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Article

JOURNAL OF EXPERIMENTAL PSYCHOPATHOLOGY

Journal of Experimental Psychopathology
January-March 2019: 1–11

DOI: 10.1177/2043808719834451
journals.sagepub.com/home/jepp
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Out with the old and in with the new: The role of intolerance of uncertainty in reversal of threat and safety

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Abstract

Intolerance of uncertainty (IU) is associated with difficulty in updating contingencies from threatening to safe during extinction learning. However, it is unknown whether high IU individuals have difficulty (1) generally with updating threat to safe associations when contingencies change or (2) specifically with updating threat to safe associations during extinction learning, where direct threat is omitted. To address this question, we recorded IU, expectancy ratings, and skin conductance in 44 healthy participants during an associative learning paradigm, where threat and safety contingencies were reversed. During acquisition and reversal, we observed larger skin conductance response (SCR) magnitude and expectancy ratings for threat versus safety cues. However, during reversal, higher IU was associated with larger SCR magnitude to new threat versus new safety cues, compared with lower IU. These results were specific to IU-related variance, over shared variance with trait anxiety (State-Trait Anxiety Inventory, Trait Version). Overall, these findings suggest that individuals high in IU are able to reverse threat and safety associations in the presence of direct threat. Such findings help us understand the recently revealed link between IU and threat extinction, where direct threat is absent. Moreover, these findings highlight the potential relevance of IU in clinical intervention and treatment for anxiety disorders.

Keywords

Acquisition, anxiety, conditioning, reversal, threat, uncertainty

Date received: 7 August 2018; accepted: 5 February 2019

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Introduction

The ability to discriminate and adjust behavior to stimuli that predict threatening or safe outcomes is vital for survival and protection against anxiety and stress disorders (LeDoux, 1998; Milad & Quirk, 2012; Shin & Liberzon, 2009). An organism can learn to associate neutral cues (conditioned stimulus, e.g., a visual stimulus such as a shape) with threatening outcomes (unconditioned stimulus, [US], e.g., shock, loud tone) or safe outcomes. Repeated presentations of a neutral cue with a threatening outcome then result in defensive responding to the cue alone (conditioned response). Importantly, learned threat and safe associations can be updated when the outcome changes. For example, (1) if a neutral cue no longer predicts a threatening outcome, then defensive responding to the neutral cue ceases; this process is known as extinction; (2) if a neutral cue previously associated with safety starts to predict threat, then defensive responding to the neutral cue increases.

A large body of research has shown that individuals who have anxious traits or who are clinically anxious show stronger threat acquisition and reduced extinction (for reviews, see Lonsdorf & Merz, 2017; Milad & Quirk, 2012). Notably, recent research from our laboratory and others has shown that individual differences in intolerance of uncertainty (IU), a transdiagnostic dispositional tendency to find uncertain situations aversive and anxiety provoking (Carleton, 2016a, 2016b; Dugas, Buhr, & Ladouceur, 2004), play a critical role in threat acquisition (Chin, Nelson, Jackson, & Hajcak, 2016) and extinction (Dunsmoor, Campese, Ceceli, LeDoux, & Phelps, 2015; Lucas, Luck, & Lipp, 2018; Morriss, Christakou, & van Reekum, 2015, 2016; Morriss, Macdonald, & van Reekum, 2016). For example, under 50% reinforcement during acquisition, high IU individuals have been shown to exhibit greater discrimination in startle response—indicative of a negative affective background state—to threat versus safety cues (Chin et al., 2016). Furthermore, during an acquisition phase with 50% reinforcement and generalization stimuli (cues that look similar to the CS), high IU individuals have also been observed to show greater generalization in skin conductance response (SCR)—a measure of sympathetic arousal—across threat and safety cues (Morriss, Macdonald, et al., 2016). However, a few studies have not found any significant differences in physiological responding during acquisition for individuals with high versus low IU (Dunsmoor, Campese, et al., 2015; Lucas et al., 2018). Findings are more consistent for IU and threat extinction. For example, high IU individuals have been found to show generalized SCR across threat and safety cues during early extinction and to show continued skin conductance responding to threat versus safety cues during late extinction (Morriss, Christakou, et al., 2015, 2016). Moreover, in an extinction phase with generalization stimuli, high IU individuals display a generalized pattern for SCR across threat and safety cues (Morriss, Macdonald, et al., 2016). These findings were specific to IU, over and above trait anxiety.

The current understanding of the results presented above is that during extinction there is a period of uncertainty regarding the change of outcome, and this may induce uncertainty-related anxiety in high IU individuals, which subsequently disrupts extinction in high IU individuals. However, it remains unclear as to whether high IU individuals have difficulty (1) generally with updating threat to safe associations when contingencies change or (2) specifically with updating threat to safe associations during extinction where the US omitted. The latter would be expected, given that recent conceptualizations of IU suggest that the absence of information (e.g., omission of US in extinction) may be more threatening than having some information (e.g., US moves to another stimulus in reversal): "IU is an individual's dispositional incapacity to endure the aversive response triggered by the perceived absence of salient, key, or sufficient information, and sustained by the associated perception of uncertainty" (Carleton, 2016b, p. 31). The question above can be addressed by adopting a threat reversal paradigm, where both threat and safety contingencies are reversed (Costa, Bradley, & Lang, 2015; Kluge et al., 2011; Li, Schiller, Schoenbaum, Phelps, & Daw, 2011; Mertens & De Houwer, 2016; Morris & Dolan, 2004). Importantly, during threat reversal, the US remains present. Therefore, IU findings from threat reversal can be contrasted against the IU findings from the threat extinction literature, to assess the importance of US presence versus absence on the updating of threat and safe associations.

Despite the richness that threat reversal paradigms offer in understanding the flexibility of learned associations, little research has been conducted on threat reversal in relation to individual differences in anxiety. Given the important role of uncertainty in anxiety (Carleton, 2016a, 2016b; Grupe & Nitschke, 2013) and that current therapies are based on associative learning principles (Milad & Quirk, 2012), examining

the link between IU and the reversal of threat and safe associations may provide crucial information relevant to IU conceptualization and future IU-related disorder diagnosis and treatment.

Here we used threat and safety cues during acquisition and reversal, in order to assess the relationship between individual differences in self-reported IU and updating of learned threat and safety associations. We measured SCR and expectancy ratings while participants performed the acquisition and reversal phases. We used an aversive sound as an unconditioned stimulus and visual shape stimuli as conditioned stimuli, similar to previous conditioning research (Morriss, Christakou, et al., 2015, 2016; Morriss, Macdonald, et al., 2016; Neumann, Waters, & Westbury, 2008; Phelps, Delgado, Nearing, & LeDoux, 2004). We used a 50% reinforcement rate during both acquisition and reversal to maintain conditioning (Grady, Bowen, Hyde, Totsch, & Knight, 2016; Jenkins & Stanley, 1950; Leonard, 1975; Livneh & Paz, 2012) and to induce greater uncertainty.

In general, we hypothesized that, during threat acquisition and reversal, SCR and expectancy ratings would be higher to the threat (CS+) versus safety cues (CS−). Furthermore, we explored which of the two alternative hypotheses for IU and updating of learned threat and safety associations during acquisition would be supported. Based on previous opposing findings in the literature as reviewed above, during acquisition high IU individuals would be prone to either (1) greater discrimination (Chin et al., 2016) indicated by larger SCR and expectancy ratings to the threat versus safety cues or (2) less discrimination and have larger SCR and expectancy ratings for both threat and safety cues (Morriss, Macdonald, et al., 2016). Given the lack of research on reversal and IU, we based our exploratory hypotheses on the extinction and IU literature specifically: If high IU individuals *generally* have difficulty updating threat-to-safe associations when contingencies change, then we should observe less discrimination in SCR and expectancy ratings for threat and safety cues during reversal. However, if high IU individuals *only* have difficulty when updating threat and safety associations during extinction *when the US is omitted* (per prior research), we should observe reversal of threat and safety associations for the SCR and ratings. For both acquisition and reversal, we tested the specificity of IU effects by controlling for individual variation reported on the commonly used Spielberger's State-Trait Anxiety Inventory, Trait Version (STAI) (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983).

Method

Participants

Forty-four students took part in this study (M_{age} = 20.45, SD_{age} = 3.18; 33 females and 11 males). For this study, the sample size was not based on a formal power calculation. However, our sample size was matched with comparable experiments using psychophysiological measures to examine conditioning and individual differences in anxiety (e.g., Chin et al., 2016; Morriss, Christakou, et al., 2016). All participants had normal or corrected-to-normal vision. Participants were recruited through the University of Reading Psychology Panel. The procedure was approved by the University of Reading's Research Ethics Committee.

Procedure

Participants arrived at the laboratory and were informed on the procedures of the experiment. Firstly, participants were taken to the testing booth and given a consent form to sign as an agreement to take part in the study. Second, to assess anxious disposition, we asked participants to complete a series of questionnaires presented on a computer in the testing booth. Next, physiological sensors were attached to the participants' nondominant hand. Participants were simply instructed (1) to maintain attention to the task by looking and listening to the colored squares and sounds presented, (2) to respond to the rating scale that followed each block (see "Conditioning task" below for details) using the keyboard with their dominant hand, and (3) to sit as still as possible. Participants were presented a conditioning task on the computer, while electrodermal activity, interbeat interval (IBI), and ratings were recorded. Altogether, the experiment took approximately 25 min.

Conditioning task

The conditioning task was designed using E-Prime 2.0 software (Psychology Software Tools Ltd., Pittsburgh, Pennsylvania, USA). Visual stimuli (CS+ and CS−) were presented using a screen resolution of 800 × 600 with a 60-Hertz refresh rate. Participants sat at approximately 60 cm from the screen. Visual stimuli were light blue and yellow squares with 183 × 183 pixel dimensions that resulted in a visual angle of

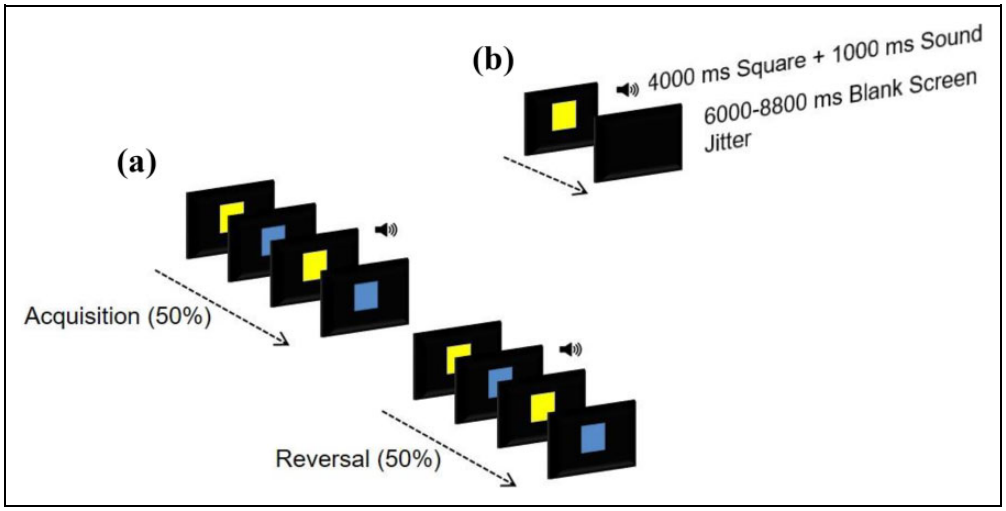

Figure 1. Image depicting (a) the experimental phases of the experiment and (b) examples of trial timing.

5.78° × 9.73°. The sound stimulus (US) consisted of a fear inducing female scream (Morriss, Christakou, et al., 2015, 2016; Morriss, Macdonald, et al., 2016).

Acquisition and reversal phases were each presented in two separate blocks, totaling four blocks for the experiment as a whole (see Figure 1). In acquisition, one of the squares (blue or yellow) was paired with the aversive sound 50% of the time (CS+), while the other square (yellow or blue) was presented alone (CS−). The 50% pairing ratio was designed to maximize the unpredictability of the US following the CS+. In reversal, the CS+ and US association was reversed so that the former CS+ became the new CS− and the former CS− became the new CS+. The 50% pairing ratio was maintained during the reversal phase. Participants were uninstructed about the conditioning procedure, the pairing rate, and contingency change during reversal. The acquisition phase consisted of 24 trials (6 CS+ paired, 6 CS+ unpaired, 12 CS−) and the reversal phase consisted of 32 trials (8 new CS+ paired, 8 new CS+ unpaired, 16 CS−). Each block therefore consisted of 12 trials during acquisition and 16 trials during reversal. The reversal phase was longer to allow time for participants to update the learned contingencies. Experimental trials within the conditioning task were pseudorandomized: The first trial of the acquisition and reversal phases started with a trial that was paired. Thereafter, the order of all remaining trials was fully randomized. Conditioning contingencies were counterbalanced, with half of the participants receiving the US with a blue square and the other half of participants receiving the US with a yellow square. The presentation times of the task were 4,000 ms square, 1,000 ms sound (coterminated with the square), and 6,000–8,800 ms intertrial interval (see Figure 1).

At the end of each block, participants were asked to rate the expectancy of the sound stimulus when preceded by the blue square or the yellow square using 9-point Likert-type scales ranging from 1 (*Don't Expect*) to 9 (*Do expect*). Two other 9-point Likert-type scales were presented at the end of the experiment. The first one asked participants to rate the valence of the sound stimulus from 1 (*Negative*) to 9 (*Positive*). The second one asked the participants to rate the arousal of the sound stimulus from 1 (*Calm*) to 9 (*Excited*).

Questionnaires

To assess anxious disposition, we presented the following questionnaires on a computer: STAI (Spielberger et al., 1983) and IU (Buhr & Dugas, 2002; Freeston, Rhéaume, Letarte, Dugas, & Ladouceur, 1994). Similar distributions and internal reliability of scores were found for the anxiety measures, STAI ($M = 43.11$; $SD = 10.85$; range = 25–67; $\alpha = .93$) and IU ($M = 63.3$; $SD = 22.3$; range = 28–111; $\alpha = .96$). The STAI and IU scores were significantly positively correlated, $r(42) = .81$, $p < .001$.

Rating data scoring

The E-Data Aid tool in E-Prime was used to reduce rating data for each subject by calculating their average responses for each experimental condition: Acquisition CS+ Early; Acquisition CS− Early;

Acquisition CS+ Late; Acquisition CS− Late; Reversal New CS+ Early; Reversal New CS− Early; Reversal New CS+ Late; and Reversal New CS− Late.

Physiological acquisition and scoring

Physiological recordings were obtained using AD Instruments (AD Instruments Ltd., Chalgrove, Oxfordshire, England) hardware and software. Electrodermal activity was measured with dry MLT116F silver/silver chloride bipolar finger electrodes that were attached to the distal phalanges of the index and middle fingers of the nondominant hand. A low constant-voltage alternate current excitation of 22 mV_{rms} at 75 Hz was passed through the electrodes, which were connected to an ML116 Galvanic Skin Response Amp, and converted to digital current before being digitized and stored. IBI was measured using a MLT1010 Electric Pulse Transducer, which was connected to the participant's distal phalange of the ring finger. An ML138 Bio Amp connected to an ML870 PowerLab Unit Model 8/30 amplified the electrodermal and IBI signals, which were digitized through a 16-bit analog to digital converter at 1,000 Hz. IBI signal was used only to identify movement artifacts and was not analyzed. The electrodermal signal was converted from volts to microsiemens using AD Instruments software.

CS+ paired trials were discarded from the analysis to avoid the sound confound (for the examination of US responses to the CS+ paired trials, see Supplementary Material). Data from the CS+ unpaired and CS− trials were included. SCRs were scored when there was an increase in skin conductance level exceeding .03 microsiemens (Dawson, Schell, & Filion, 2000). The amplitude of each SCR was scored as the difference between the onset and the maximum deflection prior to the signal flattening out or decreasing. SCR onsets and respective peaks were counted if the SCR onset was within .5–3.5 s (CS response) following CS onset (Dunsmoor, Murty, Davachi, & Phelps, 2015; Hartley, Fischl, & Phelps, 2011; Morriss, Chapman, Tomlinson, & van Reekum, 2018; Spoormaker et al., 2011). Trials with no discernible SCRs were scored as zero.

SCR amplitudes were square root transformed to reduce skewness (Dawson et al., 2000). Trials with motion artifacts, as identified by distortions in both electrodermal and IBI signals, were discarded from the analysis; .2% (4 of 1,848) of trials were removed from the analysis due to movement artifacts. SCR magnitudes were calculated from the remaining trials by averaging SCR square root transformed values and zeros for each contingency and block, creating the following conditions: Acquisition CS+ Early; Acquisition CS− Early; Acquisition CS+ Late; Acquisition CS− Late; Reversal New CS+ Early; Reversal New CS− Early; Reversal New CS+ Late; and Reversal New CS− Late. SCR magnitudes were finally *z*-scored to control for interindividual differences in skin conductance responsiveness (Ben-Shakhar, 1985) related to dryness and thickness of the skin and the surface area of the finger relative to the skin conductance electrode.

Learning assessment

To assess whether participants learned the association between the neutral cue and aversive sound, we calculated separate conditioned response scores for ratings and SCR magnitude from the acquisition and reversal phases. The conditioned response scores were the CS+ trials to the CS− trials for each phase. A positive differential response score indicated a larger response for CS+ relative to CS−, indexing a conditioned response. The learning criterion procedure has been suggested to be problematic (Lonsdorf et al., 2017); however, we used it for comparison with other laboratories that commonly use this procedure. We considered participants "learners" if they displayed a positive differential response in either phase (ratings: Acquisition 43 learners, 1 nonlearner; Reversal 41 learners, 3 nonlearners; SCR: Acquisition 34 learners, 10 nonlearners; Reversal 25 learners, 19 nonlearners). A similar learning criterion has been published elsewhere (Morriss, Macdonald, et al., 2016). Based on this criterion, only four of the 44 participants displayed no differential response in both acquisition and reversal. However, as removing these participants did not change the results reported here, for reasons of completeness, we decided to include these four participants.

Ratings and SCR magnitude analysis

The analysis was conducted using the mixed procedure in SPSS 21.0 (SPSS, Inc., Chicago, Illinois, USA). We conducted separate multilevel models (MLMs) on ratings and SCR magnitude from acquisition and reversal. For ratings and SCR magnitude, we entered Stimulus (CS+ and CS−) and Time (Early and Late) at Level 1 and individual subjects at Level 2. We included the following individual difference

Table 1. Summary of means (SD) for each dependent measure as a function of condition during the acquisition and reversal phases.

	Acquisition				Reversal			
	Early		Late		Early		Late	
Measure	CS+	CS−	CS+	CS−	CS+	CS−	CS+	CS−
SCR magnitude ($\sqrt{\mu S}$)	0.55 (0.79)	0.09 (0.48)	0.31 (0.61)	−0.15 (0.41)	0.04 (0.67)	−0.13 (0.28)	−0.02 (0.56)	−0.16 (0.29)
Expectancy rating	6.23 (1.74)	1.64 (1.43)	6.89 (1.48)	1.27 (.59)	6.50 (1.34)	3.23 (1.80)	6.70 (1.62)	2.55 (1.80)

Note. Expectancy rating, 1 = *Don't Expect* and 9 = *Do Expect*; SCR magnitude ($\sqrt{\mu S}$) and square root transformed and z-scored skin conductance magnitude measured in microsiemens. SD = standard deviation; SCR = skin conductance response.

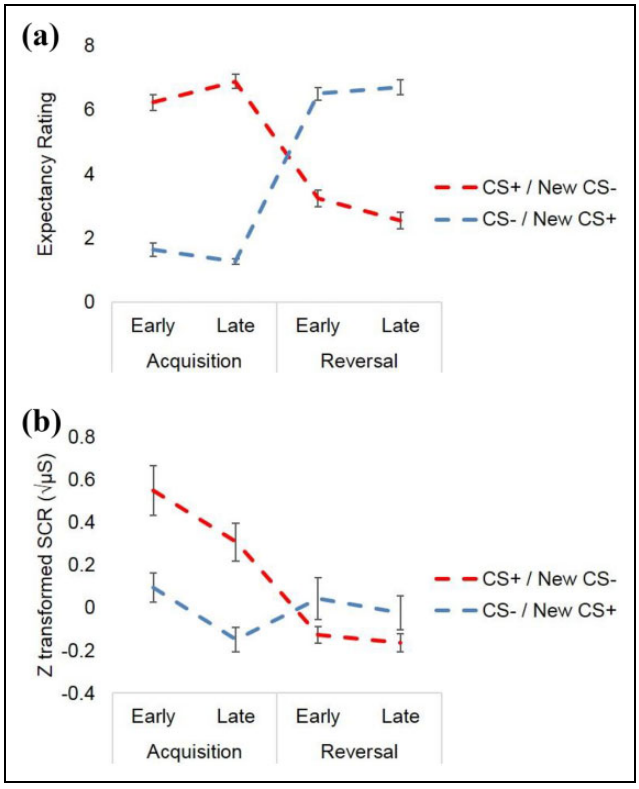

Figure 2. Line graphs displaying (a) expectancy ratings and (b) SCR magnitude scores to the CS+ and CS− during the experiment. For all phases, participants reported greater expectancy of the sound with the CS+, compared with the CS−. In addition, larger SCR magnitude responses were found for the CS+ versus CS− during acquisition and reversal. Bars represent standard error of the mean. Expectancy rating, 1 (*Don't expect*)–9 (*Do expect*). SCR magnitude ($\sqrt{\mu S}$) and square root transformed and z-scored skin conductance magnitude measured in microsiemens. SCR = skin conductance response.

predictor variables into the MLMs: IU and STAI. In all models, we used a diagonal covariance matrix for Level 1. Random effects included a random intercept for each individual subject, where a variance components covariance structure was used. Fixed effects included Stimulus and Time. We used a maximum likelihood estimator for the MLMs.

Where a significant interaction was observed with IU, we performed follow-up pairwise comparisons on the estimated marginal means of the relevant conditions estimated at specific IU values of +1 SD or −1 SD of mean IU, adjusted for the control variable (STAI). These data are estimated from the MLM of the entire sample, not unlike performing a simple slopes analysis in a multiple regression analysis. Similar analyses have been published elsewhere (Morriss, Macdonald, et al., 2016; Morriss, McSorley, & van Reekum, 2018).

Results

Ratings

On average, the participants rated the sound stimulus as aversive ($M = 2.05$ $SD = 0.91$, range 1–4, where 1 = *Very negative* and 9 = *Very positive*) and arousing (M = 7.11, $SD = 1.33$, range 4–9, where 1 = *Calm* and 9 = *Excited*).

For the expectancy ratings, during acquisition, participants reported greater expectancy of the sound with the CS+, compared with CS−, Stimulus: $F(1, 123.240) = 659.340$, $p < .001$, (for descriptive statistics of ratings, see Table 1 and Figure 2(a)). Reflecting learning over time, follow-up tests revealed the expectancy rating of the sound with the CS+ to increase from early acquisition to late acquisition, $p < .05$, Stimulus × Time: $F(1, 123.240) = 6.624$, $p = .011$, and the expectancy rating of the sound with the CS− to remain low across early to late acquisition, $p = .104$. No other significant main effects or interactions with IU or STAI were found for the ratings during acquisition, max $F = .997$.

During reversal, participants reported greater expectancy of the sound with the NewCS+, compared with NewCS−, Stimulus: $F(1, 122.423) = 329.755$, $p < .001$. Follow-up pairwise comparisons suggest

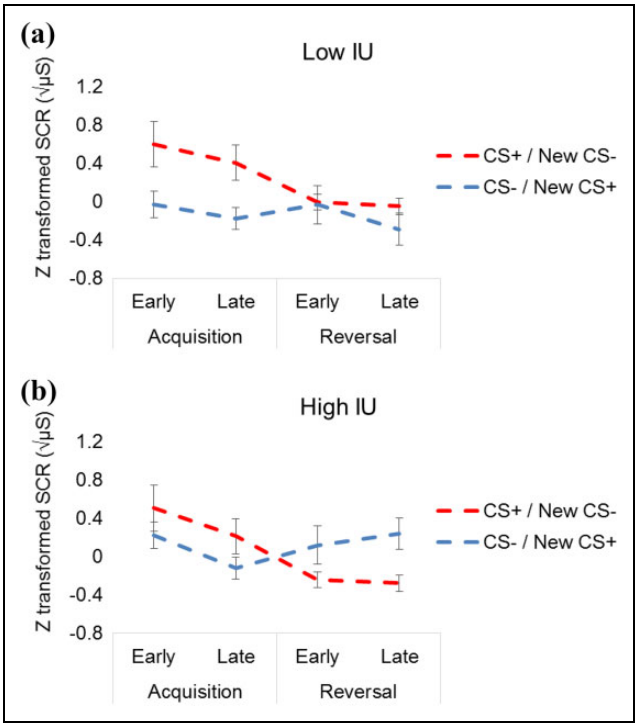

Figure 3. Line graphs depicting IU estimated at +1 SD or −1 SD of mean IU (controlling for STAI) from the multilevel model analysis for SCR magnitude during acquisition reversal. Higher IU was associated with greater discrimination in SCRs to CS+ versus CS− during reversal. No significant IU-related differences were observed during acquisition. Bars represent standard error at +1 SD or −1 SD of mean IU. Square root transformed and z-scored SCR magnitude (μS) and skin conductance magnitude measured in microsiemens. IU = intolerance of uncertainty; SD = standard deviation; STAI = State-Trait Anxiety Inventory, Trait Version; SCR = skin conductance response.

that the expectancy rating of the sound with the NewCS+ was high during this phase and did not change across early acquisition to late acquisition, $p = .436$, and the expectancy rating of the sound with the NewCS− dropped across early to late acquisition, $p = .036$, Stimulus × Time: $F(1, 122.423) = 4.691$, $p = .032$. No other significant main effects or interactions with IU or STAI were found for the ratings during reversal, max $F = 2.289$.

SCR magnitude

For SCR magnitude, during acquisition, participants displayed larger SCR magnitude to the CS+, compared with CS−, Stimulus: $F(1, 135.204) = 27.726$, $p < .001$ (see Table 1 and Figure 2(b)). Furthermore, SCR magnitude dropped from early acquisition to late acquisition without an effect of stimulus type, Time: $F(1, 135.204) = 7.821$, $p = .006$. No other significant main effects were found, nor were there significant interactions with IU (or STAI) for the SCR magnitude during acquisition, max $F = .978$.

During reversal, participants displayed larger SCR magnitude to the NewCS+, compared with the NewCS−, Stimulus: $F(1, 118.858) = 4.891$, $p = .029$. As predicted, MLM revealed a significant interaction between Stimulus × IU during reversal, $F(1, 118.858) = 5.418$, $p = .022$ (see Figure 3).[1,2] Further inspection of follow-up pairwise comparisons for reversal revealed that low IU was associated with an absence of differential responding between the NewCS+ versus NewCS− during reversal, $p = .353$. High IU was associated with greater differential responding to the NewCS+ versus NewCS− during reversal, $p = .002$. No other significant main effects or interactions with IU or STAI were found for SCR magnitude during reversal, max $F = 2.694$.

Discussion

In the current study, we showed that individual differences in self-reported IU modulate threat reversal. Our data suggest that during an associative learning experiment with acquisition and reversal phases, high IU is associated with greater differential SCR between threat and safety cues during reversal. No significant relationships were found between IU and expectancy ratings. The skin conductance findings for IU are specific to variability explained by IU, over shared variability with STAI. These results further our understanding of IU's role in the updating of threat and safety associations in the presence and absence of threat, which may be important in the maintenance of uncertainty-induced anxiety.

For both threat acquisition and reversal phases, greater expectancy ratings and skin conductance magnitude were observed for threat versus safe cues, suggesting evidence of conditioning across the sample (Costa et al., 2015; Li et al., 2011; Mertens & De Houwer, 2016; Morris & Dolan, 2004). However, the extent of conditioning on skin conductance magnitude during reversal varied substantially with individual differences in IU. During reversal, higher IU was associated with larger SCR magnitude to new threat versus new safety cues, compared with lower IU. These results suggest that high IU individuals may be prone to greater conditioning in the presence of uncertain threat, compared with low IU individuals. This effect may be driven by uncertainty relevance. For individuals high in IU, uncertainty is more

motivationally relevant, as they find uncertainty aversive and anxiety-provoking, while individuals low in IU either don't care much about, or even welcome, uncertainty. The lack of reversal in low IU individuals may be maladaptive in the long term. Future research should vary the relevance of the US and assess the full spectrum of IU, as it may open up new avenues of research that will be relevant to psychopathology and therapy.

In a broader context, the reversal finding with IU enriches our understanding of previous research where high IU has been found to predict reduced threat extinction (Morriss, Christakou, et al., 2015, 2016; Morriss, Macdonald, et al., 2016). Comparing across these experiments, we can speculate that the reason for high IU individuals being able to update threat to safe associations during reversal but not extinction may stem from the amount of information available. For example, there is some familiarity with the reinforcement rate, such that CSs are associated with a 50% partial reinforcement rate during both acquisition and reversal. Furthermore, during reversal, the learned threat is simply moved onto another stimulus, while in extinction, the learned threat is completely omitted. The lack of any previously learned threat outcome in extinction may induce greater anxiety in high IU individuals. This finding fits with the modern definition of IU by Carleton (2016b). Further work is needed to clarify how the presence and absence of information modulates anxiety in individuals who score high in IU.

The findings reported here feed into a wider research movement examining the role of uncertainty in anxiety disorders (Carleton, 2016a, 2016b; Grupe & Nitschke, 2013). Recent research has begun to examine whether IU can be targeted in treatment for anxiety disorders, and initial findings show promise for patients with generalized anxiety disorder (GAD) and social anxiety disorder (Dugas & Ladouceur, 2000; van der Heiden, Muris, & van der Molen, 2012). Our preliminary findings highlight how IU interacts with fundamental associative learning processes such as threat conditioning, which are relevant for current exposure-based therapies for anxiety disorders (Milad & Quirk, 2012). It is unclear, however, what type of IU-related biases interact with threat conditioning mechanisms; for example, one potential bias could be heightened expectation of threat under uncertainty, particularly when direct threat is absent as in extinction. Nonetheless, such findings pave the way for new lines of research to address the relevance of IU-related biases on threat conditioning mechanisms as potential risk markers and intervention targets. For example, future research may focus on how discrimination during threat extinction can be improved in high IU individuals, by exposing participants to more safe stimuli or by asking participants to use different appraisal strategies related to accepting or tolerating uncertainty.

In the current study, we did not observe IU to modulate threat acquisition. This result is at odds with some previous research from our laboratory and others, where high IU individuals have been shown to have (1) larger SCR magnitude across threat and safety cues during partial reinforcement (Morriss, Macdonald, et al., 2016) and (2) greater discrimination in startle response for threat versus safe cues (Chin et al., 2016). The differences in findings may reflect differences in experimental paradigms and measures. For example, there may be other differences between the studies which may influence the results, such as the threat level of unconditioned stimuli (e.g., sound versus shock), the number of stimulus types (e.g., the use of generalization stimuli), and the number of trials. Furthermore, the startle response is under control of the central nucleus of the amygdala, among other (Koch, 1999), and the inclusion of startle probes introduces more ambiguity in the experimental design (Lonsdorf & Merz, 2017). Further research is needed to assess the role of IU in threat acquisition.

Self-reported expectancy ratings were not found to reflect individual differences in IU in our sample. While correspondence between ratings and SCR magnitude was observed, differences between self-reported and psychophysiological measures of emotion are often reported (Mauss, Levenson, McCarter, Wilhelm, & Gross, 2005). To our knowledge, only a few studies have observed IU effects on ratings during threat conditioning (Morriss, Macdonald, et al., 2016; Sjouwerman, Scharfenort, & Lonsdorf, 2017). The majority of research examining the effects of IU on threat acquisition and extinction has found significant relationships between IU and psychophysiological measures such as startle response and skin conductance (Chin et al., 2016; Dunsmoor, Campese, et al., 2015; Morriss, Christakou, et al., 2015, 2016; Morriss, Macdonald, et al., 2016; Sjouwerman et al., 2017). We therefore think that IU may be a more suitable predictor of bodily responses during threat conditioning. The lack of relationship between psychophysiological and rating measures for IU may also

be due to the time between phasic cue events and rating periods in the experiment, where recall of expectancy was required for each block.

The design specifics of the current study should be further addressed in future research to assess the robustness and generalizability of the findings reported here. Firstly, future studies should use stimuli that vary in aversiveness and different reinforcement rates to elucidate whether IU modulates the updating of threat and safe associations differently based on these factors. Secondly, the sample contains mainly female participants, and future studies should more carefully balance their sample in terms of gender. Lastly, the current study may have been more sensitive to individual differences if low and high IU individuals were selected or oversampled. However, it is important to note that the mean IU score in the current sample is (1) approximately10 points higher than those reported in student samples from North America (Buhr & Dugas, 2002; Carleton, Norton, & Asmundson, 2007) and (2) approximately 7 points above the clinical cutoff used for patients with GAD (Dugas & Ladouceur, 2000). Therefore, the sample in this study is likely relevant for clinical research.

In conclusion, these initial results provide some insight into how IU modulates threat and safe associations in the presence and absence of threat, which may be relevant for understanding uncertainty-induced anxiety and related psychopathology (Carleton, 2016a, 2016b; Grupe & Nitschke, 2013).

Acknowledgments

The authors thank the participants who took part in this study. To access the data, please contact Dr. Jayne Morriss.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This research was supported by the Centre for Integrative Neuroscience and Neurodynamics at the University of Reading.

Supplemental material

Supplemental material for this article is available online.

Notes

1. In the untransformed skin conductance response data, the same pattern of results is observed for the interaction of Stimulus × Intolerance of uncertainty during reversal, $F(1, 95.368) = 5.760$, $p = .018$.
2. To assess that the interaction of Stimulus × Intolerance of uncertainty (IU) during reversal was not driven by US habituation, we ran an additional multilevel model including the average skin conductance response magnitude of the US response during reversal as a covariate. In this model, we observed the same result for Stimulus × IU during reversal, $F(1, 95.368) = 4.757$, $p = .031$, suggesting that this effect was not driven by US habituation.

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