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Maximizing the generalization of fear extinction: Exposures to a peak generalization stimulus

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ABSTRACT

Experimental research has shown that generalization of fear extinction from a generalization stimulus (GS) is minimal compared to generalization of fear extinction from the conditional stimulus itself (CS+). This poses a challenge to extinction-based treatments of anxiety because the exact CS is often not known or unavailable. However, experimental studies failed to disentangle differences in stimulus identity (CS + or GS) from differences in the level of fear (GS typically elicits less fear than CS+). Here, we test the hypothesis that a high level of fear is key to extinction learning and generalization, rather than the identity of the stimulus under extinction (CS + or GS). For that purpose, we took advantage of the peak-shift phenomenon that describes the conditions under which a GS can elicit equal or higher levels of responding, compared to the CS+. Hence, we compared the generalizability of fear extinction following exposure to the CS + itself, to a 'weak' GS that elicits less fear, and to a 'peak' GS that elicits as much fear as the CS+. First, the results replicated, with a new set of stimuli, the observation that extinction of a skin conductance response and US-expectancy generalizes only weakly from a weak GS to CS+. Second, extinction generalized strongly from a peak GS towards CS+, as hypothesized. Third, extinction with the peak GS even outperformed extinction with the CS+, as it generalized more strongly across the generalization gradient. Together, these results support exposure treatment strategies that focus on the fear-eliciting potential of stimuli (often described as a fear hierarchy), rather than their learning history. We propose that stimulus typicality and/or intensity may explain the enhanced effects of a 'peak' GS over the CS+ in enhancing the generalization of fear extinction.

1. Introduction

Anxiety disorders, with a lifetime prevalence of 28.8%, are a widespread mental health problem (Kessler et al., 2005). Fear generalization, the broadening of fear over stimuli and contexts, has been considered a pathogenic process in various anxiety disorders (American Psychiatric Association, 1994; Dunsmoor & Paz, 2015; Dymond, Dunsmoor, Vervliet, Roche, & Hermans, 2015; Struyf, Zaman, Vervliet, & Van Diest, 2015). Notably, patients with panic disorder or generalized anxiety disorder display wider generalization of de novo conditioned fears in the laboratory, compared to healthy individuals (Greenberg, Carlson, Cha, Hajcak, & Mujica-Parodi, 2013; Lissek et al., 2014; Lissek & Grillon, 2010). It follows that any successful treatment for anxiety will have to promote equal or stronger generalization of its beneficial effects to counter the widely generalized fears.

Exposure therapy is an effective psychotherapeutic treatment and involves repeatedly exposing a patient to a dreaded situation or object within a safe therapeutic context (Hofman & Smits, 2008; Norton & Price, 2007). This procedure is thought to engage a fear extinction process that leads to the desired reduction of fear (Craske, Treanor, Conway, Zbozinek, & Vervliet, 2014).[1] Arguably, a new inhibitory CS—US association is formed during extinction learning that suppresses the earlier fear association (CS—US). As such, exposure therapy does not erase the fear association but leaves open the possibility that the fear returns when the effect of the inhibitory association wanes. Relapse is indeed a problem for exposure therapy, with estimates ranging from

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[1] This does not imply that exposure therapy only consists of fear extinction nor that fear extinction is the only mechanism responsible for the effects of exposure therapy. On the other hand, fear extinction is a crucial element of exposure therapy and since we use extinction of conditioned fear as a laboratory substitute for exposure therapy all our inferences will be limited to the fear extinction aspect of exposure therapy.

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19% to 62% (Craske & Mystkowski, 2006). It has been suggested that a failure to generalize the beneficial effects of fear extinction contributes to return of fear (Craske, Hermans, & Vervliet, 2018). More specifically, it has been extensively shown in both pre-clinical and clinical analog studies that fear may return in a new context after successfully extinguishing fear in another context (e.g., loss of fear in therapeutic session but again fearful at home; e.g., Effting & Kindt, 2007; Milad, Orr, Pitman, & Rauch, 2005; Mineka, Mystkowski, Hladek, & Rodriguez, 1999). Similarly, generalization of extinction over perceptually similar stimuli is limited (Barry, James, Vervliet, & Hermans, 2015; Vervliet, Vansteenwegen, & Eelen, 2004). As a clinical example of dog phobia after a bite incident, repeated exposures to another dog (generalization stimulus; GS) will often reduce fear of that dog, but may fail to generalize to other dogs. Other dogs would then continue to elicit fear, including the dog that bit you (the original conditional stimulus, CS+). The situation is different when fear extinction is achieved via exposures to the original CS+: This procedure does generalize the extinction effects readily across perceptually similar stimuli (Vervliet et al., 2004). Based on these laboratory findings, we can conclude that exposure therapy with the original CS + would probably outperform exposure therapy with generalization stimuli. Unfortunately, the original CS+ is often unknown or unavailable.

The empirical research on generalization of fear extinction from a GS is characterized by a potential confound, i.e. the GS elicited less fear than the original CS+ in these studies (e.g., Dubin & Levis, 1973; Vervliet et al., 2004; Vervoort, Vervliet, Bennett, & Baeyens, 2014). This reflects so-called generalization decrement: The level of conditional responding (fear) typically decreases with increasing dissimilarity (Honig & Urcuioli, 1981). One reason why extinction generalizes weakly from a GS to the CS + may simply be that the fear association is not fully activated by the GS and therefore not fully extinguished. The remaining, non-extinguished fear association will produce a 'return' when the original CS+ is encountered again. Thus, it remains to be seen whether fear extinction generalizes inherently different from a GS, or whether the observation of limited generalization is due to a difference in activation of the acquired fear association by these stimuli. This requires a methodology that allows equating the level of fear to the CS+ and the GS.

We and others have shown that generalization does not always involve a decrease in conditional responding (Ghirlanda & Enquist, 2003; Hanson, 1959; Purtle, 1973; Struyf, Iberico, & Vervliet, 2014). Under specific conditions, GSs can elicit a similar or even a stronger response than the original CS+. This occurs when the stimuli lie on an intensity dimension, that is, when the GS is a more intense version of the CS+ (e.g., a more intense tone). The more intense GS elicits equal or higher levels of conditioned responding, compared to the CS+. But even when GS and CS + are of equal intensity, a shift in the peak of responding can occur towards the GS. This has been observed in differential conditioning procedures, where the CS+ is paired with the US, but another stimulus on the dimension is not (CS-). For example, Dunsmoor and LaBar (2013) showed that when a blue-green CS+ is paired with an aversive US and a green CS- is not paired with the US, later tests with blue GSs elicit equal levels of fear as the CS + itself. Thus, fear is pushed away from the CS- towards the opposite side of the CS + on the dimension. For our current purpose, it follows that using an intensity dimension and/or a differential conditioning procedure makes it possible to create a GS that produces a level of fear equal to the CS+. This allows us to compare the generalizability of extinction between a GS and a CS+, independently from the level of fear. In more general terms, such comparison will allow us to test whether extinction generalization fares best by identifying and applying the original CS+ during exposures, or by identifying and applying the most fear-eliciting stimulus (CS + or GS).

The current paradigm is based on the procedure of Dunsmoor, Mitroff, and LaBar (2009), which used facial expressions along a dimension of increasing fear intensity, i.e. emotionally expressive faces of the same identity morphed between neutral and fearful endpoints. More specifically, they showed that, after fear acquisition, different facial expressions elicited various levels of fear (generalization of conditioned fear), and most importantly, the most fearful facial expression elicited as much fear as the CS+. Our experiment consists of a differential conditioning procedure, where a fearful facial expression (CS+) is repeatedly paired with a highly annoying, but not painful stimulus (e.g., electrical shock; US; induction of fear) and a relatively neutral facial expression (CS-) is not followed by the US (induction of safety). Subsequently, fear extinction occurs by recurrently presenting the CS + or a GS without being followed by the US. More specifically, participants received extinction with either CS+, a GS that elicits less fear than CS+ (weak GS) or a GS that elicits at least as much fear as CS + (peak GS). Finally, generalization of fear extinction is tested by exposing participants to new facial expressions that have never been associated with the US. In this way the current study will be able to disentangle the confound in generalization of fear extinction research by investigating the generalizability of extinction of the CS+, a weak GS and a peak GS. We have chosen to not fully extinguish fear during the extinction phase to avoid missing possible differences between the stimuli in their generalization of extinction due to a potential floor effect. More specifically, if full extinction of the CS + would generalize perfectly across the generalization gradient (i.e., none of the GSs elicit fear), then it would be impossible to evaluate whether generalization of extinction of one of the GSs is even more pronounced. We hypothesize that, compared to generalization of fear extinction of the CS+, extinction of the weak GS will result in more fear across the generalization gradient, while extinction with the peak GS will result in similar levels of fear overall.

2. Method

2.1. Participants

Eighty-four participants (mean age = 22.61 years, SD = 6.10, 69 women) participated in exchange of course credits or a small reimbursement. Exclusion criteria included psychiatric or neurological disorders, other serious medical conditions and use of medication. The study was approved by the university ethics committee.

2.2. Stimuli and apparatus

The stimuli were various faces on a fear intensity dimension, as used by Dunsmoor et al. (2009), presented against a black background (see Fig. 1). The US was an individually selected electric shock with an intensity that was assessed as certainly uncomfortable but not painful. It was generated by a DS7A constant current stimulator (Digitimer) and delivered to the wrist of the dominant hand by two electrodes (V91-01,8 mm; Coulbourn). A conductive gel was applied between the electrical conductor and the skin. In order to assess fear at the physiological level, electro dermal activity was measured during the entire computer task. A Coulbourn Instruments coupler (model V71-23, Allentown, PA) was used. The apparatus was attached to the palm of the participant's non-dominant hand via a pair of sintered-pellet silver chloride electrodes with a diameter of 8 mm filled with K-Y gel. Across the electrodes, a constant voltage of 0.5 V was sent. To assess fear at the subjective level all CS/GS presentations were accompanied by a US-expectancy rating scale on the bottom of the screen. The scale ranged from 0 ("certainly no shock") to 10 ("certainly shock"), with 5 labeled as "uncertain". Participants were instructed to respond by mouse-clicking on the corresponding point of the rating scale. Stimulus presentations and behavioral measurements were controlled by Affect 4 software (Spruyt, Clarysse, Vansteenwegen, Baeyens, & Hermans, 2009).