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Cognitive processes during fear acquisition and extinction in animals and humans:

Implications for exposure therapy of anxiety disorders

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Abstract

Anxiety disorders are highly prevalent. Fear conditioning and extinction learning in animals often serve as simple models of fear acquisition and exposure therapy of anxiety disorders in humans. This article reviews the empirical and theoretical literature on cognitive processes in fear acquisition, extinction, and exposure therapy. It is concluded that exposure therapy is a form of cognitive intervention that specifically changes the expectancy of harm. Implications for therapy research are discussed.

Keywords

Cognitive processes; Fear acquisition; Extinction; Exposure therapy; Cognitive-behavioral therapy; Anxiety disorders; Amygdala; Prefrontal cortex; d-Cycloserine

Anxiety disorders, such as social phobia, specific phobias, panic disorder, and post-traumatic stress disorder are among the most common mental disorders in the population. The most effective strategies for treating anxiety disorders include exposure therapy with or without cognitive strategies, and pharmacotherapy, such as selective serotonin reuptake inhibitors (for a review, see Barlow, 2002). Exposure therapy is rooted in behaviorism and learning theories in psychology that began in the early 1900s (Watson, 1924). Especially influential was Mowrer (1939) who hypothesized that fears are acquired through repeated presentations of a neutral stimulus (conditioned stimulus; CS) and a pain-producing or fear-eliciting stimulus (unconditioned stimulus; US). He observed that the strength of the fear response in rats is determined by the number of repetitions of association between the CS and US, and the intensity of the unconditioned response.

Mowrer (1939) further noted that the repeated presentation of the CS in the absence of the US leads to extinction, the gradual decrease of the conditioned response. This process has been regarded as primarily responsible for exposure therapy in humans from the early beginnings of experimental studies in psychology (Watson & Rayner, 1920) to the contemporary field of neuroscience (e.g., Bouton, Mineka, & Barlow, 2001; Davis, Ressler, Rothbaum, & Richardson, 2006; Quirk, 2006). For example, Davis et al. (2006) recently wrote: "In exposure therapy the patient is repeatedly exposed for prolonged periods to a feared object or situation in the company of a supported therapist and hence in the absence of aversive consequences (extinction training)" (p. 369). It is further generally assumed that extinction training is an "automatic, unconscious, and low-level process" (Lovibond, 2004 p. 495), separate from

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higher-order cognitive processes. On the contrary, a review of the neuroscience literature indicates that “it may reasonably be predicted that extinction involves more complex processes than acquisition and, hence, may depend on additional brain regions and/or be affected differently by pharmacological manipulations” (Lovibond, 2004; p. 499). In this review, I will explore the processes of fear acquisition and extinction learning and will later discuss novel pharmaceutical approaches to enhance the extinction processes during exposure therapy.

Animal research suggests that extinction is a form of acquired inhibition that suppresses a fear response. In other words, extinction is probably not simply an unlearning or forgetting but rather a new form of learning that changes the CS-US contingency in such a way that the CS no longer signals an aversive event and thereby inhibits the expression of the fear response (e.g., Bouton, 1993, 2004; Myers & Davis, 2002; Pearce & Bouton, 2001; Rescorla, 1996). Further evidence against the idea that extinction is simply an unlearning or forgetting comes from experiments showing spontaneous recovery of a previously conditioned fear response (Robbins, 1990), renewal (Bouton & Bolles, 1979; Rodriguez, Craske, Mineka, & Hladeck, 1999), and reinstatement of fear (Bouton & Swartzentruber, 1991; Dirikx, Hermans, Vansteenwegen, Baeyens, & Eelen, 2004; Hermans et al., 2005; Rescorla & Heth, 1996).

Laboratory studies implicate the amygdala during fear extinction. For example it has been shown that the neuronal firing in the lateral nucleus in response to a CS diminishes over time when the US is no longer delivered (Quirk, Repa, & LeDoux, 1995; Repa et al., 2001). Another brain area that is apparently involved in extinction learning is the medial prefrontal cortex, probably mediating or regulating amygdala activity in rats (Milad & Quirk, 2002) and humans (Phelps, Delgado, Nearing, & LeDoux, 2004). The following review will present evidence that is consistent with the view that higher-order cortical processes are closely involved in fear acquisition and extinction learning in animals and humans (Delgado, Olsson, & Phelps, 2006; Lovibond, 2004). It will be argued that extinction learning and exposure therapy are forms of cognitive intervention that specifically changes harm expectancy. It should be noted that I will not present an exhaustive review of learning processes, but rather a focused, clinically relevant discussion of models that are derived from Pavlovian conditioning and their associations with cognitive theory and therapy.

1. Cognitive processes in models of fear acquisition

1.1. The simple conditioning model

The idea that direct conditioning is primarily responsible for fear acquisition in humans was the dominant view for many decades. For example, the study of Little Albert by Watson and Rayner (1920) has frequently been used as an example of fear conditioning in humans. In the experiment, Watson and Rayner (1920) first presented Little Albert, an 11-month old orphan with several objects including a rat, a rabbit, a fur coat, and a dog. Little Albert did not show any signs of fear or other negative emotional reactions towards these objects. However, the infant cried in response to the US, which was a loud noise made by banging a heavy hammer against a steel bar. During the conditioning trial, the experimenters presented the infant with a rat (CS). Each time the infant reached for the rat, the US was also presented. After seven trials over the course of 1 week, the subject was presented with only the rat. As predicted, the boy exhibited signs of fear and avoidance. The experimenters then presented Albert with other hairy objects, including a rabbit, a fur coat, and a dog. The boy reacted similarly distressed to each of these objects, suggesting that the response generalized to other objects with hair. A similar reaction was observed 5 days and, to a lesser degree, 31 days after the initial conditioning trial. When the subject was tested in a different context (by moving him to a different room) the fear response was still noticeable but significantly decreased. Watson and Rayner's (1920) classical experiment has often been used to illustrate the basic principles of fear conditioning, generalization, the context effect, and extinction in a human infant. Other

authors, however, identified a number of methodological limitations that make the findings ambiguous and difficult to interpret. For example, at least during the first two trials, the loud noise was contingent on Little Albert's touching the rat. Therefore, operant and instrumental conditioning might have accounted for Little Albert's response. A more in depth critique of Little Albert and its relevance to classical fear conditioning can be found in Harris (1979).

In later years, a number of empirical studies and theories further questioned some aspects of Mowrer's model, such as the assumption of temporal contiguity of the CS and the US. For example Rescorla (1988) assumed that the crucial aspect in conditioning is the information that one stimulus gives about another (i.e., the CS-US contingency). According to this view, conditioning only occurs if the probability of the US in the presence of the CS is different than in its absence. Other theorists, in contrast, argue that contingency is neither necessary nor sufficient for conditioning (e.g., Bitterman, 2006; Papini & Bitterman, 1990).

In addition to traditional Pavlovian conditioning, fear can also be acquired without directly experiencing the CS and US. For example, Mineka and colleagues demonstrated that young Rhesus monkeys learn quickly to acquire a fear of snakes simply by observing another monkey responds fearfully to them. Similarly, observing another monkey responding nonfearfully can effectively prevent the acquisition of this fear following later exposure to models behaving fearfully (e.g., Mineka & Zinbarg, 2006). In other words, fear can be acquired by observing two events contiguous in time: the snake and the fear response to the snake exhibited by another monkey. Moreover, fear can be prevented or inhibited through observation, suggesting the involvement of higher-order cognitive processes.

1.2. The preparedness theory

Common fears are not randomly distributed. For example, cars are considerably more dangerous to pedestrians than are dogs or snakes. This had led some researchers to assume that animals and humans specifically acquire fears of objects that were once potentially harmful or dangerous (e.g., snakes or predators), and for which the capacity to recognize and respond quickly to this potential danger would be advantageous for one's survival and reproductive fitness. This "preparedness theory" (Seligman, 1971) was an early attempt to explain human fears in the context of evolutionary psychology. The theory (also known as the "selective association model") states that humans are biologically "prepared" to acquire the fear of certain objects or situations that used to threaten the survival of our species. This model was developed to explain the rapid acquisition and seeming irrationality of common phobias, as well as their high resistance to extinction. Phobic fear was seen as a noncognitive and irrational response that is fundamentally different from conditioned fear in the laboratory (Seligman, 1971).

Consistent with the preparedness theory, Öhman and his colleagues (Öhman, Erixon, & Lofberg, 1975; Öhman & Soares, 1998) found that conditioned responses (using skin conductance measures) to fear-relevant CS's (e.g., pictures of spiders and snakes) took longer to extinguish than responses to fear-irrelevant stimuli (e.g., pictures of flowers and mushrooms). However, a number of experimental studies question the validity of various postulations of the model (see McNally, 1987, for a review). For example, latent inhibition has been used to explain the belongingness between stimuli and fear response. Latent inhibition is the phenomenon that simple prior exposure to a CS before the CS and US are ever paired together reduces the amount of subsequent conditioning to the CS when paired with the US (e.g., McLaren & Mackintosh, 2000).

Another postulation by the model that has not been supported is the assumption that fear acquisition of prepared stimuli is a primitive form of learning with little cognitive involvement. For example, Dawson, Shell, and Banis (1986) measured skin conductance response and US expectancy online (i.e., the expectancy that the US will follow the CS). The results showed

that US expectancy ratings mirrored skin conductance response and both measures suggest the same resistance to extinction effect. Similar findings were also reported by Davey (1992). The author argued that the heightened expectation of aversive outcomes following the presentation of feared stimuli may generate and maintain a learned association between fear and expectation. This cognitive bias could explain why some stimuli, but not others, become associated with aversive outcomes (Davey, 1992, 1995).

1.3. The neo-conditioning model

Learning through verbal communication and observation seems to be particularly common in humans (e.g., Hygge & Öhman, 1978; Rachman, 1977). As a result, theorists have considered modifications of the simple conditioning models to explain how fear in humans can be acquired. These modifications place a particular emphasis on cognitive processes. Specifically, Rachman (1976, 1977) proposed a model, which has become known as the “neo-conditioning” model. This model suggests that fear can be acquired through three different pathways: (1) classical conditioning (the pathway that is identical to Mowrer’s model); (2) modeling; and (3) vicarious/information transmission. The indirect pathway allows for conditioning to occur even when CS and US are separated in time, as long as the subject learns the relationship between events (Rachman, 1991). An additional pathway was later added to account for fears that are apparently inherited, such that they appear without any relevant associative learning experiences, either direct, or indirect (Menzies & Clarke, 1995; Poulton & Menzies, 2002).

Rachman’s (1976,1977) conditioning model is plausible and received preliminary support from various studies (Öst & Hugdahl, 1981,1983;Stemberger, Turner, Beidel, & Calhoun, 1995). However, a number of other retrospective and prospective studies raised questions about the validity of this model. For example, some studies failed to identify any conditioning events (McNally & Steketee, 1985;Menzies & Clarke, 1995) or reported that such events occurred many years after the onset of the phobia (Hofmann, Ehlers, & Roth, 1995). Furthermore, when giving the choice, most phobic individuals choose panic attacks as the most important reason for their phobia (Hofmann et al., 1995;McNally & Steketee, 1985). Finally, many individuals who did experience such conditioning events did not develop any fears (DiNardo, Guzy, & Bak, 1988).

As noted elsewhere (McNally, 2002a,b; McNally & Steketee, 1985), the inconsistencies reported in the literature may be related to the different definitions of a conditioning event that the various studies used. Some studies defined a conditioning event as the CS-US pairing in which the US is a potentially harmful or traumatizing event (such as a car accident or dog bite). In contrast, others used a more liberal definition and considered a panic attack as a possible US in the presence of the CS (e.g., Barlow, 2002). This obviously raises the important question why uncued panic attacks happen in the first place (for a discussion, see Bouton et al., 2001).

1.4. The modern learning theory perspective

Öhman and Mineka (2001) present evidence for a selective associative model and the existence of an evolutionarily evolved fear module that shows four characteristics, each shaped by evolutionary contingencies: (1) selectivity with regard to the input (i.e., the fear module is sensitive to stimuli that have been correlated with threatening encounters in the evolutionary past); (2) automaticity (i.e., the evolutionarily fear-relevant stimuli can trigger the module in the absence of any conscious awareness); (3) encapsulation (i.e., the module is resistant to conscious cognitive influences); and (4) specialized neural circuitry (i.e., the module is controlled by a specific neural circuit that has been shaped by evolution).

A further elaboration of the contemporary learning theory perspective on the etiology of anxiety disorders was provided by Mineka and Zinbarg (2006). This model assumes that, aside from

direct or vicarious traumatic conditioning experiences, a number of other factors influence CS-US conditioning. These factors include the perceptions of controllability and predictability of stressful events, the properties of the CS (such as fear relevance, temporal proximity to stressful events, etc.), and a number of vulnerabilities (temperament, as well as social and cultural learning history).

The case of post-traumatic stress disorder (PTSD) might illustrate some of these factors. PTSD is the only anxiety disorder that includes a direct conditioning event in its diagnostic definition. Consistent with the conditioning model, war veterans with PTSD who are exposed to trauma cues by watching a video clip of a combat scene typically show intense emotional responses that are elicited by the specific trauma cues, which are the conditioned stimuli that were previously paired with the traumatic event (e.g., Foa, Zinbarg, & Rothbaum, 1992). However, exposure to trauma is not sufficient to develop PTSD. Although the majority of individuals in a large community sample (59.2%) reported stressful events that can be considered in the diagnosis of PTSD, only 9.2% of these events led to the DSM-IV diagnosis of PTSD (Breslau & Kessler, 2001). Even when considering the subjective distress criterion, only 12% of these events culminated in PTSD. These data suggest that trauma exposure is not sufficient to develop PTSD. Prior experiences with uncontrollable events (Mineka & Zinbarg, 2006), the intensity of autonomic arousal following the trauma (Pitman et al., 2002), and a number of individual characteristics, such as intelligence (Macklin et al., 1998), all determine whether a potentially traumatizing event will or will not lead to PTSD in a particular person.

The modern learning perspective of fear acquisition by Öhman and Mineka (2001) and Mineka and Zinbarg (2006) places a particular emphasis on cognitive processes, such as the controllability and predictability of the aversive event. At the same time, however, Öhman and Mineka (2001) assume that the fear module is impenetrable to conscious cognitive control (i.e., is encapsulated). In other words, once confronted with a snake, the fear module of a snake phobic is activated and cannot be aborted easily by any cognitive strategies. Öhman and Mineka (2001) hypothesize that the fear module originated and is neurologically located in the subcortical areas of the brain, especially the limbic structure. Therefore, the judgment of the fear relevance is a “quick and dirty” process that rather risks false positives than false negatives by proceeding without neocortical influence (LeDoux, 1996). However, Öhman and Mineka (2001) caution that the encapsulation assumption should not be taken to imply that cognitions are unimportant in phobias, because the amygdala, the neural node of the fear network in humans, is reciprocally connected with areas of the frontal lobe that serve to regulate emotions. Therefore, the fear circuitry in rats suggests that the amygdala and its projections are involved in both the acquisition and expression of conditioned fear (e.g., Davis, 1992; LeDoux, 1996).

In sum, the simple Pavlovian conditioning model (Mowrer, 1939; Watson, 1924) shows a number of significant weaknesses as a model of fear acquisition in humans. As a result, a number of alternative models were discussed, including the preparedness theory (e.g., Seligman, 1971), the neo-conditioning theory (Rachman, 1976, 1977, 1991), the nonassociative model (e.g., Poulton & Menzies, 2002), and modern learning theories (e.g. Bouton et al., 2001; Mineka & Zinbarg, 2006; Öhman & Mineka, 2001). As pointed out by McNally (2002b), none of these theories can fully account for all cases, and some of them became so complex that it has been difficult to test them in the laboratory, let alone in clinical practice. Common features of contemporary theories of fear acquisition include the consideration of temperamental variables, such as anxiety sensitivity (McNally, 2002a), and cognitive processes. These cognitive processes are evident in observational and informational learning, as well as during direct conditioning events. Specifically, it has been demonstrated that US expectancies and the perception of controllability and predictability about stressful events are essential aspects of fear conditioning in humans.

For the remainder of this discussion, I will refer to US expectancies and the perception of controllability and predictability of future events as *cognitive processes*. The goal is to identify these processes in extinction learning and exposure therapy and to discuss the implications for clinical research. It remains unclear whether these cognitive processes causally implicate fear mechanisms or whether they are simply epiphenomenal correlates to the actual mediator. Nevertheless, there is sufficient evidence to conclude that extinction learning and exposure therapy are not simply automatic, unconscious, and low-level processes. Instead, higher-order cognitive processes that modulate harm expectancy and the perception of control are closely linked to extinction learning and exposure therapy. Therefore, although often attempted in treatment component analyses, I will conclude that it is impossible to conduct successful exposure therapy without also changing these cognitive processes.

2. Cognitive processes in extinction learning

Fear acquisition and extinction involve the learning of associations between passively observed events. It is typically assumed that animals only learn about causal relations by using basic associative mechanisms. However, a recent experiment has shown that rats can perform causal reasoning without the reliance on associative processes (Bleisdell, Sawa, Leising, & Waldmann, 2006). Causal reasoning allows the animal to predict outcomes on the basis of observation. Furthermore, a number of experimental studies have shown that cognitive factors directly modulate the CS-US contingency. Specifically, reductions in CS-US expectancy are correlated with reductions in CRs during the course of extinction (Biferno & Dawson, 1977; Lipp & Edwards, 2002), and extinction is associated with a reduction in the strength of the CS-US expectancy (Shell, Dawson, & Marinkovic, 1991). It has further been shown that experimentally induced autonomic fear responses can be eliminated by simply informing subjects that the US will no longer follow the CS (Grings, 1973). Moreover, extinction can be disrupted by adding a stimulus that serves as a safety signal (Lovibond, Davis, & O'Flaherty, 2000). These findings suggest that extinction is caused by changes in expectancies and contingency beliefs that are stored in long-term memory (Lovibond, 2004). In other words, extinction results in new learning about CS-US expectancy (namely that the CS no longer signals a US), which competes with the previously learned knowledge (namely that the US is followed by the CS).

An experiment by Phelps et al. (2001) further demonstrates the effects of verbal instructions on the biological correlates of fear acquisition. Participants in this study were told that one of two CS's (the CS+) was associated with the possibility of an aversive shock, while the other CS (CS-) signaled safety. The subjects never actually received a shock during the experiment. The researchers recorded brain activity using fMRI and found left amygdala activation when comparing CS+ and CS- trials. Furthermore, CS+ trials resulted in greater skin conductance response than CS- trials. The results of this study demonstrate that providing verbal instructions to explain the CS-US contingency has the same effect as Pavlovian CS-US pairing.

In sum, the literature on cognitive processes in extinction learning suggests that extinction is accompanied by changes in the CS-US contingency. Moreover, verbal instructions can directly modify extinction processes by changing this contingency, which could also explain the mechanism of exposure therapy. Similarly, a number of psychological theories point to cognitive processes as the primary mechanism of change during exposure therapy.

3. Cognitive processes in exposure therapy

Cognitive therapy implies that changes in cognitions are responsible for treatment gains. However, cognitive therapy is not limited to cognitive modification; the client's emotional and behavioral responses are of equal importance. Effective cognitive therapy targets all aspects of an emotional disorder, including emotional experience, behavior, and cognitions.

Accordingly, Beck (1985) distinguishes among the intellectual, the experiential, and the behavioral approaches, all of which are important aspects of cognitive therapy. As part of the intellectual approach, clients learn to identify their misconceptions, test the validity of their thoughts, and substitute them with more appropriate concepts. The experiential approach helps clients to expose themselves to experiences in order to change these misconceptions. The central element of the behavioral approach is to encourage the development of specific forms of behavior, which leads to more general changes in the way patients view themselves and the world.

In cognitive therapy, cognitions are assumed to play a crucial role in the maintenance and development of the anxiety response. For example, in individuals with panic disorder, the catastrophic misinterpretation of the rush of physical sensations experienced during a panic attack is assumed to exacerbate their distress and perpetuate their difficulties (Clark, 1986). Some cognitions are seen as specific to certain anxiety disorders. For example, in the case of social phobia, the focus is usually placed upon the consequence of public scrutiny and subsequent negative evaluation. In contrast, individuals with agoraphobia feel distressed about the inability to escape or get help in case they develop panic or panic-like symptoms in a variety of situations.

Although some of the cognitions typically associated with each diagnosis may be disorder-specific, there are a number of commonalities of cognitions across the anxiety disorders. For example, all maladaptive anxiety-related cognitions are assumed to be future-oriented perceptions of danger or threat (e.g., what is about to happen, what will happen). This sense of danger may involve either physical (e.g., having a heart attack) or psychological (e.g., anxiety focused on embarrassment) threat. During treatment, the patient is provided with an opportunity to challenge these beliefs by conducting hypotheses by exposing herself to situations that are likely associated with the expected harmful consequences. In other words, the patient is encouraged to re-evaluate harm expectancy which, as I reviewed earlier, appears to be the commonality between extinction learning and exposure therapy.

It has further been shown that repeated experiences with uncontrollable aversive events can lead to pathological emotional states, such as anxiety and depression (e.g., Barlow, 2002). Therefore, it has long been suggested that the degree to which people view events as within their control may be a fundamental mediator of psychopathology and treatment (e.g., Rotter, 1966). Modern emotion theories assume that the unexpected experience of bursts of emotions may lead to anxiety disorders in vulnerable individuals because they view their own emotions or bodily reactions as out of control (Barlow, 2002). In the case of panic disorder, for example, vulnerable individuals may unexpectedly experience a brief and intense burst of fear and subsequently develop anxiety over the possibility of the reoccurrence of this response in an uncontrollable manner. It is hypothesized that all anxiety disorders share a lack of perceived control over negative emotional and bodily reactions. Similar predictions have been made based on related models that assume that decreased harm expectancy (Foa & Kozak, 1986; Zoellner, Echiverri, & Craske, 2000) and enhanced self-efficacy (Bandura, 1986; Jones & Menzies, 2000) are causally related to improvements during exposure therapy. Again, this is consistent with the notion that changes in the CS-US expectancy are common elements of fear reduction in extinction learning, exposure therapy and cognitive-behavioral therapy.

4. Implications for therapy research

Exposure is an important, if not the most important, treatment component of effective interventions for the range of anxiety disorders, including social phobia (e.g., Feske & Chambless, 1995), panic disorder and agoraphobia (e.g., Clum, Clum, & Surls, 1993), obsessive-compulsive disorder (e.g., Abramowitz, 1997), post-traumatic stress disorder (e.g.,

Foa et al., 1999), and specific phobias (e.g., Öst, Svensson, Hellstrom, & Lindwall, 2001). A case in point is social phobia. The prominent model of social phobia is the cognitive perspective, which assumes that effective psychological treatment needs to change the person's self-perception in a more positive direction (Clark & Wells, 1995). Therefore, some investigators argued that a treatment that specifically targets dysfunctional beliefs about social situations should be more effective than simple exposure procedures. The literature reports eight controlled clinical studies in which investigators directly compared cognitive-behavioral therapy to exposure therapy without explicit cognitive interventions (Butler, Cullington, Munby, Amies, & Gelder., 1984; Emmelkamp, Mersch, Vissia, van der Helm, 1985; Gelernter et al., 1991; Hofmann, 2004; Hope, Herbert, & White, 1995; Mattick & Peters, 1988; Mattick, Peters, & Clark, 1989; Scholing & Emmelkamp, 1993a,b). In only two of the trials did the effects of cognitive-behavior therapy exceed those of exposure alone at post-treatment (Butler et al., 1984; Mattick & Peters, 1988). These component analyses studies were based on the assumption that simple exposure procedures are sub-optimal because the mechanism of change is via extinction learning, which is not mediated by cognitive changes. However, based on the present review, there is no evidence to support this assumption. Instead, the empirical evidence suggests that exposure procedures without explicit cognitive intervention strategies have very similar effects than comprehensive cognitive-behavioral treatments, simply because exposure therapy is mediated through changes in cognitions, and specifically changes in CS-US (harm) expectancy.

The efficacy of exposure therapy as compared to other, more comprehensive, treatment approaches has been surprising to many researchers. Moreover, it has been surprising that exposure therapy not only alleviates specific anxiety symptoms but is also associated with improvement in general functioning and results in significant cognitive changes. For example, after reviewing the outcome literature of CBT and exposure therapy without explicit cognitive intervention for social phobia, Feske and Chambless (1995) wrote:

“Overall, CBT and exposure yielded very similar pre-post and prefollow-up effect for self-report measures of social phobia, cognitive symptoms, and depressed/anxious mood. Moreover, there was no evidence of differential dropout between the two treatment modalities. These findings are disappointing in light of the enthusiasm for CBT. In particular, investigators had hoped that CBT would lead to greater improvement in cognitive distortions associated with social phobia and would thus produce more generalized and durable treatment effects than exposure without explicit cognitive components” (pp. 712-713).

These findings are only surprising if we assume that exposure therapy (and extinction) only involves primitive, automatic, and low-level processes that need to be supplemented with cognitive therapy to effectively target dysfunctional cognitive processes. If, on the other hand, we assume that exposure therapy is cognitively mediated, we would expect exposure therapy to have very similar effects as more comprehensive treatments, such as cognitive therapy. In fact, my research group has found that repeated exposures to feared public speaking situations lead to very similar short-term reductions of social anxiety symptoms than a comprehensive cognitive-behavioral treatment that targets a variety of dysfunctional thoughts related to social phobia (Hofmann, Moscovitch, Kim, & Taylor, 2004). Moreover, it has been shown that treatment changes during cognitive-behavioral therapy and exposure therapy are both mediated via changes in cognitions (Hofmann, 2004). These results are consistent with previous studies suggesting that simple exposure procedures lead to significant improvements in negative self-perception (Hofmann, 2000) and other negative cognitions (Newman, Hofmann, Trabert, Roth, & Taylor, 1994). These data illustrate the importance of cognitive processes in exposure therapy. Although the precise mechanism of treatment change during exposure therapy remains unclear, it can be concluded that repeated exposure practices (whether with or without explicit cognitive strategies) change harm expectancy, among other things. The effect of exposure

therapy on other cognitive variables, such as changes in negative self-perception in social phobia, is difficult to explain at this stage and will require additional research.

Recognizing the importance of cognitive processes in fear acquisition, extinction, and exposure therapy offers a new possibility for intervention research, namely to improve the effects of exposure therapy with pharmacological interventions that are believed to act as cognitive enhancers. Animal research has shown that fear and extinction learning are both blocked by antagonists at the glutamatergic *N*-methyl-d-aspartate (NMDA) receptor, which is critically involved in learning and memory. For example, intra-amygdala infusions of an NMDA receptor antagonist shortly before extinction training dose-dependently block extinction (Falls, Miserendino, & Davis, 1992). Moreover, d-cycloserine (DCS), a partial NMDA agonist dose-dependently enhances extinction in rats (Ledgerwood, Richardson, Cranney, 2003, 2004; Walker, Ressler, Lu, & Davis, 2002). Interestingly, DCS can still facilitate extinction when given up to about 3 h after extinction training, which suggests that DCS acts to facilitate memory consolidation of extinction (Richardson, Ledgerwood, & Cranney, 2004).

In an initial effort to demonstrate the utility of DCS as a method to enhance exposure therapy in humans, Ressler et al. (2004) randomized 28 subjects with a DSM-IV diagnosis (APA, 1994) of specific phobia of heights (acrophobia) to 2 sessions of virtual reality exposure therapy preceded in double-blind fashion by administration of single doses of placebo or DCS (50 or 500 mg) taken 2-4 h prior to each of the sessions. Exposure therapy combined with DCS resulted in significantly larger reductions of acrophobia symptoms at 1 week and 3 months following treatment with no difference in efficacy between the 2 doses and no reports of adverse effects from DCS administration. Subjects receiving DCS also showed significantly greater decreases in post-treatment skin conductance fluctuations during the virtual exposure and significantly greater improvement compared to placebo on general measures of real-world acrophobia symptoms that were evident early in treatment and were maintained at 3 months.

In another double-blind placebo-controlled study, 27 patients with a principal DSM-IV diagnosis of social anxiety disorder (social phobia) were assigned to either receive 5 exposure group sessions plus DCS (50 mg) or 5 exposure group sessions plus pill placebo (Hofmann et al., 2006). The exposure practices of increasing difficulty consisted of giving speeches about topics, chosen by the therapists, in front of the other group members or confederates and a video camera. The level of social anxiety was assessed at baseline, post-treatment, and 1 month after the last session (1-month follow-up). The results showed that patients who received DCS prior to the exposure sessions showed greater reduction in their social anxiety than patients who received placebo prior to the exposures. The difference between the two groups increased linearly with time, with the greatest treatment effects of DCS being evident at follow-up.

Together, the clinical outcome studies by Hofmann et al. (2006) and Ressler et al. (2004) provide support for the use of a cognitive enhancer to augment exposure therapy in patients with anxiety disorders. However, the evidence is still preliminary and a number of additional studies around the world are currently being conducted to replicate and extend these early findings and to dissect the specific mechanism.

5. Conclusion

Mowrer's (1939) model of fear acquisition was an important step toward understanding fear conditioning and extinction in humans. It was readily adopted as a model for fear acquisition and anxiety reduction in humans. However, the view that extinction learning is a low-level process that does not involve any higher-order cognitive processes was an overly simplistic and misleading conceptualization. As a result, early models of fear acquisition (e.g., Mowrer, 1939; Seligman, 1971; Watson, 1924, Watson & Rayner, 1920) were revised to include the

role of cognitive processes (Mineka & Zinbarg, 2006; Öhman & Mineka, 2001; Rachman, 1976, 1977). In humans, these processes are not only evident in cases of observational and informational learning, but can also be seen in changes of US expectancies and perception of controllability and predictability. Similarly, it appears that extinction learning and exposure therapy involve higher-order cognitive processes. Specifically, the present review of the literature suggests that a reduction in US expectancy mediates extinction learning and exposure therapy, as well as cognitive-behavioral therapy.

This view is consistent with a number of psychotherapy models that emphasize the prediction of harm (Foa & Kozak, 1986), perception of control (Barlow, 2002; Clark, 1986, Rotter, 1966), and sense of competence in mastering potential threat (Bandura, 1986) during exposure procedures. In essence, the present review of empirical data and theoretical models suggests that fear extinction in animals and exposure therapy in humans share similar cognitive processes that are associated with changes in CS-US expectancy. I conclude that exposure therapy is a form of cognitive intervention that specifically changes harm expectancy.¹

Comparing conditioning studies with psychotherapy studies is not without problems — humans are more complex than animals; exposure therapy is more complex than extinction training; and anxiety is more complex than fear. Contemporary emotion theorists characterize fear (but not anxiety) as a “basic” emotion. Basic emotions are believed to occur in all human beings, across all cultures. They fulfill useful, evolutionarily adaptive functions in dealing with fundamental life-tasks by mobilizing quick and adaptive reactions in response to threatening situations (e.g., Ekman, 1992; Izard, 1992; Öhman, 1992; Plutchik, 1980; Tomkins, 1963). In contrast to fear, anxiety is conceptualized as a cognitive association that connects basic emotions (such as fear) to events, meanings and responses (Barlow, 2002; Izard, 1992). These cognitive associations are less “hardwired” than basic emotions and, therefore, vary widely depending on the individual and the situation. Although fear and anxiety are different, both are adaptive emotional responses to threat. If these emotions become maladaptive (e.g. excessive in intensity, frequency or duration), they may develop into anxiety disorders.

A closer examination of the animal literature on conditioning and extinction makes it difficult to distinguish fear and anxiety simply based on the involvement of cognitive processes. The present review suggests that even primitive Pavlovian fear conditioning and extinction are modulated and mediated by cognitive processes. Specifically, extinction in animals is closely associated with changes in CS-US expectancy, and exposure therapy in humans is closely associated with changes in perception of predictability of stressful events, among other cognitive variables.

Knowing the neuroscience literature, it should come as no surprise that cognitive processes are critically important in even primitive forms of learning. The fear circuitry in rats suggests that the amygdala and its projections with areas of the frontal lobe are involved in both the acquisition and expression of conditioned fear (e.g., Davis, 1992; LeDoux, 1996). Moreover, rats can predict outcomes simply on the basis of observation (Bleisdell et al., 2006), which points to complex cognitive processes even in rodents during fear and extinction learning.

¹One of the reviewers correctly pointed out that it might be difficult to ascertain the expected US in all phobia cases. For example, very few individuals with height phobia have experienced a fall from high places. Similarly, it is unlikely that a panic attack is the feared consequence, because exposure to heights typically produces intense fear and is, therefore, a highly likely and expected event. Instead, patients with height phobia may be more likely to report fear of losing control and jumping or fainting and falling, although they never experienced such an event. As I reviewed earlier, most phobias are unlikely to be the result of a direct CS-US pairing. Observation and informational learning are more likely pathways to establish CS-US expectancy that change as a result of exposure intervention.

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