Available online at www.sciencedirect.com
ScienceDirect
Behavior Therapy 46 (2015) 611–626
Behavior Therapy
www.elsevier.com/locate/bt

Generalization of Fear to Respiratory Sensations

Mathias Schroijen
Meike Pappens
University of Leuven

Koen Schruers
University of Leuven
Maastricht University

Omer Van den Bergh
Bram Vervliet
Ilse Van Diest
University of Leuven

Interoceptive fear conditioning (IFC), fear generalization and a lack of safety learning have all been hypothesized to play a role in the pathogenesis of panic disorder, but have never been examined in a single paradigm. The present study aims to investigate whether healthy participants (*N* = 43) can learn both fear and safety to an interoceptive sensation, and whether such learning generalizes to other, similar sensations. Two intensities of inspiratory breathing impairment (induced by two pressure threshold loads of 6 and 25 cm$H_2$0) served as interoceptive conditional stimuli (CSs) in a differential conditioning paradigm. An inspiratory occlusion was used as the unconditioned stimulus (US). Generalization was tested 24 h after conditioning, using four generalization stimuli with intensities in-between CS+ and CS- (GSs: 8-10.5-14-18.5 cm$H_2$0). Measures included US-expectancy, startle blink EMG responses, electrodermal activity and respiration. Perceptual discrimination of interoceptive CSs and GSs was explored with a discrimination task prior to acquisition and after generalization. Results indicate that differential fear learning was established for US-expectancy ratings. The group with a low intensity CS+ and a high intensity CS- showed the typical pattern of differential fear responding and a similarity-based generalization gradient. In contrast, the high intensity CS+ and low intensity CS- group showed impaired differential learning and complete generalization of fear. Our findings suggest that interoceptive fear learning and generalization are modulated by stimulus intensity and that the occurrence of discriminatory learning is closely related to fear generalization.

Keywords: Interoceptive fear conditioning; Generalization; Dyspnea; Perceptual discrimination; Panic disorder

The present study was supported by a KU Leuven grant (PF/10/005) to the Centre for Excellence of Generalization Research in Ill Health and Psychopathology.

Address correspondence to Mathias Schroijen, MSc, or Ilse Van Diest, Ph.D., Centre for Excellence on Generalization Research in Ill Health and Psychopathology, Research Group Health Psychology, University of Leuven, Tiensestraat 102, 3000 Leuven, Belgium; e-mail: mathias.schroijen@ppw.kuleuven.be or ilse.vandiest@ppw.kuleuven.be.

Human fear conditioning is extensively used as an experimental model to study and understand the etiology and maintenance of panic and anxiety disorders (Bouton, Mineka, & Barlow, 2001; Mineka & Zinbarg, 2006). In fear conditioning, an initially neutral conditioned stimulus (CS) is paired with an intrinsically aversive stimulus (unconditioned stimulus, US) and through associative learning the CS–US pairing results in the CS becoming a predictive signal for imminent threat, typically eliciting conditioned fear responses (CR). These conditioned fear responses may consist of physiological arousal, subjective apprehension, or verbal responses and avoidance behavior (Lang, 1971). In differential fear conditioning paradigms, two CSs are used, of which one is paired with an aversive US (CS+: learned danger cue) and the other is presented in the absence of the US (CS-: learned safety cue), resulting in larger fear responses to the CS+ versus the CS-. Pathological forms of fear learning are considered hallmarks of psychopathologies, including anxiety disorders, depression, and posttraumatic stress disorder (Pollak et al., 2008). For instance, a meta-analysis across 453 anxiety patients and 455 healthy comparisons suggested enhanced fear-responding to the CS- instead of elevated differential responding to the CS+ as one of the robust conditioning correlates of clinical anxiety (Lissek et al., 2005). The enhanced fear-responding to the CS- may imply enhanced generalization of conditioned fear from the danger cue (CS+) to the resembling safety cue (CS-).

Generalization of fear is a learning mechanism whereby fear responses to a CS extend to a range of stimuli (generalization stimuli, or GSs) that resemble the original CS (Pavlov, 1927; Pearce, 1987; Rescorla & Furrow, 1977; Watson & Rayner, 1920). It allows an organism to extrapolate from one experience to other similar events without the necessity to experience them and, as such, fear generalization can provide an adaptive advantage. However, overgeneralization of fear to nonthreatening situations can be maladaptive and through excessive proliferation of cues that trigger anticipatory anxiety, fear generalization is considered a critical mechanism in the evolution from an initial panic attack to panic disorder (American Psychiatric Association, 2000). Although described extensively in the older conditioning literature (see Ghirlanda & Enquist, 2003, for a review), human fear generalization has regained interest only lately. To demonstrate generalization of conditioned fear, Lissek et al. (2008) used a differential conditioning procedure in which an electric shock was used as US, a large/small circle as CS+, a small/large circle as CS- and eight intermediate-sized circles as generalization stimuli. The strongest fear responses were observed to those circles that were perceptually most similar to the CS+ and fear responding decreased systematically with larger differences from CS+ (Lissek et al., 2008). The continuous downward slope of fear responding to stimuli with gradually less perceptual similarity to the CS+ is called the generalization gradient (Pavlov, 1927) and the strength of fear generalization is indexed by the steepness of the gradient whereby steeper gradients reflect less fear generalization (Lissek et al., 2014).

Because fear generalization seems to depend on the perceptual resemblance of the generalization stimulus to the CS+, the ability to discriminate between stimuli is a relevant factor. Interestingly, several findings have documented perceptual changes concomitant with fear learning (see Zaman et al., 2015, for an overview). For example, fear learning enhances the olfactory system's sensitivity in both animals (Kass, Rosenthal, Pottackal, & McGann, 2013) and humans (Åhs, Miller, Gordon, & Lundström, 2013; Li, Howard, Parrish, & Gottfried, 2008). Resnik, Sobel, & Paz (2011) on the other hand demonstrated that aversive conditioning decreased (auditory) discrimination for tones around the CS+, whereas perceptual discrimination for tones around the CS- was improved. Moreover, the physical "CS+/CS-" distance in auditory fear conditioning importantly moderates the effect, resulting in (a) increased discrimination when both CSs closely resemble and (b) decreased discrimination with increasing physical distance between CSs (Aizenberg & Geffen, 2013). Together these findings suggest that modulation of perceptual discrimination may be importantly connected with stimulus generalization.

Overgeneralization of conditioned fear to exteroceptive, visual stimuli has been identified as a pathogenic marker of panic (Lissek et al., 2010) and generalized anxiety disorder (Lissek, 2012: Lissek et al., 2014). In particular for panic patients, Lissek et al. (2010) showed a proclivity toward overgeneralization of conditioned fear and the authors suggest that the fear system of panic patients, compared to healthy individuals, is more easily triggered by less robust threat information. The model as used by Lissek et al. (2010) is very well suited to investigate exteroceptive (e.g., agoraphobic) components of panic disorder, but may not necessarily allow firm conclusions on, for instance, fear responses to somatic arousal that are elicited by fear itself (fear-of-fear). Interoceptive sensations have been hypothesized to play an important role in panic disorder (Barlow, 2002; Bouton et al., 2001), but studies investigating fear generalization to interoceptive fear conditioning (IFC) remain very scarce. Therefore, the present study aimed to investigate fear learning and generalization with interoceptive stimuli, and to explore changes in perceptual discrimination of these interoceptive stimuli in relation to fear generalization.

In contrast to exteroceptive stimuli, interoceptive stimuli are only privately perceived and are often characterized by a vague/systemic location and blurred on- and offset boundaries. Given their perceptually ambiguous nature, strong generalization effects may easily arise with interoceptive stimuli. However, despite its clinical relevance, generalization of interoceptive fear conditioning has not been studied. Fear conditioning paradigms