Running title: Intolerance of uncertainty and threat extinction

**I doubt it is safe: A meta-analysis of self-reported intolerance of uncertainty
and threat extinction training**

*Jayne Morriss, *Shannon Wake, Charlotte Elizabeth & Carien M. van Reekum

Centre for Integrative Neuroscience and Neurodynamics

School of Psychology and Clinical Language Sciences

University of Reading

Reading

UK

*Joint first authorship

Correspondence:

Jayne Morriss

Centre for Integrative Neuroscience and Neurodynamics

School of Psychology and Clinical Language Sciences

University of Reading

Earley Gate, Whiteknights Campus

RG6 6AH Reading

United Kingdom

(0)118 378 7937

j.e.morriss@reading.ac.uk

Abstract

Background. Intolerance of uncertainty (IU), the tendency to find uncertainty distressing, is an important transdiagnostic dimension in mental health disorders. Higher self-reported IU has been linked to poorer threat extinction training (i.e., the updating of threat to safe associations), a key process that is targeted in exposure-based therapies. However, it remains to be seen whether IU-related effects during threat extinction training are reliably and specifically driven by the IU construct or a particular subcomponent of the IU construct over other self-reported measures of anxiety.

Methods. A meta-analysis of studies from different laboratories (experiment $n = 18$; sample $n = 1006$) was conducted on associations between different variants of self-reported IU (i.e., 27-item, 12-item, inhibitory and prospective subscales), trait anxiety and threat extinction training via skin conductance response. The specificity of IU and threat extinction training was assessed against measures of trait anxiety.

Results. All of the self-reported variants of IU, but not trait anxiety, were associated with threat extinction training via skin conductance response (i.e., continued responding to the old threat cue). Specificity was observed for the majority of self-reported variants of IU over of trait anxiety.

Conclusions. The findings suggest that the IU construct broadly accounts for difficulties in threat extinction training and is specific over other measures of self-reported anxiety. These findings demonstrate the robustness and specificity of IU-related effects during threat extinction training and highlight potential opportunities

Running title: Intolerance of uncertainty and threat extinction

for translational work to target uncertainty in therapies that rely on threat extinction principles such as exposure therapy.

Keywords: Threat, Anxiety, Extinction, Intolerance of Uncertainty, Skin Conductance, Exposure Therapy

Introduction

The formation and adjustment of threat and safety associations are crucial for wellbeing and protection against psychopathology (1-3). Principles of associative threat and safety learning have provided a theoretical framework for animal and human models of the development, treatment and relapse of anxiety, obsessive-compulsive, trauma and stress disorders (4-8). Importantly, principles of associative threat and safety learning underscore modern therapies such as exposure therapy (9). Exposure-based therapies aim to reduce anxiety symptoms by gradually exposing patients to the particular objects or situations that make them feel anxious (10). The gradual exposure is thought to challenge old threat associations (i.e., once my employer processed my payslip and the payment was late) by providing alternative new safe associations (i.e., last week my employer processed my payslip, the payment was on time) (11). However, after exposure therapy completion, many patients experience a return of anxiety symptoms (9, 12). The reason for high relapse rates after exposure therapy remain unclear. One potential factor that may hinder progress during exposure therapy is uncertainty (i.e., when my payslip is next processed, how can I be sure that I will be paid on time?). Changes to contingency, such as threat to safety, may not be evident in the first instance; it may take several experiences to realise that a cue that once signalled threat now signals safety. Uncertainty (also referred to as ambiguity) over the change in contingency from threat to safety may prolong the learning of new safety associations generally (13, 14) but particularly for individuals who find uncertainty anxiety-provoking (15).

Intolerance of Uncertainty (IU) has been defined as “an individual's dispositional incapacity to endure the aversive response triggered by the perceived absence of salient, key, or sufficient information, and sustained by the associated

perception of uncertainty” [(16), p.31]. IU is a lower-order factor that underlies higher-order constructs related to negative affectivity such as neuroticism (16, 17). For example, self-reported IU: (1) accounts for unique variance in anxiety and depression symptomology when controlling for neuroticism (18, 19) and has been shown to mediate the relationship between anxiety and depression symptomology and neuroticism (20). Notably, IU is a transdiagnostic dimension, with high levels of self-reported IU observed in a number of mental health disorders such as anxiety, obsessive-compulsive, trauma and stress disorders (20, 21). Given IU’s potential promise as a transdiagnostic target for mental health interventions (22-25), understanding the neurobiological basis of IU has become paramount (26, 27).

From animal and human evidence, it is well established that uncertainty plays a fundamental role in the neurobiology of anxiety and stress (28-33). However, only recently has research began to emerge on the importance of individual differences in IU in associative threat and safety learning mechanisms (27, 34). Several studies, albeit from the same laboratory (34), have shown that during threat extinction training, individuals with high IU exhibit greater skin conductance responding (SCR) to cues that no longer signal threat (15, 35-39). However, presentations of disrupted threat extinction training in individuals with high IU appears varied. The majority of studies have found specificity of IU, over other self-reported anxiety measures in predicting differences in SCR to: (1) both learned threat and safety during early trials, (2) greater SCR to learned threat cues versus safety cues during late trials (36, 37) or (3) greater SCR to learned threat cues across all trials (15, 35). Several studies have also reported no association between IU and SCR during threat extinction training (39-41).

There is also debate concerning what self-reported IU scale or subscale is more suitable for examining cognitive, affective, and behavioural facets of anxiety (42, 43). Historically, the Intolerance of Uncertainty Scale (IUS) with 27 items was developed to distinguish anxiety-related features in participants presenting with Generalised Anxiety Disorder (GAD) (44, 45). Currently, the most prominent IUS questionnaire is the 12-item measure, which can be derived from the 27-item measure (46). Both the 27-item and 12-item IUS measures have robust psychometrics such as good internal reliability, convergent validity and discriminant validity (18, 43, 47). Carleton et al.'s (2007) 12-item IUS measure is viewed as superior to the 27-item IUS measure because it removes high inter-item correlations and factor instability, and it delineates from a unilateral scale into two subscales. The two subscales consist of prospective IU (P-IU), which refers to the desire for predictability and active seeking of certainty, and inhibitory IU (I-IU), which refers to paralysis of cognition and action in the face of uncertainty (48). The two IUS subscales also show evidence of good internal reliability, convergent validity and discriminant validity (18, 47). An additional benefit of the two-factor scale is that it may reveal further specificity between aspects of IU and cognitive, affective and behavioural facets of anxiety. For instance, the P-IU subscale has been specifically linked to excessive avoidance of cues that no longer signal threat (49, 50). The majority of studies examining IU and threat extinction training have used the 27-item IU scale (15, 35-39, 51). In order to further understand IU's role in threat extinction training, however, it would be beneficial to compare associations between different IU scales/subscales and indices of threat extinction training. It is possible that IU may broadly account for differences in threat extinction training or a particular

component of IU (i.e., prospective or inhibitory) is related to differences in threat extinction training.

Assessing the robustness and specificity of IU-related effects during threat extinction training could help characterize neurobiological models of uncertainty-based maintenance of anxiety (26, 27), with implications for future work aiming to test, develop or modify existing exposure-based treatments (25, 52) that are more appropriate for a particular individual or group (53-56). In the current study, we conducted a meta-analysis of eighteen threat extinction training experiments from different laboratories (sample $n = 1006$), to examine whether IU reliably predicts threat extinction training captured via skin conductance response (i.e., the most dominant measure used to assess threat conditioning in the literature (57)).

We compared associations between the IU 27-item, 12-item and IU-prospective and -inhibitory subscales with SCR during threat extinction training (i.e., difference scores between learned threat and safety cues). Additionally, we examined associations between measures of trait anxiety (i.e., STAI-T (58) and STICSA (59)) with SCR during threat extinction training. Then, we assessed the specificity of relationships between IU and threat extinction training against measures of trait anxiety. There were several reasons for comparing IU against measures of trait anxiety. Firstly, trait anxiety captured by STAI-T is one of the most commonly used self-reported anxiety measures in the threat conditioning literature (34). Secondly, the construct of trait anxiety is considered to be closely related to (60), or synonymous with the construct of neuroticism (i.e., broader negative affect) (61), whereas IU is considered to be a lower-order factor and related to a particular part of the neuroticism construct (16) (i.e., the need for predictability or controllability (61)).

We hypothesised that the IU 27-item and 12-item scales would be reliably and specifically associated with threat extinction training. However, given the lack of research on the IU subscales and threat extinction training, we did not have any specific hypotheses as to how the IU subscales would relate to SCR during threat extinction training.

Methods and Materials

For the meta-analysis, PRISMA-guidelines were followed (62). The protocol for the meta-analysis was not preregistered. The relevant files from the meta-analysis (i.e., search records, master data file, and meta-analysis output from R) are located on the Open Science Framework (OSF) through the following link: (<https://osf.io/8ad2q/>). All aspects related to the literature search, data collation, data reduction and data analysis were conducted by at least two independent investigators (J.M, S.W and C.E).

Data Search and Inclusion Criteria

An overview of our data search is provided in Fig 1. Firstly, a literature search was conducted in four digital databases (PubMed, BioRxiv, PsyArXiv, and the Open Science Framework) using the following terms: “Intolerance of Uncertainty” AND (Conditioning” or “Extinction”). Secondly, to ensure that any published or unpublished studies were not missed, datasets were called for via social media posts (i.e., Twitter) and by emailing experts in the field known to conduct threat conditioning experiments (51 experts contacted). The literature search and call for data were conducted between 19.06.2020-16.10.2020. After removing duplicate results, records were screened against the following eligibility criteria: (1) had to use

a standard differential threat extinction training protocol with a paired (CS+ presented with an aversive outcome [US] such as a shock or loud noise), an unpaired conditioned stimulus (CS+ in the absence of an US) and a control stimulus (CS-), (2) had to measure SCR, and (3) had to measure self-reported IU. Next, the authors of eligible published studies were contacted regarding their willingness to share details on their design and their individual-level data (i.e. SCR, self-reported IU scores, and any additional self-reported trait anxiety scores). Based on the literature search, call for data on social media and emailing of experts in the field, 16 records (15, 35-37, 39, 40, 51, 63-71) met the inclusion criteria and were available for the meta-analysis (14 published and 2 unpublished records; 18 experiments; sample $n = 1006$; see Table 1).

Data Quality Check

Authors with eligible records were contacted via email and were asked to provide details of their study by completing a template spreadsheet (i.e., author list, title, sample size, and characteristics, exclusion criteria, measures collected, reinforcement rate, CS type, US type, CS length, ITI length, number of trials in extinction, SCR scoring type (trough – peak; baseline-peak), SCR value, SCR value criterion, SCR transformations, SCR non-responding). The data quality was checked by examining whether each eligible record used an experimental conditioning task (57) and SCR extraction technique (72, 73) that matched the typical recommendations for the field.

There are a variety of ways to measure and extract SCR. However, similar results for SCR have been observed when using different design choices (i.e., different interstimulus timing) (74) or pre-processing pipelines (e.g., scoring

windows) (75). While there is substantial heterogeneity in the exclusion criteria used for SCR non-responding and non-learning in the field (76), for the current meta-analysis, SCR exclusion criteria was relatively similar across studies. The majority of records excluded participants who displayed non-responding in SCR (i.e., none ($n = 5$), 10% ($n = 4$) or 33.3% ($n = 3$) of responses meeting SCR criterion or used no non-responding criteria to exclude ($n = 4$)) and only 2 out of 16 records excluded participants based on non-learning in SCR. All studies were maintained in the meta-analysis.

Data Collation

Authors of the original studies were asked to provide individual-level data for their SCR, IU questionnaire (IU-27, IU-12, P-IU or I-IU), and trait anxiety questionnaire measures in a spreadsheet with wide format. Authors were able to share trial-wise or averaged SCR data and itemised or total score questionnaire data. Then, each eligible records' associated data file was organised and prepared for data reduction.

Data Reduction

SCR: In keeping with a variety of metrics used in the literature to capture the process of threat extinction (57), four separate SCR difference score metrics were computed for each experiment; whole phase extinction $[(CS+) - (CS-)]$, early extinction $[(\text{first } 6\text{--}10 \text{ } CS+ \text{ trials}) - (\text{first } 6\text{--}10 \text{ } CS- \text{ trials})]$, late extinction $[(\text{last } 6\text{--}10 \text{ } CS+ \text{ trials}) - (\text{last } 6\text{--}10 \text{ } CS- \text{ trials})]$, and the double-difference extinction score $[(CS+ - CS-)_{\text{early}} - (CS+ - CS-)_{\text{late}}]$. While there is some interdependence between the different SCR difference scores, organising the SCR data in this manner allows for the assessment of threat and safety discrimination overall, and across time (57). For 4 experiments, only the

early extinction training metric was analysed (64, 65, 69, 70). This was due to these studies having too few extinction learning trials to examine SCR across the whole phase, during late extinction, and comparing early versus late extinction (i.e., the studies only had 9 or 10 total trials per CS type).

IU: Scores from four separate IU scales (IU-27, IU-12, I-IU, and P-IU) were generated from the Intolerance on Uncertainty Scale (IUS; (44)) (see Table 2). The IUS comprised of 27 items that are rated on a 5-point Likert Scale. The IU-12 score is generated from 12 items from the IUS. Two experiments only administered the IU-12 (40, 63), and therefore are not included in the analysis of the IU-27 scale. The I-IU (Inhibitory IU) and P-IU (Prospective IU) are two subscales measuring separate components of IU and are generated from either the IU-27 or IU-12 scale. Where 2 or more items were missing for the IUS, values were interpolated based on the average item score ($n = 14$).

Trait Anxiety: 15 out of the 18 studies measured trait anxiety using the STAI-T or the STICSA as an alternative self-report measure of anxiety. The State-Trait Anxiety Inventory – Trait (STAI) (58) consists of 20 trait anxiety items rated on a 4-point Likert scale. The State-Trait Inventory for Cognitive and Somatic Anxiety (STICSA) (59) consists of 21 items that are rated on a 4-point Likert scale.

Analyses

Correlation and partial correlation analyses were performed in SPSS (SPSS, Inc; Chicago, Illinois) for each dataset. To examine whether IU or trait anxiety was related to threat extinction training in each experiment, correlations were conducted

between the IU-scales (IU-27, IU-12, I-IU, and P-IU), variants of trait anxiety (STAI-T or STICSA), and SCR difference scores (whole phase, early, late, and double-difference) during the threat extinction training phase (see Supplementary Table 1 and 2). To assess the specificity of IU over other self-report measures of anxiety in each experiment, partial correlations were conducted between the IU-scales (IU-27, IU-12, I-IU, and P-IU) and SCR difference scores (whole phase, early, late, and double-difference) during the threat extinction training phase, controlling for STAI-T or STICSA (see Supplementary Table 3).

The r values from the correlations and partial correlations were converted into Hedges' g effect size values. Fixed-effect meta-analyses were carried out in RStudio (RStudio, Inc; Boston, MA) on the effect sizes from the correlations and partial correlations separately, to generate a pooled effect size for every IU-scale (IU-27, IU-12, I-IU and, P-IU), trait anxiety variant (STAI-T, STICSA) and difference score (early, late, whole phase and double-difference) across the 18 experiments. Benjamini-Hochberg corrections (77) were applied to the correlations (corrected value, $p < .025$) and partial correlations (corrected value, $p < .018$).

Results

Relationships Between IU and SCR During Threat Extinction

All of the self-reported variants of the IU scale (IU-27, IU-12, I-IU, and P-IU) were significantly associated with SCR difference scores during late extinction training and across the entire extinction phase [corrected p 's $< .025$, for statistics see Table 3]. The significant meta-analytic effect sizes for relationships between self-reported IU and SCR differences scores during late extinction training and the entire extinction phase were small to medium [Hedges g between 0.2-0.35; see Table 3 and Figure

2A & B] and yielded fairly low heterogeneity across studies [I^2 between 0-32.5%; see Table 3].

Only the IU-27 (not IU-12, I-IU, or P-IU) was significantly associated with SCR double-difference scores during extinction training [corrected $p < .025$, for statistics see Table 3]. None of the self-reported variants of the IU scale (IU-27, IU-12, I-IU, and P-IU) were significantly associated with SCR difference scores during early extinction training [p 's $> .3$, see statistics see Table 3 and Supplementary Table 4].

Relationships between Trait Anxiety and SCR During Threat Extinction

No significant relationships were found between trait anxiety and SCR difference scores [corrected p 's $> .1$, see statistics see Table 4].

Relationship Between IU and SCR During Threat Extinction When Controlling for Measures of Trait Anxiety

Even though trait anxiety was not significantly related to threat extinction training, it is important to establish specificity of IU over trait anxiety due to shared variance between these constructs [correlation between IU-12 and STAI-T, $r(802) = .568$, $p < .001$; correlation between IU-12 and STICSA, $r(115) = .217$, $p = .003$]. When controlling for trait anxiety, IU-12, P-IU and I-IU (but not IU-27) were significantly associated with SCR difference scores during late extinction training [corrected p 's $< .018$, for statistics see Table 5]. Moreover, when controlling for trait anxiety, IU-27, IU-12, and P-IU (but not I-IU) were significantly associated with SCR difference scores across the entire extinction phase [corrected p 's $< .018$, for statistics see Table 5]. The meta-analytic effect sizes for significant relationships between self-reported IU and SCR differences scores during late extinction training and the entire

extinction phase, when controlling for self-reported trait anxiety, were small to medium [Hedges g between 0.24-0.31; see Table 5] and showed fairly low heterogeneity across studies [I^2 between 0-26.9%; see Table 5].

When controlling for trait anxiety, none of the self-reported variants of the IU scale (IU-27, IU-12, I-IU and, P-IU) were significantly associated with SCR double-difference scores [corrected p 's between .029 and .06] or SCR difference scores during early extinction training [corrected p 's > .3, see statistics see Table 5].

Publication Bias Assessment

Publication bias was assessed using Egger's regression tests and funnel plots for the two most prominent results across the meta-analyses conducted, i.e., meta-analyses examining the relationship between IU-12 and SCR difference scores during late extinction learning and the entire extinction phase. The Egger's tests were not significant for studies included in meta-analyses examining the relationship between IU-12 and SCR difference scores during the late extinction phase, $t = 1.42$, $p = .18$, and across the entire extinction phase, $t = 1.19$, $p = .26$. This result, and the symmetry of the funnel plots presented in Figure 2C & D suggest that there is very little evidence for publication bias.

Discussion

Threat extinction is a key principle underlying exposure-based therapies (5). Here, in a meta-analysis of 18 experiments, we show that IU, the tendency to find uncertainty distressing (16, 17, 44), consistently and specifically impairs threat extinction training, indexed by greater SCR to cues that no longer signal threat. The findings consolidate the role of IU-related biases in threat extinction training and have clear

implications for neurobiological models of uncertainty-related maintenance of anxiety (27, 31, 32) and future translational work aiming to target IU in exposure-based therapies (26).

All of the self-reported variants of IU were associated with greater SCR to learned threat versus safety cues: (1) across threat extinction training, and (2) during the late trials of threat extinction training. No relationships were found between trait anxiety (STAI and STICSA) and SCR difference scores metrics during threat extinction training. Importantly, the majority of the IU-related effects during threat extinction training remained, particularly for the 12-item variant of the IUS, when controlling for self-reported measures of trait anxiety such as STAI and STICSA. Taken together, these findings suggest that the IU construct broadly, and not a sub-component of the IU construct (i.e., prospective or inhibitory), accounts for difficulties in updating threat to safety, and that such effects are specific to IU, over other self-report measures of trait anxiety (i.e., STAI and STICSA). Moreover, these results suggest that the IU construct, which is in part related to the need for predictability/controllability facet of the neuroticism construct (16), is more predictive of threat extinction learning, than trait anxiety constructs that strongly overlap with multiple facets of the neuroticism construct (60, 61).

In previous research, a few studies observed differences in SCR to both learned threat and safety cues during the early trials of threat extinction training (36, 37). However, the meta-analysis showed that none of the self-reported variants of IU were reliably associated with SCR to learned threat or safety cues during the early trials of threat extinction training. During the early part of extinction training, participants begin to learn that the conditioned stimulus is no longer being reinforced with an aversive outcome (i.e., a shock or loud sound). However, the time it takes

participants to learn that a contingency change has occurred may differ depending on the reinforcement rate used during the prior acquisition phase (78, 79). Notably, the original studies that found a relationship between IU and early extinction used a 100% reinforcement rate during acquisition (36, 37), where the change in contingencies between acquisition and extinction are more obvious. Within the current meta-analysis, the reinforcement rates during acquisition varied substantially across studies (i.e., 37.5-100%) which may explain the lack of IU-related effects during early extinction.

While the IU-related effects across extinction training by time may seem unintuitive, given that contingency uncertainty may be greatest during early extinction training, the findings are in line with modern IU theory. Based on Carleton's definition of IU (16), aversive responses triggered by the perceived absence of information are sustained by the perception of uncertainty. In the case of extinction learning, individuals with high IU, relative to low IU may sustain the perception of uncertainty for longer, resulting in the maintenance of a conditioned response. Indeed, the lack of information about the omission of threat throughout the extinction phase may cumulatively add to the perception of uncertainty in individuals with high IU (i.e., "I didn't hear the sound on the last trial. Maybe it will happen on the next trial?").

Importantly, the findings from the present meta-analysis highlight the relevance of IU in threat extinction training, a key process that is targeted in exposure-based therapies (5-7), and therefore has implications for clinical work. A next step for experimental work would be to identify the extent to which IU-related difficulties in threat extinction training are transdiagnostic using a research domain criteria approach (53, 55, 56). For instance, it is unclear whether IU is associated

with poorer threat extinction training within a specific or broader cluster of mental health disorders. Translational research could identify whether existing evidence-based therapies such as cognitive behavioural therapy (i.e., which often involve exposure sessions with cognitive restructuring techniques) are effective in reducing IU-related biases across disorders or whether further modification (i.e., prolonged exposure-based therapy) to these treatments (25, 52) are needed to target IU-related biases in a particular disorder or within a broader set of disorders (26). Answering these questions would allow for precision psychiatry (54), where clinicians could select a particular type of therapy for individuals with high IU in those disorders or cases in which it is relevant.

The meta-analysis had several strengths. Firstly, the meta-analysis data were more heterogeneous than that typically found from a single study (i.e., data from different laboratories and from different sample types). Secondly, despite differences in design and data reduction techniques, IU was still the dominant anxiety construct in predicting threat extinction training behaviour via SCR, suggesting that IU-related effects are particularly robust in the face of additional 'noise' and error variance.

Future work should focus efforts on replicating IU-related effects in non-English speaking countries, in non-WEIRD samples (80) and in other readout measures (57) to further assess the generalisability, reliability, and specificity of IU-related effects during threat extinction training. Furthermore, the meta-analyses primarily used data from same-day or next-day uninstructed threat extinction training with only one session, limiting the generalisability of the results to real-world exposure-based therapies (i.e., which typically involve instructions about assessing the likelihood of aversive events and often comprise of more than one session) (8). Promisingly, several studies have shown that higher IU is associated with poorer

threat extinction retention 24 hours later, and that this can be alleviated either through extending (i.e., longer session) or by introducing a novel stimulus (i.e., pairing the CS+ with a benign tone) during threat extinction training (41, 51).

However, further research is needed to assess the impact and stability of IU-related effects across more extinction training sessions and extended periods of time (51), as well as to identify whether biological mechanisms modulated by IU can be altered via therapeutic and/or pharmacological interventions, in order to extrapolate the clinical relevance of IU in the treatment of anxiety and stress disorders (26).

Overall, the findings from the meta-analysis demonstrate the robustness, and specificity of IU-related effects during threat extinction training. Furthermore, the findings highlight potential opportunities for experimental and translational work to examine how IU modulates threat extinction learning across different disorders with an anxiety component and whether existing therapies that rely on threat extinction principles (i.e., exposure therapy) need to be modified to target IU-related biases.

Acknowledgements

We would like to thank all of the authors who shared their data for the meta-analysis: AM Apergis-Schoute, FE Arntz, T Blow, RN Cardinal, DM Christmas, J Dunsmoor, A Fryer, Z Gazman, E Goldfarb, J Kanen, M Kuhn, O Lipp, TB Lonsdorf, K Lucas, C Luck, PM McEvoy, J Niehaus, O Pascucci, E Phelps, J Pomeroy, A Price, TW Robbins, BJ Sahakian, R Scharfenort, HB Simpson, R Sjouwerman, S Steinman, Y Stovezky, A Thompson, LD de Voogd, & R Yellowlees. The meta-analysis was supported by a: (1) NARSAD Young Investigator Grant from the Brain & Behavior Research Foundation (27567) and (2) an ESRC New Investigator Grant (ES/R01145/1) awarded to Jayne Morriss.

Disclosures

The authors have no conflicts of interest to declare.

Author Contributions

J.M. conceived the initial study, and J.M., S.W., C.v.R. contributed to the design of the study. Data collection was carried out by C.E., & J.M., (literature search), J.M., & C.v.R (online call for data), and J.M. & C.E. (collation). Data reduction was carried out by S.W. & J.M. Analyses were performed by J.M & S.W. and data interpretation by J.M. The paper, including introduction (C.E., J.M.), method (S.W., J.M.), results (J.M., S.W.) and discussion (J.M.), was written, critically revised, and approved for publication by all named authors.

References

1. Shin LM, Liberzon I (2009): The neurocircuitry of fear, stress, and anxiety disorders. *Neuropsychopharmacology*. 35:169-191.
2. LeDoux J, Daw ND (2018): Surviving threats: neural circuit and computational implications of a new taxonomy of defensive behaviour. *Nature Reviews Neuroscience*. 19:269-282.
3. VanElzakker MB, Dahlgren MK, Davis FC, Dubois S, Shin LM (2014): From Pavlov to PTSD: the extinction of conditioned fear in rodents, humans, and anxiety disorders. *Neurobiology of Learning and Memory*. 113:3-18.
4. Jacoby RJ, Abramowitz JS (2016): Inhibitory learning approaches to exposure therapy: A critical review and translation to obsessive-compulsive disorder. *Clinical Psychology Review*. 49:28-40.
5. McNally RJ (2007): Mechanisms of exposure therapy: how neuroscience can improve psychological treatments for anxiety disorders. *Clinical Psychology Review*. 27:750-759.
6. Carpenter JK, Pinaire M, Hofmann SG (2019): from extinction learning to anxiety treatment: Mind the gap. *Brain Sciences*. 9:164.
7. Milad MR, Quirk GJ (2012): Fear extinction as a model for translational neuroscience: ten years of progress. *Annual Review of Psychology*. 63:129-151.
8. Craske MG, Treanor M, Conway CC, Zbozinek T, Vervliet B (2014): Maximizing exposure therapy: an inhibitory learning approach. *Behaviour Research and Therapy*. 58:10-23.
9. Boschen MJ, Neumann DL, Waters AM (2009): Relapse of successfully treated anxiety and fear: theoretical issues and recommendations for clinical practice. *Australian & New Zealand Journal of Psychiatry*. 43:89-100.

10. Barlow DH (2002): *Anxiety and its disorders: The nature and treatment of anxiety and panic*, 2nd ed. New York, NY, US: Guilford Press.
11. Foa EB, Kozak MJ (1986): Emotional processing of fear: exposure to corrective information. *Psychological Bulletin*. 99:20.
12. Bandelow B, Michaelis S, Wedekind D (2017): Treatment of anxiety disorders. *Dialogues in Clinical Neuroscience*. 19:93.
13. Bouton ME (2002): Context, ambiguity, and unlearning: Sources of relapse after behavioral extinction. *Biological Psychiatry*. 52:976-986.
14. Levy I, Schiller D (2021): Neural computations of threat. *Trends in Cognitive Sciences*. 25:151-171.
15. Morriss J, van Reekum CM (2019): I feel safe when i know: Contingency instruction promotes threat extinction in high intolerance of uncertainty individuals. *Behaviour Research and Therapy*. 116:111-118.
16. Carleton RN (2016): Into the unknown: A review and synthesis of contemporary models involving uncertainty. *Journal of Anxiety Disorders*. 39:30-43.
17. Carleton RN (2016): Fear of the unknown: One fear to rule them all? *Journal of Anxiety Disorders*. 41:5-21.
18. McEvoy PM, Mahoney AE (2011): Achieving certainty about the structure of intolerance of uncertainty in a treatment-seeking sample with anxiety and depression. *Journal of Anxiety Disorders*. 25:112-122.
19. Boelen PA, Reijntjes A (2009): Intolerance of uncertainty and social anxiety. *Journal of Anxiety Disorders*. 23:130-135.
20. McEvoy PM, Mahoney AE (2012): To be sure, to be sure: Intolerance of uncertainty mediates symptoms of various anxiety disorders and depression. *Behavior Therapy*. 43:533-545.

21. McEvoy PM, Hyett MP, Shihata S, Price JE, Strachan L (2019): The impact of methodological and measurement factors on transdiagnostic associations with intolerance of uncertainty: A meta-analysis. *Clinical Psychology Review*. 73:101778.
22. Boswell JF, Thompson-Hollands J, Farchione TJ, Barlow DH (2013): Intolerance of uncertainty: A common factor in the treatment of emotional disorders. *Journal of Clinical Psychology*. 69:630-645.
23. Oglesby ME, Allan NP, Schmidt NB (2017): Randomized control trial investigating the efficacy of a computer-based intolerance of uncertainty intervention. *Behaviour Research and Therapy*. 95:50-57.
24. Robichaud M, Dugas MJ (2006): A cognitive-behavioral treatment targeting intolerance of uncertainty. *Worry and its psychological disorders: Theory, assessment and treatment*. 289-304.
25. Einstein DA (2014): Extension of the transdiagnostic model to focus on intolerance of uncertainty: a review of the literature and implications for treatment. *Clinical Psychology: Science and Practice*. 21:280-300.
26. Shihata S, McEvoy PM, Mullan BA, Carleton RN (2016): Intolerance of uncertainty in emotional disorders: What uncertainties remain? *Journal of Anxiety Disorders*. 41:115-124.
27. Tanovic E, Gee DG, Joormann J (2018): Intolerance of uncertainty: Neural and psychophysiological correlates of the perception of uncertainty as threatening. *Clinical Psychology Review*. 60:87-99.
28. Brosschot JF, Verkuil B, Thayer JF (2017): Exposed to events that never happen: Generalized unsafety, the default stress response, and prolonged autonomic activity. *Neuroscience & Biobehavioral Reviews*. 74:287-296.

29. Brosschot JF, Verkuil B, Thayer JF (2016): The default response to uncertainty and the importance of perceived safety in anxiety and stress: An evolution-theoretical perspective. *Journal of Anxiety Disorders*. 41:22-34.
30. Hirsch CR, Meeten F, Krahé C, Reeder C (2016): Resolving ambiguity in emotional disorders: The nature and role of interpretation biases. *Annual Review of Clinical Psychology*. 12:281-305.
31. Grupe DW, Nitschke JB (2013): Uncertainty and anticipation in anxiety: an integrated neurobiological and psychological perspective. *Nature Reviews Neuroscience*. 14:488-501.
32. Peters A, McEwen BS, Friston K (2017): Uncertainty and stress: Why it causes diseases and how it is mastered by the brain. *Progress in Neurobiology*. 156:164-188.
33. Pulcu E, Browning M (2019): The misestimation of uncertainty in affective disorders. *Trends in Cognitive Sciences*. 23:865-875.
34. Lonsdorf TB, Merz CJ (2017): More than just noise: Inter-individual differences in fear acquisition, extinction and return of fear in humans-Biological, experiential, temperamental factors, and methodological pitfalls. *Neuroscience & Biobehavioral Reviews*. 80:703-728.
35. Morriss J (2019): What do I do now? Intolerance of uncertainty is associated with discrete patterns of anticipatory physiological responding to different contexts. *Psychophysiology*. e13396.
36. Morriss J, Christakou A, Van Reekum CM (2015): Intolerance of uncertainty predicts fear extinction in amygdala-ventromedial prefrontal cortical circuitry. *Biology of Mood & Anxiety Disorders*. 5:1.

37. Morriss J, Christakou A, Van Reekum CM (2016): Nothing is safe: Intolerance of uncertainty is associated with compromised fear extinction learning. *Biological Psychology*. 121:187-193.
38. Morriss J, Saldarini F, Van Reekum CM (2019): The role of threat level and intolerance of uncertainty in extinction. *International Journal of Psychophysiology*. 142:1-9.
39. Wake S, van Reekum CM, Dodd H, Morriss J (2020): The Impact of Intolerance of Uncertainty and Cognitive Behavioural Instructions on Safety Learning. *Cognitive Therapy and Research*. 44:931-942.
40. Lucas K, Luck CC, Lipp OV (2018): Novelty-facilitated extinction and the reinstatement of conditional human fear. *Behaviour Research and Therapy*. 109:68-74.
41. Dunsmoor JE, Campese VD, Ceceli AO, LeDoux JE, Phelps EA (2015): Novelty-facilitated extinction: providing a novel outcome in place of an expected threat diminishes recovery of defensive responses. *Biological Psychiatry*. 78:203-209.
42. Bottesi G, Noventa S, Freeston MH, Ghisi M (2019): Seeking certainty about Intolerance of Uncertainty: Addressing old and new issues through the Intolerance of Uncertainty Scale-Revised. *PloS one*. 14:e0211929.
43. Hong RY, Lee SS (2015): Further clarifying prospective and inhibitory intolerance of uncertainty: Factorial and construct validity of test scores from the Intolerance of Uncertainty Scale. *Psychological Assessment*. 27:605.
44. Freeston MH, Rhéaume J, Letarte H, Dugas MJ, Ladouceur R (1994): Why do people worry? *Personality and Individual Differences*. 17:791-802.

45. Birrell J, Meares K, Wilkinson A, Freeston M (2011): Toward a definition of intolerance of uncertainty: A review of factor analytical studies of the Intolerance of Uncertainty Scale. *Clinical Psychology Review*. 31:1198-1208.
46. Carleton RN, Norton MPJ, Asmundson GJ (2007): Fearing the unknown: A short version of the Intolerance of Uncertainty Scale. *Journal of Anxiety Disorders*. 21:105-117.
47. Khawaja NG, Yu LNH (2010): A comparison of the 27-item and 12-item intolerance of uncertainty scales. *Clinical Psychologist*. 14:97-106.
48. Carleton RN, Mulvogue MK, Thibodeau MA, McCabe RE, Antony MM, Asmundson GJ (2012): Increasingly certain about uncertainty: Intolerance of uncertainty across anxiety and depression. *Journal of Anxiety Disorders*. 26:468-479.
49. Flores A, López FJ, Vervliet B, Cobos PL (2020): Prospective intolerance of uncertainty is associated with maladaptive temporal distribution of avoidance responses: An extension of Flores, Lopez, Vervliet, and Cobos (2018). *Journal of Behavior Therapy and Experimental Psychiatry*. 68:101527.
50. Flores A, López FJ, Vervliet B, Cobos PL (2018): Intolerance of uncertainty as a vulnerability factor for excessive and inflexible avoidance behavior. *Behaviour Research and Therapy*. 104:34-43.
51. Morriss J, Wake S, Lindner M, McSorley E, Dodd H (2020): How many times do I need to see to believe? The impact of intolerance of uncertainty and exposure experience on safety-learning and retention in young adults. *International Journal of Psychophysiology*. 153:8-17.
52. Knowles KA, Olatunji BO (2018): Enhancing Inhibitory Learning: The Utility of Variability in Exposure. *Cognitive and Behavioral Practice*. 26:186-200.

53. Insel TR (2014): The NIMH research domain criteria (RDoC) project: precision medicine for psychiatry. *American Journal of Psychiatry*. 171:395-397.
54. Fernandes BS, Williams LM, Steiner J, Leboyer M, Carvalho AF, Berk M (2017): The new field of 'precision psychiatry'. *BMC medicine*. 15:1-7.
55. Morris SE, Cuthbert BN (2012): Research Domain Criteria: cognitive systems, neural circuits, and dimensions of behavior. *Dialogues in Clinical Neuroscience*. 14:29.
56. Cuthbert BN (2015): Research Domain Criteria: toward future psychiatric nosologies. *Dialogues in Clinical Neuroscience*. 17:89.
57. Lonsdorf TB, Menz MM, Andreatta M, Fullana MA, Golkar A, Haaker J, et al. (2017): Don't fear 'fear conditioning': Methodological considerations for the design and analysis of studies on human fear acquisition, extinction, and return of fear. *Neuroscience & Biobehavioral Reviews*. 77:247-285.
58. Spielberger CD, Gorsuch RL, Lushene RE (1970): Manual for the state-trait anxiety inventory.
59. Ree MJ, French D, MacLeod C, Locke V (2008): Distinguishing cognitive and somatic dimensions of state and trait anxiety: Development and validation of the State-Trait Inventory for Cognitive and Somatic Anxiety (STICSA). *Behavioural and Cognitive Psychotherapy*. 36:313-332.
60. Clark DA, Beck AT (2011): *Cognitive therapy of anxiety disorders: Science and Practice*. Guilford Press.
61. Barlow DH, Sauer-Zavala S, Carl JR, Bullis JR, Ellard KK (2014): The nature, diagnosis, and treatment of neuroticism: Back to the future. *Clinical Psychological Science*. 2:344-365.

62. Moher D, Shamseer L, Clarke M, Gherzi D, Liberati A, Petticrew M, et al. (2015): Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews*. 4:1.
63. Thompson A, McEvoy PM, Lipp OV (2018): Enhancing extinction learning: Occasional presentations of the unconditioned stimulus during extinction eliminate spontaneous recovery, but not necessarily reacquisition of fear. *Behaviour Research and Therapy*. 108:29-39.
64. Sjouwerman R, Niehaus J, Kuhn M, Lonsdorf TB (2016): Don't startle me—Interference of startle probe presentations and intermittent ratings with fear acquisition. *Psychophysiology*. 53:1889-1899.
65. Sjouwerman R, Scharfenort R, Lonsdorf TB (2020): Individual differences in fear acquisition: multivariate analyses of different emotional negativity scales, physiological responding, subjective measures, and neural activation. *Scientific Reports*. 10:15283.
66. de Voogd LD, Phelps EA (2020): A cognitively demanding working-memory intervention enhances extinction Research article. *Scientific Reports*. 10.
67. Steinman S et al. (2020): Does novelty facilitate extinction in individuals with anxiety disorders or obsessive compulsive disorders. Unpublished raw data.
68. Goldfarb E, Dunsmoor J, Blow T, Phelps E (2020): Elemental and configural threat learning bias extinction generalization. . *Neurobiology of Learning and Memory*. 180:107405.
69. Sjouwerman R, Lonsdorf TB (2020): Individual differences in intolerance of uncertainty in fear learning. Unpublished raw data.
70. Kanen JW, Arntz FE, Yellowlees R, Christmas DM, Price A, Apergis-Schoute AM, et al. (2020): Effect of tryptophan depletion on conditioned threat memory

expression: role of intolerance of uncertainty. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*.

71. Wake S, Morriss J, Johnstone T, van Reekum CM, Dodd H (2021): Intolerance of uncertainty, and not social anxiety, is associated with compromised extinction of social threat. *Behaviour Research and Therapy*.103818.
72. Dawson ME, Schell AM, Filion DL (2000): The Electrodermal System. In: Cacioppo JT, Tassinary LG, Berntson GG, editors. *Handbook of Physiology*, 2nd ed. Cambridge, UK: Cambridge University Press, pp 200-223.
73. Boucsein W, Fowles DC, Grimnes S, Ben-Shakhar G, Roth WT, Dawson ME, et al. (2012): Publication recommendations for electrodermal measurements. *Psychophysiology*. 49:1017-1034.
74. Breska A, Maoz K, Ben-Shakhar G (2011): Interstimulus intervals for skin conductance response measurement. *Psychophysiology*. 48:437-440.
75. Pineles SL, Orr MR, Orr SP (2009): An alternative scoring method for skin conductance responding in a differential fear conditioning paradigm with a long-duration conditioned stimulus. *Psychophysiology*. 46:984-995.
76. Lonsdorf TB, Klingelhöfer-Jens M, Andreatta M, Beckers T, Chalkia A, Gerlicher A, et al. (2019): Navigating the garden of forking paths for data exclusions in fear conditioning research. *Elife*. 8:e52465.
77. Benjamini Y, Hochberg Y (1995): Controlling the false discovery rate: a practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society Series B (Methodological)*.289-300.
78. Grady AK, Bowen KH, Hyde AT, Totsch SK, Knight DC (2016): Effect of continuous and partial reinforcement on the acquisition and extinction of human conditioned fear. *Behavioral Neuroscience*. 130:36.

79. Leonard DW (1975): Partial reinforcement effects in classical aversive conditioning in rabbits and human beings. *Journal of Comparative and Physiological psychology*. 88:596.

80. Henrich J, Heine SJ, Norenzayan A (2010): Beyond WEIRD: Towards a broad-based behavioral science. *Behavioral and Brain Sciences*. 33:111.

Figure Captions

Figure 1. A schematic of the literature search.

Figure 2. Forest plots demonstrating a small-medium effect size across studies for the relationships between the IU-12 item scale and skin conductance difference scores (CS+ - CS-) during late extinction (A) and across the entire extinction phase (B). Funnel plots were symmetrical indicating little publication bias for studies in the meta-analyses examining the relationship between IU-12 and SCR difference scores during the late extinction (C) and across the entire extinction phase (D). In sum, individuals with higher IU continue to respond to learned threat cues in the absence of reinforced threat, indicating difficulty in updating threat associations to safe associations. Note, 4 experiments not included due to a lack of trials for late and entire extinction phase analysis.

Table 1. Study Characteristics and Experimental Parameters										
Study	IU Scale Administered	Trait Anxiety Measure Administered	Reinforcement Rate	Instruction Type	CS Type	US Type	CS Length (ms)	ITI Length (ms)	N Trials Extinction	SCR Scoring Window (ms after trial onset)
Goldfarb et al. (2021)	IU-27	STAI-T	73%	Uninstructed	Tones and coloured squares	Electric shock	6000	8000 – 10000	24 (12+, 12 CS-)	500 - 6000
Kanen et al. (2021)	IU-27	STAI-T	37.5%	Uninstructed	Coloured squares	Electric shock	4000	10000	20 (10 CS+, 10 CS-)	500 - 4500
Lucas et al. (2018)	IU-12	N/A	50%	Uninstructed	Angry male caucasian faces	Electric shock	8000	22000, 24000 or 26000	32 (16 CS+, 16 CS-)	1000 – 4000
Morriss et al. (2015)	IU-27	STAI-T	100%	Uninstructed	Coloured squares	Female scream	1500	3000 – 6450	32 (16 CS+, 16 CS-)	0 – 7000
	IU-27	STAI-T	100%	Uninstructed			1500			0 – 7000

Morriss et al. (2016)					Coloured squares	Female scream		3000 – 6450	32 (16 CS+, 16 CS-)	
Morriss & van Reekum, Exp 1 (2019)	IU-27	STAI-T	50%	Uninstruct ed	Coloured squares	Female scream	4000	6000 – 8800	32 (16 CS+, 16 CS-)	500 – 3500
Morriss & van Reekum, Exp 2 (2019)	IU-27	STAI-T	50%	Uninstruct ed	Coloured squares	Female scream	4000	6000 – 8800	32 (16 CS+, 16 CS-)	500 – 3500
Morriss & van Reekum, Exp 3 (2019)	IU-27	STAI-T	50%	Uninstruct ed	Coloured squares	Female scream	4000	6000 – 8800	32 (16 CS+, 16 CS-)	500 – 3500
Morriss (2019)	IU-27	STAI-T	50%	Uninstruct ed	Coloured squares	Female scream	4000	6000 – 8800	32 (16 CS+, 16 CS-)	500 – 3500
Morriss et al. (2020)	IU-27	STICSA	50%	Uninstruct ed	Coloured squares	Female scream	4000			500 – 3500

								6000 – 8800	32 (16 CS+, 16 CS-)	
Sjouwerma n et al. (2016)	IU-27	STAI-T	100%	Uninstruct ed	Black shapes (i.e., grid or spiral) on a backgrou nd picture of water	Electric shock	6000	1000 0 – 1300 0	18 (9 CS+, CS-)	900 - 4000
Sjouwerma n et al. (2020)	IU-27	STAI-T	100%	Uninstruct ed	Black geometric al symbols on coloured backgrou nd	Electric shock	6000	1000 0 - 1300 0	18 (9 CS+, CS-)	900 - 4000
Sjouwerma n & Lonsdorf (Unpublishe d)	IU-27	STAI-T	100%	Uninstruct ed	Black geometric al symbols on coloured backgrou nd	Electric shock	6000	1100 0 - 1300 0	18 (9 CS+, CS-)	900 - 3500

Steinman et al. (Unpublished)	IU-27	STAI-T	53.33%	Uninstructed	Angry male caucasian faces	Electric shock	6000	12000	40 (20 CS+, 20 CS-)	500 - 6000
Thompson et al. (2018)	IU-12	N/A	100%	Uninstructed	Coloured images of animals (fish and birds)	Electric shock	6000	13000 - 17000	24 (12 CS+, 12 CS-)	1000 - 6000
de Voogd (2020)	IU-27	N/A	37.5%	Uninstructed	Pictures of snakes	Electric shock	6000	18000 – 22000	40 (20 CS+, 20 CS-)	500 - 6500
Wake et al. (2020)	IU-27	STICSA	50%	Uninstructed	Coloured squares	Female scream	4000	6000 – 8800	32 (16 CS+, 16 CS-)	500 – 3500
Wake et al. (2021)	IU-27	STAI-T	50%	Uninstructed	Neutral female caucasian faces	Electric shock and critical verbal statements	4000	6000 – 8800	332 (16 CS+, 16 CS-)	500 – 3500
STAI-T, State-Trait Anxiety Inventory-Trait; STICSA, The State-Trait Inventory for Cognitive and Somatic Anxiety; CS, Conditioned stimulus; US, Unconditioned stimulus; N, Number; ITI, Inter-trial interval.										

Table 2. Summary of Means, Standard Deviations and Range of scores for each IU-scale in the eighteen experiments.													
Study	N	IU-27			IU-12			I-IU			P-IU		
		M	SD	Range	M	SD	Range	M	SD	Range	M	SD	Range
Goldfarb et al. (2021)	49	63.00	14.59	29 - 100	28.63	7.67	14-46	9.94	3.48	5-20	18.69	5.19	9-31
Kanen et al. (2021)	47	52.57	13.74	31-85	24.70	7.17	13-39	8.15	2.77	5-15	16.55	5.09	8-25
Lucas et al. (2018)	24	N/A	N/A	N/A	32.92	9.13	18-55	11.54	4.67	5-23	21.38	5.09	12-32
Morriss et al. (2015)	14	50.86	16.32	27-85	24.14	8.28	12-39	8.36	2.71	5-13	15.79	6.36	7-26
Morriss et al. (2016)	34	62.88	18.99	31-116	28.5	9.1	12-52	10.41	4.16	5-21	18.1	5.93	7-31
Morriss & van Reekum, Exp 1 (2019)	29	66.66	16.83	33-94	30.41	7.95	15-46	11.14	3.32	5-17	19.28	4.95	10-31
Morriss & van Reekum, Exp 2 (2019)	39	66.21	17.46	33-104	31.64	9.3	15-51	11.31	3.8	5-18	20.33	6.61	9-35

Running title: Intolerance of uncertainty and threat extinction

Morriss & van Reekum, Exp 3 (2019)	42	63.36	17.61	33-103	29.48	9.17	15-48	10.07	3.67	5-19	19.4	6.16	10-32
Morriss (2019)	46	64.15	17.36	31-94	29.96	8.22	14-45	10.63	3.33	5-18	19.33	5.56	9-29
Morriss et al. (2020)	70	64.53	19.82	32-122	29.23	8.57	16-58	10.56	4.1	5-25	18.67	5.34	9-33
Sjouwerman et al. (2016)	54	57.65	18.38	27-121	26.70	8.74	12-55	10.35	3.80	5-24	16.35	5.67	7-31
Sjouwerman et al. (2020)	267	62.77	18.44	27-135	28.62	8.74	12-60	11.18	4.12	5-25	17.44	5.45	7-35
Sjouwerman & Lonsdorf (Unpublished)	86	53.49	14.74	27-93	24.50	7.02	12-45	9.06	2.93	5-18	15.44	4.74	7-27
Steinman et al. (Unpublished)	27	75.22	19.82	42-117	34.41	8.86	19-52	13.11	4.53	6-21	21.30	5.14	12-31
Thompson et al. (2018)	24	N/A	N/A	N/A	28.00	8.39	16-47	9.54	3.56	5-18	18.46	5.12	11-29
de Voogd (2020)	24	58.17	19.89	32-103	27.25	9.00	17-47	9.04	3.61	5-17	18.21	5.94	10-30

Running title: Intolerance of uncertainty and threat extinction

Wake et al. (2020)	46	64.21	21.9	28-110	29.15	10.39	12-52	10.64	3.96	5-18	18.51	6.86	7-34
Wake et al. (2021)	84	64.68	17.92	35-113	29.61	8.31	15-49	10.89	3.56	5-19	18.71	5.49	8-33

Table 3.

Pooled effect sizes and heterogeneity (percentage of variability in the effect size) for the IU scales (IU-27, IU-12, I-IU, and P-IU) and difference scores (early, late, whole phase and double-difference) for SCR during extinction.

	<i>g</i>	(95% CI)	<i>k</i>	<i>N</i>	<i>p</i>	<i>I</i> ²
IU-27						
Early Ext	-0.01	(-0.14; 0.11)	16	958	.822	45.6%
Late Ext	0.35	(0.17; 0.53)	12	504	<.001	17.2%
Whole Phase Ext	0.29	(0.11; 0.46)	12	504	.001	1.5%
Double-Difference	-0.28	(-0.45; -0.1)	12	504	.002	31.8%
IU-12						
Early Ext	0.06	(-0.06; 0.19)	18	1006	.341	44.9%
Late Ext	0.24	(0.08; 0.41)	14	552	.005	29.9%
Whole Phase Ext	0.28	(0.11; 0.45)	14	552	.001	1.1%
Double-Difference	-0.12	(-0.28; 0.05)	14	552	.180	38.2%
I-IU						
Early Ext	0.03	(-0.09; 0.16)	18	1006	.621	40.4%
Late Ext	0.25	(0.08; 0.42)	14	552	.004	10.9%
Whole Phase Ext	0.22	(0.05; 0.39)	14	552	.010	0%
Double-Difference	-0.15	(-0.32; 0.02)	14	552	.090	43%
P-IU						
Early Ext	0.07	(-0.06; 0.19)	18	1006	.301	42%
Late Ext	0.20	(0.04; 0.37)	14	552	.017	32.5%
Whole Phase Ext	0.23	(0.06; 0.39)	14	552	.008	10%
Double-Difference	-0.08	(-0.25; 0.09)	14	552	.348	20%

Table 4.

Pooled effect sizes and heterogeneity (percentage of variability in the effect size) for the trait anxiety scores (STAI-T and STICSA) and difference scores (early, late, whole phase and double-difference) for SCR during extinction

	<i>g</i>	(95% CI)	<i>k</i>	<i>N</i>	<i>p</i>	<i>I</i> ²
Trait Anxiety						
Early Ext	0.016	(-0.11; 0.15)	15	920	.805	8.5%
Late Ext	0.043	(-0.14; 0.22)	11	479	.638	0%
Whole Phase Ext	0.146	(-0.03; 0.325)	11	479	.112	0%
Double-Difference	-0.017	(-0.2; 0.16)	11	479	.852	21.1.%

Table 5.

Pooled effect sizes and heterogeneity (percentage of variability in the effect size) for the IU scales (IU-27, IU-12, I-IU, and P-IU) and difference scores (early, late, whole phase and double-difference) for SCR during extinction when controlling for trait anxiety scores (STAI-T or STICSA).

	<i>g</i>	(95% CI)	<i>k</i>	<i>N</i>	<i>p</i>	<i>I</i> ²
IU-27						
Early Ext	-0.03	(-0.16; 0.1)	15	933	.661	45.3%
Late Ext	0.14	(-0.04; 0.33)	11	479	.120	65.5%
Whole Phase Ext	0.31	(0.13; 0.49)	11	479	<.001	18.8%
Double-Difference	-0.21	(-0.39; -0.02)	11	479	.029	52.1%
IU-12						
Early Ext	0.04	(-0.08; 0.17)	15	933	.498	46.1%
Late Ext	0.28	(0.10; 0.47)	11	479	.002	26.9%
Whole Phase Ext	0.25	(0.07; 0.43)	11	479	.007	14%
Double-Difference	-0.17	(-0.35; 0.01)	11	479	.066	43%
I-IU						
Early Ext	0.004	(-0.12; 0.13)	15	933	.947	41.2%
Late Ext	0.29	(0.11; 0.47)	11	479	.002	18%
Whole Phase Ext	0.18	(0.002; 0.36)	11	479	.047	16.1%
Double-Difference	-0.18	(-0.37; -0.003)	11	479	.046	51.6%
P-IU						

Running title: Intolerance of uncertainty and threat extinction

Early Ext	0.06	(-0.07; 0.19)	15	933	.354	32.8%
Late Ext	0.23	(0.05; 0.41)	11	479	.013	22%
Whole Phase Ext	0.24	(0.06; 0.42)	11	479	.009	0%
Double-Difference	-0.13	(-0.31; 0.05)	11	479	.163	19.3%

A

B

C

D