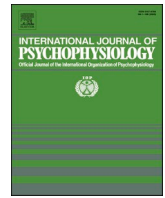


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## Neural and psychophysiological markers of intolerance of uncertainty

### 1. Introduction

Fear of the unknown is considered a primary, fundamental fear (Carleton, 2016a, 2016b; Papenfuss and Ostafin, 2021). In research settings, the fear of the unknown is commonly captured using the self-reported Intolerance of Uncertainty Scale (Carleton et al., 2007; Freeston et al., 1994), which measures the tendency to interpret and react to uncertainty negatively. Importantly, recent research has demonstrated that high levels of self-reported intolerance of uncertainty exist across many emotional disorders (e.g. anxiety, depression, stress and trauma, and obsessive-compulsive disorders) (McEvoy et al., 2019). Moreover, emerging research demonstrates that high levels of self-reported intolerance of uncertainty can be reduced to some extent through short-term interventions in the general population (Dunsmoor et al., 2015; Li et al., 2021; Morriss et al., 2020; Oglesby et al., 2017; Wake et al., 2021), and longer-term transdiagnostic (Sperling, 2022; Talkovsky and Norton, 2016), general (McEvoy and Erceg-Hurn, 2016; Palitz et al., 2019), and intolerance of uncertainty-specific (Dugas et al., 2022; Hebert and Dugas, 2019; Mofrad et al., 2020) standardised treatment protocols (e.g., cognitive behavioural therapy) in clinical populations. Given this progress, there is an increasing need for research examining the neural and psychophysiological basis of intolerance of uncertainty (Morriss et al., 2021; Tanovic et al., 2018), in order to enhance our mechanistic understanding of how intolerance of uncertainty modulates key processes relevant to the pathogenesis and treatment of emotional disorders (Einstein, 2014; Grupe and Nitschke, 2013; Hong and Cheung, 2015; Paulus et al., 2015; Shihata et al., 2016).

The aim of this special issue was to collate new, cutting-edge research on the neural and psychophysiological basis of intolerance of uncertainty, with a view towards highlighting current advances in characterising intolerance of uncertainty, to understand its utility as a key transdiagnostic dimension and treatment target for emotional disorders, and to open up novel lines of enquiry. The popularity of this topic allowed us to gather twenty empirical articles written by experts and scholars in the field that focused on the neural and psychophysiological correlates of intolerance of uncertainty under various parameters of uncertainty (e.g., risk, ambiguity), valence spaces (e.g., threat, reward), and populations (e.g., community, clinical, and developmental). The articles have been organised into subsections according to the domain or population studied: anticipation of uncertain threat and reward, associative threat and safety learning, action tendencies, performance monitoring, and developmental and clinical populations, and interventions (see Table 1).

### 1.1. Anticipation of uncertain threat and reward

Five of the articles in this special issue focused on the anticipation of uncertain threat and reward in adult nonpatient samples using a variety of neural and psychophysiological measures including functional magnetic resonance imaging (fMRI) and connectivity analysis, event-related potentials (ERP), and startle potentiation (eye-blink reflex).

Two of the five articles tested for associations between different facets of intolerance of uncertainty, startle responses, and event-related potentials to startle probes using aversive stimuli. In a large sample of adult siblings employing the No-shock, Predictable-shock, Unpredictable-shock (NPU) task (Schmitz and Grillon, 2012), Correa et al. (2022) reported a negative association between inhibitory intolerance of uncertainty, and the N100 ERP component during unpredictable threat. They also reported on potential early evidence of familial aggregation of increased N100 during unpredictable threat suggesting its potential as an endophenotype for internalising disorders. Like many implementations of the NPU task, the U condition in this study consisted of threat that is both temporally and probabilistically unpredictable. Recognizing this, Carsten et al. (2022) employed two versions of the NPU task designed to independently manipulate temporal and probabilistic unpredictability in a rigorous, preregistered study. Carsten et al. (2022) found that intolerance of uncertainty was positively associated with startle potentiation during probabilistic but not temporal unpredictability. However, Carsten et al. (2022) observed no significant associations between intolerance of uncertainty and the N100 or P300 ERP components.

Of course, the anticipation of important events is not limited to aversive valence spaces. While the two previously mentioned articles focused on the anticipation of noxious stimuli, the anticipation of appetitive stimuli is potentially equally important in understanding the role of intolerance of uncertainty in anxiety and other processes. Highlighting this, Radoman and Gorka (2022) explored anticipation of unpredictable rewards finding a positive correlation between intolerance of uncertainty and functional connectivity between the right anterior insula and dorsal anterior cingulate cortex and right dorsolateral prefrontal cortex during a task designed to manipulate the predictability of rewards.

Further, two papers used a mixed-valence design (positive, negative and neutral) to investigate the relationship between intolerance of uncertainty, affective anticipation and reactivity. Both employed the S1-S2 paradigm and scalp-recorded electroencephalography. In this task, the S1 cue is used to induce expectation about valence (positive/neutral/negative) and outcome probability of S2. Wiese et al. (2022) manipulated the probability by having either a fully predictive S1 cue (low

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**Table 1**  
Overview of the studies included in the special issue.

Domain	Paradigm	Valence Space	Population	IU marker	Outcome measure
<b>Anticipation of threat and reward</b>					
Correa et al. (2022)	No (N), predictable (P), and unpredictable (U) threat (NPU-threat task, uninstructed)	Threat	Controls and clinical (wide range of psychopathologies)	IUS-12	Electroencephalography (event-related potentials: N100, P300), startle potentiation.
Carsten et al. (2022)	No (N), predictable (P), and unpredictable (U) threat (NPU-threat task, partially instructed)	Threat	Community (students)	IUS-12	Anxiety ratings, electroencephalography (event-related potentials: N1, P3), startle potentiation
Radoman and Gorka (2022)	Probabilistic reward anticipation (NPU-reward task, instructed)	Reward	Community with wide range of psychopathologies	IUS-12	Functional magnetic resonance imaging (connectivity)
Wiese et al. (2022)	Affective probabilistic anticipation and reactivity (S1-S2 task)	Positive and negative	Community (students)	IUS-12	Arousal and valence ratings, electroencephalography (event-related potentials: SPN, LPP)
Del Popolo Cristaldi et al. (2022)	Affective probabilistic anticipation and reactivity (S1-S2 task)	Positive and negative	Community (students with absence of psychopathology)	IUS-12 (Italian version)	Arousal ratings, electroencephalography (resting-state connectivity).
<b>Associative threat and safety learning</b>					
Klingelhöfer-Jens et al. (2022)	Threat conditioning (uninstructed acquisition, delayed extinction)	Threat	Community (absence of psychopathology)	IUS-27	Fear ratings, skin conductance response, startle potentiation
Mertens et al. (2022)	Threat conditioning (partially instructed acquisition)	Threat	Community (absence of psychopathology)	IUS-27	Fear ratings, skin conductance response, startle potentiation
Wendt and Morriss (2022)	Threat conditioning (uninstructed + instructed acquisition, immediate extinction)	Threat	Community (students with absence of psychopathology)	IUS-27	Valence ratings, arousal ratings, skin conductance response, functional magnetic resonance imaging
Wroblewski et al. (2022)	Threat conditioning (instructed acquisition, delayed extinction, reinstatement)	Threat	Community (absence of psychopathology)	IUS-27 (combined in cluster analysis with STAI-T)	US expectancy ratings, valence ratings, arousal ratings, skin conductance response, startle potentiation, functional magnetic resonance imaging
Lipp et al. (2022)	Threat conditioning (habituation, uninstructed acquisition)	Threat	Community (mixture of students)	IUS-12	Valence ratings, skin conductance response
<b>Action tendencies</b>					
Cobos et al. (2022)	Threat avoidance task (contingencies partially instructed)	Threat	Community (students)	IUS-27	Response frequency, avoidance confidence, relief ratings.
Kryptos et al. (2022)	Approach-avoidance four-bandit task	Threat	Community (absence of psychopathology)	IUS-27	Participants' choices, estimated model parameters
Wake et al. (2022)	Visual discrimination and checking task	No explicit valence	Community (student)	IUS-27	Self-reported anxiety, unpleasantness, urge-to-check; checking frequency, answer accuracy, reaction times; skin conductance response, corrugator supercilii activity
<b>Performance monitoring</b>					
Malbec et al. (2022)	Error-detection task (Eriksen flanker task)	No explicit valence	Community (student)	IUS-12	Electroencephalography (event-related potentials: ERN, CRN),
<b>Developmental and clinical populations</b>					
Michalska et al. (2022)	Incremental (0 %, 25 %, 50 %, and 100 %) threat task with fear faces as the aversive stimulus	Threat	Youth (8–17 years old) with (n = 19) and without (n = 33) anxiety disorders	Anxiety disorder	Functional magnetic resonance imaging
Newsome et al. (2022)	Threat conditioning (uninstructed acquisition, immediate extinction)	Threat	Youth and adults with anxiety disorders (n = 133) and healthy controls (n = 173)	Anxiety disorder	Fear ratings, skin conductance responses, ITI-normalised startle potentiation
Jovanovic et al. (2022)	Threat conditioning (uninstructed acquisition, immediate extinction)	Threat	Community youth (9 years old)	Contingency awareness during extinction	US expectancy ratings, startle potentiation
Beatty et al. (2022)	No (N), predictable (P), and unpredictable (U) threat (NPU-threat) task with female scream	Threat	Community youth (girls 13–22 years old) and one parent	IUS-12	Event-related potentials (N100 & P300), startle potentiation, accuracy, reaction time
Lees et al. (2022)	Decision task with varying probability (10–100 %) of varying rewards (1–10 points)	Reward	Community youth (7–11 years old)	Deliberation time during uncertainty of receiving reward	Skin conductance level
<b>Interventions</b>					
Papenfuss et al. (2022)	Mindfulness intervention; No (N), predictable (P), and unpredictable (U) threat (NPU-threat task, uninstructed)	Threat	Community (student)	IUS-12	Startle potentiation

uncertainty) or S1 cue providing no information (high uncertainty). The authors focused on two specific ERP components previously linked to emotional processing: Stimulus Preceding Negativity (SPN) which reflects anticipatory activity, and the Late Positive Potential (LPP) which reflects reactive activity. Anticipatory SPN for certain-positive and uncertain stimuli was negatively associated with overall intolerance of uncertainty scores, suggesting heightened affective anticipation. S2-evoked LPP on the other hand was positively associated with intolerance of uncertainty in both certain- and uncertain-negative conditions, highlighting its role in emotional reactivity to negative stimuli. The LPP effect was driven by the prospective intolerance of uncertainty subscale. All results remained significant after controlling for self-reported trait anxiety and stress.

Del Popolo [Cristaldi et al. \(2022\)](#) manipulated the probability by the affective congruency of the S1 and S2 images (non-predictive: 50 %, moderately predictive: 75 % and fully predictive: 100 %). The authors focused on investigating the relationship between resting-state functional connectivity (RS-FC), in-task event-related potentials (N170 - anticipation stage; LPP - reactivity) and intolerance of uncertainty. The properties of the resting state networks were first characterised using graph theory measures (strength, clustering coefficient and betweenness centrality). N170 source-localised to the right superior temporal sulcus had reduced strength metric with increasing intolerance of uncertainty - this was interpreted as reduced extraction of facial information (S1). During updating (S2), intolerance of uncertainty modulated the relationship between clustering coefficients in the bilateral orbitofrontal cortex (OFC) and in-task LPP - high intolerance of uncertainty was associated with reduced modulation of event-related potentials. This was interpreted as reduced top-down inhibition of affective processing of uncertain threat in high intolerance of uncertainty. Taken together, these studies provide evidence for intolerance of uncertainty-specific (controlling for other measures) modulation of anticipatory and reactive event-related potentials during affective tasks.

### 1.2. Associative threat and safety learning

Five articles examined the relationship between individual differences in intolerance of uncertainty and associative threat and safety learning. The articles used a variety of different associative threat and safety learning phases (e.g. acquisition, extinction learning, reinstatement) and measures (e.g. fMRI, startle potentiation (eye-blink reflex), skin conductance, and ratings).

For acquisition (learning a threat association between a cue (e.g. visual stimulus) and an aversive outcome (e.g. electric shock)), regardless of whether the phase was uninstructed or instructed, no significant relationships were observed between intolerance of uncertainty and psychophysiological ([Klingelhöfer-Jens et al., 2022](#); [Mertens et al., 2022](#)) or neural measures ([Wendt and Morriss, 2022](#); [Wroblewski et al., 2022](#)). However, during uninstructed acquisition, [Lipp et al. \(2022\)](#) observed in a large sample ( $n = 217$ ) that higher intolerance of uncertainty was associated with greater skin conductance response to omitted unconditioned stimuli (i.e., electric shock). In addition, during uninstructed acquisition, two of the articles found that higher intolerance of uncertainty was related to greater self-reported ratings of anxiety, fear, and distress to the threat vs. safe cue ([Klingelhöfer-Jens et al., 2022](#); [Mertens et al., 2022](#)).

For uninstructed extinction learning (updating a learned threat association to a safe association), [Wroblewski et al. \(2022\)](#) found that higher intolerance of uncertainty was associated with: (1) reduced neural responses (e.g. in the thalamus, putamen, dorsal anterior cingulate cortex, and ventrolateral prefrontal cortex), (2) larger discriminatory startle response to the threat vs. safety cue throughout the phase, and (3) larger discriminatory skin conductance response to the threat vs. safety cue at the beginning of the phase. During uninstructed extinction learning, [Klingelhöfer-Jens et al. \(2022\)](#) did not observe a significant effect of intolerance of uncertainty on startle or skin conductance

response, but did observe a trend for intolerance of uncertainty and self-reported ratings of anxiety, fear, and distress to the threat vs. safe cue. In an extinction learning phase with different instructions (e.g. no instruction about contingencies, instructions about contingencies), [Wendt and Morriss \(2022\)](#) reported no significant effects of intolerance of uncertainty on neural measures. However, [Wendt and Morriss \(2022\)](#) found some tentative evidence that higher intolerance of uncertainty was associated with larger skin conductance response to the safety cue during extinction generally and greater ratings of unpleasantness and arousal to the safety cue after extinction.

Lastly, two studies examined reinstatement (unsignalled presentation of the aversive stimulus, followed by the threat cue without reinforcement). [Klingelhöfer-Jens et al. \(2022\)](#) found that higher intolerance of uncertainty was associated with increased fear ratings to the threat cue relative to the safety cue during a reinstatement test. However, this association was not found with startle or skin conductance responses. Furthermore, [Wroblewski et al. \(2022\)](#) did not find reliable associations with intolerance of uncertainty and either subjective ratings or psychophysiological measures during the reinstatement test. Nonetheless, [Wroblewski et al. \(2022\)](#) did find individuals with low intolerance of uncertainty to exhibit increased neural activation in regions related to the salience network to the threat cue during reinstatement test.

Notably, for the associative threat and safety experiments, most of the significant effects of intolerance of uncertainty remained while controlling for other negative affectivity measures (e.g. trait anxiety) ([Lipp et al., 2022](#); [Klingelhöfer-Jens et al., 2022](#); [Mertens et al., 2022](#)). Although, it is worth noting that in the [Wroblewski et al. \(2022\)](#) study, individuals with high intolerance of uncertainty and high trait anxiety were grouped together.

### 1.3. Action tendencies

Three articles examined whether individual differences in intolerance of uncertainty modulated action tendencies that support uncertainty reduction (e.g. avoidance, approach, and checking). [Cobos et al. \(2022\)](#) examined the relationship between intolerance of uncertainty and avoidance by using a threat avoidance conditioning experiment with limited and unrestricted avoidance availability. Primary measures included frequency of avoidance, post-trial relief ratings from trials where the aversive outcome was omitted, and avoidance confidence ratings. The authors observed that higher prospective intolerance of uncertainty (a subscale related to the desire for predictability and an active engagement in seeking certainty) was associated with greater post-trial relief ratings during the avoidance acquisition phase to the threat cues and in the test phase when avoidance availability was limited to the threat cues. The authors observed specificity for the prospective intolerance of uncertainty subscale in predicting post-trial relief during the avoidance acquisition phase but not for the test phase when avoidance availability was limited to the threat cues. Although not significant, higher prospective intolerance of uncertainty was also related to greater avoidance frequency in the test phase when avoidance availability was unrestricted to the threat cues. These findings suggest that prospective intolerance of uncertainty may play an important role in modulating avoidance behaviour under uncertain threat.

[Kryptos et al. \(2022\)](#) examined how individual differences in intolerance of uncertainty may relate to the exploration-exploitation dilemma (EED). The authors used a computational modelling framework together with both frequentist and Bayesian correlation analyses. The results showed little support for any relationship between intolerance of uncertainty and the estimated parameters of the winning model. The only significant relationship identified was between a subscale of intolerance of uncertainty (i.e., tendency to become paralysed in the face of uncertainty) and the decay rate (i.e., forgetting the values of the different options the longer they had not been chosen). The authors outlined several experimental design modifications, which may be more optimal for examining relationships between intolerance of uncertainty

and EED.

Wake et al. (2022) explored individual differences in self-reported anxiety and obsessive-compulsive features (including intolerance of uncertainty) on subjective, behavioural, and physiological indices during a visual discrimination and checking task with unrestricted and restricted checking availability. Higher scores for the self-reported anxiety and obsessive-compulsive features (all of the measures) were associated with higher subjective ratings of unpleasantness and the urge to check during the task. Furthermore, higher self-reported anxiety and obsessive-compulsive features related to general negative affect, intolerance of uncertainty, and perfectionism were associated with greater checking frequency during the task. Lastly, stronger obsessional beliefs about perfectionism and the need for certainty were related to poorer accuracy, slower reaction times, and higher engagement of the corrugator supercilii during the task, particularly when checking was unavailable. Such findings suggest that different self-reported anxiety and obsessive-compulsive features, in particular perfectionism and the need for certainty, may relate to and maintain checking behaviour in low threat contexts.

#### 1.4. Performance monitoring

One article investigated whether individual differences in intolerance of uncertainty impacted performance monitoring processes. Malbec et al. (2022) used an Eriksen flanker task in a large sample ( $n = 188$ ) to measure performance monitoring related brain activity (event-related potentials: error-related negativity (ERN); correct-response negativity (CRN)) and behaviour (accuracy, reaction times). Results revealed little evidence for a significant relationship between intolerance of uncertainty and the ERN, task accuracy or task reaction times. However, a significant relationship between intolerance of uncertainty and the CRN was observed, such that higher intolerance of uncertainty scores were associated with a larger (i.e., more negative) CRN. The authors conclude that further high-powered replications are required to ascertain whether individual differences in intolerance of uncertainty reliably modulate performance monitoring processes.

#### 1.5. Developmental and clinical populations

Heightened anticipation of uncertain threat has been proposed to constitute a key process in psychopathology, and anxiety disorders in particular (Grupe and Nitschke, 2013). Furthermore, anxiety disorders typically emerge in childhood and adolescence (Beesdo et al., 2009). Five articles in the special issue focused on examining the role of intolerance of uncertainty (or putative markers of intolerance of uncertainty) on neural and psychophysiological responses (fMRI, ERPs, skin conductance response), and startle potentiation (eye-blink reflex). Michalska et al. (2022) used parametric manipulation of threat probability during fMRI in youth with and without anxiety disorders. The findings revealed that youth with anxiety disorders—compared with controls—exhibited greater activation in the ventrolateral prefrontal cortex in response to uncertain threat as well as altered scaling of ventral striatum-subgenual anterior cingulate cortex activation with threat probability. Such work begins to identify early-emerging aberrant function in circuitry contributing to threat uncertainty in anxiety.

Newsome et al. (2022) compared anxiety patients and control comparisons, from both youth and adult populations, in terms of physiological responding during an uninstructed threat conditioning and extinction task. Regardless of age, anxiety patients and controls exhibited comparable conditioning in terms of both skin conductance response and startle potentiation. For anxiety patients, compared to controls, startle potentiation to threat cue persisted throughout the extinction learning phase. Given the capacity of startle potentiation to capture sustained, uncertain-threat anticipation states, these findings suggest that anxiety-related difficulties in extinction could be more precisely captured when considering extinction as an uncertain-threat

state. Jovanovic et al. (2022) likewise examined associations between PTSD symptoms in children and startle potentiation during threat extinction learning. Among several findings, the authors show that threat uncertainty moderates associations between exposure to trauma and PTSD symptoms in children, such that awareness (certainty) of threat may potentially buffer against symptoms. These studies used putative markers of intolerance of uncertainty (for instance diagnosis of anxiety disorder rather than self-reported intolerance of uncertainty) and correlated them with brain or physiological activity during anticipation of threat, suggesting that there may be other ways in which to capture intolerance of uncertainty in different populations,

Exploring familial markers of self-reported intolerance of uncertainty, Beatty et al. (2022) studied a sample of female adolescents and their biological parents, recording startle potentiation and event-related potentials associated with anticipation of unpredictable threat. The authors report that parental prospective intolerance of uncertainty, but not participant prospective intolerance of uncertainty, correlates with greater startle potentiation and startle probe N100 enhancement during the anticipation of unpredictable threat. Finally, Lees et al. (2022) examined risky decision making in children as it relates to uncertainty and physiological responding. Their findings suggest that longer deliberation time before decision making is associated with skin conductance response and probability of offer rejection (i.e., avoidance), pointing to a potential role of decision uncertainty and behavioural outcomes.

Together, these studies examine a wide range of responses to potential, uncertain threat in youth, indexing attention, psychophysiological, behavioural, and neural responding, and symptomatology or symptom-relevant behaviour. The consistent revealed effects of uncertain threat encourage continued work on uncertainty in developmental and clinical populations.

#### 1.6. Interventions

One paper investigated the effect of a two-week mindfulness training on startle potentiation, intolerance of uncertainty, and other self-reported anxiety-related dimensions (social anxiety, worry etc.) (Papenfuss et al., 2022). Participants completed two sessions, two-weeks apart, during which they performed NPU-threat task, as well as a battery of questionnaires. Participants were assigned into two groups: mindfulness and control. In between the two sessions, participants in the mindfulness group completed a daily 10-min mindfulness practice. At pre-intervention, higher inhibitory intolerance of uncertainty was associated with greater startle potentiation to the unpredictable threat cue. In addition, the authors reported a significant effect of the intervention on reducing social anxiety symptoms and intolerance of uncertainty scores but no significant effect on startle responses. Moreover, intolerance of uncertainty significantly mediated the effect of the intervention on reducing symptoms of social anxiety and worry.

## 2. Discussion

The special issue has highlighted that a variety of experimental paradigms can be used to induce different aspects of uncertainty (e.g. risk and ambiguity) and valence (e.g. threat, reward, negative, and positive spaces) together. All of the studies examined individual differences in intolerance of uncertainty under risk to some extent (e.g. where contingencies denoting uncertainty are known through instruction) (Kobayashi and Hsu, 2017; Payzan-LeNestour and Bossaerts, 2011). Furthermore, a handful of studies using fear conditioning paradigms examined individual differences in intolerance of uncertainty under ambiguity (e.g. where contingencies associated with uncertainty are unknown but may be learned through experience) (Morriss et al., 2021). Additionally, the special issue demonstrated that intolerance of uncertainty may be operationalised and captured using a variety of measures (e.g. self-report questionnaires using the total IU score or IU subscales, other putative markers through behavioural and subjective ratings) and



in different populations (e.g. community, developmental, clinical).

Importantly, the findings from the special issue suggest that despite methodological differences within and across the domain of study (e.g. anticipation of threat and reward, action tendencies etc) and differences in sample population (e.g. clinical, developmental), intolerance of uncertainty is specifically involved in modulating several neural and psychophysiological metrics, as well as action tendencies, and self-reported feelings/emotions. Notably, the findings from the special issue point towards expanding the role of intolerance of uncertainty (and uncertainty more broadly) in the research domain criteria framework (RDoC) (Insel et al., 2010; Insel, 2014). Currently, within the RDoC framework, intolerance of uncertainty is positioned as a self-report unit of analysis under the construct of negative valence systems and the subconstruct of potential threat (“anxiety”). However, the findings here suggest that intolerance of uncertainty is likely involved in many more RDoC framework constructs (e.g. positive valence systems, cognitive systems) and negative valence based subconstructs (e.g. acute threat (“fear”) and frustrative nonreward). Interestingly, in recent examinations of self-report units of analysis for negative valence systems within the RDoC framework, intolerance of uncertainty has been left out (Hasratian et al., 2022; Watson et al., 2017). Although, the research reported in this special issue indicates that intolerance of uncertainty may be one of the more dominant self-report units of analysis for negative valence systems within the RDoC framework.

While the broad extent of conceptual and methodological variability across the special issue highlights the wide-ranging relevance of intolerance of uncertainty to many processes, this variability also calls for efforts towards systematic investigation and operationalisations of intolerance of uncertainty on different outcome measures and within diverse sample populations (e.g. other samples from around the world; Kumar et al., 2021; Yao et al., 2021; and within non WEIRD samples; Bradford et al., 2022). Systematic investigations through cross-lab collaboration efforts, large-scale replication endeavours, and preregistration and standardisation of some methodological approaches will facilitate reproducibility (Baldwin, 2017). Furthermore, conducting such systematic investigations within a given domain of study (e.g. anticipation of threat and reward, action tendencies etc), or across domains of study, will likely be informative for more accurately representing intolerance of uncertainty within the RDoC framework (Insel et al., 2010; Insel, 2014) and other current and novel transdiagnostic models of psychopathology (e.g. how intolerance of uncertainty fits into the internalising spectra within the Hierarchical Taxonomy of Psychopathology (Kotov et al., 2017)).

In summary, we hope that this collection of novel scientific insight provides a strong foundation for the further development of new research questions, methods, and perspectives on individual differences in intolerance of uncertainty.

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