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Threat and Uncertainty in the Face of Perceptual Decision-Making in Anxiety

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Anxiety is defined as an anticipatory response to uncertain, future threats. It is unknown how anticipatory information regarding uncertainty about upcoming threatening and neutral stimuli impacts attention and perception in anxiety. Individuals with and without anxiety disorders performed two perceptual decision-making tasks in which they used threat or neutral prestimulus cues to discriminate between subsequent threatening and neutral faces. In one task, cues provided no probability information (high uncertainty). In the other, cues indicated a high probability of encountering threatening or neutral faces (low uncertainty). Under high uncertainty only, anxious apprehension was associated with worse discrimination between threatening versus neutral faces after threat cues. Additionally, anxious arousal was associated with worse discrimination after neutral cues in individuals with anxiety disorders. These findings will advance the field by spurring the development of more comprehensive and ecologically valid models in which anticipatory top–down factors influence threat perception in anxiety.

General Scientific Summary
Anxiety is characterized by anticipation of potential future threats; however, our understanding of threat-related perception in anxiety is almost entirely based on responses to threats that are acute or present. In the real-world, rather than solely reacting to threatening stimuli, we use prior knowledge such as cues and contexts to anticipate and detect threatening stimuli in our environment. Our study shows how anxiety is associated with worse utilization of prior knowledge when detecting threatening versus nonthreatening stimuli under uncertain conditions.

Keywords: perception, decision-making, anxiety, uncertainty, threat

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The National Institute of Mental Health (NIMH) and the *Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition* (*DSM–5*) define anxiety as a response to potential threat as opposed to acute, current threat, emphasizing the anticipatory nature of anxiety (American Psychiatric Association, 2013; National Institute of Mental Health, n.d.). This view has a long history in the clinical literature, with anxiety being defined as an anticipatory response to possible, but uncertain, future threats (e.g., Barlow, 2000; Grupe & Nitschke, 2013; Sarinopoulos et al., 2010). Although this definition of anxiety clearly focuses on anticipatory factors, our empirical understanding of perceptual and attentional processes in anxiety is almost entirely based on behavioral or neural responses to acute rather than potential threat (Bar-Haim et al., 2007; Bradley et al., 1999; Cisler & Koster, 2010; MacLeod et al., 1986). This has resulted in a disconnect between clinical conceptualizations of anxiety, which highlight the importance of anticipatory top–down factors (e.g., prestimulus cues, schemas, and expectations), and our understanding of attention and perception in anxiety as being driven by involuntary, bottom–up attentional capture by threatening stimuli (Öhman et al., 2001; Sussman, Jin, & Mohanty, 2016). To reconcile this gap, we examined how anticipatory factors influence perceptual decision-making in anxiety. We focused on perceptual decision-making because it is the basic process by which available sensory information is gathered and the identity of a stimulus is decided (Heekeren et al., 2008), and such decisions have critical downstream consequences for higher-order cognition and behavior.

Three overarching points highlight the importance of examining top–down factors in perceptual decision-making in anxiety. First, individuals usually experience threats in familiar environments where

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they possess prior knowledge regarding relevant and probable stimuli, and individuals frequently use their learning and prior knowledge to detect threats. For example, when cues such as park signs warn us to look out for rattlesnakes or road signs warn us to look out for black ice, we use such cues to help us detect upcoming threatening stimuli. Similarly, a socially anxious person who has been told to expect overcritical audience members when giving a presentation may use such top–down information to discriminate between critical and neutral audience members' facial expressions. Further, socially anxious persons may utilize such top–down information differently than a less anxious individual when making the same kind of decisions. Although earlier studies have examined top–down attentional factors in anxiety, such factors were orthogonal or irrelevant to threat perception and were studied by directing attention or working memory resources away from emotional targets (e.g., Bar-Haim et al., 2007; Cisler & Koster, 2010), rather than voluntarily guiding attention toward threatening targets. Additionally, studies have investigated physiological responses during threat anticipation (e.g., Schmitz & Grillon, 2012) but have failed to examine the impact of this anticipation on perception.

Empirically, the visual perception literature has investigated the role of prior knowledge via manipulation of prestimulus cues or contexts that facilitate perceptual decision-making by providing prior information regarding the relevance and probability of upcoming stimuli (Summerfield & De Lange, 2014). According to the predictive coding framework, prior knowledge assists the inference of the cause of sensory input, leading to perception (Friston, 2012). Furthermore, recent research shows that threat cues enhance subsequent perceptual decision-making to a greater extent than neutral cues (Glasgow et al., 2020; Imbriano et al., 2020; Sussman et al., 2016, 2017). Because anxiety is characterized by inflated estimates regarding the probability of encountering upcoming threats (Aue & Okon-Singer, 2015; Butler & Mathews, 1987; Nelson et al., 2010; Stöber, 1997), prestimulus threat cues may guide perceptual decision-making differently in anxiety; however, this has not been empirically investigated.

Second, exaggerated threat expectations in anxiety are primarily observed under uncertainty (Carleton, 2016; Cisler & Koster, 2010; Grupe & Nitschke, 2013). For example, trait anxiety is positively associated with greater probability estimates of negative events under uncertainty (e.g., Stöber, 1997), and human and animal research show that uncertain environments and events are linked with aberrant fear learning and increased physiological threat reactivity (Grillon et al., 2004; Grupe & Nitschke, 2013; Servatius & Shors, 1994). Although these findings bolster the view that uncertainty is integral to anxiety, there is a paucity of research investigating how anticipation and elevated expectations regarding uncertain future threat influence subsequent perceptual decision-making in anxiety.

Finally, adaptive interactions with our environment are contingent upon effective use of information, not only regarding impending threat, but also possible safety. Individuals with elevated anxiety may differ in how they use prior knowledge regarding safe or neutral stimuli when making similar perceptual decisions. Empirically, anxiety is linked with a decreased ability to utilize safety versus threat cues during fear learning (Gazendam et al., 2013), and individuals with greater anxiety tend to respond in a threat-congruent manner to cues indicative of safety (Grillon et al., 2008). Therefore, anxiety is characterized by the inability to correctly identify and utilize safety information, resulting in maladaptive threat-relevant responses to neutral or safe environments (see Brosschot et al., 2016). However, the utilization of anticipatory neutral information in perceptual decision-making in anxiety remains underexplored.

In summary, anxiety is characterized by exaggerated estimation of threat under conditions of uncertainty and worse utilization of safety cues. However, the role of anticipatory threatening, neutral, and uncertainty-related information in subsequent discrimination between threatening and neutral stimuli has not been elucidated in anxiety. In the present study, we utilized a transdiagnostic approach to examine relationships of different dimensions of anxiety—anxious apprehension (e.g., worry) and anxious arousal—with perceptual decision-making across a sample of individuals diagnosed with and without anxiety disorders. These anxiety dimensions were chosen because evidence indicates that they involve separable psychological and neural mechanisms (Sharp et al., 2015), warranting an examination of their differential effects on perceptual decision-making.

In this study, participants performed two forced-choice two-alternative perceptual decision-making tasks wherein they used prestimulus threat and neutral cues to discriminate between subsequent threatening and neutral faces. In one task, threat and neutral cues provided no information regarding the probability of encountering upcoming faces. In the other task, each cue indicated a high probability of subsequently encountering one of the two face types. As a lack of probability-related information is definitionally more uncertain than the provision of probability-related information (Hartley & Phelps, 2012), we will refer to the former task as the High Uncertainty Cue (HUC) task and the latter task as the Low Uncertainty Cue (LUC) task. In our study, the cues represent a top–down manipulation, because they provide information about upcoming stimuli that are relevant or likely. By using these cues when making perceptual decisions, participants are not relying solely on physical characteristics or salience of the presented stimuli. Specifically, the cues provide information about the relevance (threatening or neutral) and probability of encountering upcoming targets, just as in the real world where cues and contexts indicate what types of potentially upcoming stimuli (e.g., threatening or neutral) are probable, likely, or relevant. Overall, by manipulating both the salience of the stimuli and the prestimulus cues that indicate information about upcoming stimuli, we are utilizing a plausibly ecologically valid paradigm to examine how humans make decisions in their day-to-day life.

In line with earlier studies (Glasgow et al., 2020; Imbriano et al., 2020; Sussman et al., 2016, 2017), we hypothesized that prestimulus threat cues would lead to more sensitive perceptual decision-making than neutral cues overall in both tasks. As anxiety is associated with exaggerated expectations regarding threatening stimuli as well as deficient utilization of neutral information—especially under uncertain conditions—we hypothesized that higher levels of anxiety would be associated with worse discrimination between threatening and neutral faces after both prestimulus threat and neutral cues, but only in the HUC task.

Method

Participants

To determine an appropriate sample size for our study, we ran power analyses using G*Power (Faul et al., 2009). Given our prior work examining the effect of fear cues versus neutral cues on perceptual sensitivity in unselected participants (Sussman et al., 2016), power analyses revealed that 30 subjects would be needed to observe similarly large task-related effects. No study has examined relationships between self-report measures of anxious apprehension and anxious arousal with fear cue versus neutral cue perceptual sensitivity across individuals diagnosed with and without anxiety disorders. Hence, we based our power analyses on the relationship between perceptual sensitivity following fear cues and the interaction between trait anxiety and experimentally induced anxiety (Sussman et al., 2016). Using G*power, we found that we would have 80% power to detect an effect of f^2 = .339 between trait anxiety and fear cue-related *d'* with 47 participants. To detect an interaction f^2 of .372 between case status and trait anxiety with a power of 80%, we would need a sample size of 49.

To attempt to plausibly capture adequate variance in the dimensional anxiety measures within the case group, we recruited 98 participants (see Table 1). Nineteen participants were unable to complete the LUC task due to time constraints. To handle missing data in the LUC task that occurred due to task noncompletion, multiple imputation was implemented using IBM SPSS Statistics (Version 26; IBM Corp., 2019). Two hundred imputations were used to ensure both precise parameter estimates as well as more replicable standard error estimates (e.g., Von Hippel, 2020). All variables in our regression models were utilized to impute the missing data (He, 2010). Reported LUC task results reflect the values from the pooled results. Analyses conducted using the originally collected data yielded the same pattern of results. In both tasks, four different participants were excluded from analyses due to extreme behavioral performance, defined as scores ± 3 *SD* from the mean or overall task accuracy below 50%. Thus, a total of 94 participants were included in HUC and LUC analyses, respectively.

Participants were recruited from Stony Brook University and the surrounding community via fliers and electronic advertisements. Informed consent was obtained from every participant in accordance with the study protocol approved by the Stony Brook University Institutional Review Board. The recruitment and assessment protocols were designed to (a) offset issues with convenience sampling, and (b) maximize the variance in anxious arousal and anxious apprehension levels in the study sample. Specifically, to reduce issues related to convenience sampling, we recruited participants from several different outpatient psychology and psychiatry clinics at Stony Brook University, Stony Brook hospital, and the surrounding community centers and organizations using electronic and print advertisements. Stony Brook undergraduate and graduate students were also recruited for the study using similar recruitment materials. Participants completed a structured interview and questionnaires in the initial session and completed the behavioral tasks in the second session. All behavioral data was collected as part of a broader functional magnetic resonance imaging (fMRI) study. Imaging data are still being processed and will be presented in a separate article. See Table 1 for demographic and descriptive information.

Clinical Measures

Structured Diagnostic Interview for DSM–5–Research Version (SCID-5–RV)

The SCID-5–RV is a semistructured diagnostic interview that assesses clinical disorders as defined by the *DSM–5* (First et al., 2015). The patient overview, core screener, psychosis screener, anxiety disorders module, and posttraumatic stress disorder (PTSD) module were administered to all participants to examine eligibility for study participation. To reduce potential confounds, participants were excluded if they (a) endorsed symptoms of psychosis, (b) reported clinically elevated substance use, or (c) had a history of traumatic brain injury or neurological illness, as such symptoms and experiences are related to changes in perceptual processes and working memory (see Christodoulou et al., 2001; Cousijn et al., 2014; Underwood et al., 2016). As depression-related symptoms have also been linked with changes to working memory and perceptual processes, we partialed out variance in depression-specific symptoms in our models by

Table 1
Demographic Information and Descriptive Statistics

Characteristic/measure	Controls (*n* = 35)	Cases (*n* = 63)	Test statistic
Age (*M*, *SD*)	22.60 (8.72)	22.68 (8.09)	*t* = −.044
Gender (% female)	54.30	71.4	χ^2 = 3.912
Race (%)			χ^2 = 3.535
White	40.0	44.4	
Black	2.9	6.4	
Asian	37.1	22.2	
Multiracial	5.7	12.7	
Unknown/unreported	14.3	14.3	
Clinical questionnaires (*M*, *SD*)			
MASQ-AA	24.63 (9.68)	31.26 (12.11)	*t* = −2,774*
MASQ-AD	16.09 (6.33)	21.52 (7.72)	*t* = −3.540*
STAI-T	40.17 (10.16)	55.94 (10.14)	*t* = −7.347***
SCID-5 primary diagnoses (*n*, %)			
GAD		30 (31.9)	
SAD		30 (31.9)	
PD		3 (3.2)	

Note. MASQ-AA = Anxious Arousal subscale of the Mood and Anxiety Symptoms Questionnaire; MASQ-AD = Anhedonic Depression subscale; STAI-T = Trait subscale of the State-Trait Anxiety Inventory; SCID-5 = Structured Diagnostic Interview for *Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition*; GAD = generalized anxiety disorder; SAD = social anxiety disorder; PD = panic disorder. Independent-samples *t* tests were utilized to examine potential differences in continuous measures between cases and controls. Chi-squared tests were conducted to examine differences in the frequency of self-reported race and gender between cases and controls.
* $p < .05$. *** $p < .001$.

using the Anhedonic Depression subscale of the Mood and Anxiety Symptoms Questionnaire (MASQ-AD), as described below. Controls were defined as participants not diagnosed with any anxiety disorder or PTSD. Cases were defined as participants who met criteria for at least one of the following anxiety disorders: generalized anxiety disorder, social anxiety disorder, panic disorder with or without agoraphobia. We focused on these three disorders because they show the most variance in anxious apprehension and anxious arousal dimensions (Brown et al., 1998). SCIDs were administered by three trained graduate students and two trained postbaccalaureate research assistants. SCID administration was supervised by the principal investigator. Primary diagnoses for cases are listed in Table 1.

Mood and Anxiety Symptoms Questionnaire (MASQ)

Two subscales were used from the MASQ (Nitschke et al., 2001; Watson & Clark, 1991): the anxious arousal subscale (MASQ-AA; 17 items) and the short-form of the anhedonic depression subscale (MASQ-AD; eight items), which was specifically designed to assess for depressed mood (Nitschke et al., 2001). These subscales have been shown to successfully differentiate unique variance in anxious arousal versus anhedonic depression. The MASQ-AA subscale measures physiological symptoms of anxiety, whereas the MASQ-AD subscale measures low positive affect and loss of interest specific to depression. Anxious arousal is associated with frequent hypervigilance for threat and elevated physiological symptoms when such threat is perceived (Sharp et al., 2015). The MASQ-AA and MASQ-AD subscales have been shown to better differentiate symptoms specific to anhedonic depression from symptoms specific to anxious arousal compared with other measures of anxiety and depression (Nitschke et al., 2001). The ability of these two subscales to measure anhedonic depression-specific and anxious arousal-specific symptoms in comparison to other measures has been observed in both a college sample as well as a sample comprised of clinical cases and controls (Boschen & Oei, 2006; Nitschke et al., 2001).

State–Trait Anxiety Inventory–Trait Subscale (STAI-T)

The STAI-T (20 items) is a widely used subscale of the State–Trait Anxiety Inventory that purportedly measures trait-like anxiety (Spielberger et al., 1983), including negative thought patterns associated with anxious pathology (e.g., worry, concerns about the future; Nitschke et al., 1999). This scale is considered to be more representative of anxious apprehension than anxious arousal (Heller & Nitschke, 1998; Heller et al., 1997; Nitschke et al., 1999; Nordahl et al., 2019; Sharp et al., 2015); and has been shown to be highly correlated with other measures of anxious apprehension, including the Penn State Worry Questionnaire (Crittendon & Hopko, 2006; Fajkowska et al., 2017; Hofmann et al., 2005). Because the STAI-T is also considered to be a measure of negative affect, general distress, or vulnerability to psychopathology (Nitschke et al., 2001; Nordahl et al., 2019), we partialed out variance associated with anhedonic depression in all of our models. Thus, in the present study, the STAI-T was used to measure variance associated with anxious apprehension.

Stimuli

Thirty-two faces were obtained from the Nim Stim Face Set (Tottenham et al., 2009), for a total of 16 fearful faces and 16 neutral faces. To allow us to examine the top–down effects of cues, we controlled for low-level image properties, including luminance, pixel size (512 × 512), and spatial frequency using the Spectrum, Histogram, and Intensity Normalization Equation (SHINE) toolbox for MATLAB (Willenbockel et al., 2010). Controlling for such low-level image properties allows for better examination of top–down influences in face perception (Fiset et al., 2008). Poststimulus masks were generated by deconstructing several face images displaying different emotional expressions into100-pixel squares and randomly rearranging these pixels into a single image. Thus, the poststimulus masks were specifically generated to contain similar low-level image properties as the target face stimuli. Finally, we utilized fearful rather than angry faces for our stimuli, as prior work has demonstrated that fearful faces are rated as more threatening (Taylor & Barton, 2015) and provoke greater activation in threat-related neural circuits (Whalen et al., 2001).

Thresholding Task

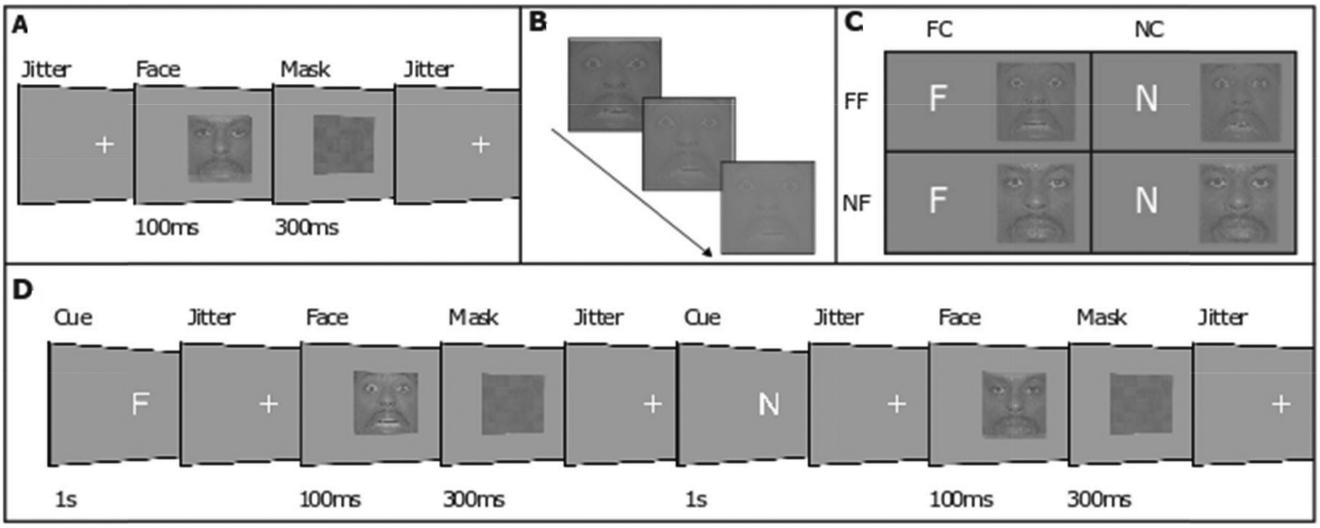
The perceptual thresholds (75% accuracy) for fearful and neutral faces for each participant were separately approximated using a two-alternative forced-choice perceptual decision-making task, similar to the paradigm utilized by Summerfield and colleagues (Summerfield et al., 2006). This thresholding task consisted of eight blocks of 32 (16 fearful faces, 16 neutral faces) trials, for a total of 256 trials presented in random counterbalanced order. At trial onset, a fixation cross appeared, which was jittered for 2 to 6 s. The fixation cross was followed by the presentation of either a fearful or neutral face (100 ms), which was followed by a stimulus mask (300 ms). Subsequent to stimulus presentation, participants decided whether the face was fearful or neutral using one of two alternative buttons on a button box. See Figure 1 for a visualization of the thresholding task timeline.

The contrast level at which each target stimulus was presented ranged from 100% to 0%, with 100% corresponding to full contrast and 0% corresponding to no contrast, resulting in the presentation of the stimulus image as a gray square. The contrast values for fearful and neutral faces were each initially presented at 10% contrast, such that the face stimulus was purposefully difficult to see on the first trial for each face type. The contrast value at which subsequent fearful and neutral faces were presented was determined by response accuracy, such that, after correct identification of a fearful or neutral face, the next trial of that face type was presented at a lower contrast value (i.e., the face was more difficult to see). Conversely, after an incorrect response, the next trial of that face type was presented at a greater contrast value (i.e., the face was easier to see). Contrast degradation for fearful and neutral faces was manipulated separately using two adaptive staircases based on the QUEST algorithm, which can be used to approximate the Bayesian estimate of the perceptual threshold of fearful and neutral faces for each participant (Watson & Pelli, 1983). Psychopy was used for data collection and task presentation (Peirce, 2007).

Cued Facial Affect Discrimination Tasks

After completing the thresholding task, subjects completed two separate cued facial affect discrimination tasks (see Figure 1), which were identical in task timeline except for three key differences. First, the face stimuli were perceptually degraded and presented at any contrast level ranging from −6% to 8% around the

Figure 1
Task Timelines



Note. (A) Example of a single trial in the threshold task. (B) Image contrasts of fearful (FF) and neutral faces (NF) were adjusted in the threshold task using two adaptive staircases. Perceptual thresholds (75% accuracy) were approximated for FF and NF. (C) Cue and stimulus pairs in the High Uncertainty Cue (HUC) and Low Uncertainty Cue (LUC) tasks consisted of FF after fear cues (FC) and neutral cues (NC), and NF after FC and NC. (D) Example of two trials in the HUC task. Participants were asked to respond to perceptually degraded FF and NF after viewing either an FC or NC. Timeline of the LUC task was identical, except that cue letters were blue instead of light gray. Faces in this figure, as well as faces used in the tasks described in the article, are from the Nim Stim Face Stimulus Set (Tottenham et al., 2009), which is a publicly available set of faces displaying different facial expressions. The actor in the stimuli in the above figure consented to have his picture used in scientific publications.

participant's previously determined perceptual threshold (Adini et al., 2004; Sussman et al., 2016, 2017). For example, if a participant's threshold for fearful faces was determined to be .1 in the thresholding task, they were subsequently shown images ranging from .108 to .094 in the cued task. Stimuli were shown at several contrast levels to experimentally control for practice effects (Sussman et al., 2016, 2017). Second, before each face stimulus, participants were shown either a fearful (FC) or neutral (NC) cue (1,000 ms) to aid their perceptual decision-making. The perceptually degraded face stimuli along with preceding cues were designed to encourage participants to use cue-related perceptual sets when making decisions about whether the faces were fearful or neutral. Lastly, there were four blocks with 20 fear cue and 20 neutral cue trials per block, resulting in a total of 160 trials (80 fear cue and 80 neutral cue trials) across the task. Only 128 cued trials were followed by degraded face stimuli, resulting in a total of 64 fearful face trials and 64 neutral face trials. The remaining 32 trials were catch trials in which cues were not followed by faces. Catch trials were included in this experiment for the purposes of neuroimaging data collection; however, these trials were not included in the behavioral analyses described in this article and will not be described in further detail.

High Uncertainty Cue (HUC) Task

In this task, cues were not predictive of upcoming face types. As such, there was an equal probability of a fearful or neutral face presentation after both fear and neutral cues on noncatch trials. Participants were not informed of this relationship between cues and subsequent faces. However, the cues did indicate the type of decision to be made, with fear cues indicating a decision of "fearful or not," and neutral cues indicating a decision of "neutral or not." Decisions were made with two alternative keys on a button box, which were labeled "Y" and "N," where a "Y" decision indicated a "yes" that the target facial expression matched the emotion indicated by the preceding cue, whereas an "N" decision indicated a "no," in that the target facial expression did not match the emotion indicated by the preceding cue. See Figure 1 for a visualization of the cue task timeline.

Low Uncertainty Cue (LUC) Task

The second cue task was identical to the first cue task, except that the cues provided information not only about the type of decision to be made, but also the probability of encountering fearful or neutral faces. Participants were informed that, after a fear cue, a subsequent fearful face was "highly likely," and after a neutral cue, a subsequent neutral face was highly likely. In reality, after fear cues, there was a 75% chance of a fearful face, and a 25% chance of a neutral face. Similarly, after neutral cues, there was a 75% chance of a neutral face, and a 25% chance of a fearful face. Thus, in this version of the cue task, the cues validly indicated a higher probability of encountering either fearful or neutral faces, and participants were generally informed of this relationship. The contingencies between cues and subsequent face types, as well as the additional instructions to participants, were the only differences between the first cue task and the second cue task, with the exception of cue letter color, which was blue instead of light gray.

As unlearning of these probabilistic relationships would be required if the LUC task was presented before the HUC task, we used a fixed task order for all subjects, in which the HUC task (i.e., the task where there was no relationship between cues and subsequent faces) was always administered before the LUC task.

Participant-Level Signal Detection Theory (SDT) Parameters

For both cue tasks, *d'* (*Z*(*hit rate*) – *Z*(*false alarm rate*)) was computed separately for responses to fearful and neutral faces after fear and neutral cues, respectively, for each participant. *d'* represents perceptual sensitivity (i.e., discriminability) between the distinct distributions of two different stimulus types (i.e., the signal distribution and the noise distribution; Stanislaw & Todorov, 1999). Thus, in this study, *d'* after fear or neutral cues represents participants' abilities to differentiate between subsequently presented face types, where fearful faces were the signal stimuli after fear cues, and neutral faces were the signal stimuli after neutral cues.

Group-Level Analyses

A similar analytical strategy was implemented for both cue tasks. Overall task effects were examined in each task by comparing *d'* after fear versus neutral cues across all participants using paired *t* tests. Given that the tasks were administered in a fixed order to avoid carry-over effects of the LUC task instructions, we did not compare cue effects between the two tasks, as such comparisons would not be easily interpretable. However, for thoroughness, these comparisons have been reported in the online supplemental materials under Supplementary Results. To examine the effect of anxiety on behavioral performance, two separate hierarchical linear regression models were conducted predicting *d'* after fear cues and neutral cues, respectively. In these models, variables were entered in four steps in the following order: (1) age and gender; (2) scores on the MASQ-AA, STAI-T, and MASQ-AD, and case status; (3) the interaction between MASQ-AA and case status; and (4) the interaction between STAI-T and case status. MASQ-AA, MASQ-AD, and STAI-*t* scores were mean-centered before inclusion. The effects of MASQ-AA and STAI-T on *d'* independent of MASQ-AD, age, and gender were of primary interest. The interaction terms were included to determine if the relationship of MASQ-AA and STAI-T on *d'* varied as a function of anxiety disorder diagnosis (i.e., case status). An examination of QQ plots showed that the residuals for fear cue and neutral cue *d'* were normally distributed in both tasks.

As *d'* incorporates both hit and false alarm rates (HR; FAR) described above, follow-up hierarchical linear regression models predicting hit rate and false alarm rate separately were conducted for all hierarchical regression models that revealed relationships between anxiety measures and *d'*. These follow-up regression models utilized identical steps and predictors as those described above to further elucidate underlying relationships between perceptual decision-making and anxiety.

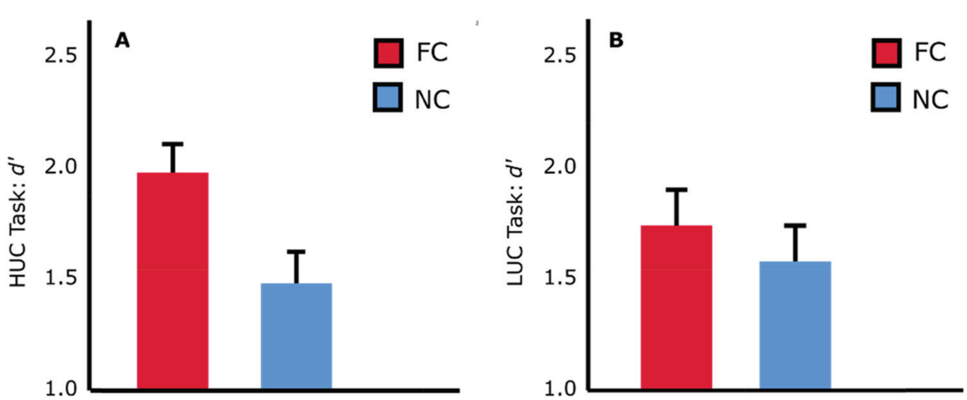
Results

Sample Characteristics

Sample demographics and clinical variables for cases and controls are presented in Table 1. Compared with controls, cases showed higher MASQ-AA, MASQ-AD, and STAI-T scores. Age was not different between cases and controls, and frequencies of self-identified race and gender did not differ between cases and controls. Age and gender were included in step one of each hierarchical linear regression model to control for these demographic factors.

To assess task reliability, we computed the split-half reliability for FC and NC *d'* in each task. Our split-half reliability analyses revealed good reliability in both tasks (HUC task: Spearman-Brown coefficient = .883; LUC task: Spearman-Brown coefficient = .848). Additionally, because reliability of difference scores may differ (Rodebaugh et al., 2016), we computed the split-half reliability for the difference between FC minus NC *d'* within each task. The split-half reliability of the difference scores revealed low and moderate split-half reliability of FC minus NC *d'* in both tasks, respectively (HUC task: Spearman-Brown coefficient = .532; LUC task: Spearman-Brown coefficient = .699).

Figure 2
HUC Task: FC Versus NC d'



Note. (A) *d'* after fear cues (FC) and neutral cues (NC) across all participants in the High Uncertainty Cue (HUC) task. (B) *d'* after FC and NC across all participants in the Low Uncertainty Cue (LUC) task. In both panels, the red (dark gray) bar indicates FC, and the blue (light gray) bar indicates NC. Error bars represent 95% confidence intervals (CIs). See the online article for the color version of this figure.

High Uncertainty Cue Task

Influence of FC and NC on Speed and Sensitivity of Perceptual Decision-Making

In accordance with our hypotheses, results revealed an effect of cue type on *d'*, such that *d'* after fear cues (M = 1.981, SE = .091) was greater than *d'* after neutral cues (M = 1.483, SE = .101), t = 5.161, $p < .001$, d = .534, 95% confidence interval (CI) of d = −1.077, 1.981 (see Figure 2). Thus, discriminability between fearful and neutral faces was enhanced after fear cues. These results were observed under conditions of high uncertainty, when the cues indicated which stimuli (fearful or neutral faces) were relevant, but the cues did not indicate the probability of encountering these subsequent stimuli. For response time results and comparisons of overall cue effects between tasks, see online supplemental materials under Supplementary Results and Supplementary Discussion.

Relationship Between Anxiety and Perceptual Decision-Making After FC

Next, we examined the effects of different anxiety dimensions on *d'* after fear cues. Hierarchical linear regression analyses (see Table 2) showed that age (B = .030, p = .013) and STAI-T (B = −.021, p = .034) but not MASQ-AA (B = .016, p = .121), MASQ-AD (B = −.019, p = .265), or case status (B = .380, p = .106), accounted for variance in FC *d'* (see Figure 3). Additionally, the interaction between MASQ-AA and case status (B = −.011, p = .543) as well as STAI-T and case status (B = .012, p = .542) did not account for variance in FC *d'*. Thus, our results revealed that higher STAI-*t* scores were associated with worse discriminability between fearful and neutral faces after FC across individuals with and without anxiety disorders.

Follow-up hierarchical linear regression models predicting hit rate and false alarm rate separately after fear cues revealed that

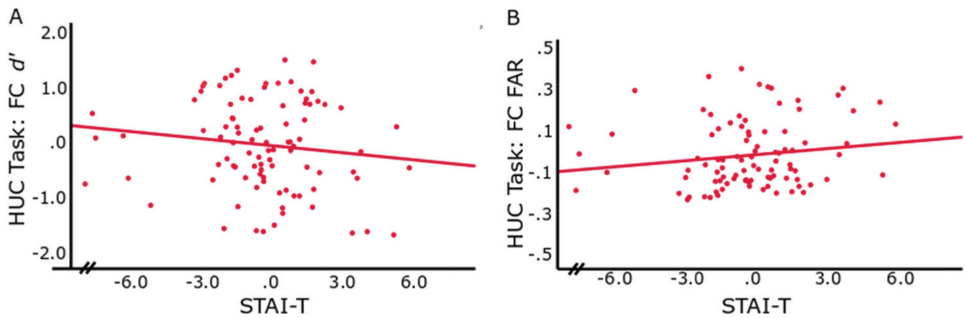
Table 2
Perceptual Sensitivity (d'): Hierarchical Regression Models

Task	DV	Step	Predictor	*B*	*t*-value	*p*-value
HUC	FC *d'*					
		1	Age	.030	2.540	.013
			Gender	−.215	−1.282	.203
		2	MASQ-AA	.016	1.565	.121
			Case status	.380	1.633	.106
			STAI-T	−.021	−2.154	.034
			MASQ-AD	−.019	−1.123	.265
		3	MASQ-AA × Case Status	−.011	−.611	.543
		4	STAI-T × Case Status	.012	.612	.542
HUC	NC *d'*					
		1	Age	.031	2.416	.018
			Gender	−.362	−1.985	.050
		2	MASQ-AA	.009	.798	.427
			Case status	.551	2.153	.034
			MASQ-AD	−.018	−.964	.338
			STAI-T	−.015	−1.405	.164
		3	MASQ-AA × Case Status	−.058	−2.983	.004
		4	STAI-T × Case Status	.001	.036	.971
LUC	FC *d'*					
		1	Age	.009	.552	.581
			Gender	−.290	−1.171	.242
		2	MASQ-AA	.026	−.882	.064
			Case status	.107	.353	.724
			STAI-T	−.001	−.036	.971
			MASQ-AD	−.030	−1.081	.280
		3	MASQ-AA × Case Status	.025	.653	.514
		4	STAI-T × Case Status	−.013	−.491	.623
LUC	NC *d'*					
		1	Age	−.011	−.567	.571
			Gender	−.275	−.901	.368
		2	MASQ-AA	−.025	−1.463	.144
			Case status	.265	.732	.464
			STAI-T	−.025	−1.260	.208
			MASQ-AD	.035	1.048	.295
		3	MASQ-AA × Case Status	.080	1.753	.080
		4	STAI-T × Case Status	−.054	−1.725	.085

Note. B = unstandardized regression coefficients; DV = dependent variable; FC = fear cue; NC = neutral cue; HUC = High Uncertainty Cue task; LUC = Low Uncertainty Cue task; MASQ-AA = Anxious Arousal subscale of the Mood and Anxiety Symptoms Questionnaire; MASQ-AD = Anhedonic Depression subscale; STAI-T = Trait subscale of the State-Trait Anxiety Inventory.

Figure 3

HUC Task: SDT Parameters and STAI-T Relationships After FC



Note. Partial plots of the relationship between the Trait subscale of the State-Trait Anxiety Inventory (STAI-T) and (A) *d'* after fear cues (FC) in the High Uncertainty Cue (HUC) task, and (B) False alarm rate (FAR) after FC in the HUC task. SDT = signal detection theory. See the online article for the color version of this figure.

higher STAI-*t* scores were associated with greater false alarms after fear cues, B = .004, $p = .037$ (see Figure 3). There were no relationships between any other predictor variables and hit rate or false alarm rate after fear cues (see Table 3). Thus, our results indicated that the relationship between worse perceptual sensitivity after fear cues and STAI-T was largely driven by increased misidentification of neutral faces as fearful.

Relationship Between Anxiety and Perceptual Decision-Making After NC

We then examined the effects of anxiety dimensions on *d'* after neutral cues. Hierarchical linear regression results (see Table 2) showed that age ($B = .031$, $p = .018$) and case status ($B = .551$, $p = .034$), but not gender ($B = -.362$, $p = .050$), MASQ-AA ($B = .009$, $p = .427$), MASQ-AD ($B = -.018$, $p = .338$), or STAI-T ($B = -.015$, $p = .164$), accounted for variance in *d'* after neutral cues. However, the interaction between MASQ-AA and case status predicted *d'* after neutral cues ($B = -.058$, $p = .004$). Further examination of this interaction revealed that, in controls, as MASQ-AA increased, *d'* after neutral cues increased, whereas in cases, as MASQ-AA increased, *d'* after neutral cues decreased (see Figure 4). The interaction between STAI-T and case status did not account for variance in neutral cue *d'* ($B = .001$, $p = .971$). Overall, our results revealed that higher MASQ-AA scores were associated with worse discriminability between fearful and neutral faces after neutral cues in cases, whereas higher MASQ-AA scores were associated with better discriminability between fearful and neutral faces after neutral cues in controls.

Follow-up hierarchical linear regression models predicting hit rate and false alarm rate separately after neutral cues revealed that the MASQ-AA by case status interaction accounted for variance in hit rate after neutral cues ($B = -.010$, $p = .036$; see Figure 4). Further examination of this interaction revealed that higher MASQ-AA scores were associated with higher hit rate for neutral faces after neutral cues in controls, whereas higher MASQ-AA scores were associated with lower hit rate for neutral faces after neutral cues in cases. No other relationships were significant (see Table 3). Overall, higher MASQ-AA scores were associated with worse perceptual sensitivity after neutral cues in individuals diagnosed with anxiety disorders, a relationship that was predominantly driven by incorrect identification of neutral faces after NC. However, the opposite pattern of results was observed in controls, wherein MASQ-AA was associated with better perceptual sensitivity and increased HR after NC.

Low Uncertainty Cue Task

Influence of FC and NC on the Sensitivity of Perceptual Decision-Making

Our results showed no differences in *d'* after fear cues ($M = 1.723$, $SE = .109$) compared with *d'* after neutral cues ($M = 1.583$, $SE = .132$), $t = 1.198$, $p = .244$ (see Figure 2). Hence, discriminability between fearful and neutral faces did not differ after fear cues versus neutral cues when the cues indicated a high probability of encountering subsequent fearful or neutral faces (i.e., under low uncertainty).

Relationship Between Anxiety and Perceptual Decision-Making After FC and NC

Hierarchical linear regression results showed that neither MASQ-AA, STAI-T, nor their respective interactions with case status accounted for variance in *d'* after either fear or neutral cues after accounting for variance in age, gender, and MASQ-AD (see Table 2).

Replication of Results Excluding Covariates

As others have noted (e.g., Miller & Chapman, 2001), the use of covariates such as age and gender can be problematic, as can the use of depression-related covariates when anxiety is a measure of interest. Thus, we reran our analyses for both tasks excluding these variables, and all the pattern of results remained the same.

Discussion

Empirical evidence is sparse regarding the effects of threatening and neutral anticipatory top–down factors on perceptual decision-making in anxiety under uncertainty. Thus, we utilized two tasks in which participants with and without anxiety disorders used anticipatory threat and neutral cues to discriminate between subsequently presented threatening and neutral stimuli under varying uncertainty.

Table 3
Hit Rate (HR) and False Alarm Rate (FAR): Hierarchical Regression Models

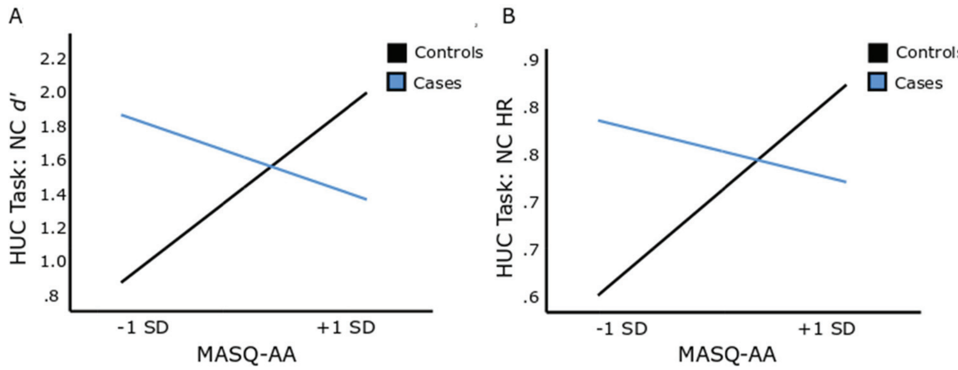
Task	DV	Step	Predictor	*B*	*t*-value	*p*-value
HUC	FC HR					
		1	Age	.003	1.368	.175
			Gender	−.019	−.693	.490
		2	MASQ-AA	.002	1.062	.291
			Case status	.074	1.883	.063
			STAI-T	−.001	−.588	.558
			MASQ-AD	−.003	−1.101	.274
		3	MASQ-AA × Case Status	−.004	−1.157	.250
		4	STAI-T × Case Status	>.001	.062	.062
HUC	FC FAR					
		1	Age	−.004	−1.559	.123
			Gender	.064	1.943	.055
		2	MASQ-AA	−.002	−1.204	.232
			Case status	−.060	−1.303	.196
			STAI-T	.004	2.121	.037
			MASQ-AD	.002	.745	.458
		3	MASQ-AA × Case Status	−.001	−.154	.878
		4	STAI-T × Case Status	−.003	−.780	.438
HUC	NC HR					
		1	Age	.004	1.430	.156
			Gender	−.076	−1.809	.074
		2	MASQ-AA	.003	1.107	.271
			Case status	.115	1.925	.057
			STAI-T	−.003	−1.242	.218
			MASQ-AD	−.004	−.875	.384
		3	MASQ-AA × Case Status	−.010	−2.135	.036
		4	STAI-T × Case Status	.002	.451	.653
HUC	NC FAR					
		1	Age	−.004	−1.751	.083
			Gender	.023	.794	.429
		2	MASQ-AA	.001	.575	.567
			Case status	−.055	−.1,333	.186
			STAI-T	.001	.815	.417
			MASQ-AD	.002	.580	.564
		3	MASQ-AA × Case Status	.005	1.569	.120
		4	STAI-T × Case Status	>.001	.016	.987

Note. *B* = unstandardized regression coefficients; DV = dependent variable; FC = fear cue; NC = neutral cue; HR = hit rate; FAR = false alarm rate; HUC = High Uncertainty Cue task; LUC = Low Uncertainty Cue task; MASQ-AA = Anxious Arousal subscale of the Mood and Anxiety Symptoms Questionnaire; MASQ-AD = Anhedonic Depression subscale; STAI-T = Trait subscale of the State-Trait Anxiety Inventory.

Results revealed that threat cues enhanced the perceptual sensitivity of subsequent decision-making to a greater extent than neutral cues under high uncertainty. Threat-specific cues may enhance subsequent perceptual decisions via several mechanisms. Such cues may increase attention before stimulus onset, which may subsequently improve stimulus detection by biasing sensory processing toward cued features (Desimone & Duncan, 1995; Okon-Singer et al., 2015). Threat cues may also give rise to more precise perceptual templates, ultimately resulting in better target detection (Lu & Dosher, 1998; Summerfield & De Lange, 2014). Finally, threat cues may increase arousal and thereby bias selective attention toward subsequent perception of relevant stimulus characteristics (Bennion et al., 2013). Congruent with predictive coding (Friston, 2012), threat cues may lead to greater precision being assigned to threatening faces and lower precision to neutral faces, leading to better discrimination. Further research is needed to examine these potential mechanisms. Notably, the differential impact of cues on subsequent discrimination between fearful and neutral faces was observed under high, but not low, uncertainty. The differential effects of the cues may not have appeared under low uncertainty because the predictive neutral cues may have guided attention to a similar degree as predictive threat cues (e.g., Calvo & Dolores Castillo, 2001).

Results revealed that dimensions of anxiety were differentially associated with worse perceptual sensitivity after anticipatory threatening and neutral cues under high uncertainty. Specifically, anxious apprehension was associated with worse discrimination between threatening and neutral stimuli after uncertain threat cues across individuals with and without anxiety disorders. As anxious apprehension is associated with exaggerated beliefs about the probability of encountering threatening stimuli and events (Grupe & Nitschke, 2013; Stöber, 1997), the uncertain threat cues may have triggered inflated threat-relevant expectations regarding upcoming facial expressions. Consequently, neutral faces may have been misinterpreted as threatening (Yoon & Zinbarg, 2008),

Figure 4
HUC Task: SDT Parameters and MASQ-AA After NC



Note. Simple slopes of the interaction between case status and the Anxious Arousal subscale of the Mood and Anxiety Symptoms Questionnaire (MASQ-AA) on (A) *d'* after neutral cues (NC) in the High Uncertainty Cue (HUC) task, and (B) hit rate (HR) after NC in the HUC task. Blue (light gray) lines represent cases. Black (dark gray) lines represent controls. SDT = signal detection theory. See the online article for the color version of this figure.

resulting in worse discrimination between face types. This is supported by our findings showing that anxious apprehension is associated with greater false alarms (misidentification of neutral faces as threatening) after threat cues.

In contrast, our results showed that anxious arousal was associated with worse perceptual sensitivity after uncertain neutral cues in participants diagnosed with anxiety disorders. Thus, top–down attentional guidance toward relevant neutral stimulus features may be impaired in pathologically anxious individuals with elevated anxious arousal, thereby impairing subsequent discrimination between threatening and neutral stimuli. Additionally, high anxious arousal in pathologically anxious populations may be associated with less precise neutral perceptual templates, ultimately resulting in worse discrimination between threatening and neutral stimuli. Consistent with this possibility, cases were increasingly worse at identifying neutral faces after neutral cues as anxious arousal increased. Contrastingly, higher anxious arousal was associated with better perceptual sensitivity after uncertain neutral cues in controls. Possibly, moderate anxious arousal in controls enhanced behavioral performance by improving anticipatory top–-down attentional guidance toward neutral stimuli (Mather & Sutherland, 2011); however, high anxious arousal in cases impaired the same performance, reinforcing findings that physiological arousal impedes performance at extreme levels (Bennion et al., 2013; Yerkes & Dodson, 1908).

Perceptual sensitivity after highly predictive threat or neutral cues was not related to either anxious arousal or anxious apprehension. Such findings are congruent with and expand upon previous empirical findings indicating that differences in threat-related responses in anxiety disappear under less uncertain conditions (Calvo & Dolores Castillo, 2001). Our results extend these findings by showing that anxiety is not associated with worse top–-down utilization of threatening and neutral cues for perceptual decision-making when cues are highly predictive of upcoming stimuli. Several factors may account for these findings. For example, the role of uncertainty in increasing attention and reactivity (Cisler & Koster, 2010; Grupe & Nitschke, 2013)—which both influence perceptual decision-making—may be less impactful during tasks with low uncertainty.

Several limitations may notably impact the generalizability of our findings. Although our study is the first to examine the effects of uncertainty in perceptual decision-making in anxiety, experimental constraints required us to always administer the experimental tasks in the same order. This lack of counterbalancing influenced our confidence in statistically comparing cross-task performance. Additionally, although we used a highly recommended transdiagnostic approach to examine effects of dimensional anxiety (Cuthbert, 2014), this resulted in the recruitment of a larger clinical versus control sample. Hence, future research should examine if our findings generalize to other representative samples. Lastly, although the STAI-T has been used as a measure of anxious apprehension as detailed above, replicating the results of the current study with other measures of anxious apprehension is warranted (e.g., PSWQ; Meyer et al., 1990).

Overall, our findings bridge the gap between clinical research, which emphasizes anticipation-related top–down factors in anxiety, and cognitive models of threat processing in anxiety, which tend to focus on bottom–up salience of threatening stimuli. Our findings highlight the top–down influence of not only threat but also neutral information on perceptual decision-making in anxiety under uncertainty. Because perceptual decision-making serves as a gateway to higher-order cognition, any anxiety-related effects at this stage are likely to propagate downstream and influence attention and behavior. By focusing on top–down threat knowledge on exteroception, our findings complement the existing literature on interoception in anxiety (Barrett & Simmons, 2015; Paulus & Stein, 2010). Additionally, our findings underscore the importance of a transdiagnostic approach (Cuthbert, 2014), as our results elucidate how specific dimensions of anxiety differentially relate to perceptual decision-making. Identification of these transdiagnostic top–down factors is an important step toward the development of increasingly effective treatments involving more fine-tuned discrimination between threat and neutral stimuli. These results may also inform the improvement of existing treatments like Attention

Bias Modification (Hakamata et al., 2010) by training top–down attentional strategies that are implemented before the arrival of threatening stimuli. Lastly, findings from the present project may assist in the development of more comprehensive, specific, and ecologically valid models in which prior knowledge relating to threat, safety, and uncertainty all play an important role in perceptual decision-making in anxiety.

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