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Evidence for Different Roles of Inhibitory and Prospective Intolerance of Uncertainty During Threat Discrimination Learning

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Uncertainty is a core component of threat and associated learning processes. One methodological factor impacting uncertainty in threat learning paradigms is the threat reinforcement rate, which refers to the proportion of times a cue is reinforced with an aversive stimulus. This study tested the effect of partial vs continuous threat reinforcement on threat / safety discrimination learning, as indexed by skin conductance response (SCR). Using a within-participants design, fifty-nine participants completed a task in which three colored shapes were paired with electric shock at reinforcement schedules of 100% (CS+), 50% (CS+) and 0% (CS-). In addition, the study examined the relationship between the Intolerance of Uncertainty scale (IU) and two subscales – inhibitory and prospective IU – with threat discrimination learning. The data show heightened SCR in the continuous vs partial reinforcement condition to all stimuli, but limited evidence of enhanced discrimination learning. Furthermore, no association was observed between total IU score and threat-safety discrimination. However, using a two-factor model of IU, findings showed higher inhibitory IU and higher prospective IU were associated with diminished and heightened threat discrimination, respectively. These results contribute to a fast-growing literature exploring how the uncertainty inherent to predictors of threat, individual differences in sensitivity to uncertainty, and interactions between these two factors, can shape the acquisition of threat memory.

I. Introduction

Threat conditioning is a process that involves learning the relationship between danger and the cues that predict its arrival (Phelps et al., 2004). For example, an individual can learn that the sound of a rattlesnake or a snarling dog signals imminent danger, providing the opportunity to freeze, flee or fight (Blanchard & Blanchard, 1988). This learning process has been extensively studied behaviorally and neurobiologically (LeDoux, 2003; Maren, 2001; Sehlmeyer et al., 2009) and is thought to play an important etiological role in stress and anxiety disorders (Bouton et al., 2001; Davey, 1992; Lissek et al., 2005). Crucial to the adaptive value of this learning process is the ability for an individual to distinguish threat cues from those that signal safety. Threat discrimination learning is usually studied in the lab by way of a standard paradigm that involves multiple presentations of a CS+ (e.g., a visual stimulus, such as a colored shape or face) paired some proportion of the time with an aversive stimulus (e.g., electric shock or scary sounds/pictures), and another stimulus, the CS-, which acts as a control and is never paired with an aversive stimulus. Over multiple presentations, participants typically develop a conditioned threat response to the CS+, but not the CS-, as indexed by some combination of physiological and/or neural response, behavior and/or self-report. Discrimination learning can be quantified by measuring the difference between responses to threat and safety cues, where larger difference scores are indicative of enhanced learning. Threat discrimination learning performance has been linked to threat-related disorder, with diminished capacity to differentiate between danger vs safety stimuli observed in individuals with high trait anxiety (Raymond et al., 2017) and in psychological disorders such as post-traumatic stress disorder (PTSD) (Grasser & Jovanovic, 2021), panic disorder (Lissek et al., 2010), and generalized anxiety disorder (Lissek et al., 2014).

Uncertainty is thought to activate the behavioral inhibition system responsible for negative affective states such as anxiety and stress (Gray, 1983; Peters et al., 2017). In-

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deed, current neurobiological evidence suggests that uncertainty plays a central role in modulating both neural and psychophysiological responses to cues that signal threat and safety (Brosschot et al., 2016; Grupe & Nitschke, 2013; Morriss et al., 2019). Within threat conditioning paradigms, uncertainty can be manipulated in a variety of different ways to assess its effect on threat discrimination learning (Lonsdorf et al., 2017; Morriss, Zuj, et al., 2021). For instance, uncertainty may be manipulated through providing participants with different instructions (e.g., uninstructed, partially instructed, fully instructed) about threat and safety contingencies (for review see, Mertens et al., 2018). One of the most common ways of manipulating uncertainty is through varying the threat reinforcement rate (the proportion of times the CS+ is paired with an aversive stimulus), which typically varies anywhere from 37.5% up to 100% (Lonsdorf et al., 2017), with rates of threat reinforcement being equated to higher levels of uncertainty as they move closer to 50%. There is evidence that uncertainty about the contingencies associated with a threat cue, as operationalized by parametric manipulation of the threat reinforcement rate, can impact threat learning processes (Dunsmoor et al., 2007; Grady et al., 2016). Dunsmoor et al (2007) showed higher self-reported US expectancy and SCR to a CS+ reinforced at 100% vs 50%. Grady et al (2016) showed a similar pattern of results, with higher self-reported US expectancy and SCR for CS+ stimuli conditioned at 100%, at mixed rates of reinforcement (50% and 100%) and at 50%, respectively. Some studies have not shown these effects. Chin et al (2016) showed higher responses to both the CS+ and CS- using a 75% vs 50% reinforcement schedule, but no difference in threat discrimination. Recent work by Zhao and colleagues (2022) used 100%, 75% and 50% reinforcement schedules and failed to find statistically significant effects during acquisition, though they did show descriptive results consistent with higher SCR to CS+ stimuli at higher reinforcement rates. Collectively, these findings support a link between decreased uncertainty about threat contingencies and enhanced threat discrimination, but results are mixed. It is important to note, however, that all of the aforementioned studies concurrently varied the threat reinforcement rate and the amount of learning experience in their experimental designs. That is, higher threat reinforcement rates corresponded to proportionally higher numbers of CS-US pairings, with Dunsmoor et al. (2007) using reinforcement rates (and # of CS-US trials) of 50% (20) and 100% (40), Grady et al. (2016) using 50% (20), 50%-100% (30), 100%-50% (30), and 100% (40), Zhao et al (2022) using 50% (4), 75% (6) and 100% (8) and Chin et al (2016) using 50% (4) and 75% (6). This is important because more learning experience could lead to enhanced threat discrimination by reducing estimation uncertainty (Payzan-LeNestour et al., 2013), thus this feature of the experimental design challenges direct attributions of enhanced threat discrimination learning to reinforcement rate alone.

Differences in threat discrimination learning can also be observed on the individual level. According to the diathesis stress model, some individuals are more susceptible to stress and anxiety disorders because of a trait vulnerability to traumatic conditioning experiences (Monroe & Simons, 1991). One such trait dimension is sensitivity to the unknown. A widely-used measure of this construct is *Intolerance of Uncertainty* (IU; Carleton et al., 2007), a transdiagnostic measure of the tendency to find uncertain or ambiguous situations aversive. Self-reported IU is shown to be higher in individuals diagnosed with anxiety disorders, obsessive compulsive disorder, and depression compared to community samples (Carleton et al., 2012; McEvoy et al., 2019), demonstrating the clinical relevance of this measure. A large body of research has shown poorer threat extinction learning (e.g., difficulty updating threat to safety) in individuals with higher IU scores (Bauer et al., 2020; Morriss et al., 2015; Morriss, Christakou, et al., 2016, 2016). But precisely how and under what conditions threat acquisition processes are mediated by individual differences in IU remains unsettled (for review, see Morriss, Zuj, et al., 2021).

A few studies have shown evidence for a relationship between IU and threat discrimination learning. Morriss, Christakou, et al. (2016)) used a fear generalization paradigm to show that high IU was associated with higher threat generalization from threat to safety cues during acquisition. Kanen et al (2021) showed higher IU was linked to poorer discrimination between two CS+s and a CS- during acquisition, as indexed by SCR. Sjouwerman et al. (2020) showed higher auditory startle to the CS- during acquisition for individuals with higher IU scores. Chin et al (2016) showed a negative association between IU and threat discrimination, as indexed by startle response, for a 50% but not 75% reinforced CS+, consistent with the notion that individuals high in IU are particularly sensitive to highly uncertain threat cues during acquisition learning. However, in contrast to these findings, many studies examining links between IU and threat/safety discrimination learning have shown no statistically significant effects (for review, see Mertens & Morriss, 2021). One possible explanation for the disparity in results is methodological differences. That is, many studies showing IU-related acquisition effects have used a within-subjects design with multiple CS+s and/or included additional startle probes (Bauer et al., 2020; Chin et al., 2016; Kanen et al., 2021; Klingelhöfer-Jens et al., 2022; Mertens et al., 2022; Morriss, Macdonald, et al., 2016; Sjouwerman et al., 2020), which may have created an extra layer of uncertainty compared to the studies not showing these effects, which have mostly used a single CS+ and no startle probes (Morriss, Zuj, et al., 2021). It could be that IU-related effects on threat discrimination are more likely to emerge when a suprathreshold level of uncertainty or complexity is reached during the learning session.

Although IU was originally conceived of as a unitary construct (Freeston et al., 1994), two sub-factors have been identified (Birrell et al., 2011; Hong & Lee, 2015) with the potential for distinct effects on threat learning processes (Birrell et al., 2011; Hong & Lee, 2015). *Inhibitory IU* is linked to paralysis of action and cognition when faced with the unknown (e.g., "when it is time to act, uncertainty paralyzes me"), while *Prospective IU* reflects the desire for predictability and active seeking of certainty in the face of un-

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certainty (e.g., "I always want to know what the future has in store for me"). Relevant to learning processes, higher inhibitory IU is associated with avoidance-oriented responses and disengagement, whereas higher prospective IU reflects an increased tendency to engage in approach-oriented, information seeking behavior (Birrell et al., 2011; Hong & Lee, 2015; Penney et al., 2020; Shihata et al., 2018). There is some preliminary, but inconsistent, evidence of differential associations between these two factors and threat-related disorders, with inhibitory IU being most commonly linked to social anxiety disorder, panic disorder, agoraphobia and depression, while prospective IU has been associated with generalized anxiety disorder and obsessive-compulsive disorder (McEvoy & Mahoney, 2011, but see Correa et al., 2019). Notably, a handful of studies from the threat of shock literature have shown that startle responses and relevant event-related potentials to instructed unpredictable threat are attenuated by inhibitory IU, but enhanced by prospective IU (Carsten et al., 2022; Correa et al., 2022; Nelson et al., 2016; Nelson & Shankman, 2011), suggesting different roles of the IU subscales in stress and anxiety. While this evidence is consistent with the possibility of differential effects of inhibitory and prospective IU on threat acquisition processes, minimal research has explored this relationship using the two-factor model for IU (Morriss, Wake, et al., 2021; Morriss, Zuj, et al., 2021).

Here, we used a standard fear paradigm to test the effect of 50% and 100% threat reinforcement on SCR. We utilized a within-participants design and conditioned participants to two CS+ stimuli, partially or fully reinforced with electric shock, presenting each CS+ in a separate block, with task order counterbalanced across participants. SCR was measured to each CS+ and the CS- in each condition. The shock was less predictable in the 50% vs the 100% condition, and, distinct from similar studies (Chin et al., 2016; Dunsmoor et al., 2007; Grady et al., 2016), we matched the number of CS-US pairings (and US presentations) across conditions such that any differences in SCR could be more directly attributed to threat reinforcement rate and not more CS-US pairings or US presentations. We hypothesized that because the threat was more certain in the 100% condition, we would observe heightened threat differentiation there (greater difference between CS+ and CS-) compared to in the 50% reinforcement condition, consistent with previous findings (Dunsmoor et al., 2007; Grady et al., 2016).

In addition, we examined how threat discrimination learning could be impacted by both individual differences in anxiety-related dispositional factors and interactions between those factors and the level of uncertainty associated with a threat cue. First, we set out to examine the relationship between total IU score and SCR during fear acquisition, hypothesizing higher total IU would be associated with diminished threat differentiation. Second, we tested for an interactive effect of total IU and threat reinforcement rate on SCR during acquisition, hypothesizing that individuals scoring higher vs lower in total IU would show poorer threat discrimination to the uncertain (50%) vs certain (100%) threat cue, in accordance with findings from threat generalization studies (Bauer et al., 2020; Morriss, Macdonald, et al., 2016). Finally, we conducted a post-hoc, exploratory analysis to test the hypothesis that higher scores on inhibitory IU would be associated with poorer discrimination learning, while higher scores on prospective IU would be linked to enhanced discrimination. This is based on evidence showing discriminant validity between these two factors, with higher prospective IU being associated with information-seeking behavior, while higher inhibitory IU is associated with information-avoidant behavior (Hong & Lee, 2015; Penney et al., 2020; Shihata et al., 2018). Because our aim was to independently examine the impact of total IU, and its inhibitory and prospective subscales, on threat acquisition, and both are highly correlated with trait anxiety, we controlled for trait anxiety in all of our individual difference analyses, similar to prior research (Klingelhöfer-Jens et al., 2022; Mertens & Morriss, 2021; Sjouwerman et al., 2020).

II. Methods

2.1. Participants

A total of seventy-two, right-handed college students provided informed, written consent to participate in this study for course credit. Of the original 72, four participants were excluded because they failed to respond to the US (electric shock) during at least one of the acquisition blocks, seven were excluded due to a scripting error (participants did not receive shocks for one of the CSPs during acquisition) and two were excluded for being out of the pre-specified age range for the study (18 – 35 years old). This left 59 participants in the final sample (Female = 34, Male = 25; Age Mean = 20.1 years; Age SD = 3.0; Age Range = 18-32; Ethnicity: 30 White, 19 Black, 7 Hispanic and 3 Asian). Data were collected from two different sites, a Midwestern private college (n = 37) and an urban public college (n = 22). Participants were recruited through an advertisement describing that the study was about memory. After contacting the research team, participants were screened for physical and mental health. Participants were excluded if they reported ever being diagnosed with a psychiatric disorder, were currently taking a prescription medication, or had suffered a head injury in the previous six months. Participants were informed during consent that they could terminate their participation at any time, for any reason, if they chose to do so. No participants voluntarily terminated their participation in the experiment. The study was approved by the Institutional Review Board at Manchester University and the University Integrated Institutional Review Board at The City University of New York (IRB approval #2018-1420).

2.2. Self-report measures

2.2.1. Intolerance of Uncertainty Scale – 12-item version (IUS-12); inhibitory (5-item) and prospective (7-item) subscales

The IUS-12 (Carleton et al., 2007) is a short version of the Intolerance of Uncertainty Scale (IUS; (Freeston et al., 1994). The original IUS consists of 27 items designed to

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assess general sensitivity to uncertainty, as well as cognitive and behavioral tendencies in ambiguous situations. The IUS-12 has shown a strong correlation with the original scale ($r = .96$, Carleton et al., 2007). Items on the IUS-12 are rated on a five-point Likert-type scale, with values ranging from 1 (*Not at all characteristic of me*) to 5 (*Entirely characteristic of me*), with total scores ranging from 12 to 60. Higher scores indicate greater intolerance of uncertainty. The IUS-12 has demonstrated high internal consistency in undergraduate samples (α = .91, (Carleton et al., 2007). Internal consistency of the IUS-12 for the current sample was acceptable (α = .80). Inhibitory IU consists of 5 items from the IUS-12 (items 3, 6, 7, 10 and 12). Data from item 12 was corrupted for 18 participants in this study. For those participants, we calculated the mean of 3, 6, 7, and 10 for each participant and used that value for item 12. Inhibitory IU in this sample was M = 12.95, SD = 4.99, and internal consistency was acceptable (α = .88). Prospective IU consists of 7 items from the IUS-12 (items 1, 2, 4, 5, 8, 9, and 11). Prospective IU in this sample was M = 19.14, SD = 5.73, and internal consistency was acceptable (α = .79).

2.2.2. State-Trait Anxiety Inventory

The STAI (Spielberger et al., 1983) is a 40-item measure consisting of 20 measures each for state and trait anxiety. In the present study, participants only completed the STAI-trait part of the questionnaire (STAI-T). Items on the STAI-T are rated on a four-point Likert-type scale, with values ranging from 1 (not at all) to 4 (very much like me), with higher scores indicating higher trait anxiety. STAI-T in this sample was M = 39.22, SD = 9.37, and internal consistency was acceptable (α = .87).

2.3. Stimuli and procedure

We utilized a differential, cued fear conditioning procedure that took place over one day (Figure 1). The visual context consisted of a scene of a kitchen (Google Sketch Up, 2008), presented to participants on a computer screen. Three distinct cues were presented, consisting of three colored windows, embedded in the visual context, that changed color from black to green, black to blue or black to yellow, constituting the partially and fully reinforced stimuli ($CS+_{50}$ and $CS+_{100}$), and the control stimulus (CS-), respectively. Colors were matched for luminance and intensity. Colors were not counterbalanced across stimuli. While it is not uncommon for stimulus color to be counterbalanced in paradigms similar to that used here, there is no published evidence we are aware of showing differential conditioning based on color, as long as other stimulus dimensions, such as luminance and intensity, are matched. The unconditioned stimulus (UCS) was electric stimulation. Trial duration was 9 seconds, with a black window showing for 3 seconds and a color window for 6 seconds. On reinforced trials, the stimulus co-terminated with UCS. The intertrial interval (ITI) was 14 seconds, which provided sufficient time to allow SCR to return to baseline. The duration of the electrical stimulation was 200 ms. The measure of threat learning was skin conductance response (SCR) to the conditioned stimuli. SCR is an indicator of autonomic nervous system arousal (Sequeira et al., 2009).

Upon arriving on day 1, participants provided informed consent and completed the STAI-T (Spielberger et al., 1983), IUS-12 (Carleton et al., 2007) and a handedness questionnaire. We then brought participants to the experiment room and seated them in front of a computer monitor. We attached the SCR sensors to the distal phalanges of the second and third fingers on the participants' left hand and tested participants' SCR. Then, we utilized a standard work-up procedure to establish the shock level. First, we attached the sensors and told participants we would set the shock level to a point where it would be "annoying, but not painful." We then asked participants to rate a test shock on a scale of one to nine for how annoying the shock was, where "one means not annoying at all and nine means very annoying" and told participants that our goal was to get the shock to a level of seven. If the participant rated the first shock at less than a seven, we increased the voltage slightly, administered another test shock and asked the participant to rate it again. We repeated this process until the participant rated the shock at a level of seven. After the shock level was established, we told participants they would be watching a series of pictures of a room appear where the color in the window of the room would be changing. We told them "you may occasionally receive electrical shocks" and told them to "pay attention to everything you see and feel, and note any relationships you observe between the things you see and feel." During acquisition, the conditioned stimuli ($CS+_{50}$ and $CS+_{100}$) were paired with the UCS. The stimuli were presented as the changing color of a window embedded in a picture of a room (Figure 1). The $CS+_{50}$ was reinforced 50% of the time, and the $CS+_{100}$ was reinforced 100% of the time. The CS- was never paired with the UCS. Participants were presented with 36 trials (twelve $CS+_{50}$, six $CS+_{100}$ and eighteen CS-) across two blocks; different number of trials for each stimulus were presented in order to match the number of reinforced trials across stimulus type (six CS-US pairings for both the CS+s). The partial reinforcement (50%) block consisted of twelve presentations of the $CS+_{50}$, where six trials co-terminated with the UCS, and twelve presentations of the CS-. The continuous threat reinforcement block (100%) consisted of six presentations of the $CS+_{100}$, where all six trials co-terminated with the UCS, and six presentations of the CS-. Block order was counterbalanced across subjects (partial/full, n = 30; full/partial, n = 29). Participants came back for two more experimental sessions on the subsequent two days, but those data are being used in a separate project and not being reported here. After participants concluded the experiment on day three, they completed a self-report questionnaire about their experiences in the study, which included US expectancy data for the acquisition session. Unfortunately, much of this data was lost in a flood of the lab space and is no longer available.

2.4. Physiological recording and analysis

The experiment was conducted in a well-lit, temperature-controlled room adjacent to the control room in which

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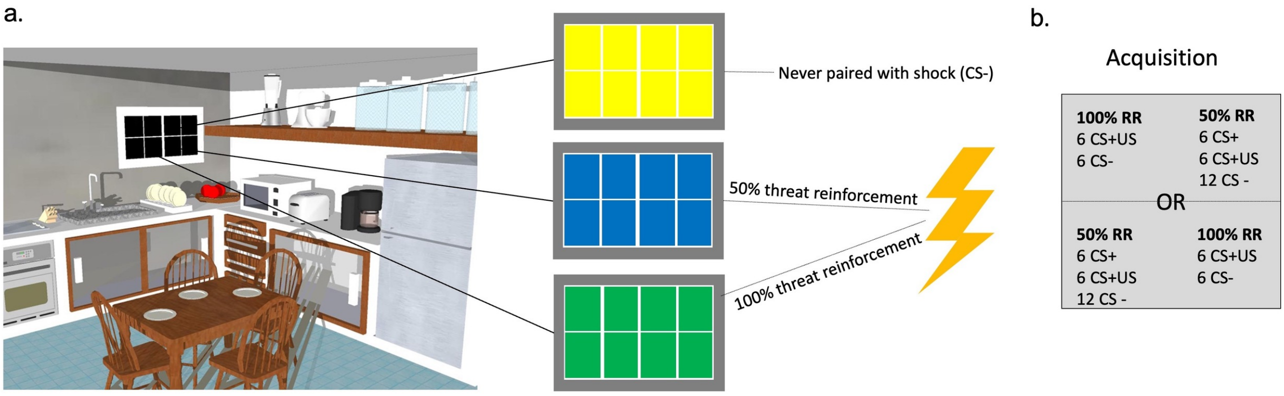

Figure 1. a. Stimuli were different colored windows embedded in a picture of a room. b. Conditioning for the 50% and 100% CS+ occurred in separate blocks during acquisition, with task order counterbalanced across participants.

the electronic equipment and experimenter were located. A stimulator (MP150 or MP160/STM100C, Biopac Systems, Goleta, GA) delivered electric stimulation through Ag/AgCl electrodes attached to the lower, inside right arm (opposite the wrist). Stimulus delivery and acquisition of the physiological data were controlled by two computers using E-Prime 3.0 (PST, Pittsburgh, PA) and AcqKnowledge software (Biopac Systems, Goleta, GA). Skin conductance response was recorded using the Biopac MP150 or MP160 at a sample rate of 2000 Hz using disposable electrodes attached to the first phalanx of the index and middle fingers of the left hand. The electrodes were 27 mm wide, 36 mm long and 1.5 mm thick, with a contact area of 11 mm in diameter (model: EL507A, Biopac Systems, Goleta, GA).

Skin conductance response (SCR) was median smoothed with a three-sample gaussian kernel to reduce noise. SCR was calculated by recording any response that began between .5 and 4.5 seconds after stimulus onset and was equal to or greater than .02 µS in magnitude, with scores below .02 µS input as zeroes (Johnson & Casey, 2015; LaBar et al., 1998). The SCR scoring window closed at stimulus offset for all stimuli. This was necessary because responses to the $CS+_{100}$ would have overlapped with responses to the UCS. Thus, we were able to use all trials for all stimuli (including all partially and continuously reinforced CS+s) in our analyses. All SCR were square rooted to normalize the distribution and range corrected by dividing each score for a given participant by that participant's highest SCR to the UCS during acquisition (Lykken & Venables, 1971). For early and late acquisition, we calculated mean response for the first half and last half of trials, respectively.

2.5. Statistical tests

To test for an effect of reinforcement rate on threat learning, we ran a repeated-measures ANCOVA consisting of within-subject factors of time (early, late), condition (50%, 100%) and stimulus type (CS+, CS-) to test for main effects and interactions. All ANCOVAs included task order (order 1: 50% -> 100%; order 2: 100% -> 50%) as a dichotomous covariate. Statistically significant three-way interactions were followed up with separate two-way ANCOVAs for each stimulus type. To fully account for the effect of the covariate, significant two-way interactions were followed up with one-way ANCOVAs (similar to Chin et al., 2016). To examine the relationship between threat learning and total IU, above trait anxiety, we ran a similar ANCOVA (with task order as a dichotomous covariate), adding total IU and trait anxiety as additional mean-centered covariates. We also tested the relationship between threat learning and the prospective and inhibitory subscales of IUS and threat learning by running an ANCOVA with the same within-subject factors as described above, but with inhibitory and prospective IU and trait anxiety as mean-centered covariates. While we did not find any significant effects of IU on threat learning, we did find significant interactive effects of prospective and inhibitory IU and stimulus type. We followed these up with hierarchical regressions (similar to previous research on IU; Morriss et al., 2015, p. 2016) for differential CS+, and CS+ and CS- separately. In each of these hierarchical regressions, task order was entered in the first block, STAI-T was entered in the second block, and inhibitory and prospective IU were entered in the third block.

To examine whether we had sufficient power to examine individual differences in IU scores and SCR, a sensitivity analysis was conducted based on a point biserial correlation model. Based on our sample size (two-tailed, $\alpha = .05$, $1 - \beta$ error probability = .8, n = 59), the effect size that we were able to detect in the present study was .33. Importantly, this small-medium effect size is comparable to that reported in a recent meta-analysis of correlational data between IU scores and SCR during threat extinction learning (Morriss, Wake, et al., 2021). An alpha of .05 was used for all statistical tests. All tests were conducted using SPSS (Version 28; IBM; Armonk, NY).

III. Results

3.1. Stimulus, time and condition

First, we conducted a repeated-measures, three-way ANCOVA with stimulus (CS+, CS-), condition (100%, 50%) and time (early, late) as within-subject factors, and task order

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Table 1. SCR (square rooted and range corrected) for stimulus, condition and time. Mean (SD)

	50%		100%	
	First half	Last half	First half	Last half
CS+	.24 (.17)	.22 (.20)	.26 (.18)	.25 (.22)
CS-	.17 (.15)	.10 (.12)	.16 (.16)	.12 (.13)

as a covariate. As expected, results indicate a main effect of stimulus (F(1, 57) = 5.93, $p = .02$, $\eta_p^2 = .09$), such that SCR was greater to the CS+ stimuli vs the CS-, suggesting that participants successfully learned the experimental contingencies. Results indicated a main effect of condition (F(1, 57) = 7.35, $p = .01$, $\eta_p^2 = .11$), such that overall SCR was greater during the full vs partial reinforcement conditions. There was no interaction between stimulus and condition (f(1, 57) = 1.48, $p = .23$), suggesting threat reinforcement rate did not mediate overall threat discrimination learning. Results indicated a main effect of time (F(1, 57) = 4.76, $p = .033$, $\eta_p^2 = .08$), such that heightened SCR was observed during early vs late trials (Table 1).

There was a time x condition interaction (F(1, 57) = 10.61, $p = .002$, $\eta_p^2 = .16$), such that there was a statistically significant decrease in SCR from early to late trials during partial reinforcement (F(1, 57) = 15.03, $p < .001$, $\eta_p^2 = .21$) but not during full reinforcement (F(1, 57) = .52, $p = .47$). Additionally, there was a stimulus x condition x time interaction (f(1, 57) = 5.12, $p = .03$, $\eta_p^2 = .08$). To follow-up this interaction, we conducted separate two-way repeated measures ANCOVAs for the CS+ (Figure 2a) and CS- (Figure 2b) with factors of condition and time. Additionally, to specifically assess threat discrimination, we also conducted a two-way repeated measures ANCOVA for the differential CS+ (Figure 2c). For the CS+ alone, there was no statistically significant two-way interaction between condition and time (F(1, 57) = .33, *ns*). For the CS- alone, there was a statistically significant two-way interaction between condition and time (F(1, 57) = 22.04, $p < .001$, $\eta_p^2 = .28$), such that there was a statistically significant decrease in SCR from early to late trials for the $CS\text{-}_{50}$ (F(1, 57) = 25.1, $p < .001$, $\eta_p^2 = .31$) but not the $CS\text{-}_{100}$ (F(1, 57) = 2.18, $p = .15$, $\eta_p^2 = .07$). For the differential CS+ there was a statistically significant two-way interaction between condition and time (F(1, 57) = 5.12, $p = .03$, $\eta_p^2 = .08$), such that there was higher SCR for the differential $CS+_{100}$ vs differential $CS+_{50}$ during early trials for (F(1, 57) = 5.72, p = .02, $\eta_p^2 = .09$) but not during late trials (F(1, 57) = .26, p = .61), suggesting faster threat discrimination for the continuously vs partially reinforced CS+.

3.2. Individual differences

To explore the association between total IU and trait anxiety scores and threat learning, we ran a repeated-measures, three-way ANCOVA with stimulus type (CS+, CS-), condition (100%, 50%) and time (first half, last half) as within-subject factors, total IU and trait anxiety as mean-centered continuous covariates and task order as a dichotomous covariate. We found no interactive effects of total IU or trait anxiety and stimulus type, condition or time (all *p*s > .05). To explore effects of the two-factor model of IU on threat learning, we ran a similar ANCOVA with inhibitory and prospective IU and trait anxiety as mean-centered continuous covariates and task order as a dichotomous covariate. There were significant interactions of stimulus and inhibitory IU (F(1, 54) = 14.53, $p < .001$, $\eta_p^2 = .21$) and stimulus and prospective IU (F(1, 54) = 4.73, $p = .03$, $\eta_p^2 = .08$). To follow up these interactions, we conducted three separate hierarchical multiple regressions using differential CS+, CS+ and CS- as the dependent variables. For the differential CS+, we computed differential CS+ (CS+ minus CS-) for acquisition, collapsed across time and condition. We controlled for task order by entering it in the first block and trait anxiety by entering it in the second block. Inhibitory and prospective IU were entered in the third block. For the first block analysis of task order, this factor was not statistically significant (f(1, 57) = .01, $R^2 = -.02$, p = .94). For the second block analysis, trait anxiety was added to the regression, and the results show the model was not statistically significant (f(2, 56) = .09, $\Delta R^2 = .003$, p = .91). For the third block analysis, inhibitory and prospective IU were added to the regression, and the data show the model was statistically significant (f(4, 54) = 4.3, $\Delta R^2 = .24$, p = .004) (Figure 3).

Results showed a significant negative relationship between inhibitory IU and differential CS+ ($\beta = -.68$, t = -3.94, $p < .001$), such that higher inhibitory IU was associated with poorer discrimination learning. These results suggest a 4.9-point increase (+1 SD) on the inhibitory subscale of IU was associated, on average, with a decrease in differential SCR of .07 µS on the threat learning task. In contrast, there was a significant positive relationship between prospective IU and SCR for the differential CS+ ($\beta = .34$, t = 2.36, $p = .02$), suggesting a 5.8-point increase (+1 SD) on this subscale of IU was associated, on average, with an increase in differential SCR of .034 µS on the task. The full model including inhibitory and prospective IU accounted for 19% of the variability in SCR for the differential CS+ (adjusted r^2). Thus, the results provide tentative evidence for distinct associations between inhibitory vs. prospective IU and threat/safety discrimination. To examine potential associations between the IU subscales and the threat and safety stimuli alone, we conducted identical hierarchical regressions for the CS+ and CS-. For the CS+, the first block analysis of task order was not statistically significant (f(1, 57) = 1.68, $R^2 = .01$, $p = .20$). For the second block analysis of trait anxiety, the model was not statistically significant (f(2, 56) = 2.56, $\Delta R^2 = .06$, $p = .09$). For the third block analysis of inhibitory and prospective IU, the model was not statistically significant (f(4, 54) = 2.4, $\Delta R^2 = .07$, $p = .06$). For the CS-, the first block analysis of task order was not statistically significant (f(1, 57) = 3.9, $R^2 < .06$, $p = .053$). For the second block analysis of trait anxiety, this factor was statistically significant (f(2, 56) = 4.3, $\Delta R^2 = .07$, $p = .02$). Results showed a significant negative relationship between trait anxiety and CS- ($\beta = .27$, t = -2.12, $p = .04$), such that higher trait anxiety was associated with higher SCR. Results also show a significant

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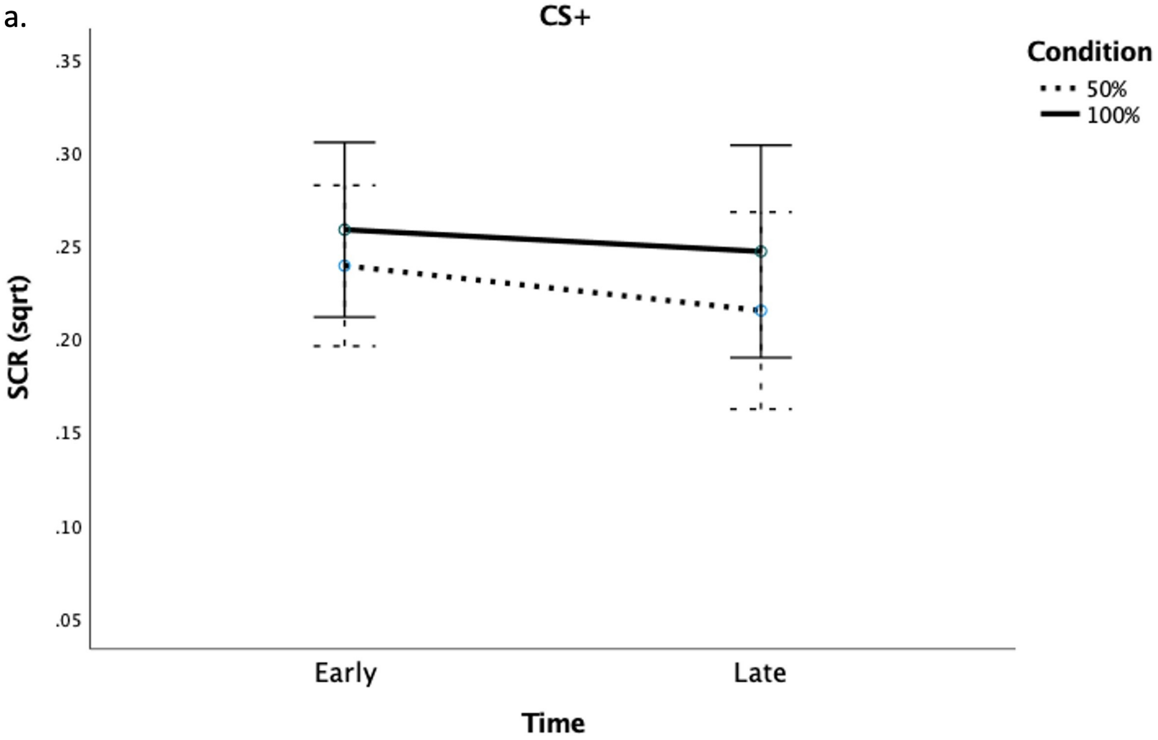

Figure 2a. There was no statistically significant interaction of time and condition for the CS+ (top).

*p < .05

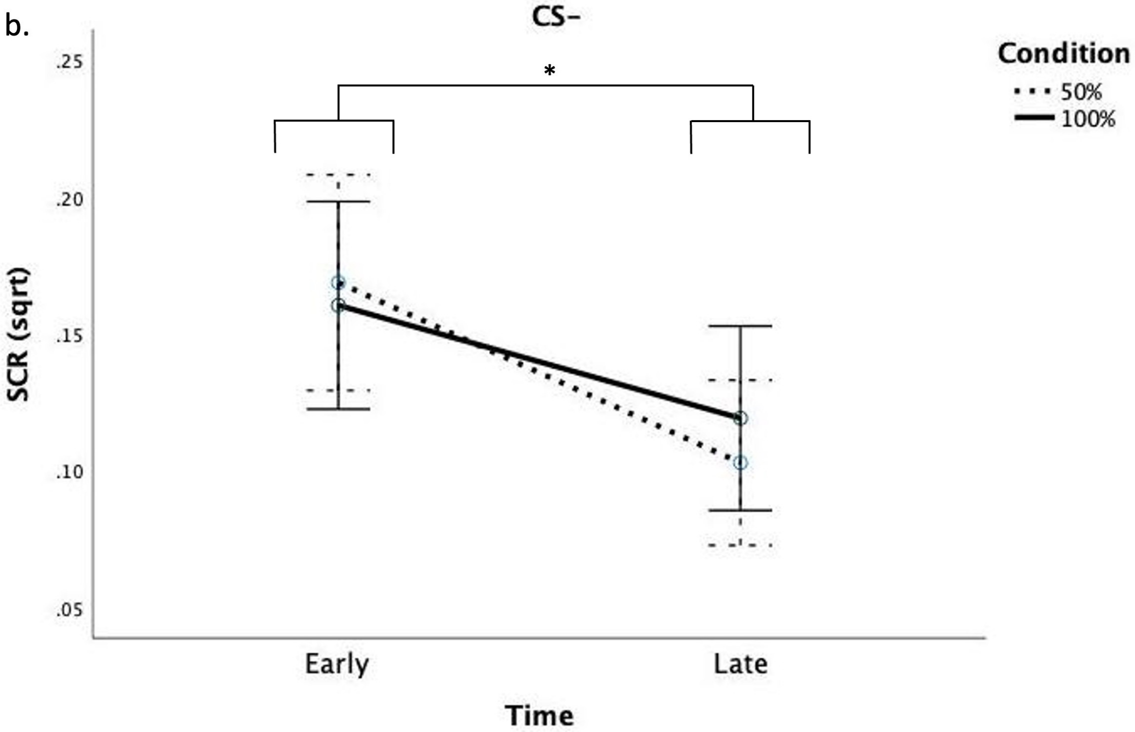

Figure 2b. There was a statistically significant interaction of time and condition for the CS- (middle), with a smaller decrease from early to late trials in the 100% vs 50% condition.

*p < .05

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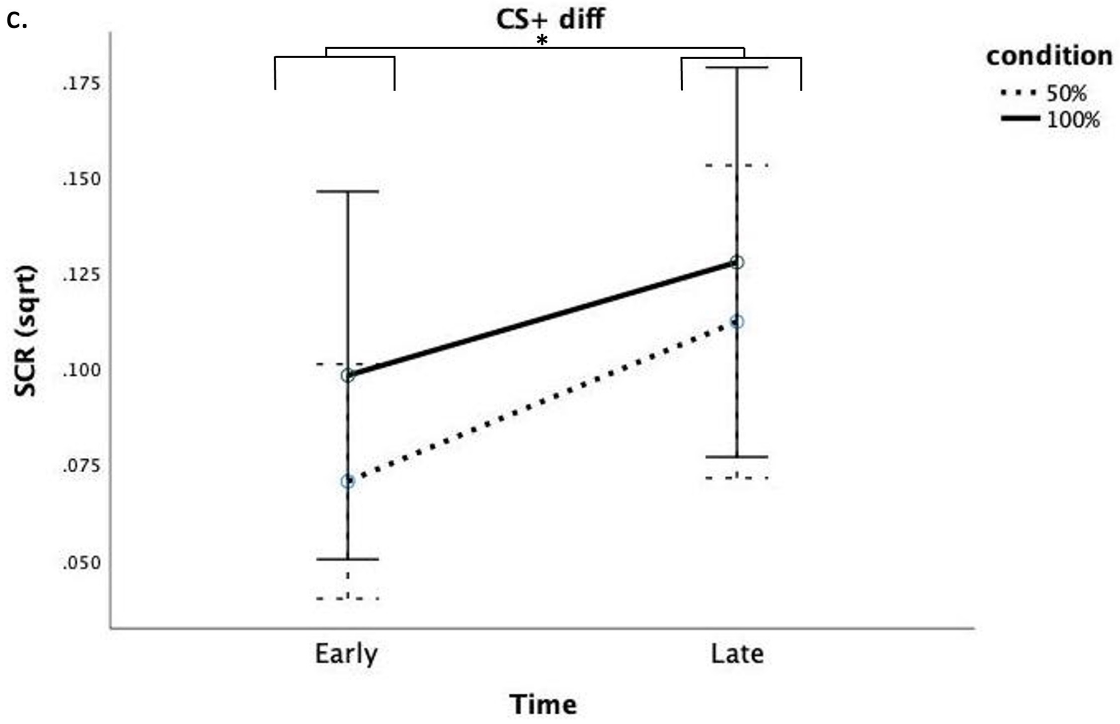

Figure 2c. There was a significant interaction of time and condition for the CS+ diff (bottom), with greater threat/safety discrimination in the 100% vs 50% condition during early vs late trials.

*p < .05

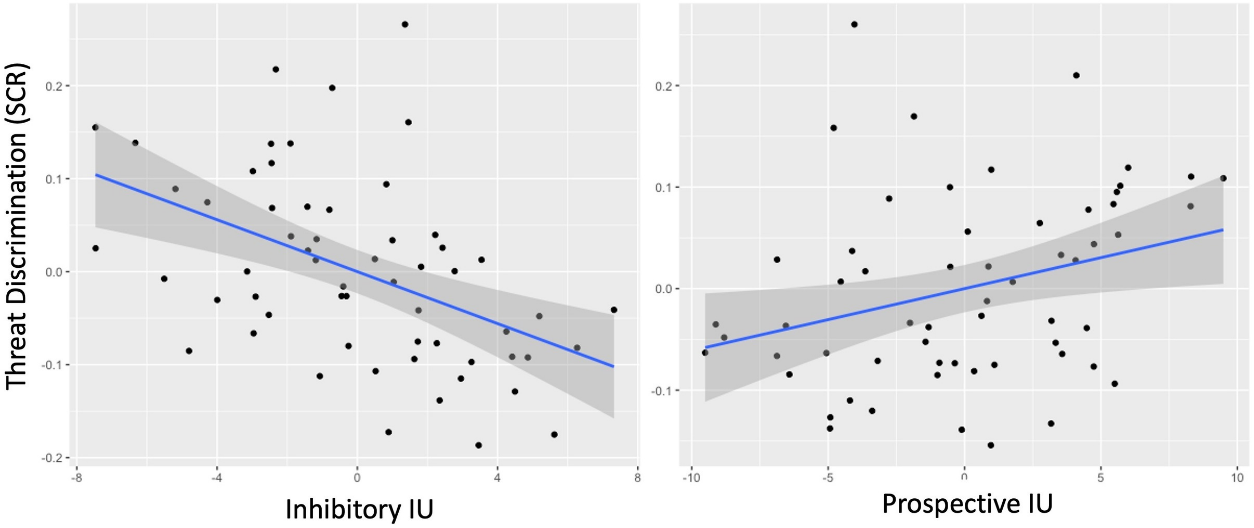

Figure 3. There was a negative correlation between threat discrimination and Inhibitory IU (β< = -.68, t = -3.94, *p* < .001) and a positive correlation between threat discrimination and Prospective IU (β = .35, t = 2.36, *p* = .02). To match the statistical results from the hierarchical regression, scatter plots were created by using the unstandardized residuals after covariates from the regression model were regressed out (covariates for each plot were task order, trait anxiety and the two subscales of IU).

effect of task order in the second block analysis (β = .30, t = 2.4, *p* = .02), such that SCR for the CS- was higher when the continuous reinforcement block occurred first vs second. For the third block analysis of inhibitory and prospective IU, the data show the model was not statistically significant (f(4, 54) = 2.35 , ΔR^2 = .02, *p* = .07). Overall, these analyses provide preliminary evidence of specific associations between the inhibitory and prospective subscales of

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IU and threat discrimination learning that were not driven by responses to the threat and/or safety stimuli alone.

IV. Discussion

The ability to discriminate between threat and safety is crucial to adaptive functioning, but the extent to which this process is modulated by the level of uncertainty associated with a threat cue, individual differences in sensitivity to uncertainty, and interactions between these two factors, has not been fully resolved. Furthermore, evidence suggests individual differences in sensitivity to uncertainty can be segmented into two distinct subscales characterized by information avoidance (inhibitory IU) vs. information seeking (prospective IU), suggesting the possibility of distinct effects of these two factors on threat learning.

Here, participants demonstrated typical threat discrimination between the CS+ and CS- for both reinforcement schedules (for review see, Lonsdorf et al., 2017). Furthermore, participants showed heightened threat reactivity for both the CS+ and CS- in the full vs partial threat reinforcement condition, consistent with previous research showing the same (Chin et al., 2016). Additionally, participants showed less habituation from early to late trials for the CS-, but not the CS+, in the full vs partial reinforcement condition. This suggests that reactivity to all stimuli, including safety cues, can be potentiated in sustained fashion in environments in which continuous threat reinforcement is occurring. The data here did not provide evidence of overall enhanced threat discrimination at higher threat reinforcement rates, in contrast to previous findings (Dunsmoor et al., 2007; Grady et al., 2016). However, in previous studies, reinforcement rate and learning experience (the number of CS-US pairings) covaried, which may have played some role in previous results. Number of learning trials was matched across conditions in the present study, and participants' showed evidence of better threat discrimination for the more certain (100%) vs less certain (50%) CS+ cue during early but not late acquisition, suggesting that while threat/safety discrimination learning was not enhanced in the continuous reinforcement condition, it did occur more quickly.

Surprisingly, in the present study, despite the use of a more complex threat acquisition experiment (e.g., three CS's, two different reinforcement rates), no significant effects of the IU total score were found for skin conductance response. The literature on the impact of the IU total score on threat learning processes is decidedly mixed. The majority of past studies using standard threat acquisition paradigms (1 CS+, 1 CS-; singular reinforcement rate of 50 or 100%) have found no significant effects of the IU total score on psychophysiological or self-report measures (for review see Morriss, Zuj, et al., 2021). However, several recent positive findings using more complex threat acquisition paradigms (e.g. multiple CSs; inclusion of startle probes) have observed significant effects of the IU total score on skin conductance response (Bauer et al., 2020; Kanen et al., 2021; Morriss, Macdonald, et al., 2016), startle potentiation (Chin et al., 2016; Sjouwerman et al., 2020), and/or fear ratings (Klingelhöfer-Jens et al., 2022; Mertens et al., 2022).

Interestingly, an exploratory analysis revealed significant effects of the IU subscales on skin conductance response in this study. In particular, higher inhibitory IU was associated with diminished threat discrimination learning, while prospective IU was associated with enhanced threat discrimination learning. Moreover, these effects held when controlling for trait anxiety. Unfortunately, it is difficult to compare the IU subscale-based effects during threat learning from this study to others from the threat conditioning literature due to the scarcity of data. However, there is some supporting evidence for a similar pattern of results in Bauer et al's (2020) multi-lab study. Bauer et al. (2020) reported in their supplementary materials that: (1) higher inhibitory IU was associated with reduced threat discrimination between CS+ and other generalisation stimuli via skin conductance responses (1 out of 3 replication studies), and (2) higher prospective IU was associated with greater threat discrimination between the CS+ and other generalisation stimuli via skin conductance response and an event-related potential known as the late positive potential (1 out of 3 replication studies). Outside the threat conditioning literature, the IU subcale effects reported here are in line with several studies from the threat of shock literature, which have found inhibitory IU to attenuate and prospective IU to enhance startle responses and relevant event-related potentials to instructed unpredictable threat (Correa et al., 2022; Nelson et al., 2016; Nelson & Shankman, 2011). In sum, the IU subscale-based effects reported here follow on from prior research suggesting that the two IU subscales may be related to different cognitive and behavioural tendencies (Birrell et al., 2011; Hong & Lee, 2015).

At the moment it is unclear as to why in this study, effects were found for the IU subscales, rather than the IU total score. Speculatively, it may be explained by sample variation in the IU questionnaire. For instance, it is possible that there was more variation between the IU subscales in this study, compared to previous studies. To elucidate and confirm IU subscale-based effects during threat learning, the field would benefit from a meta-analysis of existing data sets (e.g. Morriss, Wake, et al., 2021) and/or systematic international multi-lab studies in diverse populations (Gatzke-Kopp, 2016; Henrich et al., 2010).

One limitation of the present study is that we only report a single outcome measure, SCR. There are multiple outcome measures available for use in threat learning research beyond SCR, including self-report, fear potentiated startle and BOLD fMRI, all of which are likely to tap slightly different underlying processes (Lonsdorf et al., 2017). Research using single output measures is problematic to the extent that findings are heterogenous and synthesizing across the literature can be difficult. In this study, we did collect self-reported US expectancy and evaluative ratings, in addition to SCR, but, as described, a portion of that data was lost. However, there is minimal evidence of a relationship between IU and subjective experience of expectancy (e.g. US expectancy, CS evaluative responses) in the threat learning literature (for review see Morriss, Zuj, et al., 2021). Future research exploring response coherence across systems, and factors that mediate it, will be necessary in order to ef-

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fectively synthesize the fast-growing literature on threat learning and regulation. Another limitation of this study is the relatively small sample size compared to that recommended to achieve a stable estimate for a correlation coefficient (e.g., between. n = 150 and 250 in a typical study; see Schönbrodt & Perugini, 2013). Future attempts to replicate this finding should use larger samples.

Controlling for the number of CS-US pairings across conditions in this study necessarily meant that we would have twice as many presentations for the CS+$_{50}$ vs the CS+$_{100}$. This could be considered a limitation to the extent that more habituation could have occurred for the partially-reinforced, more frequently presented CS+, potentially leading to attenuated physiological responses that result in diminished measures of threat discrimination learning for that stimulus compared to the fully reinforced, less frequently presented one. Alternatively, it's possible that a response bias is introduced when unequal numbers of USs and CS-US pairings are used, as in previous studies (Chin et al., 2016; Dunsmoor et al., 2007; Grady et al., 2016). On that basis, the novel methodological approach taken here could be considered warranted, despite the risk of differential habituation across conditions.

In conclusion, this study showed that the presence of certain threat was associated with heightened threat reactivity for both danger and safety stimuli. Additionally, an exploratory analysis showed threat discrimination occurred more slowly for more uncertain threat cues. Individual differences in Intolerance of Uncertainty, a dispositional measure of the tendency to find uncertainty aversive, did not predict threat discrimination learning performance. However, using a two-factor model of IU, this study provided tentative evidence of different relationships between the IU subscales and threat discrimination learning. Specifically, higher inhibitory vs prospective IU scores were associated with diminished and enhanced threat discrimination, respectively. While this result warrants replication, it provides further supporting evidence that the two subscales of IU may be associated with different cognitive and behavioral tendencies in the face of uncertainty. Overall, these findings demonstrate how the acquisition of threat and safety memories can be shaped by both the uncertainty inherent to a stimulus and differences in sensitivity to uncertainty on the level of the individual. Continued research exploring the relationship between threat learning processes and dispositional measures such as the two-factor IU is important and could contribute to the development of novel or optimized symptom- and individual-level diagnostic and treatment approaches for threat-related disorders.

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Author Contributions

DCJ developed and designed the experiment. VH, BU and STQ collected and scored the data. DCJ and JM analyzed the data. DCJ and JM wrote the manuscript. All authors approved the final submitted version of the manuscript.

Competing Interests

The authors declared that they had no conflicts of interest with respect to their authorship or the publication of this article.

Data Accessibility Statement

All the participant data can be found on the project page at OSF: https://osf.io/yvaqw

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