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Published in:
International Journal of Psychophysiology

DOI:
10.1016/j.ijpsycho.2022.04.011

Publication date:
2022

Document Version
Publisher's PDF, also known as Version of record

International Journal of Psychophysiology 177 (2022) 67–75

Contents lists available at ScienceDirect

International Journal of Psychophysiology

journal homepage: www.elsevier.com/locate/ijpsycho

The relationship between Intolerance of Uncertainty and conditioned fear acquisition: Evidence from a large sample

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ARTICLE INFO

Keywords:
Fear conditioning
Intolerance of Uncertainty
Psychophysiology
Individual differences

ABSTRACT

Despite being considered a valid model for the etiology of anxiety disorders, the fear conditioning paradigm does not always show clear correlations with anxious personality traits that constitute risk factors for the development of anxiety disorders. This may in part due to error variance and the fact that fear conditioning studies are typically underpowered to investigate inter-individual differences. In the current study, we focus on the relationship between conditioned fear acquisition and Intolerance of Uncertainty (IU). In a re-analysis of a large previous study (N = 120), which was conducted using a healthy student sample and a partial reinforcement procedure (75%) with words as Conditioned Stimuli (CSs), the relationship between IU and several outcome measures (i.e., fear ratings, expectancy ratings, skin conductance responses, and startle responses) during fear acquisition was examined. We find that IU is positively related to fear ratings towards the CS+ ($r = 0.29$), even when controlling for the shared variance with trait anxiety. Furthermore, we find a subtle relationship between IU and startle responses to the CS− ($r = -0.23$), though this correlation did not survive correction for the shared variance with trait anxiety. Taken together, we replicate some of the correlations previously reported in the literature. However, we recommend that future studies employ even larger samples and more advanced statistical techniques such as structural equation modelling to investigate the correlations between fear acquisition indices and anxious traits in a fine-grained manner.

1. Introduction

Fear- and anxiety-based disorders are the most common class of mental disorders (Baxter et al., 2013; Carpenter et al., 2019). They are associated with great economic costs and have a debilitating effect on patients' lives (Kessler et al., 2005; Craske et al., 2009). Yet, despite the high prevalence and severity of these psychiatric complaints, many patients' symptoms are left unrecognized or are inadequately treated (Craske et al., 2009). Insights gained from the Pavlovian conditioning model of fear are of great value to improve the recognition, treatment and relapse of anxiety and related disorders (Carpenter et al., 2019; Morriss et al., 2021).

The principle behind fear conditioning is to examine one's ability to discriminate between (conditioned) threat and safety cues, an ability that improves the organism's survival chances (Lonsdorf et al., 2017). In the Pavlovian fear conditioning paradigm, the contingent presentation of an initial neutral stimulus (conditioned stimulus or CS) and an aversive cue (unconditioned stimulus or US; e.g., an electric shock or annoying sound) trigger an associative learning process (Tzovara et al., 2018). Because of the repeated CS-US pairings, the neutral stimuli becomes conditioned and evokes a learned fear response (conditioned response or CR). The acquired fear can manifest in various ways, such as through physiological responses (e.g., skin conductance responses or SCRs and fear potentiated startle or FPS), behavioral responses (e.g., avoidance responses to prevent or escape from a threatening stimulus), and/or emotional reactions (e.g., subjective ratings of increased fear or distress; Waters et al., 2009). The degree of fear acquisition depends on several factors, such as how many repetitions have been shown of the paired stimuli (CS-US), the reinforcement rate (i.e., the amount of the presentation of the CS+ that are paired with the US), the type of instructions given (Mertens et al., 2021b), and the evolutionary relevance of the CSs (Reiss, 1980; Öhman and Mineka, 2001). Given its status as a model of fear acquisition, it is relevant to examine which inter-individual differences modulate Pavlovian fear conditioning, as they

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https://doi.org/10.1016/j.ijpsycho.2022.04.011
Received 31 December 2021; Received in revised form 23 March 2022; Accepted 26 April 2022
Available online 30 April 2022

may potentially constitute risk factors for the development of pathological fear.

Several personality factors have been argued to modulate fear learning processes (Lonsdorf and Merz, 2017), of one specifically being the unwillingness to tolerate uncertainty. Indeed, a plethora of evidence suggests that Intolerance of Uncertainty (IU) reflects a transdiagnostic feature in anxiety and stress-related disorders (Wright et al., 2016; Holaway et al., 2006; Peters et al., 2017; Carleton et al., 2012). IU is considered a dispositional trait, that entails an excessive resistance to accept the possibility that a negative event may take place in the near future, regardless of how slim that chance is (Buhr and Dugas, 2002; Holaway et al., 2006). Thus, individuals who have a high intolerance of uncertainty find uncertain situations upsetting and distressing (Buhr and Dugas, 2009;) and therefore may consider many events in life intolerable given that ambiguity is ever-present (Buhr and Dugas, 2002). Given this central role of IU in many different anxiety disorders, it is expected that this trait would also modulate Pavlovian fear conditioning.

To date, research on the link between variations in IU and threat responding is still quite limited and, among the few studies conducted, the evidence seemingly suggests IU is related to impaired fear responding only under contexts with greater uncertainty (Lonsdorf and Merz, 2017; Morriss et al., 2021). For instance, studies that have used a 100% reinforcement rate (i.e., the CS is paired with the US on every trial), have shown that IU does not affect psychophysiological responding to either the threat or safety cues (i.e., both the CS+ and CS−; Morriss et al., 2016a). Indeed, it is only when partial reinforcement rates were used (i.e., reinforcement rates in which the US is not paired with the CS on every trial) that more clear associations were found between IU and the acquisition of fear. For instance, Chin et al. (2016) found that IU was related to differential FPS with a study design using a 50% reinforcement rate but this correlation disappeared when a 75% reinforcement rate was applied. Moreover, Morriss et al. (2016b) used a 50% reinforcement rate and their acquisition phase included both CSs and generalization stimuli (i.e., stimuli that resemble the CSs). They found that high IU relative to low IU was related to larger SCR magnitude to safety cues (Morriss et al., 2016b). Thus, it appears that less uncertainty within the experimental design blocks the manifestation of interindividual variability in fear learning (Arnaudova et al., 2013; Lissek et al., 2006), whereas increased uncertainty helps to find these individual differences (Lonsdorf and Merz, 2017). However, it should be mentioned that not all studies using a low reinforcement rate could replicate these findings (Morriss et al., 2020; Wake et al., 2020; Wake et al., 2021). Particularly, Dunsmoor et al. (2015) used a 33% reinforcement rate but did not find a correlation between IU scores and SCR to the CS+. Similarly, Arnaudova et al. (2013) were not able to report a correlation between IUS and differential US-expectancy ratings.

Another experimental feature that may influence the uncertainty in the experimental design is the inclusion of (unpredictable) startle probes. For instance, Sjouwerman et al. (2016) have argued that startle probe presentations attenuate CS+/CS− discrimination during fear acquisition. The inclusion of startle probes likely increases uncertainty in the experimental design, allowing for the emergence of individual differences (Sjouwerman et al., 2016). However, in a study by Mertens and Morriss (2021) which used a 75% reinforcement rate and included startle probes, no relationship between IU scores and SCR or FPS was found. Therefore, the available evidence regarding the relationship between IU and fear acquisition in Pavlovian fear conditioning remains inconclusive (Lonsdorf and Merz, 2017; Morriss et al., 2021).

These inconsistent findings are potentially in part caused by sampling variability, as all the reported studies used a relatively limited number of observations (Biau et al., 2008). Indeed, in all of the aforementioned studies, the sample sizes consisted of no more than 69 participants. One exception is the recent study performed by Sjouwerman et al. (2020). With a sample size of 356 participants, these authors found a significant negative correlation between IU and CS+/CS− discrimination for both SCR and FPS (using uncorrected univariate analyses), while no association was found for differential fear ratings. However, the correlations with IU disappeared after correction for multiple testing. Nonetheless, one limitation of this study was that these authors used a 100% reinforcement schedule in their study, for which it could be argued that this rate may attenuate the link between individual differences in IU and fear acquisition (Lissek et al., 2006).

Aside from the study by Sjouwerman et al. (2020), these small sample sizes (i.e., largest N = 69) only provide excellent statistical power (i.e., 0.90) to detect correlation coefficients of 0.36 or larger (Faul et al., 2007). Another major limitation of small sample sizes is the increased risk of false-positive results (Hackshaw, 2008). Small studies have the tendency to overestimate the magnitude of an association (Hackshaw, 2008), whereas larger samples provide more accurate estimates of the true association and may even indicate the absence of an association. Therefore, it is important to interpret the available results carefully as they may not yield reliable nor precise estimates of the true underlying effect (Hackshaw, 2008). For this reason, sufficiently powered studies are important to investigate whether there is an actual association between IU and fear acquisition, particularly under conditions of increased uncertainty (i.e., when using partial reinforcement; Morriss et al., 2021).

In the present report, we aim to contribute to the research on the link between IU and fear acquisition, making use of the data collected by Mertens et al. (2021a). Here, a relatively large study was conducted (N = 120), in which participants acquired a conditioned fear response towards a word during the acquisition phase (i.e., *mini* or *enormous*) using a partial reinforcement scheme (i.e., 75%). In this study, the focus was on fear generalization towards conceptually related words (i.e., *small*, *medium*, and *large*; Mertens et al., 2021a) during a fear generalization phase. However, the data generated in this study also allows us to investigate the hypothesis of whether an association exists between IU and fear acquisition. Given that the majority of the existing evidence points in the direction of a positive association, we hypothesized to find a positive link between IU and fear acquisition. That is, individuals with high self-reported IU were expected to show a stronger fear response towards the CS+ relative to the CS−, whereas the reverse is assumed for low IU. The use of a large sample allows for greater statistical power to detect smaller effect sizes (i.e., up to a correlation of 0.30 with a statistical power of 0.90; see Section 2.1). Hence, the current study allows us to find more reliable results to help solve the unclarity regarding the relationship between IU and fear acquisition in classical conditioning that is currently present in literature.

2. Method

The methods of this study have been described in detail in the article by Mertens et al. (2021). Therefore, we only provide a briefer overview of the main methodological details of the study. For a more elaborate description of the methodology applied, we direct readers to the original article (Mertens et al., 2021a, b). The materials, raw datafiles, working datafiles, and supplementary materials can be obtained through the Open Science Framework (OSF): https://osf.io/k36ba/.

2.1. Participants

The required sample size was calculated on the basis of an a priori power calculation using G*Power (Faul et al., 2007). A final sample of 120 subjects (37 men and 83 women) completed the study and met all the data quality and inclusion criteria (in order to detect correlation of $r = 0.30$ with a power of 90% and an adjusted alpha-level of 0.017, see Section 3.2). The data of 11 additional participants was excluded based on the preregistered data quality checks of the original study (see Section 3.1.1). All participants ranged in age between 18 and 35 years ($M_{age} = 22.63$, $SD_{age} = 2.76$), were native Dutch speakers, and did not suffer from a neurological nor a psychiatric disorder. They had normal or corrected-to-normal hearing and vision, and reported to use no

medication that could affect either their attention, reaction time and/or memory (Mertens et al., 2021a). Participants received an incentive in return for their participation either in monetary form (i.e., 8 euro for an hour) or they received a course credit.

2.2. Materials

2.2.1. Stimuli

Five words were used as the conditioned stimuli (i.e., CS− and CS+) and generalization stimuli (GSs). All words were related to size. The outer extremes (i.e., *enorm* and *mini*) served as the conditioned stimuli. Either one or the other was used as the CS+ via counterbalancing both stimuli across participants. The stimuli were shown in the middle of the screen, using the font 'Arial' in size 36. Participants were presented these words on a 21 in. computer screen (HP EliteDisplay E231) with a resolution of 1920 × 1080 pixels.

The US was a 500 ms electric shock (i.e., 9 pulses of 2 ms with an inter-pulse interval of 60 ms) that was sent to the wrist of the dominant hand, with the use of a Digitimer DS7A device (see https://digitimer.com). When setting up the equipment, participants could indicate the level of shock that would be used during the experiment so that it is not painful to them, yet very unpleasant (Mertens and De Houwer, 2016).

2.2.2. Outcome measures

2.2.2.1. Anxious traits assessment. Three psychological constructs were measured using self-report questionnaires, of which (i) the State-Trait Anxiety Inventory, trait version (STAI-T; Spielberger et al., 1983; Dutch version: van der Ploeg et al., 2000), (ii) the behavioral inhibition subscale of the BIS/BAS Scales questionnaire (Carver and White, 1994; Dutch version: Franken et al., 2005) and (iii) the Intolerance of Uncertainty Scale (IUS; Freeston et al., 1994; Dutch version: de Bruin et al., 2006) were included to measure trait anxiety, behavioral inhibition and intolerance of uncertainty respectively. Within the current manuscript, we only focus on IUS and STAI-T. Given that trait anxiety may confound the relationship between IUS and fear acquisition, we controlled for the shared variance with this variable, as is common in the literature (Morriss et al., 2021). Therefore, we briefly describe the characteristics of these two scales.

The STAI measures two types of anxiety — state anxiety which is a transient form of anxiety (STAI-S; 20 items) and trait anxiety, a stable personality trait (STAI-T; 20 items). In this report, we only focus on the STAI-T scores (further referred as simply "STAI"). Respondents gave their answers on a 4-point Likert scale going from 1 ("Not at all/Almost never") to 4 ("Very much so/Almost always"). The internal consistency of the STAI-T was 0.87 in the current sample.

The IUS entails 27 items that assess the emotional, cognitive, and behavioral reactions to ambiguous events, implications of being uncertain and attempts to control the future (Buhr and Dugas, 2002; Freeston et al., 1994). Participants gave their answer on a 5-point Likert scale ranging from 1 ("Not at all characteristic of me") to 5 ("Entirely characteristic of me"). The higher the score one achieves on this scale, the less tolerant to uncertainty. The internal consistency of the IUS was 0.86 in the current sample. Variably, this scale is scored using two subscales: prospective IU and inhibitory IU (McEvoy and Mahoney, 2011). For exploratory purposes, we have also used these two subscales in our analyses. The results did not differ substantially from the analyses using the complete scale (see the supplementary materials).

2.2.2.2. Physiological assessment. Two physiological indications of fear were measured, including skin conductance response (SCRs) and fear potentiated startle. The SCRs were assessed with the use of two BioSemi GSR electrodes (BioSemi, Amsterdam, the Netherlands) that were attached to the palm of the non-dominant hand. Assessment of the fear potentiated startle was done using four BioSemi FLAT active electrodes, of which two were attached under the left eye (i.e., specifically targeting the orbicularis oculi muscle) and two on the forehead, therefore serving as ground electrodes. To elicit the startle reflex, a 50 ms white noise probe (95 dB) was presented.

2.2.2.3. Fear ratings. Participants were asked how anxious they felt when they were presented with the CSs and the GSs after each phase (i.e., after the acquisition phase and the generalization phase). They were instructed to indicate their answer on a scale from 1 ("not anxious") to 100 ("very anxious").

2.2.2.4. US expectancy ratings. The extent to which participants expect the US being delivered (i.e., shock expectancy) was assessed using a 9-point Likert scale going from 1 ("Definitely no shock") to 9 ("Definitely a shock"). This Likert scale was presented at the bottom of the screen upon presentation of the words, during all three phases. Participants indicated their expectation via a mouse click on one of the respective numbers shown in the scale. The first response is the one that was recorded.

2.3. Design and procedure

This study consists of a within-subjects design, however, there was one between-subjects factor applied, namely that of counterbalancing (i.e., allocation of words *mini* vs. *enorm*). The generalization paradigm consists of three phases in the following respective order: (i) a practice phase, (ii) an acquisition phase and (iii) a generalization phase. In all three phases, participants were presented words that each refer to a different size (Mertens et al., 2021a), two of which constituted the conditioned threatening stimulus and a safe stimulus (i.e., CS+ and CS−). During the acquisition phase, the CS+ was paired with the US according to a partial reinforcement scheme (i.e., 75%). During the generalization phase, participants were also exposed to so-called generalization stimuli that had a semantic relationship with the CS+ and CS− (i.e., words relating to different sizes). The paradigm used was inspired by the generalization paradigm using perceptual stimuli by Lissek et al. (2008). Table 1 provides a schematic overview of the study design.

The computer task was generated and presented using Inquisit software (v4). Subjects were welcomed into a dimmed and soundproof room and were seated away from the computer screen at a distance of approximately 60 cm. While being seated there, shock electrodes were attached and participants were asked to indicate how far they can tolerate the pain, to set up the suitable threshold (see Mertens and De Houwer, 2016; Mertens, Bouwman, & Engelhard, 2021). Following this, ground electrodes and the electrodes for physiological measurement were applied (SCRs and startle responses). Participants were put on headphones and were asked to fill in the questionnaires inquiring about their personality. Next, participants received instructions regarding the

Table 1
Schematic overview of the procedure of the study. The numbers refer to the number of trials within the phase.

Practice phase	Acquisition phase	Generalization phase
3 arbitrary words (0% RR)	8 CS+ ("mini" or "enormous"; 75% RR) 8 CS− ("mini" or "enormous"; 0% RR)	8 CS+ ("mini" or "enormous"; 50% RR) 8 CS− ("mini" or "enormous"; 0% RR) 8 GS1 ("tiny" or "large"; 0% RR) 8 GS2 ("medium"; 0% RR) 8 GS3 ("tiny" or "large"; 0% RR)

Note: CS+ = condition stimulus paired with the unconditioned stimulus (i.e., electric shock); CS− = safe stimulus; GS = generalization stimulus; RR = reinforcement rate.

task, explaining them that they would see words appearing on the screen and that these will sometimes be followed by an electrical shock. Participants were informed that they have to predict the probability of the US appearing by indicating a number on the Likert scale. After being given the instructions, participants started the experiment with a practice phase of three trials to get them acquainted with the task. Here, three arbitrary words (i.e., table, lamp, and chair) were shown and not followed by a US. After completion of the practice phase, participants were confronted with nine startle probes with an inter probe interval of either 19, 21, or 23 s, to let participants habituate to the startle probe. Hereafter, participants started the second phase, that is the phase of fear acquisition. The CSs were shown for a duration of 8 s, and participants were asked to make predictions about the US. Seven seconds after the CS was presented, a startle probe was introduced. US was delivered at CS+ offset in six out of eight trials (equal to a reinforcement rate of 75%). The CS− was never followed by the US. During the inter-trial-interval (ITI), startle probes were presented when no words were shown. After finishing the second phase, subjects were inquired about their feelings of fear when the CS− and CS+ was presented. Response options ranged from 1 ("Not anxious") to 100 ("Very anxious"). When respondents' answers were recorded, a break of 10 min was introduced. After this, the generalization phase started. During this phase, all stimuli (i.e., both CSs and all GSs) were presented for a duration of 8 s each, and after 7 s, a startle probe was introduced. Unlike the acquisition phase, only four out of eight CS+ trials were reinforced (i.e., 50% reinforcement rate; Lissek et al., 2008).

After completion of all three phases, the following questions were asked to see whether participants understood the task and whether manipulation was successful. First, respondents were asked to list all used words in increasing order. After this, two retrospective questions were asked to check whether participants picked up on the CS-US contingency: (i) participants were first asked which word was followed by an electric shock, (ii) how certain they were about their answer (1 = completely certain, 2 = fairly certain, 3 = fairly uncertain, 4 = completely uncertain). Finally, participants provided fear ratings for both CSs and all GSs with answering options ranging from 1 ("not anxious") to 100 ("very anxious"). At the end of the study, participants received a debriefing regarding the purpose of the study and their incentives were given.

3. Data analysis approach

3.1. Preprocessing steps

3.1.1. Data exclusions

Participants were excluded from the final analysis if they failed to meet three preregistered criteria (see Mertens, Bouwman, & Engelhard, 2021). First, respondents who did not learn the CS-US pairing, as assessed by the contingency questions, were excluded from the analysis (i.e., when they indicated the wrong word as the CS+ and/or when they were fairly uncertain or completely uncertain about the answer; n = 4 excluded). The reason for this exclusion criteria is that contemporary theories of fear conditioning propose that contingency awareness is a prerequisite for successful fear conditioning (Lovibond and Shanks, 2002; Mertens and Engelhard, 2020), and therefore participants who are unaware of the CS-US contingency are expected to show little or no relevant variance. Second, if participants list the words in any other order than the following: *mini*, *klein*, *medium*, *groot* and *enorm*, their data was not included in the analysis (n = 2 excluded). Third and final, when participants' psychophysiological data quality was not in line with the minimal quality standards required, their data was not considered in the analysis (n = 2 excluded). The quality of this data was first examined via means of visual inspection. For instance, flat lines or highly noisy data refer to a disconnection of electrodes (Mertens, Bouwman, & Engelhard, 2021). Additionally, data of participants were excluded when no SCRs were observed towards the US (i.e., threshold of 0.02 μS; see below) or when there were more than 50% unusable startle response datapoints (i.e., negative peak values or missing data points; Mertens, Bouwman, & Engelhard, 2021). In addition to these three preregistered data quality criteria, the data of three additional participants was excluded because they did not complete the whole experiment.

Note that participants were not removed from the final analysis based on their responses on the outcome fear measures, as this can potentially bias the results (Lonsdorf et al., 2017).

3.1.2. Skin conductance response

Electrodermal measurements were analyzed using BrainVision Analyzer software (Brain Products, Munich, Germany). The skin conductance signal was downsampled to 10 Hz (Mertens, Bouwman, & Engelhard, 2021). Responses were calculated by subtracting the mean SCRs 2 s prior to the CS onset from the highest value that is recorded during the complete 7 s CS-US interval (Pineles et al., 2009; Mertens, Bouwman, & Engelhard, 2021). A response threshold of 0.02 μS was used for the SCRs (Boucsein et al., 2012; Mertens and De Houwer, 2016), so that responses below this defined cut-off were replaced by 0. To account for inter-individual variance, participants' SCR scores were divided by its maximum response (Boucsein et al., 2012). The SCR amplitude measures were square-root transformed to correct for skewness and to normalize their distribution (Dawson et al., 2007).

3.1.3. Startle response

Fear potentiated startle was analyzed using BrainVision Analyzer. The electromyographic signal was filtered (28–500 Hz passband), rectified, and then smoothed using a low-pass filter with a 15.9 Hz cut-off frequency (Blumenthal et al., 2005). The response amplitude were calculated by subtracting the maximum startle response (within a range of 21–150 ms after stimulus onset) from the average startle response during baseline (−30 to 20 ms after stimulus onset). To avoid that unusually large blinks affect the data outcome, blink magnitudes were standardized using T-score transformation (a conversion of the z-score) (Blumenthal et al., 2005).

3.2. Statistical analysis

All subsequent data analysis was conducted using IBM SPSS statistics (version 28). First, zero-order correlational analysis was performed between the IUS and the four outcome measures of conditioned fear responding (i.e., fear ratings, US expectancy ratings, SCR and FPS) to assess the link between IU and fear acquisition. Then, to control for the influence of the STAI, a partial correlational analysis was performed between the IUS and the four respective outcome measures while taking into account trait anxiety. For each outcome measure, we examined the association with IUS by looking at average responses during the acquisition phase to the CS+ only, the CS− only, and the difference score (i.e., CS discrimination), which was calculated by subtracting the CS− response from the CS+ response. A multiple testing correction method was used to control for the fact that four different outcome measures were included. The Holm-Bonferroni sequential rejective method (Holm, 1979) was applied to avoid inflation of the overall type-I error rate of 0.05. The *p*-values of the tests were ordered from lowest to highest. Considering the Holm-Bonferroni is a step-down procedure, hypotheses are rejected one step at a time. We first compared the smallest *p*-value to a Holm-adjusted alpha i.e., the original alpha level that is divided by the number of tests being performed). The next smallest *p*-value is compared with a Holm-adjusted alpha for one fewer test than used in our previous correction (Holm, 1979). Once the *p*-value is larger than our adjusted significance level ($p_{(k)} > \alpha$), the comparison procedure is terminated and all remaining hypotheses are considered non-significant.

4. Results

Zero-order correlational analyses revealed a significant positive correlation between IUS and fear ratings in response to the learned threat cue (i.e., CS+; $r = 0.285$, $p = 0.002$), indicating that individuals with a higher adversity for uncertainty report greater fear ratings to the learned threat cue during fear acquisition. This positive association remained significant after correction for multiple comparisons (alpha cut-off = 0.0125). Associations between IUS and expectancy ratings were not statistically significant, $r = -0.006$, $p = 0.108$, for which the Holm-Bonferroni comparison procedure was terminated (alpha cut-off = 0.01). The remaining correlations between IUS and SCR ($r = 0.064$, $p = 0.484$) and IUS and FPS ($r = -0.104$, $p = 0.257$) were thus also considered to be non-significant.

Further, partial correlational analyses (i.e., controlling for STAI-T) revealed again a significant positive association between IUS and fear ratings to the CS+ ($r = 0.228$, $p = 0.013$), even when controlling for the shared variance with the STAI. However, the significance of this positive correlation disappeared after correction for multiple testing (alpha cut-off = 0.0125) and hence, the Holm-Bonferroni comparison procedure was terminated. The other associations remained non-significant (see Table 2).

When looking at the responding towards the safe cue (i.e., CS−), zero-order correlational analysis revealed a significant negative correlation between FPS and IUS ($r = -0.234$, $p = 0.010$), indicating that increased self-reported IU is related to a decreased startle response to the CS−. This negative association remained significant after correcting for multiple comparisons (alpha cut-off = 0.0125). The correlation between IU and fear ratings towards the CS− was non-significant, $r = 0.155$, $p = 0.090$, for which the Holm-Bonferroni comparison procedure was ended (alpha cut-off = 0.01). Other correlations involving SCR and FPS remained non-significant for the CS− responses (see Table 3). As for the partial correlational analyses, all associations between the four outcome measures and IUS were non-significant after controlling for the shared variance with the STAI (lowest p-value = 0.110; see Table 3).

Finally, regarding CS discrimination, zero-order correlational analysis revealed a significant positive correlation between differential fear ratings and IU ($r = 0.203$, $p = 0.026$). However, after the multiple testing correction, this positive correlation was non-significant (alpha cut-off = 0.0125). IUS did not correlate significantly with differential SCR ($r = 0.063$, $p = 0.494$), FPS ($r = 0.093$, $p = 0.314$) nor the US expectancy ratings ($r = -0.07$, $p = 0.108$). Partial correlational analyses controlling for the shared variance with the STAI returned no significant association between IUS and any of the outcome measures (lowest p-value = 0.071; see Table 4). Tables 2–4 depict the correlations between IU and the learned fear cue (i.e., CS+), safe cue (i.e., CS−), and the differential scores (i.e., the difference between the CS+ and CS− scores). The complete correlational matrices are reported in the Supplementary Materials (retrievable through the OSF page; see Section 2). Figs. 1–3 depict the correlations between IUS and all the four outcome measures for the CS+, CS− and CS+/CS− difference scores.

Table 2
Correlation coefficients and p-values reported for the relation between intolerance of uncertainty and the learned threat cue (CS+).

Outcome measures	IUS (Pearson correlation)	IUS and STAI (partial correlation)
Fear ratings		
Correlation	0.285	0.228
p-Value	0.002*	0.013
Expectancy ratings		
Correlation	−0.006	0.107
p-Value	0.945	0.246
SCR		
Correlation	0.064	0.154
p-Value	0.484	0.095
FPS		
Correlation	−0.104	−0.021
p-Value	0.257	0.821

Note: All p-values that remained significant after Holm-Bonferroni correction are indicated by an asterisk (*). IUS = Intolerance of Uncertainty Scale; STAI = State-Trait Anxiety Inventory — trait version; SCR = Skin Conductance Response; FPS = Fear Potentiated Startle.

Table 3
Correlation coefficients and p-values reported for the relation between intolerance of uncertainty and the safety cue (CS−).

Outcome measures	IUS (Pearson correlation)	IUS and STAI (partial correlation)
Fear ratings		
Correlation	0.155	0.114
p-Value	0.091	0.217
Expectancy ratings		
Correlation	0.097	0.023
p-Value	0.292	0.806
SCR		
Correlation	0.028	0.080
p-Value	0.764	0.390
FPS		
Correlation	−0.234	−0.147
p-Value	0.010*	0.110

Note: All p-values that remained significant after Holm-Bonferroni correction are indicated by an asterisk (*). IUS = Intolerance of Uncertainty Scale; STAI = State-Trait Anxiety Inventory – trait version; SCR = Skin Conductance Response; FPS = Fear Potentiated Startle.

5. Discussion

The primary objective of this study was to explore the relation between self-reported IU and conditioned fear acquisition as measured using fear ratings, US expectancy ratings, SCR and FPS. To this end, we used a pre-existing dataset generated by Mertens et al. (2021a, b), which

Table 4
Correlation coefficients and p-values reported for the relation between intolerance of uncertainty and the difference score (CS+/CS− discrimination).

Outcome measures	IUS (Pearson correlation)	IUS and STAI (partial correlation)
Fear ratings		
Correlation	0.203	0.166
p-Value	0.026	0.071
Expectancy ratings		
Correlation	−0.070	0.046
p-Value	0.450	0.617
SCR		
Correlation	0.063	0.130
p-Value	0.494	0.158
FPS		
Correlation	0.093	0.095
p-Value	0.314	0.304

Note: All p-values that remained significant after Holm-Bonferroni correction are indicated by an asterisk (*). IUS = Intolerance of Uncertainty Scale; STAI = State-Trait Anxiety Inventory – trait version; SCR = Skin Conductance Response; FPS = Fear Potentiated Startle.

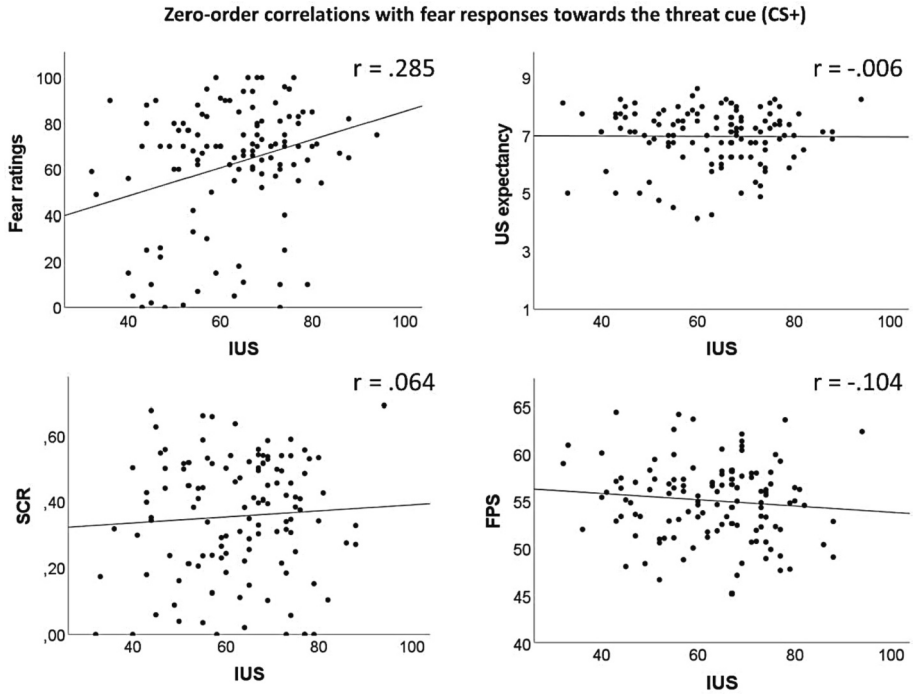

Fig. 1. Correlations between the Intolerance of Uncertainty Scale (IUS) and all four fear conditioning outcomes (fear ratings, US expectancy ratings, SCR, and FPS for the threat cue (CS+).

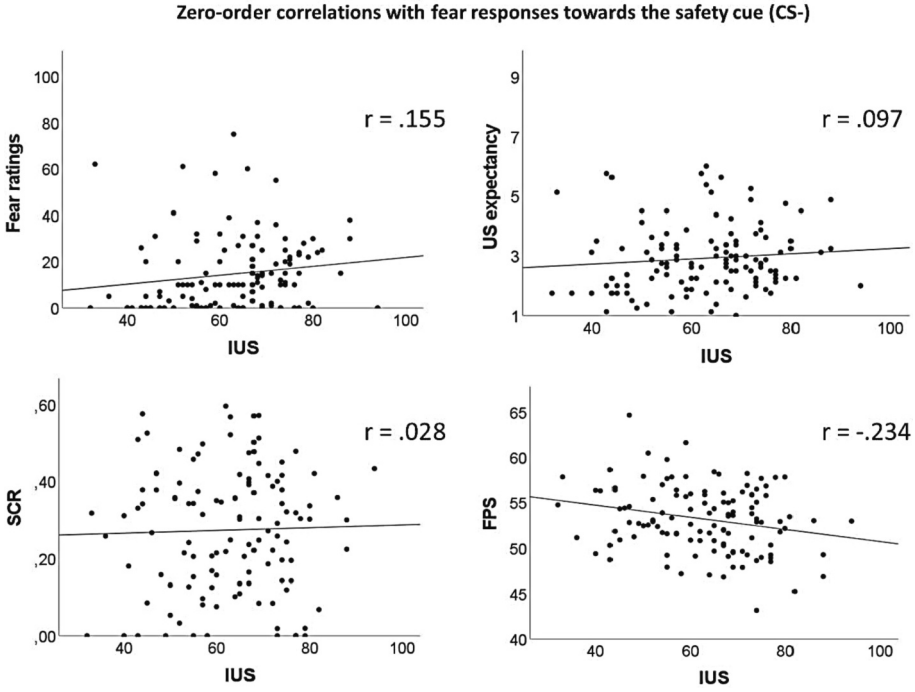

Fig. 2. Correlations between the Intolerance of Uncertainty Scale (IUS) and all four fear conditioning outcomes (fear ratings, US expectancy ratings, SCR, and FPS for the CS−.

we could use to examine whether IU relates to conditioned fear acquisition. By doing so, this evidence would add to and extend our current knowledge of the role of IU in Pavlovian fear acquisition. We predicted a positive association between differential fear acquisition and IU, which would indicate that individuals who score higher on IU show greater fear towards the learned threat versus safe cue (i.e., CS+ vs. CS−).

We found that IU was positively correlated with fear ratings to the learned threat cue (CS+). However, IU was not related with skin conductance, the startle response or the US expectancy ratings towards the CS+. In line with these findings, Klingelhöfer-Jens et al. (2021) similarly found that IU was associated with fear ratings to the threat cue (CS+), yet not with skin conductance nor FPS during the acquisition phase. Furthermore, this positive correlation found between fear ratings and IU corroborates some reports in the literature indicating that self-

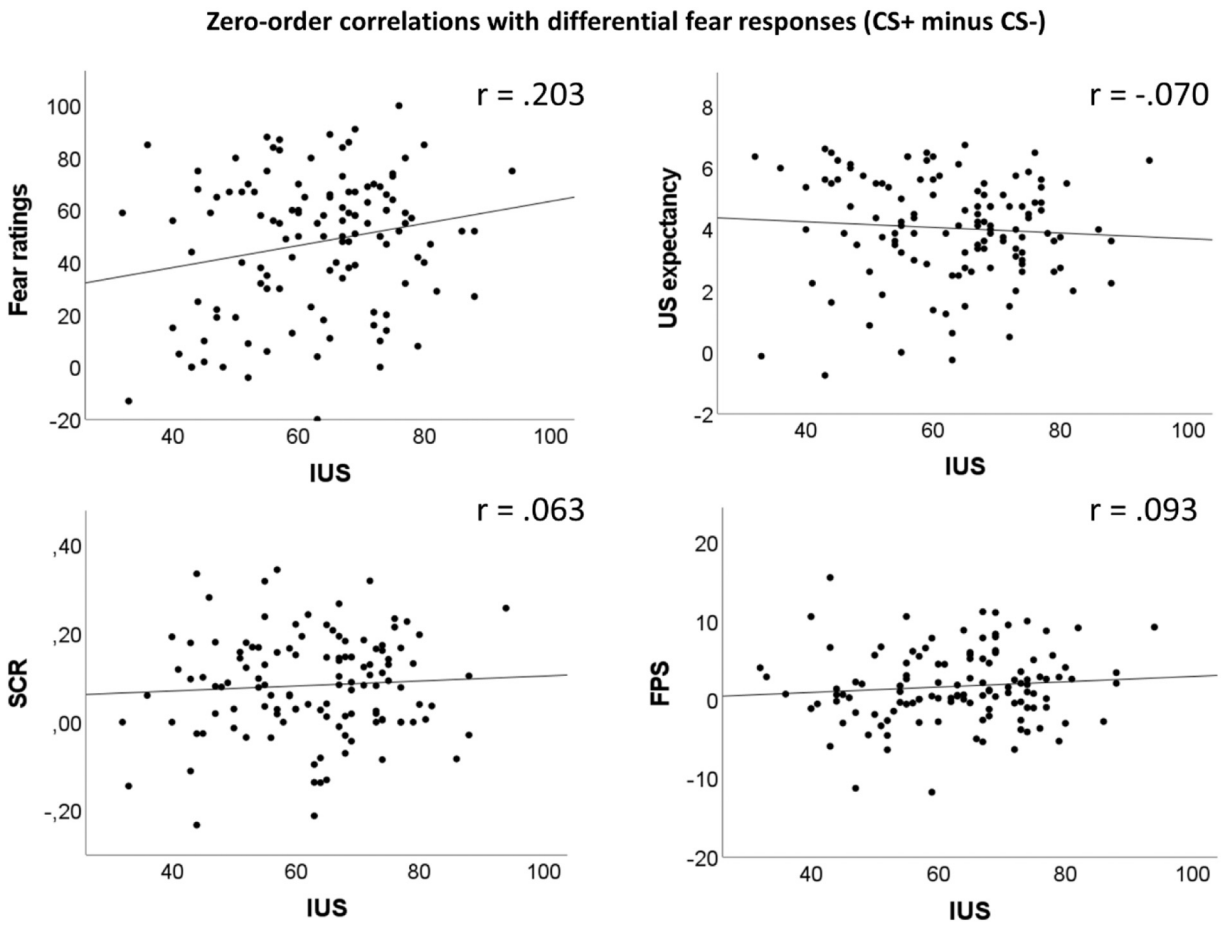

Fig. 3. Correlations between the Intolerance of Uncertainty Scale (IUS) and all four fear conditioning outcomes (fear ratings, US expectancy ratings, SCR, and FPS for the CS+/CS− difference scores.

report ratings are sometimes more reliably correlated to anxious personality traits than physiological measurements (Sep et al., 2019; Mertens et al., 2019; Sjouwerman et al., 2017; Morriss et al., 2021a, b). These findings invite further research to examine this relation of IU and subjective fear ratings to the CS+ more extensively during fear conditioning procedures (Klingelhöfer-Jens et al., 2021).

Additionally, we found a significant negative correlation between IU and FPS towards the learned safety cue (CS−). This was somewhat surprising, given that a previous meta-analysis found that patients with an anxiety disorder tend to show *higher* fear responses towards the CS− compared to healthy controls (Duits et al., 2015). Furthermore, Sjouwerman et al. (2020) reported a positive correlation between IU and startle responses to the CS− under a 100% reinforcement schedule. Hence, the observed negative correlation between IU and FPS towards the CS− does not seem to align up with the literature. However, it can be noted that both the negative correlation observed here ($r = -0.234$) and the positive correlation previously reported by Sjouwerman et al. (2020; $r = 0.168$) were quite small. Therefore, these small correlations may reflect sampling variability.

Furthermore, when accounting for the shared variance with trait anxiety, IU was not significantly correlated with either SCR or FPS. This was also surprising, given that several studies have found a relation between IU and skin conductance with differing reinforcement rates (e.g., Sjouwerman et al., 2017; Bauer et al., 2020; Morriss et al., 2016b), though other studies did not report such a relation (see Morriss et al., 2021; Klingelhöfer-Jens et al., 2021). The same applies for the started response, for which the relationship with IU remains inconclusive because of mixed findings. Particularly, whereas one study found a positive correlation between IU and differential startle responding during fear acquisition only during a 50% but not a 75% reinforcement schedule (Chin et al., 2016), another study found a subtle negative correlation between IU and differential startle responding when using a continuous reinforcement (Sjouwerman et al., 2020). Furthermore, Mertens and Morriss (2021) could not find a correlation between startle responses and IU at all using a 75% reinforcement schedule, whereas Klingelhöfer-Jens et al. (2021) could not find a relationship when using a 100% reinforcement schedule. Taken together, the evidence with regard to the relationship between psychophysiological responses and IU is mostly mixed and inconclusive at present.

The lack of clear evidence for a significant relation between IU and physiological measures during acquisition training can possibly be accounted for by random variance (e.g., sampling error, movements of participants distorting the physiological signal, etc.; see Ney et al., 2018). In addition, it is possible that the psychophysiological measures of fear used in this study do not measure the same underlying learning process, or they may index different components of the same learning mechanism (e.g., Bach and Melinscak, 2020). For instance, SCR may reflect the learning of the CS-US contingency and related attentional processes, whereas startle may reflect the defensive responding based on this learning. This may (partly) explain why the relationship with IU varies across different outcome measures (Bach and Melinscak, 2020). Furthermore, the varying findings may be explained by parameter choices which change the level of uncertainty during the acquisition phase (Morriss et al., 2021). That is, inconclusive findings may be explained by differences in (i) the reinforcement rate with the US (i.e., partial vs. continuous rate), (ii) contingency instructions, and (iii) the temporal predictability and frequency at which the startle probes are presented (Klingelhöfer-Jens et al., 2021; Sjouwerman et al., 2016; Chin

et al., 2016). Indeed, as threat reinforcement alters the predictability of an aversive stimulus, differences between reinforcement rates applied in these study designs may have changed the relationship between psychophysiological measures and IU (i.e., the relationship being generally stronger under conditions with greater uncertainty; Chin et al., 2016). More systematic research manipulating the reinforcement rates and other parameters of uncertainty (e.g., instructions, startle probes) within the same study will help to better clarify this issue. All in all, more studies are needed to determine (1) whether physiological measures are related to IU; and (2) which methodological choices potentially moderate this relationship.

Some strengths and limitations of this work can be noted. With regard to strengths, the relatively large sample size and the inclusion of four different measures of both subjective and physiological fear responding can be noted. Furthermore, a partial reinforcement scheme was used in the current study, which is needed to create sufficient uncertainty in the fear conditioning task to detect correlations with inter-individual differences (Lissek et al., 2006). With regard to limitations, it can be noted that the sample size was still relatively limited to detect smaller correlations (i.e., $r < 0.3$) and the fact that the sample consisted of only healthy university students. Ideally, even larger and more representative samples are needed to draw firmer and more generalizable conclusions. Nonetheless, it can be questioned whether investing in even larger sample sizes to detect small correlations is worthwhile. It is possible that Pavlovian fear acquisition is a relatively uninformative paradigm to study inter-individual differences in anxiety proneness and that different paradigms (or variations of the fear conditioning paradigm; e.g., fear generalization) may be more optimally suited for this purpose. This latter question is an important topic of investigation for future meta-scientific work.

In conclusion, in the current study, we could replicate a number of findings previously reported in the literature (i.e., a positive relationship between IU and fear ratings to the CS+ and a negative relationship between IU and startle responses to the CS− during fear acquisition). However, despite using a larger sample, it still remains challenging to interpret the mostly subtle relationships between the outcome measures and IU. The variability of the methodological aspects of the studies in the literature complicates the interpretation of the findings. Furthermore, an additional challenge is that the different personality factors (i.e., IUS and STAI) and the different outcome measures (i.e., fear ratings, expectancy ratings, SCR, and startle) are related to each other. This complicates te interpretation of specific correlations, because the explained variance is partly shared with other relevant constructs. To investigate these different correlations between related measures, more advanced statistical techniques are needed. As such, our recommendation for the literature would be to (1) collect even larger samples; (2) systematically investigate the effects of methodological variations (e.g., reinforcement rate and inclusion of startle probes); and (3) to use structural equation modelling to investigate the relationship between anxious personality traits and different outcome measures of fear in a more fine-grained manner (see Sjouwerman et al., 2020).

Declaration of competing interest

The authors have no conflicts of interest to declare.

Data availability

A link to the Open Science Framework project containing the data is provided in the manuscript.

Acknowledgements

This work was supported by a Vici grant (453-15-005) from the Netherlands Organization for Scientific Research (NWO) awarded to Iris Engelhard.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijpsycho.2022.04.011.

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