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Threat Intensity Widens Fear Generalization Gradients

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Research in nonhuman animals reveals threat-sensitive generalization of defensive behavior that favors widespread generalization when threat intensity is high and limited generalization (i.e., specificity) when threat intensity is low. Here, we used Pavlovian fear conditioning to systematically investigate whether threat intensity widens behavioral generalization gradients to stimuli that decreasingly resemble a learned threat cue. Using a between-subjects design, volunteers underwent fear conditioning with a tone paired with either a high-intensity or low-intensity aversive stimulus prior to a test of fear generalization to novel tones. Results showed no effect of threat intensity on initial acquisition of conditioned fear. However, volunteers who underwent fear conditioning with a high-intensity aversive stimulus exhibited widespread generalization of autonomic arousal (skin conductance responses) as compared to volunteers who received a low-intensity aversive stimulus. These results show a transition from normal (selective) to overgeneralized fear as threat intensity increases, and have implications for understanding overgeneralization characteristic of trauma- and stress-related disorders.

Keywords: Pavlovian fear conditioning, anxiety, arousal, shocks, generalization

Detection and quick reactions to signals of threat in the environment help ensure survival when threat is imminent. However, cues in the environment associated with threat (e.g., the sound of rustling leaves in the forest) do not always portend impending danger (e.g., a harmless scurrying animal and not a predator). Excessively responding to any sign of threat constitutes a waste of time and energy, but a failure to respond appropriately could be disastrous (e.g., ignoring the signs of a stalking predator). Accordingly, research shows that animals balance the trade-off between generalization and specificity by factoring the intensity of a potential threat, sometimes referred to as "threat-sensitive generalization" (Ferrari, Messier, & Chivers, 2008). If threat intensity is low, defensive behavior is limited to cues strongly and directly associated with threat; if threat intensity is high, animals generalize defensive behavior broadly to a wide range of cues that might portend danger but that have not been directly associated with threat ("better safe than sorry"). Put simply, the higher the risk of serious harm, the more widespread the fear. This relationship between threat intensity and generalization of defensive behavior emulates symptoms of psychiatric conditions characterized by excessive fear and anxiety to harmless cues following extremely intense emotional events, best exemplified by posttraumatic stress disorder. Here, we investigated whether threat-sensitive fear generalization is an empirical phenomenon in humans by varying threat intensity and measuring gradients of threat-related responses from a known threat to similar but harmless stimuli.

The importance of outcome intensity to Pavlovian learning is formalized in a number of influential learning models (Pearce & Hall, 1980; Rescorla & Wagner, 1972; Wagner, 1981), and has been empirically validated in fear-conditioning studies that vary footshock intensity in rodents (Ader, Weijnen, & Moleman, 1972; Annau & Kamin, 1961; Baldi, Lorenzini, & Bucherelli, 2004; Cordero, Merino, & Sandi, 1998; Davis & Astrachan, 1978). In fear conditioning, the subject learns the association between a conditioned stimulus (CS) and an aversive unconditioned stimulus (US). The CS–US association establishes the CS as a reliable indicator of impending threat, thereby initiating increases in autonomic activity, endocrine changes, and defensive behaviors. At weak shock intensities, rodents show little or no defensive behavior (Baldi et al., 2004; Phillips & LeDoux, 1992). At moderate shock intensities, defensive behavior emerges selectively to the cue or context predictive of shock (i.e., CS+). At high shock intensities, rodents not only respond to the CS+ but also generalize to unpaired stimuli or contexts (i.e., CS−; Baldi et al., 2004;

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Laxmi, Stork, & Pape, 2003), a process subserved by a loss of cue specificity in lateral amygdala neurons (Ghosh & Chattarji, 2015).

Although the role of US intensity in animal learning is acknowledged, the question remains whether fear conditioning with a high-intensity US leads to stronger and more generalized fear in humans. Additionally, in the existing laboratory animal research on effects of shock intensity, fear generalization is defined as increased responding to a single unpaired cue or context; it is therefore unclear if high-intensity outcomes lead to widespread generalization to graded stimuli that vary in similarity to the CS+, or if generalization gradually weakens as similarity to the CS+ diminishes.

In the present study, volunteers first underwent Pavlovian fear conditioning to a tone CS+ paired with either a low-intensity or high-intensity aversive event (shown in Figure 1A and described in detail in the Method section) and an unpaired tone (CS−). Volunteers were then tested for generalization to a range of novel tones spanning a frequency continuum. Incorporating a wide range of test stimuli provides a comprehensive estimate of intradimensional discrimination training—learning both what is a threat (CS+) and what is safe (CS−)—on similarity-based generalization gradients (Ghirlanda & Enquist, 2003; Hanson, 1959; Kahnt & Tobler, 2016; Spence, 1937; Thomas, 1993). Half of the novel tones were intermediate along the frequency continuum between the CS− and CS+, and half extended beyond the CS+ in a direction opposite the CS−. We predicted that a high-intensity threat would induce widespread behavioral generalization to intermediate tones and a shift in maximal behavioral generalization toward tones more unlike the learned safety signal. In contrast, we predicted that a low-intensity threat would promote specificity, as reflected by a sharp gradient centered on the CS+ and weak generalization to surrounding novel tones.

Method

Participants

Forty-three healthy volunteers gave written informed consent approved by the University Committee on Activities Involving

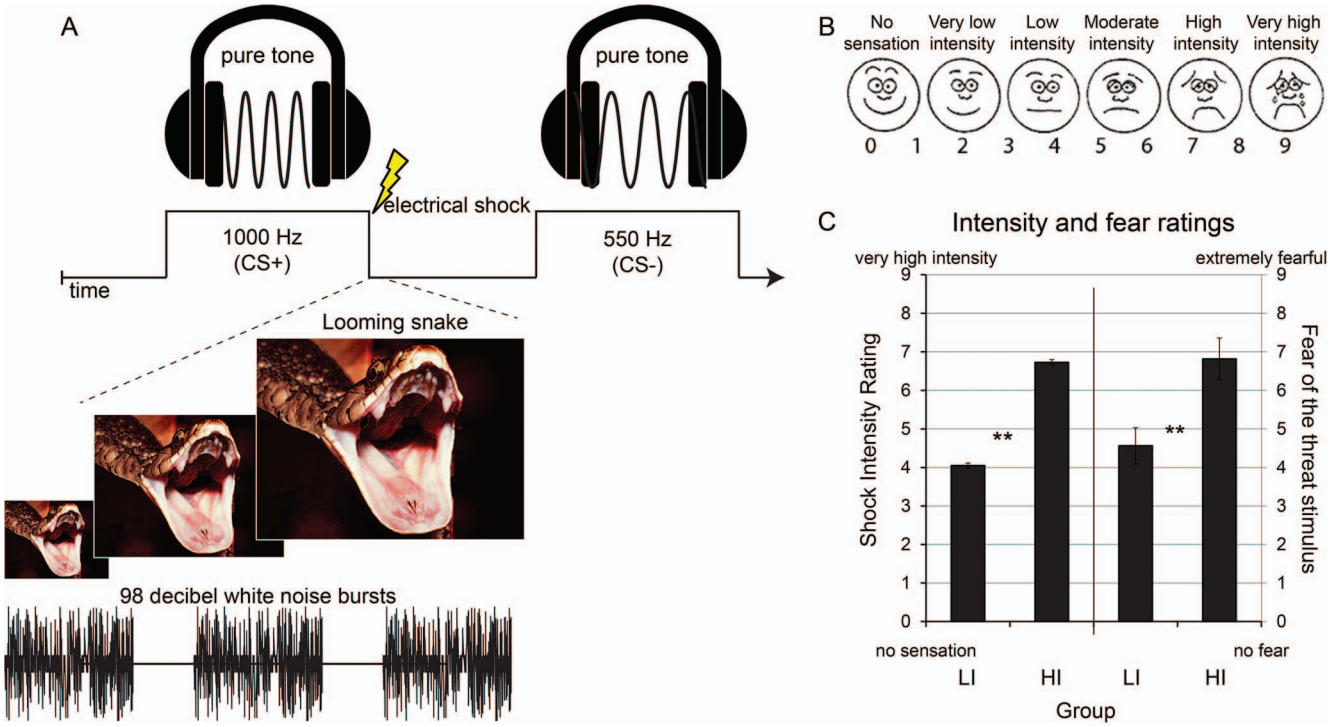

Figure 1. Fear conditioning design and subjective intensity and fear ratings for Experiment 1. (A) Discriminative fear conditioning included pure-tone conditioned stimuli paired (CS+, 1,000 Hz) or unpaired (CS−, 550 Hz) with an aversive unconditioned stimulus (US). One group (not depicted) underwent low-intensity fear conditioning that included a low-intensity electrical shock to the right wrist on 40% of CS+ trials. The other group (depicted) underwent high-intensity fear conditioning that included a multimodal US composed of a high-intensity electrical shock, static white noise bursts (~98 dB), and a looming image of a snake, presented simultaneously on 40% of CS+ trials. A different picture of a snake was used on each trial. (B) A shock work-up procedure was used to calibrate shock to either a low or high level of subjective intensity, between groups. In the low-intensity group, the shock work-up procedure ceased when the volunteer indicated the shock was "very low" to "low." For the high-intensity group, the calibration ceased when the volunteer indicated the shock was at least "high-intensity." (C) Postexperimental subjective ratings of intensity of the electrical shock and ratings of fear of the aversive US were greater in the high-intensity (HI) than in the low-intensity (LI) group. Error bars reflect standard errors of the mean. ** $p < .01$. See the online article for the color version of this figure.

Human Subjects at New York University. One volunteer was excluded from the final analysis due to normalized mean skin conductance responses (SCRs) that were >3 *SD* from the group mean. The final sample included 20 volunteers (12 females; mean age ± *SD*: 23.25 ± 4.30) assigned to the low-intensity (LI) group and 22 volunteers (13 females; 23.59 ± 3.97) assigned to the high-intensity (HI) group.

Procedures

Low- and high-intensity US calibration and design. The electrical shock was a 200-ms pulse delivered to the right wrist using disposable pregelled electrodes connected to a Grass Medical Instruments stimulator (Warwick, RI). Shocks were calibrated using an ascending staircase procedure starting with a low voltage setting near a perceptible threshold. After each calibration pulse, volunteers provided an assessment of subjective intensity using a modified Pain Intensity Scale (Figures 1B and 1C) anchored from "no sensation" to "very high intensity." For the LI group, the shock calibration ceased when the volunteer indicated the shock was "very low" to "low" in how subjectively intense the shock felt. For the HI group, the calibration ceased when the volunteer assessed the shock as feeling "high intensity" or stronger.

Importantly, there are unique considerations for studying the effects of threat intensity in humans that go beyond increasing the voltage of the electrical shock. One practical and ethical concern is that the physical (objective) intensity of the shock is limited out of concern for subject safety. Thus, there is a restricted range by which the experimenter can vary voltage levels. Furthermore, unlike laboratory animal research, human volunteers have control in determining the subjective intensity of the shock during the initial shock calibration procedure, have the ability to remove shock electrodes, and know that they can choose to terminate an experiment at any time. Accordingly, there are unique practical considerations to a systematic study of US intensity in humans that are less germane to this type of investigation in laboratory animals (see, e.g., Boren, Sidman, & Herrnstein, 1959). A further methodological challenge to varying shock intensities between subjects is that, due to individual differences in the electrode-skin circuit impedance, there is not a one-to-one correspondence between voltage and subjective intensity (Tursky & Watson, 1964). As a consequence, it is not possible to maintain the identical shock intensity level using constant voltage stimulators; a low shock voltage setting for one volunteer may be considered extremely painful to another volunteer, and vice versa. Shock intensity can also vary within the same individual over the course of a shock study due to increases or decreases in sweating, which will affect the conductance of the skin (and therefore the intensity of the shock) considerably. Therefore, due to safety concerns, variability in the electrode-skin circuit impedance, and variability in subjective pain tolerance thresholds, a threat that consists merely of an electrical shock calibrated to subjective level of "high intensity," are unsatisfactory for the goal of the present study.

To safely augment the aversive US in the HI group, the electrical shock to the wrist (calibrated to a high subjective intensity as described above) was combined with a simultaneous aversive static burst of white noise (~98 dB) and looming images of a snake (Figure 1A). For the HI group, each component of the multimodal US was presented simultaneously at the offset of the tone with no lag between tone offset and US. For the LI group, the US consisted of only the low-intensity shock. Note that while the quality of the US was different between groups (a multimodal US vs. only a shock) the stated goal of this study was to investigate the effects of high- versus low-intensity events on learning and generalization; that the objective components of the US differ between groups is in fact the essence of the manipulation. Furthermore, as multisensory aversive events are the types of experiences encountered in naturalistic environments—and implicated in trauma and stressor-related disorders—this US can be considered more ecologically valid and provides a closer approximation of real-world fearful experiences. Finally, we note that despite the use of different USs between groups, the reported dependent measures were anticipatory responses (evoked prior to when the US would occur) for tones that were never paired with the US or CS+ trials unpaired with the US.

Because the high-intensity US consisted of an image of a snake, volunteers in the HI group completed the Snake Phobic Questionnaire (SNAQ; Klorman, Weerts, Hastings, Melamed, & Lang, 1974) at the completion of the study to assess snake phobia (scores can range from 0 to 31). Mean SNAQ score was 10.09 (*SD* = 6.37)—comparable to healthy populations—and volunteers all fell below the criterion of phobia scores set at within 1 *SD* from the mean of patients with a specific phobia of snakes (Fredrikson, 1983).

Fear conditioning. The experiment occurred across two phases, discriminative fear conditioning and generalization, separated by a 5-min break during which time volunteers passively viewed a silent video of a train traveling through British Columbia (see also Dunsmoor, Mitroff, & LaBar, 2009). Stimuli consisted of pure-tone sine waves presented binaurally at a moderate volume (<60 dB) through headphones (Sennheiser HD-280 PRO) for 2.5 s each and separated by a 7- to 8-s intertrial interval. Stimulus presentation was controlled using E-Prime 2.0 (Psychology Software Tools, Sharpsburg, PA). CSs were a 1,000-Hz tone and a 550-Hz tone that signaled the presence (CS+) or absence (CS−) of the US, respectively. Fear conditioning included 12 presentations each of unpaired CS+ and CS−. An additional eight CS+ trials were paired with the US (40% reinforcement rate). Because CS duration was short, all CS+ trials paired with shock were excluded from analysis to mitigate potential confounds introduced by the US.

After fear conditioning, volunteers were presented with six novel tones of increasing frequency ranging between the CS- and CS+ (650, 800, and 900) and extending beyond the CS+ (1,100, 1,200, and 1,350) in a direction opposite the CS−. During the generalization test, tones (including unpaired CS+ and CS−) were presented seven times each. An additional five CS+ trials paired with shock were included during the generalization test to prevent extinction and habituation over the course of the lengthy generalization test (steady-state generalization testing; see also Blough, 1975; Dunsmoor et al., 2009; Lissek et al., 2008).

In all phases, volunteers rated shock expectancy on a three-alternative Forced-Choice Scale corresponding to "no risk," "moderate risk," and "high risk" for receiving the US, based on prior fear-conditioning studies (Coelho, Dunsmoor, & Phelps, 2015; Lissek et al., 2008). Volunteers were instructed that their button presses did not affect the outcome on a trial in order to mitigate the potential for volunteers to attribute the outcome to their choice or

reaction times (i.e., to prevent an illusory correlation). Volunteers were told to pay attention and try to learn the association between the tones and the shock, but no explicit information was given regarding the CS–US contingencies. Presentation was pseudorandomized so that no more than three presentations of the same tone occurred in a row. After generalization testing, volunteers underwent a hearing test, which validated that all volunteers had normal hearing and the capacity to discriminate between each tone frequency used in the experiment.

Psychophysiology Collection and Data Analysis

SCRs were acquired from the hypothenar eminence of the left palmar surface using disposable pregelled snap electrodes connected to the MP-100 BIOPAC System (BIOPAC Systems). Analysis of SCRs used procedures previously described (Dunsmoor, Campese, Ceceli, LeDoux, & Phelps, 2015). In brief, an SCR was considered related to CS presentation if the trough-to-peak deflection occurred 0.5–3 s following CS onset, lasted between 0.5 and 5.0 s, and was greater than 0.02 μS. Responses that did not fit these criteria were scored as zero. SCR values were obtained using a custom Matlab (The Mathworks Inc., Natick, MA) script that extracts SCRs for each trial using the above criteria (Green, Kragel, Fecteau, & LaBar, 2014), and subsequently inspected by an independent blinded rater. CS+ trials paired with the US were excluded from all analyses. Raw SCR scores were square-root-transformed prior to statistical analysis to normalize the distribution (Lykken & Venables, 1971). Results were analyzed separately for fear conditioning and the generalization test by repeated-measures analysis of variance (ANOVA) incorporating Stimulus as a within-subjects factor and Group as a between-subjects factor, and followed where necessary by paired-samples *t* tests or independent-samples *t* tests. We focused further analysis on SCRs to tones immediately adjacent to the CS+ in both groups, as these stimuli are the most confusable for the CS+ and therefore the likeliest to elicit a generalized response. A similar approach was used by Lissek and colleagues (2014, 2010) to investigate the change in generalization from the CS+ to the most similar generalized stimulus, and by Dunsmoor and LaBar (2013) to investigate generalization to tones immediately above and below the CS+ frequency. Thus, a planned ANOVA was conducted using the CS+ (1,000 Hz), and 900 and 1,100 Hz tones including Group as a between-subjects factor. Greenhouse-Geisser correction was used when assumption of sphericity was not met. All analyses were considered significant at $\alpha < .05$ (two-tailed).

Results

Shock Intensity and Fear Ratings

Subjective shock intensity prior to fear conditioning was higher in the HI ($M \pm SD$: 7.18 ± 0.33) than the LI (4.05 ± 0.32) group, $t(40) = 31.198$, $p < .001$. Postexperimental ratings (shown in Figure 1C) remained higher in the HI than the LI group, $t(40) = 4.64$, $p < .001$. Volunteers were also asked at the conclusion of the study how much they had feared the US (note: data from this question were not recorded for four subjects); self-reported fear was stronger in the HI than in the LI group, $t(36) = 2.90$, $p = .006$.

Fear Conditioning

SCRs. Analysis of SCRs during acquisition (Figure 2A) revealed a main effect of Stimulus (CS+, CS−), $F(1, 40) = 34.16$, $p < .001$, $\eta^2 = 0.461$, but no effect of Group ($p = .26$) and No Stimulus × Group interaction ($p = .39$). Planned *t* tests between CS+ and CS− confirmed successful fear acquisition in the LI, $t(19) = 3.27$, $p = .004$, and the HI, $t(21) = 5.10$, $p < .001$, groups. Mean SCRs on CS+ trials were not different between LI ($M \pm SEM$: 0.58 ± 0.10) and HI (0.73 ± 0.07) groups ($p = .24$).

Expectancy ratings. Shock expectancy ratings during acquisition (Figure 3A) were likewise characterized by a main effect of Stimulus, $F(1, 40) = 132.72$, $p < .001$, $\eta^2 = 0.768$, with no effect of Group ($p = .79$) and No Stimulus × Group interaction ($p = .3$).

Generalization Test

SCRs. Analysis of the entire generalization gradient revealed main effects of Stimulus, $F(4.955, 198.182) = 10.01$, $p < .001$, $\eta^2 = 0.2$, and Group, $F(1, 40) = 12.03$, $p = .001$, $\eta^2 = 0.231$, but no interaction ($p = .21$; Figure 2B). A significant linear trend, $F(1,$

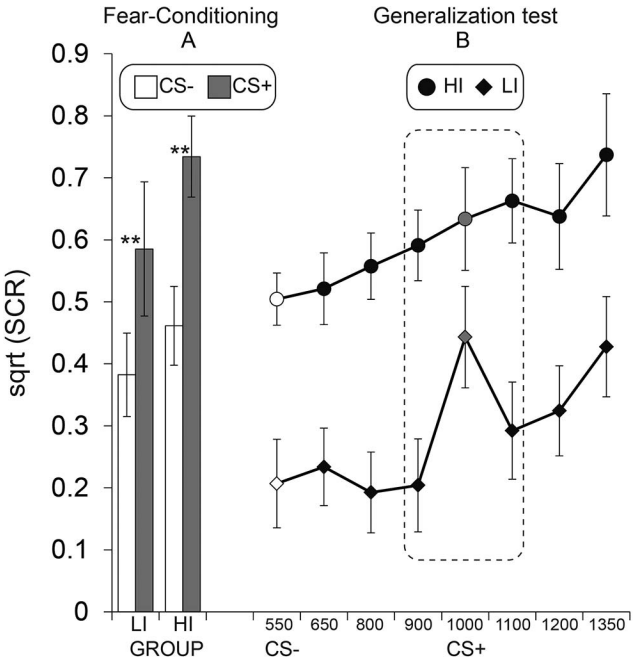

Figure 2. Skin conductance responses (SCRs). (A) Fear conditioning involving either a low-intensity (LI) unconditioned stimulus (US) or a high-intensity (HI) US both lead to successful fear acquisition as defined by greater SCRs on conditioned stimulus (CS) trials intermittently paired (CS+) versus unpaired (CS−) with the US. (B) The group that underwent fear conditioning to a CS+ paired with a low-intensity US (square) produced effectively no generalization of SCRs to novel tones between the CS+ and CS− frequencies. In contrast, the group that underwent fear conditioning to a CS+ paired with a high-intensity US (circles) showed widespread generalization of SCRs. Dashed rectangle indicates a priori analysis of threat-sensitive generalization for stimuli adjacent to the CS+. Data from CS+ trials included trials unpaired with the US only. Shaded and open symbols denote CS+ and CS−, respectively. Error bars reflect standard errors of the mean. ** $p < .01$. sqrt = square root.

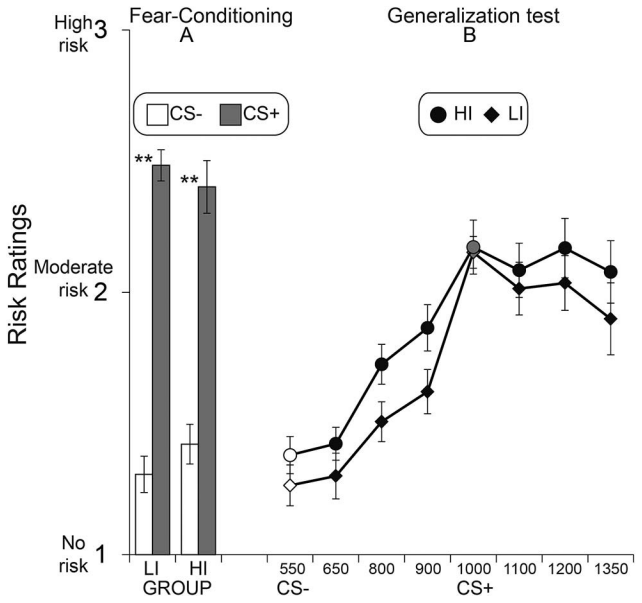

Figure 3. Expectancy ratings. (A) Fear conditioning involving either a low-intensity (LI) unconditioned stimulus (US) or a high-intensity (HI) US both lead to successful fear acquisition as defined by greater shock expectancy on conditioned stimulus (CS) trials intermittently paired (CS+) versus unpaired (CS−) with the US. (B) Both groups exhibited a decremented gradient of expectancy between the CS+ and CS− that decreased as similarity to the CS+ diminished, with no difference between groups. Expectancy in both groups was skewed to the right of the CS+, reflecting a shift in expectancy in a direction opposite of the learned safety signal, CS−. Data from CS+ trials only included trials not paired with the US. Shaded and open symbols denote CS+ and CS−, respectively. Error bars reflect standard errors of the mean. ** $p < .01$.

40) = 27.08, $p < .001$, was suggestive of an asymmetrical gradient skewed toward stimuli opposite the CS+ most unlike the CS−, that is, an area shift (Dunsmoor & LaBar, 2013). As evidence of an area shift, SCRs to stimuli opposite the CS− (mean of 1,100, 1,200, 1,350 Hz) were heightened relative to stimuli between the CS+ and CS− (mean of 650, 800, 900 Hz) in both the HI, $t(21) = 3.45$, $p = .002$, and LI, $t(19) = 3.16$, $p = .005$, groups.

Notably, while both groups exhibited somewhat linear gradients of SCRs along the frequency continuum, there were noticeable between-groups differences in the amount of generalization to stimuli surrounding the CS+. In line with our a priori hypothesis, the LI group exhibited an abrupt and pronounced decrease in SCRs to generalization stimuli surrounding the CS+, whereas generalization was markedly elevated to these same stimuli in the HI group (cf. Lissek et al., 2014). Given our a priori hypothesis regarding threat-sensitive generalization to stimuli surrounding the learned threat cue, we focused the ANOVA on the CS+ and stimuli most similar to the CS+ and 900 and 1,100 Hz (Figure 2B, dashed rectangle). This revealed a significant effect of Stimulus, $F(1.682, 67.275) = 5.80$, $p = .007$, $\eta^2 = 0.127$; Group, $F(1, 40) = 10.9$, $p = .002$, $\eta^2 = 0.214$; and a Stimulus × Group interaction, $F(1.682, 67.275) = 3.46$, $p = .036$, $\eta^2 = 0.08$. Follow-up t tests revealed a significant decrease in SCRs in the LI group between the CS+ and 900 Hz, $t(19) = 3.16$, $p = .005$, and 1,100, $t(19) = 2.58$, $p = .003$, Hz tones, while the same comparison in the HI group showed no differences ($ps > .5$). Finally, while SCRs to the CS+ were not different between groups ($p = .11$), mean SCRs to the 900-Hz, $t(40) = 4.02$, $p < .001$, and the 1,100-Hz, $t(40) = 3.51$, $p = .001$, tones were greater in the HI group than in the LI group.

We also examined whether discriminatory (CS+ vs. CS−) fear conditioning induced a shift in the maximal SCR to a stimulus along the frequency continuum most unlike the learned safety signal—the 1,350-Hz tone. Referred to as a peak shift (Honig & Urcuioli, 1981), this effect can be defined as a significant shift in the maximal response to a stimulus other than the CS+. We detected a moderate but significant peak shift in the HI group, such that mean SCRs to the 1,350-Hz tone were heightened relative to the CS+, $t(21) = 2.08$, $p = .049$, $d = .44$. Importantly, while the LI group did show an area shift as detailed above (i.e., mean SCRs to stimuli opposite the CS− heightened relative to stimuli between the CS+ and CS−), there was no peak shift from the CS+ to the 1,350-Hz tone ($p = .81$).

Expectancy ratings. Shock expectancy ratings (Figure 3B) were characterized by a main effect of Stimulus, $F(3.672, 146.889) = 40.08$, $p < .001$, $\eta^2 = 0.501$, with a linear trend, $F(1, 40) = 70.05$, $p < .001$, but no effect of Group ($p = .13$) and no Stimulus × Group interaction ($p = .83$). In line with the SCR gradient, expectancy to stimuli opposite the CS− (mean of 1,100, 1,200, 1,350 Hz) were heightened relative to stimuli between the CS+ and CS− (mean of 650, 800, 900 Hz) in the HI, $t(21) = 5.19$, $p < .001$, and LI, $t(19) = 5.39$, $p < .001$, groups. Unlike the SCR gradient, however, analysis of shock expectancy to the CS+ and tones immediately adjacent to the CS+ (900 and 1,100 Hz) did not reveal a significant Stimulus × Group interaction ($p = .2$).

Discussion

That more intense outcomes lead to stronger conditioning is a basic tenet of nearly all models of classical conditioning (e.g., Rescorla & Wagner, 1972), and is a core assumption of learning theory accounts of psychopathology (e.g., Foa, Steketee, & Rothbaum, 1989). While the present results did not show stronger fear conditioning with a high-intensity US, an intense outcome did promote widespread generalization of conditioned fear to harmless stimuli that resembled a learned threat following fear conditioning. These results provide new empirical support for threat-sensitive generalization (Ferrari et al., 2008) in humans and extends recent findings in laboratory animals (Baldi et al., 2004; Ghosh & Chattarji, 2015) by showing that threat-sensitive fear generalization is widespread and extends beyond a single unpaired stimulus.

Threat-sensitive fear generalization accords with the view that generalization is adaptive when a potential threat is intense (Åhs, Miller, Gordon, & Lundström, 2013; Laufer, Israeli, & Paz, 2016; Resnik & Paz, 2015; Resnik, Sobel, & Paz, 2011). Put another way, when a potential threat presents minimal harm, it may be advantageous to discriminate between those cues that are known to signal threat from similar cues that only might signal threat in order to avoid unnecessarily wasting time and energy. In contrast, when a potential threat poses the risk of intense harm, it may be advantageous to disregard stimulus differences and respond to a range of cues, even to cues that are clearly dissimilar from those experienced in the past, because failing to react could be catastrophic (Dunsmoor & Murphy, 2015; Dunsmoor, Prince, Murty,

Kragel, & LaBar, 2011; Laufer et al., 2016; Likhtik & Paz, 2015). Thus, in a dynamic environment where stimuli assume multiple forms from one experience to the next, the balance between discrimination and generalization may shift in accordance with the consequences of ignoring signals of threat.

It is also notable that a high-intensity US did not promote stronger fear acquisition. This finding was surprising insofar as it is widely recognized that moderate to strong footshocks produce stronger fear acquisition than weak footshocks in rodents (Baldi et al., 2004; Phillips & LeDoux, 1992). It also shows that a shock intensity even somewhat lower than in most human fea-conditioning research (in which the subjective threshold is typically "aversive but tolerable") is sufficient to generate differential CRs. What can explain equivalent conditioned SCRs and estimates of risk between the low- and high-intensity groups? One possibility is that, although the low-intensity US was subjectively weak, its mere presence was sufficient to induce anticipatory anxiety on CS+ trials. This idea fits with prior research showing that human research subjects would rather take a strong shock immediately than a weak shock that is delayed by up to several seconds, presumably because the anticipation or dread of waiting for a weak shock is more unpleasant than the shock itself (Berns et al., 2006). In the context of the present findings, the anticipation of shock—even a weak shock—may be the force driving autonomic responses ("the waiting is the worst part"). In a similar way, the mere instruction that a stimulus will be paired with shock is enough to induce increases in sympathetic arousal and amygdala activity (Olsson & Phelps, 2007). This explanation is also in line with clinical literature showing that the subjective perception of the level of harm posed by a threat mediates the development of posttraumatic stress disorder (PTSD; King, King, Vogt, Knight, & Samper, 2006; Rubin, Berntsen, & Bohni, 2008; Solomon, Mikulincer, & Benbenishty, 1989; van Wingen, Geuze, Vermetten, & Fernández, 2011), and drives emotion-related brain activations in PTSD (Morey et al., 2015; van Wingen et al., 2011) more than the actual level of harm.

Another possibility to explain equivalent fear acquisition is that the high-intensity US was not sufficiently intense. The question is raised, would an extremely intense or painful shock have produced more robust conditioned SCRs to the CS+ than we observed here? Here, we used an augmented multimodal US rather than simply increasing voltage levels between subjects for reasons elaborated in the Method section (e.g., the ceiling on "intense" electrical shock intensity for human volunteers is likely lower than studies that have explicitly investigated the result of shock intensity on fear generalization in laboratory animals). Although subjective ratings for this novel multimodal US—consisting of simultaneous presentations of a physical shock, aversive noise, and a "biologically prepared" stimulus (pictures of a looming snake)—confirmed that subjects found it fearful, it does remain a laboratory approximation of a real-world intense threat event. Yet, it is not clear that an extremely intense or painful outcome would drastically alter the fear conditioning results, per se; animal research tends to show the largest increase in CRs as footshocks increase from low to moderate, with little additional behavioral effect (Baldi et al., 2004; Boren et al., 1959; Phillips & LeDoux, 1992)—or even decrements (Davis & Astrachan, 1978; Leaton & Borszcz, 1985; Witnauer & Miller, 2013)—at extreme shock levels.

The present results extend nonhuman animal research by testing generalization to a range of stimuli, and not just to a single unreinforced CS−. Testing intradimensional generalization to stimuli above and below the CS+ along a sensory dimension allowed us to examine how broadly conditioned behavior generalizes from a learned threat as a function of similarity. This also revealed an unexpected finding; specifically, despite overall lower generalized SCRs to unreinforced tones, the low-intensity group did show an uptick in SCRs to a tone that was highly dissimilar from the CS+, 1,350 Hz. One post hoc explanation of this uptick in arousal to a highly dissimilar tone is that subjects learned a relational rule during discriminatory fear conditioning that high-pitched tones are more dangerous than low-pitched tones. This could have led to transposition (Kohler, 1939; Spence, 1937) of threat value to the most "extreme" generalized stimulus (in terms of pitch), even in subjects for whom generalized arousal was overall reduced.

One possible neurophysiological explanation for broad fear generalization is that high-intensity fear conditioning promotes short-latency plasticity in the lateral amygdala, whereby neurons switch from specific (CS+ only) to generalized as shock intensity increases (Ghosh & Chattarji, 2015). Neurons in the auditory thalamus have also been implicated in fear generalization; increasing transcription factors in the auditory thalamus enhances fear generalization following low-intensity fear conditioning to resemble fear generalization seen with high-intensity training (Han et al., 2008). Fear conditioning induced receptive field plasticity in primary auditory cortex may also play a role in behavioral generalization (Weinberger, 2007). However, Ghosh and Chattarji (2015) found that reversible inactivation of the auditory cortex following high-intensity fear conditioning did not prevent behavioral generalization, suggesting that the amygdala but not the auditory cortex is a critical site of overgeneralization (see also Armony, Servan-Schreiber, Romanski, Cohen, & LeDoux, 1997).

Although primary predictions centered on the effects of US intensity on generalized physiological arousal, it is important to note the lack of between-groups differences on explicit ratings of shock expectancy. Instead, both groups displayed similar gradients of expectancy that diminished linearly between the CS− and CS+ but skewed away from the CS−. Thus, we cannot conclude that US intensity has any effect on explicit measures of shock expectancy. We note however that the design was not optimized to detect subtle differences in shock expectancy, as we used a restricted three-alternative Forced-Choice Scale. We also note a previous fear-generalization study using the same ratings scale that detected between-groups differences in measures of SCR unaccompanied by any differences in explicit shock expectancy (Dunsmoor & Murphy, 2014). A more sensitive measure of explicit risk may be needed to detect possible differences in generalization following high- versus low- intensity threat conditioning.

In summary, the current study provides new empirical evidence of threat-sensitive generalization in humans, providing new insight into when normal fear transitions to overgeneralized fear. While generalization of threat learning is adaptive to survival, broad overgeneralization of fear and anxiety is characteristic of a host of psychiatric conditions. Indeed, emerging research has begun to characterize broad fear generalization in PTSD (Morey et al., 2015), generalized anxiety disorder (Cha et al., 2014; Laufer et al., 2016), and panic disorder (Lissek et al., 2010) relative to psycho-

logically healthy comparison subjects (see Dunsmoor & Paz, 2015, for a review). Further research is needed to translate neurophysiological findings from laboratory animals to humans and to determine how high-intensity threat affects the neurocircuitry implicated in the acquisition, expression, and regulation of conditioned fear.

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