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Gradients of Fear Potentiated Startle During Generalization, Extinction, and Extinction Recall—and Their Relations With Worry

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It is well established that fear conditioning plays a role in the development and maintenance of anxiety disorders. Moreover, abnormalities in fear generalization, extinction, and extinction recall have also been associated with anxiety. The present study used a generalization paradigm to examine fear processing during phases of generalization, extinction, and extinction recall. Specifically, participants were shocked following a CS+ and were also presented with stimuli that ranged in perceptual similarity to the CS+ (i.e., 20%, 40%, or 60% smaller or larger than the CS+) during a fear generalization phase. Participants were also presented with the same stimuli during an extinction phase and an extinction recall phase 1 week later; no shocks were presented during extinction or recall. Lastly, participants completed self-report measures of worry and trait anxiety. Results indicated that fear potentiated startle (FPS) to the CS+ and GS ± 20% shapes was present in generalization and extinction, suggesting that fear generalization persisted into extinction. FPS to the CS+ was also evident 1 week later during extinction recall. Higher levels of worry were associated with greater FPS to the CS+ during generalization and extinction phases. Moreover, individuals high in worry had fear response gradients that were steeper during both generalization and extinction. This suggests that high levels of worry are associated with greater discriminative fear conditioning to threatening compared to safe stimuli and less fear generalization to perceptually similar stimuli.

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It has long been established that classical conditioning of fear plays an integral role in the development and maintenance of anxiety-related psychopathologies (for reviews see Mineka & Oehlberg, 2008; Mineka & Zinbarg, 2006). Broadly, fear conditioning is an associative learning process through which a neutral stimulus (i.e., conditioned stimulus; CS) becomes associated with, and eventually predicts, the occurrence of a fear-eliciting unconditioned stimulus (i.e., US) after repeated pairings (Delgado, Olsson, & Phelps, 2006; Lissek et al., 2005; Pavlov & Anrep, 1927; Pavlov, 1927). Several mechanisms have been proposed to explain how aberrant fear conditioning could contribute to anxiety, such that anxious compared to nonanxious individuals display: (a) easier conditionability (Orr et al., 2000); (b) failure to inhibit fear to stimuli that signal safety (Davis, Falls, & Gewirtz, 2000); and (c) overgeneralization of fear to stimuli that are perceptually similar to a CS (Lissek et al., 2008, 2009).

Theories of overgeneralization of fear have garnered increased empirical attention in recent years. Generalization is a learning process through which a fear response can become elicited by stimuli that are similar to the CS (Lissek et al., 2009; Pavlov, 1927). In fear generalization paradigms, fear responses are examined to both the presentation of a CS+ (the "+" indicates reliable prediction of the US—typically electric shock) as well as a range of generalization stimuli (GS; never paired with the US) that vary in perceptual similarity to the CS+ (Lissek et al., 2008). This results in a gradient of fear responding. In both animal and healthy human samples, the most common generalization gradient appears as a steep slope (and/or slightly curvilinear), with fear responding that is maximal to the CS+ and decreases to GS as they decrease in similarity to the CS+ (Armony, Servan-Schreiber, Romanski, Cohen, & LeDoux, 1997; Greenberg, Carlson, Cha, Hajcak, & Mujica-Parodi, 2013a; Hajcak et al., 2009; Lissek et al., 2008; Vervliet, Kindt, Vansteenwegen, & Hermans, 2010).

Fear generalization may be particularly relevant to anxiety disorders because different gradients of fear may be thought of as individual differences in fear learning that could explain why some individuals are at risk for anxiety disorders while others are not. For instance, while a steep or curvilinear generalization gradient may be indicative of average/normal generalizing tendencies, a more flattened, linear, and less steep fear gradient would likely indicate stronger generalization tendencies and a weaker tendency to differentiate threat from safety; such a pattern may be more characteristic of anxious psychopathology.

In a test of these predictions, Lissek and colleagues (2010) assessed fear potentiated startle (FPS) response to a CS+ as well as perceptually similar stimuli in individuals with panic disorder (PD) and healthy controls. Results indicated that PD patients exhibited startle potentiation to the CS+, and this generalized to the three most similar/closest GS, which resulted in a fear response gradient that was less steep and less curvilinear than that of healthy controls. Self-reported risk of shock to each stimulus corroborated the physiological findings such that perceived risk was highest to the CS+ and generalized in PD patients compared to controls (Lissek et al., 2010). Similar results have been found in generalized anxiety disorder (GAD) as well: gradients of both FPS and perceived risk of shock were less steep in GAD patients compared to controls (Lissek et al., 2014).

Other research has not found evidence of overgeneralization in GAD. Specifically, Greenberg and colleagues (2013b) found that GAD patients and healthy controls exhibited equivalent fear generalization gradients as assessed by neural reactivity measured using fMRI (e.g., insula, anterior cingulate cortex, supplementary motor area, and caudate), pupillary response, and shock likelihood ratings. Yet, activity in the ventromedial prefrontal cortex (vmPFC), an area implicated in fear inhibition, differentiated GAD patients from controls—flatter neural generalization gradients were present in GAD compared to controls. Hence, support for overgeneralization in GAD is mixed.

In addition to the capability of organisms to learn fear, it is also possible to extinguish conditioned fear. After repeated exposures of a CS+ that is no longer paired with a US, fear responses gradually diminish and the association is weakened/extinguished. Researchers identify two unique processes in extinction: extinction learning (the initial decline in fear responding that creates a new extinction memory) and extinction recall (the later retrieval of extinction memories after some time delay; Milad et al., 2009; Quirk, Russo, Barron, & Lebron, 2000). Just as individuals with anxiety have displayed aberrant fear conditioning and generalization, they have also exhibited deficient extinction learning (Orr et al., 2000; Peri, Shakhar, Orr, & Shalev, 2000) and deficient recall of extinction memories (Milad et al., 2008, 2009). For instance, after undergoing fear conditioning, patients with posttraumatic stress disorder (PTSD) compared to healthy controls continued to exhibit enhanced skin conductance response to a CS+ during extinction trials (Orr et al., 2000). In another investigation, Milad and colleagues (2009) had patients with PTSD and healthy controls go through a fear conditioning and extinction phase and then return the following day to engage in an extinction recall phase. PTSD patients compared to controls displayed impairment in extinction recall, evidenced by equivalent skin conductance responses to extinguished and nonextinguished CS+ (Milad et al., 2009).

The aforementioned research in anxiety disorders has separately implicated deficiencies in fear generalization, extinction, and extinction recall. The primary goal of the present study was to comprehensively examine all of these processes in the same sample of individuals using a generalization paradigm. To this end, we examined fear response gradients in a large sample during experimental phases of fear generalization, extinction, and extinction recall 1 week later in time. Specifically, participants first underwent a fear generalization task in which they were exposed to a CS+ in addition to a range of GS stimuli (the same as reported in Hajcak et al., 2009); fear responses were assessed using the eyeblink startle reflex. We hypothesized that fear generalization gradients would mimic previous studies, such that startle response would peak at the CS+ and steadily decrease as stimuli appeared less similar to the CS+. In addition, we hypothesized that self-reported shock likelihood would coincide with the patterns observed in startle response. Extinction and extinction recall analyses were more exploratory. It is possible that generalization of fear to GS may persist into extinction or even 1 week later during extinction recall. Conversely, it is also possible that extinction might abolish the generalization gradient.

A secondary goal of the present study was to examine how fear gradients in these experimental