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Through the Eyes of Anxiety: Dissecting Threat Bias via Emotional-Binocular Rivalry

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Abstract

An extensive body of research has demonstrated that anxious individuals abnormally process threat-related content. Yet, the manner in which clinical anxiety affects the selection of threatening signals and their maintenance within consciousness is yet to be explored. The present study used an emotional binocular rivalry (e-BR) procedure, in which pictures of faces depicting either fearful or neutral expressions competed with pictures of a house for conscious perception. We assumed that first- or cumulative-preferred perception of faces with fearful over neutral expression (i.e., initial or sustained threat bias, respectively) stand for preferential selection or maintenance of fear content in awareness, correspondingly. Unmedicated patients with social anxiety disorder (SAD) and panic disorder (PAD) were compared to healthy controls for threat-related perceptual biases in the e-BR. At first perception of face, both SAD and PAD patients showed a greater initial threat bias than healthy controls. In contrast, at cumulative dwell-time of face, patient groups demonstrated a diminished sustained threat bias relative to healthy controls, yet in a different manner. SAD patients showed a sustained threat bias, though it was smaller than in healthy controls. Furthermore, increased levels of reported anxiety among SAD patients were associated with enhanced sustained perception of neutral faces. PAD patients, on the other hand, showed no sustained threat bias and a diminished cumulative perception of fearful faces with increased levels of anxiety traits. These findings indicate that anxiety disorders commonly involve an initially enhanced selection of threat signals into awareness, followed by disorder-specific manifestation of diminished preferred maintenance of threat in awareness.

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Keywords

social anxiety disorder; panic disorder; threat bias; binocular rivalry; information processing

Privileged processing of threat signals is necessary in order to adaptively cope with potential dangers in the environment (Nesse, 1999; Oatley & Johnson-Laird, 1987). Yet, an exaggerated tendency to preferentially process threat signals is considered to be responsible for the emergence and persistence of anxiety in some individuals (e.g., Beck & Clark, 1997; Mathews & MacLeod, 1985). Indeed, enhanced processing of threat was demonstrated in patients with anxiety disorders in different cognitive tasks, which include attention allocation (for a review, see Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van Ijzendoorn, 2007; e.g., MacLeod, Mathews, & Tata, 1986) or interpretation (Calvo & Castillo, 1997; Richards, 2004; Yoon & Zinbarg, 2008). For instance, relative to controls, patients with anxiety were slower in color naming words that depicted threat than neutral content in the emotional Stroop task (McNally, Riemann, & Kim, 1990; for a review, see J. M. Williams, Mathews, & MacLeod, 1996) and faster in responding to targets that follow threat cues rather than neutral cues in the dot-probe task (Bradley, Mogg, White, Groom, & de Bono, 1999). Furthermore, studies have shown that the heightened threat-related bias among anxiety disorder patients may persist under conditions of restricted awareness, such as with subliminal exposure times (Mogg, Bradley, Williams, & Mathews, 1993; Öhman & Soares, 1994).

While there is abundant evidence for the effect that anxiety has on the allocation of processing resources toward threat, it is still unclear in what manner anxiety may contribute to the initial selection of threat content into awareness and to its sustained maintenance in conscious perception. The current study used an emotional binocular rivalry (e-BR) procedure in order to investigate the effect of clinical anxiety on biased perception of threat signals while dissecting its initial and sustained components. Binocular rivalry occurs when two different images are presented dichoptically and simultaneously, but the observer is only aware of one image at a time and is less aware or completely unaware of the other (Wheatstone, 1838 cited in Blake & Logothetis, 2002). Thus, even though the visual input remains constant, the perceptual experience with each image spontaneously and involuntarily oscillates between two possible states, full (dominant) or restricted (suppressed) awareness (for a review, see Blake, 2001). This phenomenon largely mimics our natural vision in a controlled fashion, which involves the ongoing partial selection of multiple inputs that are either assigned to or excluded from aware processing (Gibson, 1979). Accumulating neuroimaging and psychophysical studies reveal that the dominant percept in BR is processed by the same mechanisms associated with any other normal viewing and is therefore subjected to the influence of high level, elaborated top-down processes. At the same time, the suppressed image in BR is associated with diminished processing in multiple cortical sites; therefore, it is less affected by its high-level attributes (for further details, see Blake & Logothetis, 2002). It is important to note that it has been recently proposed that the processes underlying the first perceptual selection of an image at the onset of BR are mainly affected by low-level factors and differ from those underlying the subsequent overall perceptual predominance (Carter & Cavanagh, 2007).

Image predominance in BR depends not only on the salience of its physical properties, such as luminance or contrast (Levelt, 1965) but also on the salience of its higher level attributes (Blake & Logothetis, 2002). For example, perceptually meaningful (Yu & Blake, 1992), personally relevant (Bagby, 1957) and, importantly, emotion-provoking images have been found to be perceived for longer durations in BR than images with contrasting qualities (Alpers & Pauli, 2006; Alpers, Ruhleder, Walz, Muhlberger, & Pauli, 2005; Bannerman,

Milders, De Gelder, & Sahraie, 2008; Coren & Russell, 1992). This bias toward emotion-provoking stimuli cannot be merely explained by the changes in low-level stimulus features between emotional and nonemotional content since several studies have shown that the predominance of neutral images can be biased when assigning them an emotional content, for example by using aversive conditioning (Alpers et al., 2005) or by pairing them with a negative gossip (Anderson, Siegel, Bliss-Moreau, & Barrett, 2011). Furthermore, the emotional state of the observer may also affect the perceptual predominance in BR, as the same pictures were found to be perceived differentially under different emotional states. Specifically, it has been shown that observers under induced (Anderson, Siegel, & Barrett, 2011) or reported (Gray, Adams, & Garner, 2009) negative affective states tend to preferentially perceive faces with negative expressions rather than neutral or positive expressions. Beyond the momentary emotional state, the tendency to experience negative emotions repeatedly (i.e., emotional traits) was also found to affect the predominance of affective pictures in BR. Accordingly, increased levels of depressive symptoms were associated with diminished predominance of emotional over neutral faces (Yoon, Hong, Joormann, & Kang, 2009). Further, increased reported tendency to experience anxiety in healthy participants was associated with higher frequency of initially perceived negative faces (i.e., fearful and angry; Gray et al., 2009) and with accelerated rate of alterations between two rivaling neutral percepts (Nagamine et al., 2007).

Notwithstanding, despite these accumulating data on the effect of mental states on conscious perception in BR, this has not been directly examined with regard to clinical states such as anxiety. To portray the role that clinical anxiety may have on the selection and maintenance of perception of threat cues, we applied the e-BR procedure (Figure 1a) to unmedicated patients with social anxiety disorder (SAD) and panic disorder (PAD), and to healthy controls. By using the e-BR procedure, we wished to unveil how patients with conceptually different mechanisms of heightened anxiety preferentially perceive faces over a house when the faces depicted fearful or neutral expressions (i.e., threat bias). Based on the distinction between the processes associated with first and cumulative perception in BR (Carter & Cavanagh, 2007), the use of the e-BR paradigm enabled us to dissect processing levels of threat bias into initial selection and sustained maintenance, respectively (referred as; initial and sustained threat bias; see Figure 1b and methods for details). We specifically hypothesized that both anxiety groups would show greater initial threat bias than healthy participants based on the evidence for greater sensitivity to threat under conditions of subliminal compared to supraliminal exposure (i.e., low-level processing) among anxious individuals with different diagnoses (Bar-Haim et al., 2007). In contrast, we expected that the anxiety groups would differ in their sustained threat bias. SAD is manifested as fear of being negatively evaluated by others in social situations (American Psychiatric Association, 2000), and is associated with biased allocation of attention toward negative stimuli, especially when they depict social threat (Rapee & Heimberg, 1997). We therefore hypothesized that, relative to the other groups, SAD patients would experience greater sustained threat bias. PAD, on the other hand, is characterized by the occurrence of sudden anxiety attacks with no apparent external trigger that involve both physiological and cognitive manifestations of fear (e.g., tachycardia or fear of dying, respectively [American Psychiatric Association, 2000]). Consequently, PAD patients are thought to be especially concerned with their own physical and mental health, thus to be more vigilant toward internal bodily sensations such as heartbeats (Ehlers & Breuer, 1996; Kroeze & van den Hout, 2000). We therefore hypothesized that PAD patients would not show an abnormal sustained threat bias. Additionally, we expected that the severity of clinical anxiety will correlate with predominance biases.

Method

Participants

The clinical sample consisted of 17 patients diagnosed with social anxiety disorder (SAD, 10 females, $M_{\text{age}} = 33.4$, age range: 18–54 years) and 16 patients diagnosed with panic disorder (PAD; 12 females; $M_{\text{age}} = 29.8$ years, age range: 20–51 years). All patients were off medication and were recruited to the study in the affective psychophysiology laboratory, NIMH, Bethesda, Maryland. The healthy control group consisted of 18 nonpsychiatric volunteers that were recruited by advertisements (13 females; $M_{\text{age}} = 27.5$ years, age range: 18–54 years). All participants had normal or corrected-to-normal symmetric visual acuity. Prior to the experiment participants provided informed consent approved by the Institutional Review Board (IRB) of the National Institute of Mental Health (NIMH) Intramural Research Program.

Diagnoses of both patients and healthy controls were determined by the Structured Clinical Interview for *DSM-III-R* (SCID; American Psychiatric Association, 2000), administered by one of four staff psychologists (interrater Kappa of .76) from the affective psychophysiology laboratory at the NIMH. In addition, all patients were independently assessed by a senior psychiatrist to confirm the SCID diagnosis. Among SAD patients, eight had psychiatric comorbidities of general anxiety disorder (GAD; $n = 2$), major depression disorder (MDD; $n = 3$), specific phobia ($n = 1$), MDD and specific phobia ($n = 1$), and adjustment disorder ($n = 1$). Among PAD patients, one met criteria for PAD with agoraphobia and five had psychiatric comorbidities of MDD ($n = 2$), MDD and specific phobia ($n = 2$, of which one was also diagnosed with subthreshold GAD), MDD and subthreshold posttraumatic stress disorder ($n = 1$).

Participants were excluded from statistical analysis if they systematically experienced substantially low rates of changes in percepts in either fearful or neutral face conditions (i.e., less than four changes in each of the trials), or if they had at least two trials with substantially delayed response times (i.e., initial button press latency of more than 20 s). After this elimination process, the final study cohort was comprised of 16 SAD patients (11 females, $M_{\text{age}} = 32.9$), 14 PAD patients (11 females, $M_{\text{age}} = 28.7$), and 16 healthy controls, (11 females, $M_{\text{age}} = 25.7$).

Materials and Procedure

e-BR stimuli—Photographs of eight faces (4 males), each displaying either a fearful or a neutral expression, were selected from a standardized set of facial expressions (Ekman & Friesen, 1975). A photograph of a house was selected to closely match the overall area of the facial images. Mean luminance and contrast were matched for all stimuli of both categories. Color filters were then applied to construct sets of “red only” and “green only” face and house stimuli, and the opacity of the resulting images was adjusted to 50% to make them semitransparent. Red houses were then overlaid on green faces, and vice versa, to create a fully balanced set of composite face-house stimuli. A black and white circle, subtending approximately 0.3° of visual angle, was positioned in the center of each display to serve as a fixation point. To ensure that the two images in each face-house composite were presented dichoptically, participants wore spectacles with one red and one green filtered lens (Kodak Wratten Filters). The face-house pairs, subtending approximately 11.5° of visual angle, were presented for 40 s as overlaid displays on a uniform gray background stimuli using “Presentation” software (Neurobehavioral systems, Inc.) on a Dell notebook with a 15” monitor.

e-BR procedure—The entire experimental run, which lasted 14 minutes, consisted of eight trials of rivalry and eight trials of replay condition, interleaved with 10 s of blank epochs. Half of face-house pairs were comprised of faces with fearful (*F*) expressions and the other half of faces with neutral (*N*) expressions. Each rivalry trial was followed by a replay trial and presented in a fixed order [*N-F-F-N-N-F-N-F*]. Each replay trial was identical to the prior rivalry trial with the important exception that the switches between the face and house images were now stimulus-driven, based on the reported dwell times (i.e., duration of perceiving each stimulus) during the prior rivalry epoch. The replay data were intended for a future imaging study and are not included in the current study. Participants were requested to fixate on a small black central dot and to perform a face-house categorization task by indicating their perception of a face or a house by pressing one of two keyboard buttons, disregarding the emotional content of the faces. The continuous report of participants' altering perception using key press was automatically recorded by the presentation software. Prior to the experimental run, participants completed a short practice session, which was composed of four different sets of face-house pairs, of which faces depicted neutral expressions. At the end of the task, the participants were asked to fill out several anxiety questionnaires (see below).

Self-report measures of anxiety—The Spielberger State–Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983) was used as a general measure for the levels of both momentary anxiety (state) and long-lasting tendency to experience anxiety (trait). The Fear Questionnaire (FQ; Marks & Mathews, 1979) was used as a general measure for phobias, which is composed of agoraphobia, social phobia, and blood injury phobia subgroups. Due to technical difficulties, not all participants filled out the questionnaires (16 out of 16 SAD patients, 9 out of 14 PD patients and 11–13 out of 16 controls).

Data Analysis

The data were extracted using in-house software that was developed with Matlab (MathWorks, Natick, MA) and then analyzed using SPSS 12.0 and STATISTICA 7.0 software (StatSoft, Inc., Tulsa, OK). For each rivalry trial, we initially calculated per each emotional condition (i.e., fearful or neutral) and percept type (i.e., face or house) the cumulative viewing time and the frequency of first percepts. Outlier cumulative viewing times were defined per each percept and emotional condition (i.e., per each of four percepts) as the viewing times that exceeded two standard deviations from the average of the entire group. These outlier events, which constituted a total of four percent out of the entire data, were removed from further analysis. To account for differences in response times, we additionally extracted the latency of initial button press relative to stimulus onset. We additionally estimated the average rate of alterations between face and house percepts (i.e., switch rates) separately for fearful and neutral conditions.

These raw measures were then used to calculate several indices of predominance of face, which were employed in previous emotional BR studies (e.g., Alpers & Gerdes, 2007): (1) The *initial predominance of face (IPF) index* was calculated separately for the fearful and neutral conditions as the frequency of first percepts of face minus the frequency of first percepts of house divided by the total number of trials (Figure 2a). This measure was used to estimate whether the emotional expression of a face (i.e., neutral or fearful) affects the incidence of its immediate selection into awareness. Since the IPF measure does not distribute normally, we could not directly assess the interaction between group and emotional expression in the initial predominance of face using a single statistical test, such as two-way repeated measures analysis of variance (ANOVA). To address this obstacle, we added a direct estimate of the effect of emotion on initial faces predominance and used it for

comparison between the groups, which we termed *Initial Bias for Fear (IBF) index*. The IBF index was calculated as the frequency of first percepts of faces with fearful expressions minus the frequency of first percepts of faces with neutral expressions divided by the total number of trials in which faces were perceived first (Figure 2b). By inspecting these initial awareness indices, we were able to estimate the involvement of lower level, rapid processing of threat in anxiety. (2) *The sustained predominance of face (SPF) index* was calculated separately for the fearful and neutral conditions as the cumulative viewing time of face minus the cumulative viewing time of the house divided by the sum of the viewing time of face, the viewing time of house and the initial button press latency (Figure 2c). This measure was used to estimate how the sustained preferred perception of face over house is affected by the emotional expression that the face depicts (i.e., neutral or fearful). By inspecting this ratio, we wished to quantify the extent of the involvement of higher level, elaborated processing of threat in anxiety.

Further, to examine whether anxiety trait and/or state contributed to the variance in the face predominance indices in the groups, we calculated correlations between each face predominance index and anxiety scores in each group. In order to control for the effect that the switch rates in each condition and initial button press latencies had on the SPF index, these measures were added as covariates.

Results

Group Characteristics

One-way ANOVA with group (SAD, PAD, controls) as a between-subject variable and questionnaire scores as a dependent variable revealed, as expected, a significant difference between the groups in the STAI-trait [$F(2, 35) = 29.3, p < .001$], STAI-state [$F(2, 35) = 17.9, p < .001$], and FQ questionnaires [$F(2, 35) = 5.3, p < .05$]. Additional post hoc LSD tests revealed that both SAD and PAD patients scored higher on all of these anxiety questionnaires compared to the healthy controls (see Table 1). There were no significant age [$F(2, 39) = 1.92, p = .16$] or gender ratio [$\chi^2(2) = 1.74, p = .42$] differences between the groups.

Raw Perceptual Measures

We first used the cumulative viewing time as a dependent measure in a $3 \times 2 \times 2$ mixed design ANOVA with group (SAD, PAD, Control) as a between-subjects factor, emotion type (Fear, Neutral) and category (Face, House) as within-subjects repeated measures and with average switch rates at fear and neutral conditions and the initial button press latencies as covariates. This analysis revealed a significant three-way interaction of category $\times$ emotion $\times$ group [$F(2, 40) = 3.22, p = .05$] with a main effects of category [$F(2, 40) = 6.94, p < .05$] and a two-way interaction of emotion $\times$ category [$F(2, 40) = 4.81, p < .05$; see Figure 1c]. A group (SAD, PAD, Control) $\times$ emotion (Fear, Neutral) mixed ANOVA with switch rate as dependent variable revealed enhanced switching during the neutral epochs [$F(1, 43) = 18.84, p < .0001$, main effect for emotion] with no further interaction of Group $\times$ emotion (see Figure 1d). For further delineation of the relationship between the groups and perceptual biases we used the specific indices as follow.

Initial Predominance

We first examined whether the groups differed in their initial threat bias by using the direct IBF index (see data analysis section for further details). Kruskal-Wallis nonparametric test, with IBF index as a dependent variable and group as a between-subjects factor, revealed a significant difference between all three groups in their initial fear dominance [$\chi^2(2) = 6.09, p < .05$]. We then performed separate Mann-Whitney tests to compare between each patient

group and controls and found that both PAD [$z = 2.29, p < .05$] and SAD [$z = 1.93, p = .05$] patient groups showed greater initial bias for fear relative to healthy controls (see Figure 2a). As we assumed, both anxiety groups did not differ in this initial bias for fear [$z = 0.19, p = .85$], thus we pooled them together ($n = 30$) for further post hoc within-group comparisons of IPF for neutral and fearful expressions. Wilcoxon's nonparametric test revealed that among the anxiety patients, the IPF for fearful expressions was significantly higher than the IPF for neutral expressions [$z = 1.96, p = .05$] while no such initial threat bias was found for the healthy controls [$z = 1.06, p = .28$, see Figure 2b].

Spearman correlations were applied to explore the relations between IPF indices and anxiety measures. This analysis showed that among SAD patients, levels of reported anxiety traits positively correlated with IPF for fearful expressions [FQ-social: $r_s = .67, p < .05$, Bonferroni corrected for within-group comparisons] as well as with IPF for neutral expressions [FQ-social: $r_s = .67, p < .05$, Bonferroni corrected for within-group comparisons, see Table 2].

Sustained Predominance

The mean SPF index was entered into a 3×2 mixed ANOVA design, with group (SAD, PAD, Control) as a between subjects factor, emotion (Fear, Neutral) as a within subjects repeated measure and with average switch rates at fear and neutral conditions and the initial button press latencies as covariates. Figure 2c shows that the SPF was significantly higher for fearful than neutral expressions [$F(1, 40) = 9.475, p < .001$, main effect for emotion], more so for the healthy group [$F(2, 40) = 3.4, p < .05$, two-way interaction of group $\times$ emotion]. To further clarify this two-way interaction of group and emotion, we performed planned comparisons between and within each group. For the SAD and healthy groups, but not for PAD group, there was a significantly greater predominance of faces with fearful than neutral expressions, meaning a significant sustained threat bias [SAD: $F(1, 40) = 5.95, p < .02$, Healthy: $F(1, 40) = 25.6, p < .001$, PAD: $F(1, 40) = 1.4, p = .24$]. A direct comparison between the groups for this sustained threat bias revealed that relative to healthy controls, PAD patients showed significantly diminished sustained threat bias [$F(1, 40) = 6.13, p < .02$]. The SAD group also showed a trend toward a diminished sustained threat bias relative to the healthy controls [$F(1, 40) = 3.45, p = .07$]. Lastly, this diminished sustained threat-bias emotion that was revealed in the patient groups relative to healthy controls seemed to emerge from an enhanced SPF for faces with neutral expressions [PAD: $F(1, 40) = 9.14, p < .01$, SAD: $F(1, 40) = 6.04, p = .02$] rather than a diminished SPF for faces with fearful expressions [PAD: $F(1, 40) = 0.00, p = .98$, SAD: $F(1, 40) = 0.04, p = .84$].

Partial correlations between the SPF indices and anxiety measures further revealed an interesting dissociation between the patient groups (see Table 3); Among SAD patients, enhanced social anxiety (as measured by the social phobia subscale in the FQ questionnaire) was associated with enhanced SPF for neutral faces ($r = .73, p = 0.01, n = 16$, Bonferroni corrected for within-group comparisons). In contrast, among PAD patients, higher injury anxiety (as measured by the fear of blood and injury subscale in the FQ questionnaire) was marginally associated with diminished SPF for faces with fearful expressions ($r = -0.91, p < .08, n = 9$, Bonferroni corrected for within-group comparisons).

Discussion

The current study used an e-BR procedure in order to characterize how clinical anxiety affects the initial selection and sustained maintenance of threat-related content in conscious perception. As far as we know, this is the first study that used BR to investigate threat processing in unmedicated anxiety patients. The results of this study are consistent with our primary hypothesis that patients with anxiety differ from healthy participants in the way that threat-related content is brought into and maintained in their awareness. At the initial

selection of faces, which is assumed to be based on low-level visual processes, both PAD and SAD patients, but not healthy controls, exhibited enhanced threat bias. However, at the sustained maintenance level, which is considered to involve top-down processes, anxiety patients exhibited different threat bias than healthy participants. This diminished processing had different manifestations in the anxiety groups; while SAD patients exhibited sustained threat bias, though marginally smaller than healthy controls PAD patients did not show any sustained threat bias. Correlation analyses further elucidated this different relation between indices for sustained bias for face and clinical anxiety. Among SAD patients, increased levels of social anxiety were associated with enhanced sustained bias for faces with neutral expressions. On the other hand, among PAD patients, increased levels of physical anxiety were marginally associated with diminished sustained bias for faces with fearful expressions.

Initial Threat Bias in e-BR

Both groups of anxiety patients experienced greater initial threat bias than healthy controls. These findings correspond to a recent study by Gray and colleagues (2009), who have shown that increased levels of trait anxiety (among healthy individuals) are associated with increased tendency to initially perceive fearful and angry faces in BR. The increased initial threat bias among both SAD and PAD patients could be explained by a hypersensitive early threat detection process which is a common path in various anxiety disorders. This explanation corresponds with several cognitive models of anxiety disorders, which have posited that high vigilance to threat stems from an augmented preaware evaluation mechanism, involving relatively low-level processing of brainstem and subcortical limbic regions (Mathews & Mackintosh, 1998; Mogg & Bradley, 1998; Öhman, 1993; Öhman & Wiens, 2004; J. M. Williams, Watts, MacLeod, & Mathews, 1988). This proposition is in line with accumulating behavioral studies, which have shown that bias toward threat content in highly anxious individuals persisted and was even pronounced under conditions of restricted awareness or limited attention resources (MacLeod & Rutherford, 1992; Mathews & MacLeod, 1986; Mogg & Bradley, 1999, 2002; Mogg, Kentish, & Bradley, 1993; Öhman & Soares, 1994). Brain imaging studies further support the low-level model assumptions by showing selectivity of the amygdala for experimentally suppressed fearful faces relative to neutral objects under forced-biased BR procedure (Pasley, Mayes, & Schultz, 2004; M. A. Williams, Morris, McGlone, Abbott, & Mattingley, 2004). Similarly, it has been shown that anxious individuals manifest enhanced amygdala activity compared to healthy controls when processing visually masked threat-related material, even under restricted subjective awareness (Bishop, Duncan, & Lawrence, 2004; Etkin et al., 2004). However, it remains a matter of debate as to whether the threat selectivity found in the amygdala under such restricted conditions depends on a minimal, albeit critical, availability of attention resources (Bishop, Jenkins, & Lawrence, 2007; Pessoa, McKenna, Gutierrez, & Ungerleider, 2002).

Sustained Threat Bias in e-BR

As expected from previous research (Alpers & Gerdes, 2007; Alpers & Pauli, 2006; Alpers et al., 2005; Bannerman et al., 2008; Coren & Russell, 1992; Yoon et al., 2009), we observed a sustained threat bias in the e-BR among healthy participants. This bias reflects the commonly held notion that when encountering a potential proximate threat, its sustained privileged processing is beneficial (Nesse, 1999). Additionally, whereas the measure of initial predominance of face pointed to a low-level threat bias that is common to both SAD and PAD groups, the sustained threat bias portrayed disorder-specific manifestations.

SAD patients showed a sustained threat bias in the e-BR, albeit marginally smaller than healthy controls (Figure 2c). This finding is discordant with our hypothesis that SAD patients would experience enhanced sustained threat bias relative to healthy controls.

Nevertheless, our finding of enhanced threat bias at initial but not sustained processing is in accordance with studies with SAD patients, which have found that the attentional bias toward threat changed over the course of time from exposure to threat. Specifically, using different exposure durations in the dot-probe task, it has been demonstrated that SAD patients, compared to healthy controls, showed a greater attentional bias toward threat only at early latencies from threat presentation (under 500 ms) and not at longer intervals (e.g., Mogg, Philippot, & Bradley, 2004). It is worth noting that in the current study we revealed that the sustained predominance of faces with neutral expressions was higher among SAD patients than controls (see Figure 2c). Additionally, this enhanced sustained sensitivity for neutral faces was associated with increased levels of reported social anxiety among the SAD group (see Table 3). These findings may be accounted for by the emotional ambiguity of a neutral face, which might be interpreted as being more threatening by SAD patients than healthy participants. This explanation is compatible with previous reports that SAD patients have a tendency to choose a threat-related interpretation when presented with ambiguous stimuli (Clark & McManus, 2002; Stopa & Clark, 2000). A recent neuroimaging study in SAD patients further illuminated the neural correlates of such sensitivity to ambiguity by demonstrating enhanced activity in brain regions that are associated with emotional arousal (e.g., the amygdala) during the anticipation for both negative and unknown ambiguous events (Bruhl et al., 2011). A possible source for this interpretation bias is that the patients could not inhibit the automatic threat meaning out of all possible meanings by exerting an effective cognitive control (Simpson & Burgess, 1985, from Richards, 2004). Indeed, previous behavioral studies have shown that socially anxious individuals are less able than healthy controls to inhibit inappropriate negative meanings of ambiguous words, when presented at short latencies (Amir, Foa, & Coles, 1998). Neuroimaging studies have suggested that the neural correlate of this deficiency among anxious individuals may be related to reduced activity in the medial prefrontal cortex (Bishop, 2007; Goldin, Manber, Hakimi, Canli, & Gross, 2009; Ray et al., 2005). Accordingly, the enhanced predominance of neutral faces during e-BR among the SAD group in our study may point to a difficulty in recruiting higher level regulation processes in the prefrontal cortex, over a relatively lower level automatic threat interpretation of an emotionally ambiguous stimulus (as shown by greater initial threat bias, more so with increasing levels of social anxiety). The relevance of this insight to treatment of SAD is demonstrated by a recent study, in which training SAD patients to disengage from negative social cues led to a long-lasting amelioration of their anxiety symptoms (Schmidt, Richey, Buckner, & Timpano, 2009).

In contrast to the SAD group, PAD patients did not show a sustained threat bias even though they demonstrated a greater initial threat bias. This diminished sustained threat bias among PAD patients was associated with increased cumulative predominance of faces with neutral expressions relative to healthy controls (Figure 2c), however with no significant relationship to the levels of reported anxiety. Nevertheless, levels of reported physical anxiety (i.e., fear of blood and injury) were marginally associated with decreased predominance of faces with fearful expressions. We therefore suggest that threat content in PAD is excessively processed at a low level, but is not subsequently accessed at higher, more elaborate levels of processing. In support of such an idea are findings that PAD patients were more sensitive to threat words when being presented subliminally (Lim & Kim, 2005; Lundh, Wikstrom, Westerlund, & Ost, 1999) or via dichotic listening (Burgess, Jones, Robertson, Radcliffe, & Emerson, 1981). Such a dual-staged abnormality could elucidate the occurrence of unexplained intense anxiety attacks in PAD, where overactive initial threat impressions are not accessible for more elaborated conscious evaluation at higher level (Klein, 1981). Another possible explanation to the blunted sustained threat bias is that PAD patients are less capable in discriminating between threat and non-threat signals in full awareness, as suggested by studies that revealed poor discrimination between danger and safety cues during fear conditioning (Lissek et al., 2009). Lastly, it can be also suggested that PAD

patients activate strategic avoidance from the experienced threat content and therefore are less selective to faces with fearful expressions (Tull & Roemer, 2007). However, this explanation in the context of BR is less plausible since image predominance cannot be easily regulated by top-down attentional processes (Meng & Tong, 2004).

In summary, the e-BR procedure allowed a unique insight into the mechanisms of perceptual biases in anxiety disorders as demonstrated by SAD and PAD patients. This fairly natural viewing procedure in BR, which was conducted over relatively long blocks (40 s), further enabled us to reveal multiple levels of abnormal threat processing. Overall, we demonstrated that perceptual biases to threatening signals may not be associated with a singular uni-level process, but rather with an interaction between low and high levels of threat processing. We specifically suggest that the dual-level abnormal threat processing observed via the e-BR among SAD and PAD patients, corresponds with the cognitive model of anxiety proposed by Beck and Clark (1997). Beck and Clark's threat processing model predicted that there is an overdomination of primitive, rigid, and reflexive cognitive schemas that largely capture cognitive resources in the face of threat cues and prevent further higher order conscious reappraisal of these cues in anxiety disorders. Accordingly, the enhanced initial threat bias among SAD and PAD patients is due to excessive (and persistent) utilization of low-level processing resources at the cost of diminishing the resource of fully aware processing leading to abnormal high-level processing that has different manifestations in SAD and PAD. While SAD patients overutilize high-level interpretation of threat, PAD patients seem to underutilize these more elaborate processes.

Limitations

Several limitations of the present study should be noted and addressed in future studies. First, groups may differ in their report of the mixed perceptual state, which was not directly measured in our study; that is, patients might more often report one category over the other according to its emotional value, either threatening or safe (Manguno-Mire, Constans, & Geer, 2005). However, the possibility of a general response bias in the periods of mixed percepts is somewhat weakened by the evident distinction between initial and sustained predominance in BR among the groups. Nevertheless, to eliminate the effect of this variable completely, future studies should add the option of reporting a mixed percept. Second, several e-BR studies have demonstrated that positively valenced images also predominate over neutral ones and that negative emotional state is associated with a decrease in this positivity bias (Anderson, Siegel, & Barrett, 2011; Gray et al., 2009). By adding faces with positive expressions to our study, the effect of anxiety on this positivity effect in BR could have been further explored and increase the content resolution of our findings. Third, since among PAD patients there was a relatively high rate of comorbidity with depression (5 out of 16), we cannot rule out the possibility that the findings of diminished bias toward threat found in this group were partly associated with their depression. To note, a recent BR study has shown that increased manifestations of depression in healthy participants were associated with reduced predominance of emotional faces (i.e., happy or disgusted) over neutral faces (Yoon et al., 2009). Although in a post hoc examination we did not find any correlation with severity of depression (as measured using the Beck Depression Inventory (Beck, Steer, & Brown, 1996), future studies should directly address this question by comparing the e-BR perceptual biases among patients with depression and PAD. Fourth, the marginal significant correlations between anxiety and perceptual measures in the PAD groups can be explained by lack of power due to the relatively small sample size in these analyses.

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Figure 1.

a) Perceptual states in the emotional BR paradigm: dichoptic stimulus presentation of faces, with either fearful or neutral expressions to one eye each. b) Derivation of two processing states in BR: (1) rapid initial selection of percept is estimated across trials by calculating the frequency at which each percept (i.e., face or house) was reported as the first percept; (2) ongoing aware processing of an image is estimated in each trial as the cumulative viewing time at each percept. c) Category and emotional effects on perception in BR: mean cumulative duration of perceiving at each percept (i.e., dwell time) for the different groups. d) Mean switching rate between percepts during fearful and neutral epochs for the different groups. Cross represents significant interaction, asterisks represents significant difference as follows: * $p < .05$, ** $p < .01$, *** $p < .001$. SAD = Social Anxiety Disorder, PAD = Panic Disorder.

Figure 2.

Perceptual indices for the anxiety patients and control groups: a) Initial bias for fear; Cross represents significant difference between the groups ($p < .05$). b) Initial predominance of faces with fearful or neutral expression. c) Sustained predominance of faces with fearful or neutral expression (gray). Cross represents significant interaction between group and emotion ($p < .05$); asterisk represents significant difference as follows: * $p < .05$, ** $p < .01$, *** $p < .001$. SAD = Social Anxiety Disorder, PAD = Panic Disorder, Cum. = Cumulative, IRT = Initial Response Time, F = fear, N = Neutral.

Table 1

Summary of Means (M) and Standard Errors (SE) for Scores on the FQ, STAI-State, and STAI-Trait Questionnaires as a Function of Diagnosis

Measure/diagnosis	SAD (<i>n</i> = 16)	PAD (<i>n</i> = 9)	Healthy (<i>n</i> = 13)
FQ	<i>M</i> = 35.37 *** <i>SE</i> = 4.13	<i>M</i> = 34.11 * <i>SE</i> = 7.62	<i>M</i> = 16.77 <i>SE</i> = 2.93
ST AI-state	<i>M</i> = 48.75 *** <i>SE</i> = 2.60	<i>M</i> = 38.22 ** <i>SE</i> = 4.34	<i>M</i> = 26.45 ^a <i>SE</i> = 1.59
ST AI-trait	<i>M</i> = 50.5 ^a *** <i>SE</i> = 1.32	<i>M</i> = 43.11 *** <i>SE</i> = 3.86	<i>M</i> = 27.9 ^a <i>SE</i> = 1.87

Note. PAD = Panic Disorder; SAD = Social Anxiety Disorder; FQ = Fear Questionnaire; STAI = State-Trait Anxiety Inventory. Significant differences between the groups were revealed by Kruskal-Wallis tests for all questionnaires ($p < .05$). The questionnaire scores per each anxiety patients group that were found to be significantly higher relative to healthy controls by post hoc Mann-Whitney comparisons are marked by an asterisk.

^a
n = 11.

*
 $p < .05$.

**
 $p < .01$.

 $p < .005$.

Table 2

Summary of Correlations Between Initial Predominance of Face and Questionnaires Scores as a Function of Diagnosis

Measure/diagnosis	SAD (<i>n</i> = 16)	PAD (<i>n</i> = 9)	Healthy (<i>n</i> = 11)
Initial Dominance Fearful Face			
FQ	0.60 ^(*)	−0.63	0.48
FQ-S	0.67 [*]		
STAI-trait	0.14	−0.36	0.09
STAI-state	0.38	0.02	0.37
Initial Dominance Neutral Face			
FQ	0.21	−0.67	0.25
FQ-S	0.66 [*]		
STAI-trait	0.31	0.46	0.09
STAI-state	0.42	−0.05	0.18

Note. Spearman correlation values are presented. Significant correlations, as revealed by t-tests per each questionnaire and diagnosis group, are marked by an asterisk as follows: (two-tailed, Bonferroni corrected for within group comparisons). PAD = Panic Disorder; SAD = Social Anxiety Disorder; FQ = Fear Questionnaire; STAI = State-Trait Anxiety Inventory. Correlations were additionally calculated separately for the three sub-scales of the FQ questionnaire: Social Phobia (FQ-S); Agoraphobia (FQ-A); Blood-Injury phobia (FQ-BI). Here we only present the sub-scales that correlated significantly with one of the indices.

^(*)
p < .08.

^{*}
p < .05.

Table 3

Summary of Correlations Between Sustained Predominance of Face and Questionnaires Scores as a Function of Diagnosis

Measure/diagnosis	SAD (<i>n</i> = 16)	PAD (<i>n</i> = 9)	Healthy (<i>n</i> = 11)
Sustained Predominance of Fearful Face			
FQ	0.21	−0.6	0.36
FQ-BI		−0.91^(*)	
STAI-trait	0.18	−0.32	0.21
STAI-state	0.41	−0.20	0.79
Sustained Predominance of Neutral Face			
FQ	0.39	−0.56	0.45
FQ-S	0.73[*]		
STAI-trait	0.26	0.51	0.23
STAI-state	0.42	0.41	0.34

Note. Partial correlation values, after controlling for the average switch rates and response times until initial button press, are presented. Significant correlations, as revealed by t-tests per each questionnaire and diagnosis group, are marked by an asterisk as follows: (two-tailed, Bonferroni corrected for within group comparisons). PAD = Panic Disorder; SAD = Social Anxiety Disorder; FQ = Fear Questionnaire; STAI = State-Trait Anxiety Inventory. Correlations were additionally calculated separately for the three sub-scales of the FQ questionnaire: Social Phobia (FQ-S); Agoraphobia (FQ-A); Blood-Injury phobia (FQ-BI). Here we only present the sub-scales that correlated significantly with one of the indices.

^(*) $p < .08$.

^{*} $p < .05$.