systematic desensitization had the undeniable virtue of being the first psychotherapy whose ingredients and procedures were so explicit as to permit controlled laboratory evaluation of its efficacy. Capitalizing on Wolpe's procedural lucidity, Lang and his students launched studies testing hypotheses about desensitization's mechanisms of action (Lang & Lazovik, 1963; Lang, Lazovik, & Reynolds, 1965). Inspired by Lang's pioneering work, psychologists conducted dozens of experiments designed to dismantle the components of desensitization and isolate its active ingredients (McGlynn, Mealiea, & Landau, 1981). Many of these analogue studies concerned fears of snakes in college students, prompting one wag to quip years later about the Great Snake Phobia Epidemic that had swept through American psychology departments during the 1960s and 1970s.

In parallel to work on systematic desensitization, other clinical innovators developed and tested implosive therapy (Stampfl & Levis, 1967) and its close cousins, imaginal (e.g., Foa, Blau, Prout, & Latimer, 1977; Watson & Marks, 1971) and *in vivo* (e.g., Watson, Mullett, & Pillay, 1973) flooding. Ironically, although advocates of both systematic desensitization and flooding appealed to animal learning and conditioning theory, each made opposing recommendations on how to treat pathological fear. Desensitizaton required the therapist to go easy, initiating only small amounts of distress in the patient, whereas flooding required the therapist to maximize anxiety for a sufficiently long duration to enable extinction of phobic fear.

The conclusions arising from this wave of theory-driven research on the mediating mechanisms of desensitization and flooding were oddly atheoretical. The trappings deemed essential for each treatment turned out to be not all that important. Progressive muscle relaxation, hierarchal presentation of imagined fear scenes, and so forth were not critical to desensitization, and maximal anxiety was not critical for flooding. Following Marks (1978), many clinicians concluded that the key element in fear reduction was simply sufficient exposure – preferably *in vivo* – to evocative cues until distress diminished. For pragmatic therapists, *why* exposure worked mattered little; *that* it worked was the key point.

2. Emotional processing theory

Theoretical agnosticism about mediating mechanisms is acceptable only when treatment works with flawless fidelity. But when patients fail to benefit, we need to know why. Dissatisfied with this atheoretical state of affairs, Foa and Kozak (1986) endeavored to elucidate the mechanisms of exposure therapy. Their classic article – "Emotional Processing of Fear: Exposure to Corrective Information" – has exerted a tremendous influence on clinical thinking and practice. As I document elsewhere (McNally, 2006), Foa and Kozak's article has earned remarkably high citation counts in the *Social Sciences Citation Index* year after year. Their emotional processing theory has been updated twice: ten years later (Foa & McNally, 1996), and 20 years later (Foa, Huppert, & Cahill, 2006).

Building on the work of Rachman (1980) and Lang (1977, 1979), Foa and Kozak proposed that fear is represented in memory as a network comprising stimulus propositions that express information about feared cues, response propositions that express information about behavioral and physiologic responses to these cues, and meaning propositions that elaborate on the significance of other elements in the fear structure. Applying a computer metaphor, Foa and Kozak characterized the fear network as a program for avoiding threat. Pathological fear, they said, amounted to errors in this program, characterized by excessive response elements, resistance to change, and impairments in processing certain types of information about danger and safety. Exposure therapy amounted to reprogramming the computational code to diminish clinical pathology. Opening the program, they argued, can be indexed by self-reports of increased fear and by heightened physiologic activity (e.g., heart rate). The job of the therapist is to provide information incompatible with pathological aspects of the program.

Absorbing patholytic information into the activated fear structure constituted emotional processing. According to Foa and Kozak, emotional processing is evinced by three phenomena: (1) activation of the fear network as apparent in heightened physiologic reactivity and self-reports of fear; (2) within-session habituation, as apparent in decreases in the magnitude of fear indices; and (3) between-session habituation, as reflected in gradual declines in the peak magnitude of fear responses across sessions.

Foa and Kozak identified several variables vital for emotional processing. First, input information should match elements in the fear network to ensure its optimal activation. To the extent that either an imaginal or *in vivo* therapy session fails to match relevant propositions in the network, the fear program will not be accessible for modification. On the other hand, if elements in the structure are tightly linked, activation of some propositions should spread to others, providing the activation required for therapeutic change. Second, the patient must attend to the relevant input for therapy to progress. Cognitive avoidance on the part of the patient will prevent activation of the structure and will prevent new, patholytic information from being incorporated.

According to Foa and Kozak, several changes occur as emotional processing unfolds. First, habituation of fear weakens associations between feared stimuli and fear responses. Meaning propositions change, such as exaggerated estimates of the probability of harm arising from feared situations, and exaggerated appraisals of how bad feared consequences really are – their negative valence – diminishes as well. The very fact that fear declines refutes the expectation that fear will persist indefinitely once activated.

3. Conceptual and empirical issues

There are several conceptual problems associated with emotional processing theory. One concern is that the propositional network characterization of fear merely restates the phenomenon it is designed to explain. Consider agoraphobia. Foa and Kozak propose that response propositions regarding bodily sensations are linked in the fear network with meaning propositions regarding danger. But does this not simply rephrase what astute clinicians knew all along? People with panic disorder and agoraphobia respond fearfully to their own bodily sensations, often misconstruing them as harbingers of imminent catastrophe (Clark, 1986). To say that these individuals are characterized by fear networks in which propositions about bodily sensations are linked to propositions about danger seems merely to recast clinical observations in a new vocabulary.

On the other hand, the network conceptualization might constitute an advance if hypotheses derived from it withstood empirical scrutiny. One of the few direct tests was conducted by Schniering and Rapee (1997). Using a lexical decision task, they probed the structure of fear memory in panic disorder patients and in healthy control subjects. On each trial, subjects saw a prime word (e.g., *bread*) followed by either a word target (e.g., *butter*) or a nonword target (e.g., *lutter*). Confirming previous research, Schniering and Rapee obtained semantic priming effects: lexical decision reaction times were faster for related word pairs (e.g., *bread* and *butter*) than for unrelated ones (e.g., *gray* and *queen*). The key word pairs, however, involved a bodily sensation (e.g., *breathless*) and a catastrophic consequence (e.g., *suffocate*). Emotional processing theory would predict that reaction times for the threat word pairs should be especially fast in panic patients for whom these concepts are presumably tightly linked in the fear network. The results, however, did not support this hypothesis. The priming effects were just as pronounced for threat word pairs in the control group as in the panic group. Therefore, the organization of these concepts in memory was similar in both groups, implying that whatever distinguishes panic patients from healthy individuals is not a distinctive fear network.

Another ambiguity concerns the claim that input information must "match" the information in the fear network for it to be activated and altered therapeutically. Propositions in an imaginal flooding script, for example, must match those embodied in the fear network for emotional processing to occur. But gauging the degree of match is not easy, especially for *in vivo* exposure sessions. Because the world is not a text decomposable into propositions, it is very difficult to design a session that "matches" the content of the fear network in any precise kind of way. For example, consider an agoraphobic individual whose exposure assignment is a trip to a shopping mall. An attempt to gauge the match between the propositional content of the exposure assignment and the fear network would require one to accomplish the impossible task of listing the propositional structure of the exposure task. But the number of facts expressible as propositions embedded in the trip to the shopping mall is infinite. This precludes any precise estimate of how well the propositional content of the session matches the content of the patient's fear network. Indeed, the impossibility of conducting a propositional analysis is apparent if one attempts to write down all the facts (propositions) embodied in the room in which one is sitting.

Further complicating matters are the two related claims that one must seek an optimal match between input and network content and that compensation for a suboptimal match may occur when the network is unusually tightly linked, as in snake phobia, such that only a minimal match may suffice to activate the fear network as activation spreads quickly throughout a highly coherent network. The difficulties inherent in telling when one's therapeutic input is on target – whether it provides an optimal match – result in inferences about adequate matching being made on the basis of the patient's magnitude of arousal or fear in response to the input. If fear is activated, one assumes that the match was reasonably good. The reasoning here seems uncomfortably circular.

Although the aforementioned ambiguities complicate clear tests of emotional processing theory, its main components do imply ways to evaluate it empirically. In fact, Foa et al. (2006) have reviewed recent studies that suggest modifications in the original Foa–Kozak theory. Thus, the original hypothesis regarding a clear relationship between within-session habituation of fear and clinical outcome has often not been confirmed (e.g., Jaycox, Foa, & Morral, 1998). But as Foa et al. (2006) point out, this disconfirmation is not fatal to the theory. More specifically, the key mechanism underlying successful exposure therapy is modification of the pathological associations in the fear network via disconfirmation of specific propositions embodied therein. For example, an agoraphobic patient exposed to elevated heart rate during interoceptive exposure will learn that cardiac arrest does not occur, and it is this disconfirmation of the tachycardia-heart attack association that drives the patholytic effect of interoceptive exposure, not within-habituation of fear *per se* during the treatment session. Of course, within-session habituation itself can disconfirm certain pathological beliefs such as "If I do not escape, my fear will continue indefinitely."

Another minor modification of the Foa–Kozak theory concerns the role of attentional distraction during exposure therapy (Foa et al., 2006). Foa and Kozak conceptualized distraction as a form of cognitive avoidance that would limit activation of the fear network, thereby impeding emotional processing. Early studies often provided data consistent with this conjecture (e.g., Grayson, Foa, & Steketee, 1982). However, some recent research suggests that distraction during exposure may actually facilitate fear reduction. For example, studying spider phobics, Johnstone and Page (2004) found that phobic-stimulus-irrelevant conversation with the patient during exposure hastened successful fear reduction, and this was especially true for those phobics with the highest initial baseline level of fear. Considering this and related studies, Foa et al. (2006) suggested that whether distraction helps or hinders emotional processing may depend on the type of anxiety disorder. For example, distraction might hinder progress in exposure for agoraphobia, whereas it might facilitate it in specific phobia.

Another interpretation of these discrepant results on distraction's effect on outcome is potentially consistent with Foa and Kozak's original formulation. That is, the effect of distraction may vary as a function of current level of fear. If fear is above an optimal level for emotional processing to occur, distraction may titrate it, thereby enhancing outcome. Determining what this optimal level happens to be represents a challenge in itself.

In summary, Foa and Kozak's (1986) emotional processing theory put us back on the right track, its limitations notwithstanding. These psychologists realized that further advances in the treatment of anxiety disorders will likely be inspired by deeper understanding of mechanisms. Inspired by Lang, they invoked concepts and findings from psychophysiology and information-processing psychology in their justly influential synthesis. At this point, it behooves us to widen the conceptual net, and to capitalize on insights arising from the neighboring discipline of neuroscience.

4. Insights from neuroscience

The field of animal learning and conditioning dominated much of psychology throughout the middle decades of the 20th century (Leahey, 2001, pp. 233–260), inspiring the founders of behavior therapy (e.g., Wolpe, 1958). With the rise of cognitive psychology and cognitive therapy, conditioning research and theory receded into the background. However, during the past decade or so, Pavlovian conditioning paradigms have enjoyed a renaissance, mainly as tools for behavioral neuroscientists keen to elucidate the neural circuitry of fear acquisition (e.g., Davis & Myers, 2002; LeDoux, 1998; McGaugh, 2003). These researchers have recently endeavored to elucidate the neural, cellular, and molecular mechanisms of the extinction of conditioned fear. Their findings furnish insights for improving psychological treatments for anxiety disorders.

Most scientists now agree that extinction does not involve the unlearning of CS–US associations (cf. Rescorla & Wagner, 1972), but rather the establishment of new, inhibitory associations that compete with the original ones (e.g., Bouton, 2002; Myers & Davis, 2002). Extinction is itself a form of learning indexed by a decline in the frequency and

magnitude of the CR. Extinction training – presentation of the CS without the US – does not abolish the original association; it establishes new inhibitory associations that suppress the emergence of the CR in response to the CS.

Abundant evidence confirms that the original CS–US associations are not severed (Bouton, 2002; Myers & Davis, 2002). First, when experimenters re-present the CS after a relatively long period of time after the conclusion of extinction training, CRs often remerge. Hence, this spontaneous recovery phenomenon indicates that extinction training did not sever the CS–US association.

Second, if acquisition occurs in context A, and extinction occurs in context B, CRs will occur once again in context A. This renewal phenomenon indicates that extinction is context-specific; animals learn that an inhibitory association regarding the "safety" of the CS in the extinction context while retaining the CS–US association in the original acquisition context. Hence, extinction training is not a matter of severing a context-independent CS–US association.

Third, if, following extinction training, the subject encounters the US alone, this can reinstate responding to the CS even though no further CS–US pairings have occurred.

Fourth, the recovery of responding can be marked following extinction training relative to the original acquisition. The fact that relearning of the CS–US association happens so quickly after the original acquisition and extinction indicates that extinction training did not eliminate the original CS–US association, but merely suppressed it.

Evidence that extinguished CSs participate in inhibitory associations comes from research showing that they function like conditioned inhibitors of fear. Conditioned inhibitors, or "safety signals", are established by nonreinforcing a new stimulus in the presence of cues that ordinarily predict the US (e.g., McNally & Reiss, 1982; McNally & Reiss, 1984; Rescorla, 1969). This new stimulus, then, signals safety in circumstances that otherwise signal danger. Extinction training establishes inhibitory learning that counteracts the expression of the CR. That is, competing excitatory and inhibitory CS–US associations become established, and their relative strength determines CR expression or the lack thereof. In one sense, extinction training renders the CS ambiguous in that it now has two meanings. There is the association with the US, and there is the association with no US ("safety"). The context in which the CS reappears may resolve the issue, and under some circumstances permitting the CRs to emerge, as in the clinical phenomenon of the "return of fear" (e.g., Rachman, 1979). For example, spider-fearful individuals who undergo exposure therapy ("extinction training") in one context often exhibit at least a partial return of fear when later tested in a different context (Mystowski, Craske, & Echiverri, 2002).

Unfortunately for people with anxiety disorders, conditioned fear is less context-specific than extinction, and the former associations seem to be more persistent than the latter ones. As Bouton (2002) has suggested, this asymmetry between the context-specificity and persistence of fear acquisition learning and fear extinction learning results from encoding priority of the first (acquisition) association over the second (extinction) one. That is, fear acquisition is encoded as the rule to which context-specific extinction is encoded as the exception. If so, this would imply that attempts to build resilience to anxiety disorders might establish nonfear associations first (mastery experiences?) which would retain an encoding priority over any later fear conditioning associations that might occur in the person's life.

4.1. Medial prefrontal cortex and fear inhibition

The aforementioned reconceptualization of extinction as new learning rather than unlearning is based on behavioral studies. This work has provided the springboard to the investigation of neural mechanisms mediating fear inhibition and extinction learning.

Considerable animal research points to the importance of the medial prefrontal cortex (mPFC) in suppressing conditioned fear. This region projects to the amygdala (e.g., Chiba, Kayahara, & Nakano, 2001), and its damage impedes extinction of learned fear (e.g., Morgan, Romanski, & LeDoux, 1993). Further evidence of the reciprocal relationship between the mPFC and the amygdala was provided by Milad and Quirk (2002), Using single-unit recording techniques, they found that firing of neurons in the mPFC was inversely correlated ($r = -0.73$) with the magnitude of spontaneously recovered fear, indexed by freezing, in rats who had undergone extinction training after Pavlovian fear conditioning. These neurons did not fire during fear conditioning or during extinction training itself. Therefore, activity in these neurons suggests that the mPFC may store long-term extinction memories that inhibit the expression of conditioned fear responses. Consolidation of these extinction memories may block subsequent expression of fear when CSs are encountered later. After conditioning other rats, Milad and Quirk then stimulated these neurons while pairing them with the tone CSs that had not previously been extinguished. Strikingly, this stimulation simulated extinction in that rats' minimal fear responses during testing mimicked that of rats who had previously had

their fears extinguished. As the authors pointed out, these findings suggest that targeted stimulation of the corresponding medial prefrontal structures via transcranial magnetic stimulation in phobic patients may further consolidate their extinction memories.

Using positron emission tomography, Shin et al.'s (2004) research group confirmed an inverse relation between activity in the mPFC and amygdala in male and female veterans of the Vietnam war who either had or did not have posttraumatic stress disorder (PTSD). Subjects listened to brief, audiotaped descriptions of their traumatic experiences and neutral experiences while in the PET scanner. During exposure to the traumatic *versus* neutral imagery scripts, both male and female veterans with PTSD exhibited decreased activation in mPFC. Only the male veterans exhibited increased activation in the left amygdala. However, for both male and female PTSD veterans, decreased activation in the mPFC was correlated with increased activation in the left amygdala and right amygdala and periamygdaloid cortex. Moreover, symptom severity during the trauma scripts was positively correlated with activation in the right amygdala and negatively correlated with activation in the medial prefrontal cortex for both male and female PTSD veterans.

The aforementioned studies on rodents and PTSD subjects imply that any intervention that can boost activity in the mPFC during exposure to fear provoking stimuli may yield therapeutic benefits. Consistent with these findings confirming the fear-inhibiting effects of prefrontal executive functions, psychologists have begun to develop attentional training programs that appear to produce lasting anxiolytic benefits (Amir, Selvig, Elias, & Rousseau, 2002; Rutherford, MacLeod, & Campbell, 2002; Vasey, Hazen, & Schmidt, 2002). Using a variant of the dot probe paradigm (MacLeod, Mathews, & Tata, 1986), these researchers found that attentional training to nonthreat cues in this cognitive paradigm results in clinically significant reductions in distress, including symptoms of generalized anxiety disorder. Although this breakthrough was not directly derived from neuroscience research, it is fully consilient with it.

4.2. Using NMDA agonists to hasten fear extinction

Behavioral neuroscientists have established that *N*-methyl-D-aspartate (NMDA) glutamatergic receptors within the amygdala play a key role in the extinction of conditioned fear (Davis, 2002). For example, administration of NMDA antagonists prevents extinction procedures from reducing conditioned fear. Accordingly, Davis and his research team reasoned that an NMDA agonist or partial agonist, such as D-cycloserine (DCS), might facilitate extinction of fear. They tested this hypothesis in a series of Pavlovian fear conditioning experiments with rats (Walker, Ressler, Lu, & Davis, 2002). After administering 10 CS–US fear conditioning trials (light paired with shock), the researchers administered either saline or three dosage levels of DCS via intraperitoneal injection prior to extinction training involving 30 nonreinforced CS presentations. Twenty-four hours later, Walker et al. used a fear-potentiated startle procedure to assay fear of the CS in the rats, all of whom were off DCS. Strikingly, DCS facilitated extinction, and did so in a dose-dependent manner. But this was true only for those DCS-treated animals that had undergone extinction training. Decrements in fear during testing were not evident for rats that had received either saline or DCS without extinction training. In further work, they replicated this basic procedure, but infused DCS directly into the basolateral region of the amygdala (Walker et al., 2002). Once again, DCS augmented fear reduction following extinction training.

These findings indicate DCS hastens extinction of conditioned fear in rats who are undergoing the "exposure therapy" of nonreinforced CS trials. It is not a treatment for fear itself. Its action is only apparent in concert with extinction training. Unlike medications, such as alprazolam, that attenuate anxiety but may undermine extinction in the long run (Marks et al., 1993), DCS only exerts its effect in conjunction with exposure.

By functioning as a partial agonist at the NMDA receptor, DCS facilitates diverse forms of learning, not just fear extinction. For example, transgenic mice that overexpress the most active NMDA receptor subunit (NR2B), exhibit enhanced learning in a diversity of paradigms ranging from spatial tasks to both acquisition and extinction of conditioned fear (Tang et al., 1999). These findings are consistent with the principle that learning and memory are based on modification of synaptic strength among neurons that are active at the same time.

As it turns out, physicians have already been using DCS, but to treat tuberculosis, not pathological fear. Fortunately, the compound produces no significant side effects, and thus is ripe for application in the anxiety disorders field. In a landmark study, the Davis group randomly assigned 28 patients with acrophobia to receive either DCS or pill placebo prior to undergoing a virtual reality exposure treatment involving a simulated ride up a glass elevator (Ressler et al., 2004). Although previous virtual reality research indicated that improvement occurs after seven sessions of 35–45 min

each (Rothbaum et al., 1995), Ressler et al. administered only two 34–45 min sessions with one pill taken between 2–4 h before the session. The results revealed no differences between the groups during the first virtual reality exposure session in terms of either self-reported fear or in terms of how high patients were willing to travel in the virtual elevator. However, as Ressler et al. expected, patients in the DCS group exhibited less fear and avoidance than the placebo group during the second exposure session. That is, DCS administered before the first exposure session facilitated extinction learning during the intersession interval. At three-month follow-up, patients who had received the DCS continued to exhibit less fear and avoidance than did those in the placebo group. Also, improvement was evident on spontaneous fluctuations in skin conductance during virtual exposure. Finally, DCS-treated patients reported twice as many exposures to high places relative to the placebo group. DCS-assisted virtual reality exposure, then, generalizes to the outside world.

In summary, patients in the DCS group exhibited extinction learning after only a single session of virtual reality exposure. After two sessions, they exhibited marked and lasting reduction in fear and avoidance. Consistent with the animal literature, the extinction learning seems to occur after extinction training. That is, to rephrase it in terms of Foa and Kozak's (1986) terms, DCS facilitates between-session habituation, not within-session habituation.

4.3. Bolstering inhibition within the amygdala

In addition to elucidating the neural circuits of fear acquisition and extinction, scientists have begun to probe the molecular basis of these processes as well. Most investigators believe that information about the CS and the US converge within the lateral nucleus of the amygdala, and output from this structure prompts expression of the behavioral indicants of fear (LeDoux, 1998).

Shumyatsky et al. (2002) have elucidated a negative feedback loop that modulates the activity of the principal neurons in the lateral nucleus of the amygdala, thereby controlling fear memories. This research group had identified a gene that codes for the neurotransmitter, gastrin-releasing peptide (GPR), which is preferentially expressed in the principal type of neuron in the lateral amygdala. Next, they searched for cells that contained the GPR receptor (GPRR), and identified a subpopulation of amygdalar interneurons that release the inhibitory neurotransmitter, gamma aminobutyric acid (GABA). Shumyatsky et al. then discovered that GPR triggers GPRR-expressing interneurons to release more GABA, further inhibiting the principal amygdalar neurons. They then created a mutant knockout mouse whose GRPR gene was disabled. These mutant mice exhibited impaired inhibition of principal amygdalar neurons which resulted in enhanced long-term potentiation of synaptic connections between cortical cells and the amygdala. Behaviorally, these mutant mice with their defective GRP-mediated negative feedback loop, exhibited persistent and enhanced fear of the CS. They were not more anxious in general (e.g., anxious avoidance of well-lit places), nor did they display enhanced learning in other contexts. Their memory enhancement was confined to memory for the "traumatic" CS.

This research suggests that interventions that can promote the overexpression of either GRP or GRPR might enhance the inhibition of fear memories, thereby hastening extinction of fear. These results will inspire a search for pharmacologic agents that can promote amygdalar expression of these genes, and perhaps promote recovery from anxiety disorders.

4.4. Blocking consolidation of traumatic memories

Research by McGaugh (2003) and his team (e.g., Cahill, Prins, Weber, & McGaugh, 1994) confirms that release of stress hormones following an emotionally intense experience consolidates memory for the episode, and that beta-adrenergic blockers, such as propranolol, can counteract the memory-strengthening effects of these hormones. Extrapolating from the neuroscience laboratory to the clinic, Pitman et al. (2002) conjectured that propranolol administered to people who have just survived a traumatic event may attenuate consolidation of the memory, making it less emotionally upsetting than it might otherwise be. To test this hypothesis, Pitman et al. randomly assigned accident victims arriving at the hospital emergency room to receive two weeks of either propranolol or pill placebo. At follow-up, both groups reported marked reduction in PTSD symptoms, but subjects who had taken propranolol were less reactive physiologically in the script-driven imagery paradigm than were those who had taken placebo. These findings suggest that administration of beta-blockers – drugs that attenuate consolidation of traumatic memories in the amygdala – may protect trauma survivors against developing PTSD.

5. Conclusions

Theories about the mechanisms underling successful exposure therapy for anxiety disorders have evolved since the pioneering work of Wolpe (1958) on systematic desensitization and Stampfl and Levis (1967) on implosive therapy. This early, theoretically-inspired clinical research produced conflicting results about the mechanisms of change, thereby prompting a period of atheoretical pragmatism in the treatment of anxiety disorders. Inspired by Lang and Rachman, Foa and Kozak (1986) were among those reviving theory in the field of anxiety disorders, chiefly by integrating new conceptual approaches (e.g., information processing) into behavior therapy for fear reduction.

Although the emotional processing approach has been fruitful, younger scholars, such as Dalgleish (2004), have questioned whether the formal architecture of Foa and Kozak's (1986) framework is sufficiently conceptually rich to accommodate the facts. Dalgleish argues that multirepresentational theories are superior to those incorporating a single format (e.g., the propositional fear networks of Foa and Kozak's theory). For example, Brewin (2001) has proposed a dual-representation theory of PTSD whereby traumatic memories are stored in two ways: verbally accessible memories akin to the declarative knowledge embodied in propositional networks, and nonlinguistic, situationally accessible memories that underlie sensory flashbacks. Dalgleish's own approach – the Schematic, Propositional, Analogue, and Associative Representational Systems (SPAARS) Model (Power & Dalgleish, 1999) – is even more complex than Brewin's, and its aim is to account for processing of all emotions, not just pathological fear, let alone PTSD. But as Dalgleish (2004) acknowledges, the theoretical power of multirepresentational theories comes at the price of potentially unwieldy complexity.

These interesting developments in cognitive theories of emotional processing of fear notwithstanding, psychological treatments for anxiety disorders have reached a plateau, and further advancements may arise from neighboring disciplines, such as neuroscience. At first brush, it seems counterintuitive that "biological" research would directly improve "psychological" treatment. And some psychologists might wonder whether an "incursion" of neuroscience into behavior therapy would presage reductionist attempts to write psychology out of the picture. Such worries are misplaced. As Chomsky (2002), pp. 53–56 recently observed, the history of science shows that mutual conceptual adjustment between scientific fields result in greater unification, not reduction of one science to a more fundamental one. For example, rather than early 20th century chemistry being reduced to physics, physical theory adapted to advances in chemistry (Chomsky, 2003). As an emergent discipline, psychology, including clinical, will not be reduced or eliminated by neuroscience (Bennett & Hacker, 2003). Accordingly, we should welcome the insights from neighboring disciplines whenever they point to ways for enhancing our treatments for anxiety disorders.

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