

#### Available online at www.sciencedirect.com

### **ScienceDirect**

Behavior Therapy 46 (2015) 661-670

## Behavior Therapy

www.elsevier.com/locate/bt

# An Event-Related Potential Investigation of Fear Generalization and Intolerance of Uncertainty

Brady D. Nelson
Anna Weinberg
Joe Pawluk
Magda Gawlowska
Greg H. Proudfit
Stony Brook University

Fear generalization is a key process in the development and maintenance of anxiety disorders. Psychobiological investigations of fear generalization have predominantly focused on defensive system activation (e.g., startle reflex), and it is unclear whether aberrant attentional processing contributes to fear generalization. The late positive potential (LPP) is an event-related potential component that indexes sustained attention and elaborative processing of motivationally salient information, and is larger in response to arousing compared to nonarousing stimuli. In the present study 48 participants completed a fear generalization paradigm using electric shocks. The LPP and retrospective risk ratings of shock likelihood were measured in response to the conditioned stimulus (CS+) and multiple generalization stimuli (GS) that varied in perceptual similarity to the CS+. In addition, intolerance of uncertainty (IU) was examined in relation to fear generalization. The LPP was enhanced for the CS+ relative to the GS, but the GS did not differ from one another. Thus, overall the LPP did not reflect fear generalization. However, the LPP to the GS differed as a function of IU, such that high Prospective IU was associated with an attenuated LPP to the GS, and this was independent of trait anxiety. Risk ratings tracked fear generalization irrespective of IU. We discuss the potential influence of IU and attentional processing on fear generalization. Overall, the present study supports the LPP as a useful tool for examining individual differences in fear generalization.

Address correspondence to Brady D. Nelson, Ph.D., Department of Psychology, Stony Brook University, Stony Brook, NY, 11794.; e-mail: brady.nelson@stonybrook.edu.

0005-7894/© 2014 Association for Behavioral and Cognitive Therapies. Published by Elsevier Ltd. All rights reserved.

Keywords: event-related potentials; fear generalization; intolerance of uncertainty; late positive potential

FEAR CONDITIONING IS A form of associative learning that is central to many etiological accounts of anxiety disorders (Craske et al., 2009; Mineka & Zinbarg, 2006). Laboratory studies of fear conditioning often examine differential conditioning, during which two (or more) conditioned stimuli (CS) are presented, one paired with an aversive stimulus (i.e., CS+) and the other not paired (i.e., CS-). A meta-analysis of fear conditioning research in anxiety disorders indicated heightened fear responding to the CS+ and CS-(Lissek et al., 2005). These results are consistent with fear generalization, the process through which the fear response is extended to stimuli that resemble the CS+ (i.e., generalization stimuli: GS).

Psychobiological investigations of fear generalization have predominantly focused on defensive system activation using the startle reflex (Lissek et al., 2008). For example, Hajcak and colleagues (2009) developed a fear generalization paradigm in which the startle reflex was recorded while viewing a CS+ (a red rectangle that was followed by an electric shock) and multiple GS that varied in perceptual similarity to the CS+ (red rectangles with gradually different lengths from the CS+, which were never reinforced). The paradigm was designed to provide a rich representation of fearful responding to complex stimuli, similar to real-world scenarios where danger and safety cues share perceptual similarities (Lissek et

al.). In the Hajcak et al. study, the startle reflex was greatest during the CS+ and declined parametrically as the GS became less perceptually similar to the CS+, producing a fear generalization gradient (e.g., CS+ > GS  $\pm$  20% > GS  $\pm$  40%). Recently, Greenberg and colleagues (2013) used functional magnetic resonance imaging (fMRI) to explore this paradigm in healthy controls and found that insula activation tracked the fear generalization gradient. Taken together, research suggests that GS activate defensive system activation in proportion to their perceptual similarity to the CS+.

It is not yet clear how attentional processes might contribute to fear generalization. One possibility is that GS that are more similar to the CS+ might also demand increased attention (relative to less similar stimuli) as individuals attempt to discriminate threat cues from safety cues. The increased attention could then prompt greater demand for the mobilization of physiological resources, in case a defensive response needs to be mounted (Lang, Bradley, & Cuthbert, 1997). One way to test this hypothesis is through the use of event-related potentials (ERPs), which are particularly useful for understanding mechanisms of attention (Luck, Woodman, & Vogel, 2000). In particular, the late positive potential (LPP) is a sustained positive deflection of the ERP signal that begins as early as 200-ms after stimulus onset and persists throughout (and beyond) stimulus presentation, and is posited to index sustained attention and elaborative processing of motivationally salient visual information (Cuthbert, Schupp, Bradley, Birbaumer, & Lang, 2000; Hajcak & Olvet, 2008; Weinberg, Ferri, & Hajcak, 2013). Fear conditioning studies have confirmed that the LPP is increased for CS+ relative to CS- (Baas, Kenemans, Böcker, & Verbaten, 2002; Böcker, Baas, Kenemans, & Verbaten, 2004; Bublatzky & Schupp, 2011), suggesting that it may provide an objective measure of increased attentional processes important to fear discrimination. However, the LPP has not been used to examine the role of attention in fear generalization.

Additionally, fear generalization appears to play an important role in the etiology and maintenance of multiple anxiety disorders, and several studies have reported that trait anxiety is associated with greater startle reflex and skin conductance response during fear generalization (Dunsmoor, White, & LaBar, 2011; Gazendam, Kamphuis, & Kindt, 2013; Haddad, Pritchett, Lissek, & Lau, 2012; although see Torrents-Rodas et al., 2013). However, anxiety is not a monolithic construct and the recent Research Domain Criteria (RDoC) initiative has emphasized examining transdiagnostic constructs that cut across multiple disorders (Cuthbert & Insel, 2010; Sanislow et al., 2010). In the present

study, we wished to examine specific anxiety-relevant transdiagnostic processes that might contribute to increased attention to safety cues that are perceptually similar to threat cues. In particular, it is possible that the *uncertainty* associated with determining whether a stimulus indicates threat (CS+) or safety (CS-) can impact attentional processing. If so, individuals who are highly averse to uncertainty may demonstrate aberrant processing of the GS. Intolerance of uncertainty (IU) is a cognitive bias that influences perceptions, interpretations, and responses to uncertain situations (Dugas, Buhr, & Ladouceur, 2004). IU has been associated with several anxiety disorders, including generalized anxiety disorder (GAD; Dugas, Gagnon, Ladouceur, & Freeston, 1998), obsessivecompulsive disorder (OCD; Tolin, Abramowitz, Brigidi, & Foa, 2003), and social anxiety disorder (SAD; Boelen & Reijntjes, 2009). Therefore, IU may be associated with fear discrimination/generalization via the uncertainty related to differentiating the CS+ and GS; however, no study has examined this relationship.

Factor analytic studies have indicated that IU is characterized by two related (but distinct) factors— Prospective IU and Inhibitory IU (Birrell, Meares, Wilkinson, & Freeston, 2011). Prospective IU characterizes "cognitive" concerns about uncertain future events, while Inhibitory IU represents "behavioral" inhibition and/or avoidance due to uncertainty (Carleton, Norton, & Asmundson, 2007). A growing number of studies have identified distinct relationships between Prospective and Inhibitory IU and psychobiological responding to uncertainty. For example, Inhibitory IU has been shown to be associated with decreased startle reflex (Nelson & Shankman, 2011) and increased insula activation (Shankman et al., 2014) while anticipating uncertain threat, whereas Prospective IU has been associated with decreased approach motivation (as indicated by a reduced frontal electroencephalography [EEG] asymmetry) while anticipating uncertain reward (Nelson, Shankman, & Proudfit, 2014). These results suggest that Prospective and Inhibitory IU may demonstrate disparate relationships with the processing of uncertainty, and we therefore separately examined their relationship with fear generalization.

In the present study, participants completed Hajcak, Castille, and colleagues' (2009) fear generalization paradigm while EEG was recorded. The LPP was examined in response to the CS+ and multiple GS that varied in perceptual similarity to the CS+. At the end of the task participants completed self-reported risk ratings (i.e., perceived shock likelihood) for the CS+ and GS. We also examined the association between Prospective and Inhibitory

IU and the LPP as well as participant assessment of the risk value of each stimulus. IU has demonstrated significant overlap with broader anxiety constructs (Norton & Mehta, 2007), and it is important to determine the *specificity* of any relationship between IU and fear generalization. Therefore, we also assessed trait anxiety and examined the association between IU and fear generalization *independent* of the broader construct of anxiety.

We had two primary hypotheses. First, we hypothesized that the LPP would differentiate the CS+ from the GS and produce a fear generalization gradient. Second, we hypothesized that IU would be associated with the LPP to the GS. Given previous evidence that Prospective and Inhibitory IU subscales demonstrate distinct relationships with the processing of uncertainty (Nelson & Shankman, 2011; Nelson et al., 2014; Shankman et al., 2014) and the exploratory nature of these analyses, we did not make specific directional hypotheses for either Prospective or Inhibitory IU.

#### Methods

#### PARTICIPANTS

Forty-eight introductory psychology students participated for course credit. The sample included 25 females and was on average 19.83 years old (SD = 1.56; range 18–25). Participants were recruited from online postings using the Stony Brook University research experiment system. Informed consent was obtained from each participant and all materials and procedures were approved by the Stony Brook University Institutional Review Board.

#### MEASURES

#### Intolerance of Uncertainty Scale

The Intolerance of Uncertainty Scale (IUS; Freeston, Rhéaume, Letarte, & Dugas, 1994) contains 27 items relating to the idea that uncertainty is unacceptable, reflects poorly on a person, and leads to frustration, stress, and the inability to take action. Items are rated on a 5-point Likert scale ranging from 1 (Not at all characteristic of me) to 5 (Entirely characteristic of me), with higher scores representing greater IU. The present study used the more parsimonious 12-item version of the IUS (Carleton et al., 2007) that excludes GAD-specific items and has been shown to have better psychometric properties. The 12-item IUS consists of 7-item Prospective IU (Cronbach's  $\alpha = .86$ ) and 5-item Inhibitory IU ( $\alpha = .85$ ) subscales. The IU scores were comparable with other investigations using undergraduate samples (Nelson & Shankman, 2011); scores were below those reported in anxious and/or depressed populations (Carleton et al., 2012).

State Trait Anxiety Inventory

The State Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983) is a 40-item self-report measure consisting of two 20-item forms assessing state anxiety (how they feel at this moment) and trait anxiety (how they feel generally). The present study used the 20-item measure of trait anxiety (STAI-Trait). Each item is measured on a 4-point Likert scale ranging from 1 (*Not at all*) to 4 (*Very much so*). STAI-Trait ( $\alpha$  = .92) scores were comparable to other investigations using undergraduate samples and below the means typically seen in anxious and/or depressed populations (Spielberger et al., 1983).

#### STIMULI

The present study employed a version of a fear generalization paradigm previously used in the context of both startle and fMRI investigations (Greenberg et al., 2013; Hajcak, Castille, et al., 2009). Visual stimuli were presented using Presentation software (NeuroBehavioral Systems; Berkeley, CA, USA) and electric shocks were delivered using PSYLAB (Contact Precision Instruments, London, United Kingdom). During the task, electric shocks were delivered following a specific CS+; a range of GS stimuli that varied in perceptual similarity to the CS + were also presented—though electric shocks were never delivered following the GS. Seven rectangles that were identical in height (56 pixels) but ranged from 112 to 448 pixels in width served as the stimuli and were presented in red against a white background on a 19-inch monitor set with a resolution of  $1024 \times 768$  pixels. The middle-sized rectangle (218 pixels wide) was always the CS+; six other GS were smaller or larger in width from the CS+ by 20%, 40%, or 60% (hereafter referred to as  $CS \pm 20\%$ ,  $CS \pm 40\%$ , and  $CS \pm 60\%$ , respectively). At a viewing distance of 25 inches, each stimulus occupied approximately 1.6° of visual angle vertically and 4.0-15.1° of visual angle horizontally.

#### PROCEDURE

The experiment was approximately 1 hour in duration and was conducted in the Department of Psychology at Stony Brook University. After obtaining written informed consent, participants were seated in a chair and EEG electrodes were applied. Shock intensity for each participant was then determined on an individual basis—participants initially received a mild shock (0.59 mA), which was raised by equal increments (0.20 mA) based on participant feedback. Participants were asked to choose a level of shock that would be uncomfortable but manageable. The experimenter

then informed participants that they would always be shocked following the presentation of the middle length rectangle (i.e., CS+) and that they would never be shocked following the presentation of all other rectangles (i.e., GS). Finally, participants completed an acquisition phase (trials presented in a random order) during which the CS+ was followed by a shock and each GS was not paired with a shock.

The remainder of the experiment consisted of 80 trials (20 trials of each type: CS +,  $CS \pm 20\%$ ,  $CS \pm$ 40%, and CS  $\pm$  60% trials) that were presented in three blocks. Participants received an electric shock following every CS+ trial (at the end of the 2 s CS + presentation), and never following any of the GS trials. The order of stimulus presentation was random, with the constraint that the 4 CS+ and GS stimuli were presented in each block. Stimuli were presented for 2 s with a 2.5 - 3.5 s intertrial interval (ITI). Finally, at the end of the task participants completed a self-report risk rating of shock likelihood and were asked, "Please rate how certain you are that you did or did not feel the shock after seeing this rectangle." Each rectangle was presented in a random order and rated using a 5-point Likert scale that ranged from 1 (Certainly not shocked) to 5 (Certainly shocked), with the midpoint being 3 (*Unsure*).

#### EEG RECORDING AND DATA PROCESSING

Continuous EEG was collected using as elastic cap and the ActiveTwo system (Biosemi, Amsterdam, Netherlands). Thirty-four electrode sites were used based on the 10/20 system as well as two electrodes on the right and left mastoids. Electrooculography generated from eye movements and eye blinks was recorded using four facial electrodes: horizontal eye movements were measured via two electrodes located approximately 1 cm outside the outer edge of the right and left eyes. Vertical eye movements and blinks were measured via two electrodes placed approximately 1 cm above and below the right eye. The EEG was digitized at a 24-bit resolution with a sampling rate of 512 Hz using a low-pass fifth order sinc filter with a half-power cutoff of 1024 Hz. Each active electrode was measured on-line with respect to a common mode sense active electrode producing a monopolar (nondifferential) channel.

EEG data were analyzed using Brain Vision Analyzer (Brain Products, Gilching, Germany). Data were re-referenced to the average of the left and right mastoids and band-pass filtered with low and high cutoffs of 0.1 and 30 Hz, respectively. Eye blink and ocular corrections were conducted

using standard established procedures (Gratton, Coles, & Donchin, 1983). A semiautomatic procedure was employed to detect and reject artifacts. The criteria applied were a voltage step of more than 50  $\mu$ V between sample points, a voltage difference of 300  $\mu$ V within a trial, and a maximum voltage difference of less than 0.50  $\mu$ V within 100 ms intervals. These intervals were rejected from individual channels in each trial. Visual inspection of the data was then conducted to detect and reject remaining artifacts. Four participants were excluded from analyses due to excessive artifacts (i.e., on greater than 50% of trials), leaving 44 participants in the final sample.

#### PRINCIPAL COMPONENTS ANALYSIS (PCA)

The LPP was scored using a principal components analysis (PCA), an empirically based method of isolating and scoring ERP components. PCA has previously been used to identify the LPP (Foti, Hajcak, & Dein, 2009). Four ERP averages (i.e., CS+, CS  $\pm$  20%, CS  $\pm$  40%, CS  $\pm$  60%) for each participant were entered into the data matrix for the PCA. These averages contained temporal information from -200 to 2000 ms as well as spatial information about each of the 32 electrode sites. Using the Matlab ERP PCA Toolbox -Version 2 (Dien, 2010a), a temporal PCA was performed first in order to capture variance across time and to maximize the initial separation of ERP components (Dien & Frishkoff, 2005), and a promax rotation was used to rotate to simple structure in the temporal domain (Dien, 2010b; Dien, Khoe, & Mangun, 2007). Following the first rotation, a parallel test (Horn, 1965) was conducted on the resulting Scree plot (Catell, 1966), in which the Scree of the actual dataset is compared to a Scree plot derived from a fully random dataset. The number of factors retained is based on the largest number of factors that account for a greater proportion of variance than the fully random dataset (see Dien, 2010a, for more information). Based on this criterion, 37 temporal factors were extracted for rotation, and the covariance matrix and Kaiser normalization were used for the PCA (Dien, Beal, & Berg, 2005).

Following the temporal PCA, a spatial PCA was performed on each temporal factor retained in the previous step in order to reduce the spatial dimensions of the datasets. Infomax was used to rotate to independence in the spatial domain (Dien, 2010b; Dien et al., 2007). Based on the results of the parallel test (Horn, 1965), three spatial factors were extracted from each temporal factor for Infomax rotation, yielding a total of 111 temporospatial factor combinations. To directly assess timing and spatial

voltage distributions, the factors were then translated back into voltages. Ten factor combinations accounted for more than 1% of the variance each (accounting for 61.8% of the total variance) and were retained for further analysis.

#### DATA ANALYSIS

Identical analyses were conducted for risk ratings and the LPP. Stimulus (CS+, CS  $\pm$  20%, CS  $\pm$  40%,  $CS \pm 60\%$ ) differences were examined using a repeated measures analysis of variance (ANOVA). For the IU analyses, a median split was used to dichotomize the Prospective IU (median = 18, Low n = 18, High n = 26) and Inhibitory IU (median = 10, Low n = 20, High n = 24) subscales. Separate analyses were conducted for Prospective and Inhibitory IU subscales. Two statistical approaches were used to examine the data. First, we conducted Stimulus (CS+, CS  $\pm$  20%, CS  $\pm$  40%, CS  $\pm$  60%) X IU (Low vs. High) mixed-measures ANOVAs with Stimulus as the within-subjects factor and IU as the between-subjects factors. Second, because we wished to examine the degree to which participants differentiated (or failed to differentiate) the CS+ from the GS, we calculated residual scores for each participant and condition. We elected to use residual scores rather than subtraction-based difference scores because methods relying on differences between averages are less effective at isolating variance unique to a particular condition, primarily because the resulting difference score remains correlated with both initial values (e.g., the average response to the CS+ and average response to CS ± 20%; Cronbach, & Furby, 1970; DuBois, 1957). Residuals are also a difference score of sorts, but reflect the difference between an individual's observed average response to the GS and the average that would be predicted from their CS + average; these residuals will be independent from the average response to the CS + but correlated with the average response to the GS. Residuals thus more successfully capture unique variance associated with the GS (Cronbach & Furby, 1970; DuBois, 1957; Traub, 1967), and may be a more reliable means of measuring the degree to which individuals differentiate the GS from the CS+ (Weinberg, Venables, Proudfit, & Patrick, 2014). Thus, three regressions were conducted, predicting the CS  $\pm$  20%, CS  $\pm$  40%, or CS  $\pm$  60% from the CS+. Standardized residuals representing variance unique to each GS after controlling for the response to the CS+ were saved for each participant and from each regression. Following this, stimulus differences were examined using Stimulus (CS ± 20%, CS  $\pm$  40%, CS  $\pm$  60%) X IU mixed-measures ANOVA.

Table 1
Descriptive Statistics and Correlation Coefficients Between Self-Report Clinical Measures

	1	2	3	4
1. Inhibitory I	U -	.79***	.92***	.83***
2. Prospective	IU	-	.96***	.68***
3. Total IU			-	.78***
4. STAI-Trait				-
M SD	10.41 4.29	19.14 6.05	29.55 9.79	42.46 10.01

Note. IU = intolerance of uncertainty; STAI = state trait anxiety inventory.

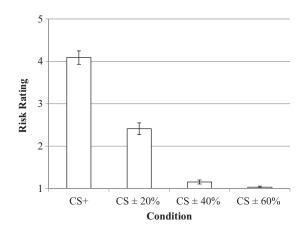
#### Results

#### SELF-REPORT CLINICAL MEASURES

Table 1 displays descriptive statistics and correlations between the IUS (Prospective and Inhibitory) and STAI-Trait. As expected, all three measures demonstrated moderate to strong positive associations.

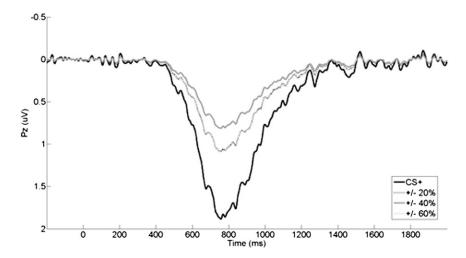
#### RISK RATINGS

Risk ratings (see Figure 1) differed across Stimuli, F(3, 129) = 201.36, p < .001,  $\eta_p^2 = .82$ , such that shock was rated as more likely following the CS+ (M = 4.16, SD = 0.96) relative to the CS ± 20% (M = 2.41, SD = 0.94), F(1, 43) = 74.05, p < .001,  $\eta_p^2 = .63$ , the CS ± 40% (M = 1.16, SD = 0.32), F(1, 43) = 374.24, p < .001,  $\eta_p^2 = .90$ , and the CS ± 60% (M = 1.03, SD = 0.17),



**FIGURE I** Risk Ratings Across the CS+ and GS. *Note*. Risk ratings were collected at the end of the fear generalization task. Error bars represent standard error. CS = conditioned stimulus; CS = conditioned stimulus; CS = conditioned stimulus;

p < .05, p < .01, p < .01, p < .001.



**FIGURE 2** PCA-Derived LPP Waveforms Across the CS  $\pm$  and GS. Note. The waveform for CS  $\pm$  40% and CS  $\pm$  60% were overlapping and appear as one line in the figure. CS  $\pm$  conditioned stimulus; GS  $\pm$  generalization stimuli; LPP  $\pm$  late positive potential; ms  $\pm$  milliseconds; PCA  $\pm$  principal components analysis.

F(1, 43) = 444.55, p < .001,  $\eta_p^2 = .91$ . In addition, shock was rated as more likely following the CS  $\pm$  20% relative to the CS  $\pm$  40%, F(1, 43) = 99.37, p < .001,  $\eta_p^2 = .70$ , and CS  $\pm$  60%, F(1, 43) = 92.76, p < .001,  $\eta_p^2 = .68$ . Finally, shock was rated as more likely following the CS  $\pm$  40% relative to the CS  $\pm$  60%, F(1, 43) = 7.28, p < .01,  $\eta_p^2 = .15$ . The pattern of results for the risk ratings was consistent with a fear generalization gradient.

There were no main effects or interactions for Prospective or Inhibitory IU using raw or residual scores for risk ratings (ps > .12). These results suggest that IU did not differentiate the risk rating fear generalization gradient.

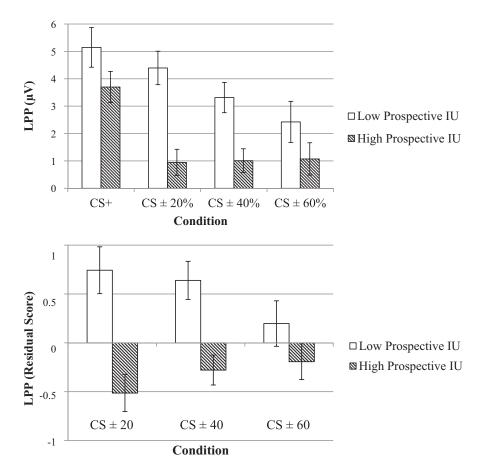
#### ERPS

Of the 10 factors retained from the PCA, one factor (accounting for 2.1% of the variance) resembled the LPP in terms of its temporal and spatial characteristics and varied as a function of Stimulus, F(3, 129) = 8.33, p < .001,  $\eta_p^2 = .16$ . As depicted in Figure 2, this factor was a positive-going deflection in the waveform that peaked at 758 ms and was maximal at fronto-central locations. The CS+ (M = 3.89, SD = 2.91) elicited a larger LPP than the CS ± 20% (M = 2.25, SD = 2.53), F(1, 43) = 11.44, p < .01,  $\eta_p^2 = .21$ , CS ± 40% (M = 1.68, SD = 2.33), F(1, 43) = 17.90, p < .001,  $\eta_p^2 = .29$ , and CS ± 60% (M = 1.68, SD = 3.01), F(1, 43) = 13.82, p < .001,  $\eta_p^2 = .24$ . However, none of the GS (i.e., CS ± 20%, CS ± 40%, or CS ± 60%) differed from one another (ps > .19). Thus, the LPP factor differentiated the CS+ from

all other stimuli—and overall did not reflect fear generalization. <sup>1</sup>

In terms of the associations between IU and the LPP, there was a main effect of Prospective IU, F(1,42) = 7.94, p < .01,  $\eta_p^2$  = .16, but no main effects or interactions for Inhibitory IU (ps > .57). As depicted in the top of Figure 3, high Prospective IU was associated with an attenuated LPP to the CS + and GS. The residual analyses also indicated a main effect of Prospective IU, F(1, 42) = 5.67, p < .05,  $\eta_p^2 = .12$ , but there were again no main effects or interactions for Inhibitory IU (ps > .66). As depicted in the bottom of Figure 3, high Prospective IU was associated with attenuated LPP residual scores to the GS. Taken together, results suggest that Prospective IU is associated with a reduced overall LPP and a reduced LPP to GS over and above what would be predicted by response to the CS+. Furthermore, Prospective IU was still associated with the LPP residual score when STAI-

<sup>1</sup> We also examined the raw grand average data prior to conducting the PCA. Data were segmented from 300–1000 ms and pooled at PO3 and PO4, where the LPP was maximal. Results indicated a main effect of Stimulus that approached significance, F(1, 43) = 2.04, p < .12,  $η_p^2 = .05$ , such that the LPP to the CS+ was greater than that for the CS ± 20%, F(1, 43) = 4.82, p < .05,  $η_p^2 = .10$ , and CS ± 40%, F(1, 43) = 4.58, p < .05,  $η_p^2 = .10$ , but not the CS ± 60%, F(1, 43) = 2.25, F(



**FIGURE 3** LPP Across the CS+ and GS as a Function of IU. *Note*. The figures depict the LPP across the CS+ and GS (top) and residual change scores for the GS (bottom) as a function of Prospective IU. Residual change was calculated by regressing the LPP to each GS on the LPP to the CS+. Error bars represent standard error. CS = CONDITION COND

Trait was included as a covariate (p < .05), indicating that the effects of Prospective IU on the GS were independent of trait anxiety.

#### Discussion

The present study replicated prior research and found that the LPP was sensitive to fear conditioning—it was enhanced for the CS+. The LPP did not differ among the GS stimuli and thus overall did not reflect fear generalization. These results differ from previous investigations that found an overall fear generalization gradient using the startle reflex (Hajcak, Castille, et al., 2009) and fMRI (Greenberg et al., 2013). However, Prospective IU was related to the LPP elicited by the CS+ and GS. Specifically, high Prospective IU was characterized by a *reduced* LPP to the CS+ and GS and attenuated fear generalization to the GS as indicated by residual scores. Furthermore, these results were independent of trait anxiety.

Finally, risk ratings followed a fear generalization gradient irrespective of IU.

These results suggest that the LPP can be used to measure individual differences in attentional process that are associated with fear generalization. Previous studies have reported a fear generalization gradient using several different measures, including the startle reflex (Lissek et al., 2008), skin conductance response (Dunsmoor, Mitroff, & LaBar, 2009), and fMRI (Greenberg et al., 2013). The current results suggest that threat cues (i.e., CS+) elicit increased sustained attention and elaborative processing indexed by the LPP relative to all GS. The GS also elicited an increased LPP consistent with fear generalization, but only in those with low IU.

Moreover, only Prospective (and not Inhibitory) IU was associated with fear generalization using the LPP. Prospective IU indexes "cognitive" concerns about future events, while Inhibitory IU represents "behavioral" inhibition and/or avoidance (Carleton et al., 2007). In the present study, participants

 $<sup>^2</sup>$  There was no association between STAI-Trait and the LPP to the CS+ and GS or the residual scores for the GS (ps > .10).

completed a passive fear generalization paradigm that required no behavioral response. Thus, even if high Inhibitory IU individuals found the GS to be unpleasant and stressful, there was no behavioral response to inhibit. On the other hand, those high on Prospective IU may have found the more "uncertain" threat cues (i.e., CS ± 20%) to be particularly unpleasant and anxiety provoking, and consequently engaged in some form of cognitive avoidance during these trials. Indeed, directing attention away from threatening stimuli has been shown to reduce the LPP (Hajcak, Dunning, & Foti, 2009; MacNamara & Hajcak, 2009), and there is evidence that anxious individuals exhibit a decreased LPP to more threatening stimuli (Weinberg & Hajcak, 2011).

Risk ratings also produced a fear generalization gradient. Specifically, shock was rated as more likely following the CS+ and decreased as the GS became less similar to the CS+. On the other hand, IU was not related to the risk ratings. There are several likely explanations for the absence of an association between IU and the risk ratings. For example, risk ratings were collected retrospectively at the end of the task and may have been susceptible to demand characteristics. Indeed, the majority of participants reported that the GS were not associated with the risk of receiving an electric shock. In addition, there was limited variance in the risk rating measurements. Specifically, the standard deviation of the risk ratings for the CS + (SD = 0.96) and GS(SD = 0.17 to 0.94) were substantially smaller compared to the LPP for the CS + (SD = 2.91) and GS (SD = 2.33 to 3.01). This suggests that while the risk ratings produced the hypothesized fear generalization gradient, there was minimal variation in this gradient and most participants were able to distinguish between the CS+ and GS. Importantly, these results highlight the potential utility of the LPP (over risk ratings) in identifying individuals who may be vulnerable to the development of anxiety disorders.

Lissek and colleagues (2010, 2014) recently examined fear generalization using the startle reflex in panic disorder (PD) and GAD. As in the present study, this research found that anxiety disorder participants demonstrated less differentiation between the CS+ and GS relative to controls. However, these results appeared to be driven by decreased startle to the CS+ (and not increased startle to the GS). In the present study, the flattened generalization gradient associated with high Prospective IU was driven by an attenuated LPP to the GS. The startle reflex is primarily a measure of defensive motivation (Lang, 1995), while the LPP is posited to index sustained attention to, and elaborative processing of, salient visual information (i.e., closer to the construct of arousal; Hajcak, Weinberg, MacNamara, & Foti, 2012). The two measures may capture different aspects of fear generalization. Indeed, it is possible that Prospective IU is associated with superior attentional capacities important for early fear discrimination but also enhanced defensive motivation toward threat. Another potential explanation for the discrepant results between the present study and the Lissek et al. is that the former focused on normative variability in an undergraduate sample while the latter was conducted using a clinical sample.

The present study had several limitations that warrant consideration. First, IU analyses relied on a median split and this may have categorized participants into artificial groups. Second, the fear generalization paradigm provided explicit instructions on the difference between the CS+ and GS, and this may have in turn contributed to the lack of an overall LPP fear generalization gradient. Third, it is possible that the LPP is not sensitive enough to detect subtle differences between GS (e.g., CS ± 40% and CS  $\pm$  60%). Fourth, participants were asked to retrospectively rate what happened, and not what they believed would happen, when confronted with the GS. The wording of this question may have contributed to the restricted range of responses and lack of association between shock likelihood ratings and IU. Future studies should consider examining participants' beliefs about the likelihood of receiving a shock when confronted with the different GS. Finally, the sample consisted of undergraduate participants with IU and STAI scores that, on average, were below those found in anxious and depressed individuals. Thus, it is unclear whether these results will generalize to clinical populations.

In conclusion, the present study found that the LPP differentiated the CS+ from the GS, but overall did not produce a fear generalization gradient. However, Prospective IU differentially impacted the LPP to GS, such that high Prospective IU was associated with an attenuated LPP, and this was independent of trait anxiety. Future studies should extend these findings by examining the association between IU and the LPP during fear generalization in individuals with anxiety disorders.

#### Conflict of Interest Statement

The authors declare that there are no conflicts of interest.

#### References

Baas, J. M. P., Kenemans, J. L., Böcker, K. B. E., & Verbaten, M. N. (2002). Threat-induced cortical processing and startle potentiation. *Neuro Report*, 13, 133–137. http://dx.doi.org/ 10.1097/00001756-200201210-00031

Birrell, J., Meares, K., Wilkinson, A., & Freeston, M. (2011). Toward a definition of intolerance of uncertainty: A review

- of factor analytic studies of the Intolerance of Uncertainty Scale. *Clinical Psychology Review*, 31, 1198–1208. http://dx.doi.org/10.1016/j.cpr.2011.07.009
- Böcker, K. B. E., Baas, J. M. P., Kenemans, J. L., & Verbaten, M. N. (2004). Differences in startle modulation during instructed threat and selective attention. *Biological Psychology*, 67, 343–358. http://dx.doi.org/10.1016/j.biopsycho.2004.01.001
- Boelen, P. A., & Reijntjes, A. (2009). Intolerance of uncertainty and social anxiety. *Journal of Anxiety Disorders*, 23, 130–135. http://dx.doi.org/10.1016/j.janxdis.2008.04.007
- Bublatzky, F., & Schupp, H. T. (2011). Pictures cueing threat: Brain dynamics in viewing explicitly instructed danger cues. Social Cognitive and Affective Neuroscience, 7, 611–622. http://dx.doi.org/10.1093/scan/nsr032
- Carleton, R. N., Mulvoque, M. K., Thibodeau, M. A., McCabe, R. E., Antony, M. M., & Admundson, G. J. (2012). Increasingly certain about uncertainty: Intolerance of uncertainty across anxiety and depression. *Journal of Anxiety Disorders*, 26, 468–479. http://dx.doi.org/10.1016/j.janxdis.2012.01.011
- Carleton, R. N., Norton, M. A. P. J., & Asmundson, G. J. G. (2007). Fearing the unknown: A short version of the intolerance of uncertainty scale. *Journal of Anxiety Disorders*, 21, 105–117. http://dx.doi.org/10.1016/j.janxdis.2006.03. 014
- Cattell, R. (1966). The Scree test for the number of factors. *Multivariate Behavioral Research*, 1, 245–276. http://dx.doi.org/10.1207/s15327906mbr0102\_10
- Craske, M. G., Rauch, S. L., Ursano, R., Prenoveau, J., Pine, D. S., & Zinbarg, R. E. (2009). What is an anxiety disorder? *Depression and Anxiety*, 26, 1066–1085. http://dx.doi.org/ 10.1002/da.20633
- Cronbach, L. J., & Furby, L. (1970). How we should measure "change": Or should we? *Psychological Bulletin*, 74, 68–80. http://dx.doi.org/10.1037/h0029382
- Cuthbert, B., & Insel, T. (2010). The data of diagnosis: New approaches to psychiatric classification. *Psychiatry*, 73, 311–314. http://dx.doi.org/10.1521/psyc.2010.73.4.311
- Cuthbert, B., Schupp, H., Bradley, M., Birbaumer, N., & Lang, P. (2000). Brain potentials in affective picture processing: Covariation with autonomic arousal and affective report. *Biological Psychology*, 52, 95–111. http://dx.doi.org/10.1016/S0301-0511(99)00044-7
- Dien, J. (2010). The ERP PCA Toolkit: An open source program for advanced statistical analysis of event-related potential data. *Journal of Neuroscience Methods*, 187, 138–145. http://dx.doi.org/10.1016/j.jneumeth.2009.12.
- Dien, J. (2010). Evaluating two-step PCA of ERP data with Geomin, Infomax, Oblimin, Promax, and Varimax rotations. *Psychophysiology*, 47, 170–183. http://dx.doi.org/10.1111/j. 1469-8986.2009.00885.x
- Dien, J., Beal, D., & Berg, P. (2005). Optimizing principal components analysis of event-related potentials: matrix type, factor loading weighting, extraction, and rotations. *Clinical Neurophysiology*, 116, 1808–1825. http://dx.doi.org/ 10.1016/j.clinph.2004.11.025
- Dien, J., & Frishkoff, G. (2005). Principal components analysis of event-related potential datasets. In T. C. Handy (Ed.), *Event-related potentials: A methods handbook* Cambridge, MA: The MIT Press.
- Dien, J., Khoe, W., & Mangun, G. (2007). Evaluation of PCA and ICA of simulated ERPs: Promax vs. Infomax rotations. *Human Brain Mapping*, 28, 742–763. http://dx.doi.org/10.1002/hbm.20304
- Dubois, P. H. (1957). *Multivariate Correlational Analysis*. New York: Harper.

- Dugas, M. J., Buhr, K., & Ladouceur, R. (2004). The role of intolerance of uncertainty in etiology and maintenance. In:
  R. G. Heimberg, C. L. Turk, D.S. Mennin (Eds.),
  Generalized anxiety disorder: Advances in research and practice (pp. 143–163). New York, NY: Guilford Press.
- Dugas, M. J., Gagnon, F., Ladouceur, R., & Freeston, M. H. (1998). Generalized anxiety disorder: A preliminary test of a conceptual model. *Behaviour Research and Therapy*, 36, 215–226. http://dx.doi.org/10.1016/S0005-7967(97) 00070-3
- Dunsmoor, J. E., Mitroff, S. R., & LaBar, K. S. (2009). Generalization of conditioned fear along a dimension of increasing fear intensity. *Learning & Memory*, 16, 460–469. http://dx.doi.org/10.1101/lm.1431609
- Dunsmoor, J. E., White, A. J., & LaBar, K. S. (2011). Conceptual similarity promotes generalization of higher order fear learning. *Learning & Memory*, 18, 156–160. http://dx.doi.org/10.1101/lm.2016411
- Foti, D., Hajcak, G., & Dien, J. (2009). Differentiating neural responses to emotional pictures: Evidence from temporal-spatial PCA. *Psychophysiology*, 46, 521–530. http://dx.doi.org/10.1111/j.1469-8986.2009.00796.x
- Freeston, M. H., Rhéaume, J., Letarte, H., & Dugas, M. J. (1994). Why do people worry? *Personality and Individual Differences*, 17, 791–802. http://dx.doi.org/10.1016/0191-8869(94)90048-5
- Gazendam, F. J., Kamphuis, J. H., & Kindt, M. (2013). Deficient safety learning characterizes high trait anxious individuals. *Biological Psychiatry*, 92, 342–352. http://dx.doi.org/10.1016/j.biopsycho.2012.11.006
- Gratton, G., Coles, M., & Donchin, E. (1983). A new method for off-line removal of ocular artifact. *Electroencephalography* and Clinical Neurophysiology, 55, 468–484. http://dx.doi.org/ 10.1016/0013-4694(83)90135-9
- Greenberg, T., Carlson, J. M., Cha, J., Hajcak, G., & Mujica-Parodi, L. R. (2013). Neural reactivity tracks fear generalization gradients. *Biological Psychology*, 92, 2–8. http://dx.doi.org/10.1016/j.biopsycho.2011.12.007
- Haddad, A. D. M., Pritchett, D., Lissek, S., & Lau, J. Y. F. (2012). Trait anxiety and fear responses to safety cues: Stimulus generalization or sensitization? *Journal of Psychopathology and Behavioral Assessment*, 34, 323–331. http://dx.doi.org/10.1007/s10862-012-9284-7
- Hajcak, G., Castille, C., Olvet, D. M., Dunning, J. P., Roohi, J., & Hatchwell, E. (2009). Genetic variation in brain-derived neurotrophic factor and human fear conditioning. *Genes*, *Brain & Behavior*, 8, 80–85. http://dx.doi.org/10.1111/ j.1601-183X.2008.00447.x
- Hajcak, G., Dunning, J. P., & Foti, D. (2009). Motivated and controlled attention to emotion: Time-course of the late positive potential. *Clinical Neurophysiology*, 120, 505–510. http://dx.doi.org/10.1016/j.clinph.2008.11.028
- Hajcak, G., & Olvet, D. M. (2008). The persistence of attention to emotion: Brain potentials during and after picture presentation. *Emotion*, 8, 250–255. http://dx.doi.org/10.1037/ 1528-3542.8.2.250
- Hajcak, G., Weinberg, A., MacNamara, A., & Foti, D. (2012). ERPs and the study of emotion. In S. J. Luck, & E. S. Kappenman (Eds.), Oxford handbook of ERP components (pp. 441–474). New York, NY: Oxford University Press.
- Horn, J. (1965). A rationale and test for the number of factors in factor analysis. *Psychometrika*, 30, 179–185. http://dx.doi.org/10.1007/BF02289447
- Lang, P. J. (1995). The emotion probe: Studies of motivation and attention. *American Psychologist*, 50, 372–385. http://dx.doi.org/10.1037/0003-066X.50.5.372

- Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (1997). Motivated attention: Affect, activation, and action. In P. J. Lang, R. F. Simons, & M. T. Balaban (Eds.), Attention and orienting: Sensory and motivational processes (pp. 97–135). Hillsdale, NJ: Erlbaum.
- Lissek, S., Biggs, A. L., Rabin, S. J., Cornwell, B. R., Alvarez, R. P., Pine, D. S., & Grillon, C. (2008). Generalization of conditioned fear-potentiated startle in humans: Experimental validation and clinical relevance. *Behaviour Research and Therapy*, 46, 678–687. http://dx.doi.org/10.1016/ j.brat.2008.02.005
- Lissek, S., Kaczkurkin, A. N., Rabin, S., Geraci, M., Pine, D. S., & Grillon, C. (2014). Generalized anxiety disorder is associated with overgeneralization of classically conditioned fear. Biological Psychiatry, 75, 909–915. http://dx.doi.org/10.1016/j.biopsych.2013.07.025
- Lissek, S., Powers, A. S., McClure, E. B., Phelps, E. A., Woldehawariat, G., Grillon, C., & Pine, D. S. (2005). Classical fear conditioning in the anxiety disorders: A meta-analysis. *Behaviour Research and Therapy*, 43, 1391–1424. http://dx.doi.org/10.1016/j.brat.2004.10.007
- Lissek, S., Rabin, S., Heller, R. E., Lukenbaugh, D., Geraci, M., Pine, D. S., & Grillon, C. (2010). Overgeneralization of conditioned fear as a pathogenic marker of panic disorder. *The American Journal of Psychiatry*, 167, 47–55. http://dx.doi.org/10.1176/appi.ajp.2009.09030410
- Luck, S. J., Woodman, G. E., & Vogel, E. K. (2000). Event-related potential studies of attention. *Trends in Cognitive Science*, 4, 432–440. http://dx.doi.org/10.1016/S1364-6613(00)01545-X
- MacNamara, A., & Hajcak, G. (2009). Anxiety and spatial attention moderate the electrocortical response to aversive pictures. *Neuropsychologia*, 47, 2975–2980. http://dx.doi.org/10.1016/j.neuropsychologia.2009.06.026
- Mineka, S., & Zinbarg, R. (2006). A contemporary learning theory perspective on the etiology of anxiety disorders: It's not what you thought it was. *American Psychologist*, 61, 10–26. http://dx.doi.org/10.1037/0003-066X.61.1.10
- Nelson, B. D., & Shankman, S. A. (2011). Does intolerance of uncertainty predict anticipatory startle responses to uncertain threat? *International Journal of Psychophysiology*, 81, 107–115. http://dx.doi.org/10.1016/j.ijpsycho.2011.05.003
- Nelson, B. D., Shankman, S. A., & Proudfit, G. H. (2014). Intolerance of uncertainty mediates reduced reward anticipation in major depressive disorder. *Journal of Affective Disorders*, 158, 108–113. http://dx.doi.org/10.1016/j.jad.2014.02.014

- Norton, P. J., & Mehta, P. D. (2007). Hierarchical model of vulnerabilities for emotional disorders. *Cognitive Behaviour Therapy*, 42, 50–63. http://dx.doi.org/10.1080/1650607070 1628065
- Sanislow, C. A., Pine, D. S., Quinn, K. J., Kozak, M. J., Garvey, M. A., Heinssen, R. K., . . . Cuthbert, B. N. (2010). Developing constructs for psychopathology research: Research domain criteria. *Journal of Abnormal Psychology*, 119, 631–639. http://dx.doi.org/10.1037/a0020909
- Shankman, S. A., Gorka, S. M., Nelson, B. D., Fitzgerald, D. A., Phan, K. L., & O'Daly, O. (2014). Anterior insula responds to temporally unpredictable aversiveness: An fMRI study. NeuroReport, 25, 596–600. http://dx.doi.org/10.1097/WNR. 00000000000000144
- Spielberger, C. D., Gorsuch, R. L., Lushene, R., Vagg, P. R., & Jacobs, G. A. (1983). Manual for the State-Trait Anxiety Inventory. Palo Alto, CA: Consulting Psychologists Press.
- Tolin, D. F., Abramowitz, J. S., Brigidi, B. D., & Foa, E. B. (2003). Intolerance of uncertainty in obsessive-compulsive disorder. *Journal of Anxiety Disorders*, 17, 233–242. http://dx.doi.org/10.1016/S0887-6185(02)00182-2
- Torrents-Rodas, D., Fullana, M. A., Bonillo, A., Caseras, X., Andión, O., & Torrubia, R. (2013). No effect of trait anxiety on differential fear conditioning or fear generalization. *Biological Psychology*, 92, 185–190. http://dx.doi.org/10.1016/j.biopsycho.2012.10.006
- Traub, R. E. (1967). A note on the reliability of residual change scores. *Journal of Educational Measurement*, 4, 253–256. http://dx.doi.org/10.1111/j.1745-3984.1967.tb00596x
- Weinberg, A., Ferri, J., & Hajcak, G. (2013). Interactions between attention and emotion: Insights from the late positive potential. In M. Robinson, E. Watkins, & E. Harmon-Jones (Eds.), *Handbook of cognition and emotion* (pp. 35–54). New York: Guilford Publications.
- Weinberg, A., & Hajcak, G. (2011). Electrocortical evidence for vigilance then avoidance in Generalized Anxiety Disorder: An event-related potential study. *Psychophysiology*, 48, 842–851. http://dx.doi.org/10.1111/j.1469-8986. 2010.01149.x
- Weinberg, A., Venables, N. C., Proudfit, G. H., & Patrick, C. J. (2014). Heritability of the neural response to emotional pictures: Evidence from ERPs in an adult twin sample. *Social Cognitive Affective Neuroscience* [Epub ahead of print.].

RECEIVED: March 5, 2014 Accepted: September 16, 2014 Available online 28 September 2014