DEPRESSION AND ANXIETY 27:234–243 (2010)

ADAA Donald F. Klein Early Career Investigator Award

DISTINCT ELECTROCORTICAL AND BEHAVIORAL EVIDENCE FOR INCREASED ATTENTION TO THREAT IN GENERALIZED ANXIETY DISORDER

Annmarie MacNamara, M.A. and Greg Hajcak, Ph.D.*

Background: *Neural activity is increasingly used in addition to behavioral measures to study anxiety and attentional biases toward threatening stimuli. Event-related potentials (ERPs) might be particularly useful because of their excellent temporal resolution. In particular, the late positive potential (LPP) reflects increased attention to emotional stimuli—and was recently found to be larger with increasing state anxiety. This study sought to examine the LPP among individuals with generalized anxiety disorder (GAD).* **Methods:** *Fifteen individuals with GAD and 15 healthy controls (HCs) viewed briefly presented pairs of aversive and neutral pictures that were presented to the left and right of, as well as above and below, fixation on each trial; ERP and behavioral measures were recorded as participants indicated whether the horizontal or vertical image pairs were the same or different.* **Results:** *Aversive pictures presented in unattended locations were associated with more errors overall, and this effect was larger in GAD than HC participants. Moreover, aversive targets elicited larger LPPs across all participants; this difference was larger in GAD than HC participants when distracters were neutral.* **Conclusions:** *Threatening stimuli presented in both target and distracting spatial locations have a greater impact on GAD than HC participants. Behavioral and ERP measures provide complimentary indices of attention toward threat in GAD. In terms of attentional control theory, behavioral interference indexes impaired processing effectiveness, whereas the LPP might index reduced processing efficiency in GAD. Both measures may provide unique windows onto how increased stimulus-driven attention to threat impacts and characterizes GAD. Depression and Anxiety 27:234–243, 2010.*

Key words: *generalized anxiety disorder; attentional bias; threat; attentional control theory; late positive potential*

Increased attention to threatening stimuli has been implicated in the development and maintenance of anxiety.[1–6] A variety of behavioral studies support the notion that anxiety biases spatial attention toward the location of threatening compared to neutral stimuli. For example, in the dot-probe paradigm,[7] one emotional and one neutral stimulus are briefly presented on the screen; following their offset, participants must respond as quickly as possible to a target that appears in the location of one stimulus. Because faster responses should occur for targets that appear in attended compared to unattended locations, an attentional bias

Department of Psychology, Stony Brook University, Stony Brook, New York

*Correspondence to: Greg Hajcak, Department of Psychology, Stony Brook University, Stony Brook, NY 11794-2500.
E-mail: greg.hajcak@stonybrook.edu

The authors report they have no financial relationships within the past 3 years to disclose.

Received for publication 4 December 2009; Revised 24 January 2010; Accepted 25 January 2010

DOI 10.1002/da.20679
Published online in Wiley InterScience (www.interscience.wiley.com).

to threat is suggested by the tendency for anxious participants to respond faster to targets that appear in the place of the threatening stimulus.[7–10] Thus, when there is competition for visual resources, anxiety may bias attention toward threatening stimuli.[11]

More recently, research has investigated attentional biases toward threatening stimuli that are presented in either task-relevant or task-irrelevant spatial locations; these studies have further examined neural correlates of biased attention toward threat. For example, Bishop et al.[12] designed a task for fMRI in which participants simultaneously viewed pictures of faces and houses: on each trial, two houses were presented in either a horizontal (i.e., to the left and right of fixation) or vertical (i.e., above and below fixation) pair—the other pair of images were faces, which could be either neutral or fearful. Participants were instructed to attend one pair of pictures on each trial and to indicate whether the target pictures were the same or different. Results showed that amygdala activation to unattended *fearful* faces was associated with state anxiety, suggesting that *task-irrelevant* threatening information receives increased processing as a function of state levels of anxiety—and that the amygdala may be a key neural structure mediating biased attention to threat in anxiety. Trait and state levels of anxiety appear to have dissociable effects on the recruitment of neural resources in studies that utilize fMRI. Work by Bishop et al.[13] found that under conditions of low perceptual load, *state* anxiety was associated with increased activity in the amygdala and superior temporal sulcus for threatening compared with neutral distracters, whereas *trait* anxiety was associated with the decreased recruitment of frontal regions associated with controlled processing on these trials. Thus, state and trait anxiety may contribute through different routes to attentional biases in anxiety, potentially explaining interactive effects found in some previous work.[14,15]

Because of their excellent temporal resolution, event-related potentials (ERPs) are also increasingly being used to index the processing of threatening stimuli in relation to anxiety.[16] Recently, MacNamara and Hajcak[17] designed a task similar to that used by Bishop et al.[12] except that all stimuli were either neutral or aversive pictures from the International Affective Picture System (IAPS).[18] On each trial, participants viewed four pictures arranged in horizontal and vertical pairs, and indicated whether two images within a pair were the same or different. Fast and accurate responding was emphasized and stimuli presented in attended and unattended locations could be neutral or aversive, whereas in Bishop et al.'s[12] study only one pair of images could be fearful because houses are necessarily neutral. To index attention to emotional stimuli, MacNamara and Hajcak[17] measured the late positive potential (LPP), a positive-going parietal ERP that begins around 200 ms following stimulus onset, and is larger for emotional compared to neutral pictures and words.[19–25]

Even though the threatening quality of the pictures was irrelevant to the task, MacNamara and Hajcak[17] found that aversive pictures elicited larger LPPs than neutral pictures; however, this pattern was only found for pictures presented in attended spatial locations. The absence of an LPP for pictures presented in unattended locations is in line with previous work suggesting that the LPP is highly sensitive to manipulations of spatial attention.[26–29] However, aversive pictures presented in unattended locations *were* associated with more errors and slower reaction times. Thus, the LPP and behavioral measures may index different processes: we hypothesize that behavioral measures reflect relatively low-level interference that does not depend on the full awareness of stimulus meaning, in line with the suggestion that attentional biases may occur relatively automatically.[6,30] On the other hand, the LPP appears to index increased attention related to the elaborated processing of stimulus meaning.[21,31,32]

From the perspective of Eysenck et al.'s[3] attentional control theory, behavioral interference suggests reduced *processing effectiveness* in the face of threatening distracters (i.e., reduced success with which a task is performed), whereas the increased LPP may index reduced *processing efficiency* (i.e., increased resources invested in the task). Importantly, MacNamara and Hajcak[17] found that *state anxiety* was uniquely correlated with an increased LPP to aversive compared to neutral pictures presented in attended locations. Because the emotional nature of *all* images in the MacNamara and Hajcak[17] task was irrelevant to the task, the increased LPP to threatening target stimuli suggested increased attention to the aversive and task-irrelevant stimulus dimension. These data provided initial support for the possibility that the LPP could be used to index increased attention to threatening stimuli as a function of anxiety. In particular, the increased LPP to the threatening nature of stimuli may index impaired processing efficiency in anxiety—a relative increase in stimulus-driven compared to goal-directed attention that is not always evident in behavioral measures of effectiveness.[3]

Although attentional control theory is often discussed in terms of normative anxiety,[3,33] there are increasing efforts to understand clinically significant anxiety in terms of biased attention to threat; for example, a recent meta-analysis by Bar-Haim et al.[8] suggested that threat-related biases of a similar magnitude may be found across several anxiety disorders. Generalized anxiety disorder (GAD) is a highly chronic and debilitating disorder associated with pathological worry, muscle tension, autonomic hyperactivity, and a level of impairment on par with that of major depression.[34–36] However, little is known about the mechanisms underlying GAD, and rates of response to treatment are poor, particularly in comparison to other anxiety disorders.[37,38] A better understanding of the mechanisms causing and maintaining

GAD could improve treatment outcomes.[39] A small number of eye-tracking and behavioral studies focusing on GAD have found evidence of increased attention toward threat;[40–42] however, one study reported conflicting results.[43] Far fewer studies have investigated *neural* response to threatening information in GAD. Specifically, two fMRI studies failed to find significant differences in amygdala reactivity to angry or fearful faces between GAD and control groups;[44,45] no studies to date have used ERPs to examine attentional bias to threat in GAD.

This study utilized the same paradigm as in MacNamara and Hajcak[17] to explore neural and behavioral biases toward threat among individuals diagnosed with GAD compared to healthy controls (HCs). In line with previous work, it was expected that aversive information would elicit larger LPPs, but only when presented in attended locations; moreover, it was predicted that aversive pictures in unattended locations would negatively impact behavioral performance across participants.[17] Based on our previous work that related state anxiety to an increased LPP,[17] it was expected that the LPP elicited by aversive compared to neutral pictures in attended locations would be larger for individuals with GAD.

METHOD

PARTICIPANTS

Fifteen individuals with GAD (2 male) and 15 HCs (4 male) participated in the study. The mean age for the GAD group was 33.53 years ($SD = 14.74$); the HCs had a mean age of 31.73 years ($SD = 11.20$). The average number of years of education was 14.87 ($SD = 2.10$) for the GAD group and 15.17 ($SD = 1.79$) for the HC group. Diagnoses were made according to the Structured Clinical Interview for the DSM-IV (SCID-I/NP).[46] Participants in the GAD group did not have any other current Axis I diagnoses, with the exception of specific phobia (two participants). None of the participants in the GAD group had a current or recent (i.e., within 12 months of study entry) major depressive episode; six had a lifetime history of a major depressive episode. Participants in the HC group did not have any current or past Axis I diagnoses, with the exception of current specific phobia (one participant). For each group, five diagnostic interviews were recorded for inter-rater reliability assessment; all 10 diagnoses were confirmed by a clinical psychologist (GH). None of the participants were taking psychotropic medications, had suffered head injuries or had serious medical conditions. All participants provided informed consent and were compensated for their time. The study was approved by the Stony Brook University Institutional Review Board (IRB).

MATERIALS

Pictures were selected from the IAPS[18] and are reported in MacNamara and Hajcak.[17] There were 48 aversive pictures (e.g., attack scenes, mutilated bodies) and 48 neutral pictures (e.g., household objects, neutral faces). Normative ratings[18] indicated that the aversive pictures were less pleasant and more arousing than the neutral pictures.[17]

Stimuli were presented on a Pentium D computer, using Presentation software.[47] Pictures were displayed in color for 250 ms at a size of 293 pixels across by 219 pixels high, or approximately 1/12 of the total monitor area (1024×768 pixels; 48.26 cm). Participants were seated approximately 60 cm from the screen.

Self-reported anxiety and depression levels were measured using the Mood and Anxiety Symptom Questionnaire (MASQ)—Short Form.[48,49] The MASQ is a 62-item self-report measure comprising four subscales, two that index anxiety symptoms: "Anxious Arousal" (17 items) and "General Distress–Anxiety Symptoms" (11 items) and two that index depressive symptoms: "Anhedonic Depression" (22 items) and "General Distress–Depressive Symptoms" (12 items). Participants indicate how much each item describes how they have felt "during the past week, including today" using a 5-point scale ranging from *1 = not at all* to *5 = extremely.*

PROCEDURE

Participants completed the MASQ;[48] next, they were told that they would be viewing pictures of varying emotional quality. Following this, participants were seated and electroencephalograph sensors (EEG) were attached. All GAD and HC participants performed multiple tasks in a random order during the experiment; results of other tasks will be reported elsewhere. Figure 1 depicts the task reported here, which was identical to that described in MacNamara and Hajcak[17] In brief, four pictures were presented simultaneously on each trial—two were positioned to the left and right, and two were positioned above and below the center of the screen; participants were told that they would be required to indicate whether two of the pictures were the same or different. In particular, participants were told that on some trials, they would make this same/different decision about the vertical picture pair, and on other trials, they would make this same/different decision about the horizontal picture pair. Picture valence (i.e., aversive or neutral) was always the same in both the horizontal and vertical pairs; in other words, neutral and aversive pictures were never mixed *within* the horizontal and vertical pairs. Before each trial, two white rectangles appeared on a black background for 1,000 ms and indicated which picture pair (i.e., horizontal or vertical) would be the targets for the same/different decision in the upcoming trial. From here on, stimuli presented in attended spatial locations will be referred to as "targets," whereas those presented in unattended locations will be referred to as "distracters." There were four trial types: neutral targets paired with neutral distracters, neutral targets paired with aversive distracters, aversive targets paired with neutral distracters, and aversive targets paired with aversive distracters. Participants used the left and right arrow keys (counterbalanced across participants) to indicate if targets were identical ("same") or different ("different"); speed and accuracy of responses were emphasized. The trial ended as soon as a participant responded or 1,800 ms after picture offset if no response was made. Participants performed 10 practice trials, followed by 320 experimental trials.

ELECTROENCEPHALOGRAPHIC RECORDING AND BEHAVIORAL RESPONSES

An elastic cap and the ActiveTwo BioSemi system[50] were used to record the continuous EEG. Thirty-four electrode sites (standard 32 channel setup plus Iz and FCz), based on the 10/20 system, were used, as well as one electrode on each of the left and right mastoids. Four facial electrodes recorded the electrooculogram generated from eye blinks and eye movements: vertical eye movements and blinks were measured with two electrodes placed approximately 1 cm above and below the right eye; horizontal eye movements were measured with two electrodes placed approximately 1 cm beyond the outer edge of each eye. Online data were referenced according to BioSemi's design, which replaces the ground electrode used in conventional

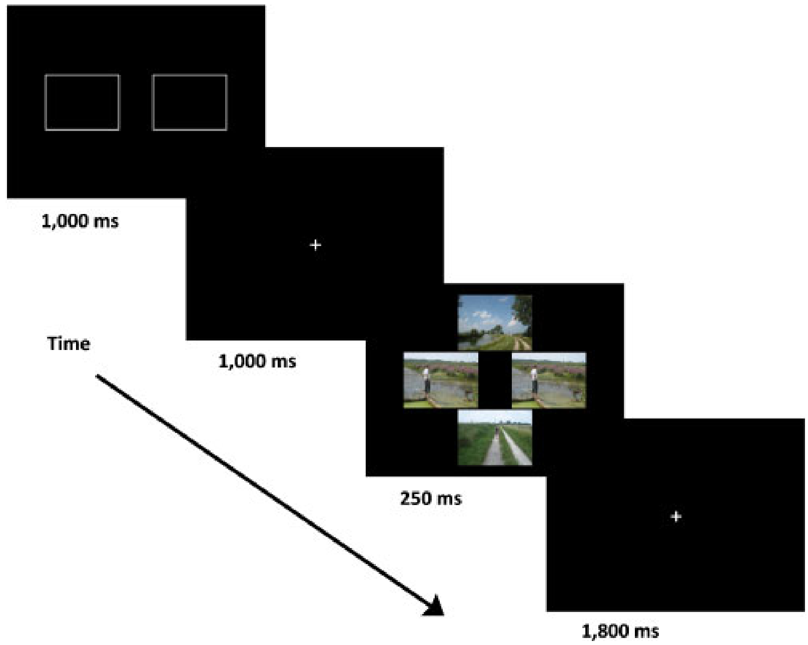

Figure 1. An example of a "same" trial from the task: two horizontal (or vertical) white rectangles were presented on a black background, directing participants' attention to the pair of upcoming "target" pictures. Following the onset of four images, participants indicated as quickly and as accurately as they could whether the pair of target images (those that replaced the rectangles) were identical ("same") or different ("different"). Fixation crosses are enlarged for illustrative purposes.

systems with two separate electrodes (the Common Mode Sense active electrode and the Driven Right Leg passive electrode). These electrodes form a feedback loop, driving the common mode potential of the participant down and reducing the effective impedance of the ground.

ActiView software[50] was used to digitize the EEG data at 1024 Hz. Off-line analyses were performed using Brain Vision Analyzer software.[51] Data were re-referenced to the average of the two mastoids and band-pass filtered with low and high cutoffs of 0.1 and 30 Hz, respectively. The EEG was segmented for each trial beginning 200 ms before picture onset and continuing for 1,200 ms (1,000 ms beyond picture onset). For each trial, the baseline was defined as the 200 ms before picture onset. Eye blink and ocular corrections were made using the method developed by Gratton et al.[52] Noisy data due to technical problems on isolated electrodes necessitated the replacement of data from C4 in one subject and Pz in another subject. Data were interpolated from the closest four electrodes in each case. Artifact analysis identified a voltage step of more than 50 μV between sample points, a voltage difference of 300 μV within a trial, and a maximum voltage difference of less than 0.50 μV within 100 ms intervals; trials were also inspected visually for any remaining artifacts. Intervals containing artifacts were rejected from individual channels in each trial. As in previous work on this task,[17] the parietal positivity was scored by averaging activity from 400 to 800 ms at four centro-parietal sites where the LPP was maximal: CP1, CP2, Cz, and Pz.

Four averages (80 trials of each condition) were created for each participant: neutral targets paired with neutral distracters, neutral targets paired with aversive distracters, aversive targets paired with neutral distracters, and aversive targets paired with aversive distracters. Behavioral data was examined for human or computer error: only trials associated with a correct response made within 1,800 ms following picture offset were included in the ERP analyses. Average reaction time per condition was determined as the average time taken to respond following picture onset on correct trials. The percentage of correct responses per condition was calculated as the number of correct trials divided by 80 trials in each condition.

The LPP, reaction time, and percentage of correct trials were evaluated with a 2 (target location: neutral, aversive) × 2 (distracter location: neutral, aversive) × 2 (group: HC, GAD) mixed-model analysis of variance. Statistical analyses were performed using PASW (Version 17.0) General Linear model software.

RESULTS

PARIETAL POSITIVITY (LPP)

Figure 2 (top) shows the scalp distributions of the amplitude differences (topographic maps) for aversive minus neutral targets (left) and aversive minus neutral distracters (right), across all participants, from 400 to 800 ms following picture onset; and (bottom) grand average waveforms for each of the four trial types at centro-parietal sites (i.e., the average of CP1, CP2, Cz, and Pz), across all participants.

Aversive compared to neutral targets appeared to elicit larger amplitudes for GAD participants when presented with neutral distracters. Figure 3 shows the ERP waveforms for each of the four trial types at centro-parietal sites for HC (left) and GAD (right) participants separately. Figure 4 shows the scalp distributions of voltage differences (topographic maps) from 400 to 800 ms after picture onset for aversive minus neutral targets when distracters were neutral (left column) and aversive (right column). Differences are shown separately for HC (top row) and GAD (bottom row) participants. As suggested by Figures 3 and 4, there was a significant three-way interaction between group, target, and distracter type ($F(1,28) = 16.74$, $P < .0005$, $\eta^2_p = .37$). Bonferroni-corrected independent samples *t* tests (critical $P = .025$) confirmed that the GAD group had larger increases in the LPP for aversive compared to neutral targets than the HC group, but only when distracters were neutral ($t(28) = 3.16$, $P < .005$); no such difference between groups was evident when the distracters were aversive ($P > .13$). Thus, when distracters were neutral, individuals with GAD were characterized by a larger electrocortical response for aversive relative to neutral targets.

Across groups, aversive compared to neutral pictures were also associated with a more positive LPP, as has been found in previous research;[19,22,23,28,31,32,53] this effect, however, was confined to aversive pictures presented in attended locations.[17] Thus, the impression from Figure 2 was confirmed statistically: the LPP was larger for aversive compared to neutral targets ($F(1,28) = 33.62$, $P < .0001$, $\eta^2_p = .55$; see Table 1 for means). There was no effect of distracter type and there were no significant two-way interactions between target and distracter type, group and target type, or group and distracter type (all Ps $> .09$). There was also no overall difference in LPP amplitude between the GAD and HC groups ($P > .71$).

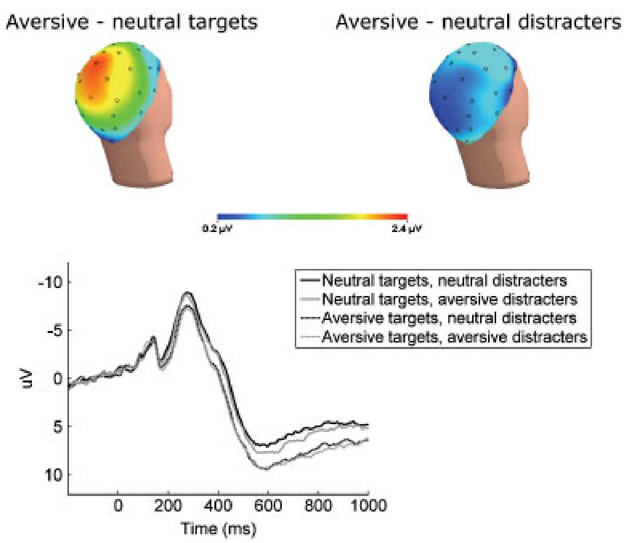

Figure 2. Top row: spatial distributions of the amplitude differences (topographic maps) for aversive minus neutral targets (top left) and aversive minus neutral distracters (top right), 400–800 ms after picture onset, across all participants. Bottom row: grand average waveforms (in µV) in each of the four conditions at centro-parietal pooling CP1, CP2, Cz, and Pz, across all participants.

BEHAVIORAL DATA

Participants generally performed well on the task ($M = 84.8$ % correct, $SD = 9.5$). The average percent of correct responses according to condition and participant group are presented in Table 1. Participants made significantly more errors on trials with aversive compared to neutral distracters ($F(1,28) = 26.82$, $P < .0001$, $\eta^2_p = .49$); error rate did not vary for target type or group and there was no interaction between target type and group (all Ps $> .22$). However, an interaction between group and distracter type ($F(1,28) = 5.24$, $P < .03$, $\eta^2_p = .16$) revealed that compared to the HC group, participants in the GAD group made significantly more errors when distracters were aversive. Group, target type, and distracter type did not interact ($P > .80$).

Average reaction times per condition and for each participant group are also presented in Table 1. There was no effect of distracter ($P > .45$) or target type ($P > .08$) on the speed at which participants performed the task. In addition, reaction time did not vary by group and there were no two-way or three-way interactions between group, target, or distracter type (all Ps $> .08$).

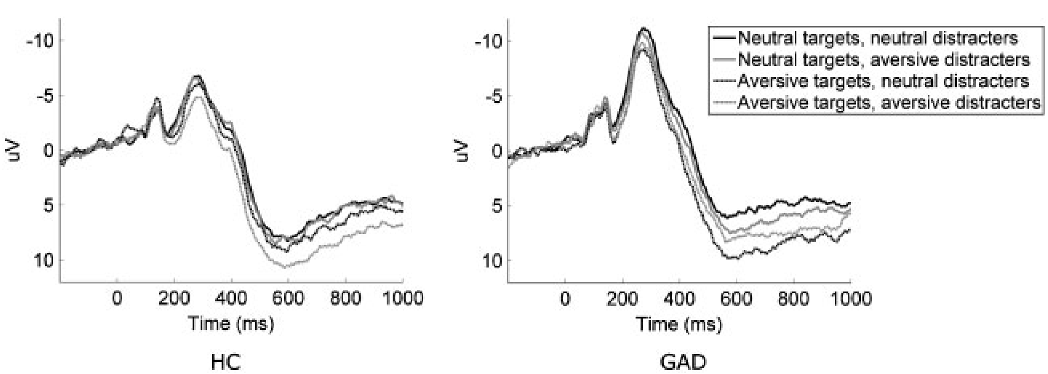

Figure 3. Grand average waveforms (in µV) for HC (left) and GAD (right) participants, in each of the four conditions, at centro-parietal pooling CP1, CP2, Cz, and Pz.

MASQ

Average scores and standard deviations for GAD and HC groups on each of the four subscales of the MASQ[48] are presented in Table 2. Compared with the HC group, participants in the GAD group had higher levels of anxiety (Anxious Arousal: $t(28) = 3.34$, $P < .005$; General Distress–Anxiety Symptoms: $t(28) = 4.94$, $P < .005$) and depressive symptoms (Anhedonic Depression: $t(28) = 2.96$, $P < .01$; General Distress–Depressive Symptoms: $t(28) = 3.33$, $P < .005$). To determine the extent to which between-group differences in the LPP and behavioral results varied with anxiety and depression level across participants, bivariate correlations were performed between scores on the four subscales of the MASQ and each of: (a) the difference in the LPP to aversive minus neutral targets paired with neutral distracters and (b) the difference in the percentage of trials on which participants responded correctly when distracters were aversive compared with when they were neutral. Individuals with greater scores on the General Distress–Anxiety Symptoms subscale had larger LPPs to aversive compared with neutral targets when distracters were neutral ($r(30) = .40$, $P < .05$); there were no other significant correlations with the LPP difference score (all $Ps > .23$). In addition, greater scores on the Anhedonic Depression subscale were associated with a smaller percentage of correct responses on trials involving aversive compared with neutral distracters ($r(30) = -.42$, $P < .05$); there were no other significant correlations with this difference score (all $Ps > .24$).

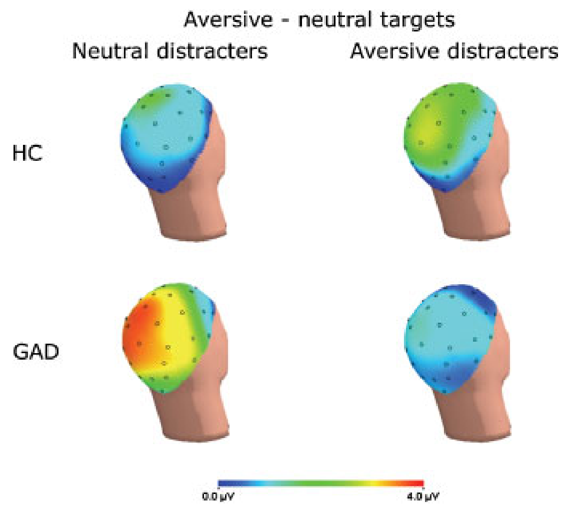

Figure 4. Spatial distributions of the amplitude differences (topographic maps) for aversive minus neutral targets on trials with neutral (left column) and aversive (right column) distracters, 400–800 ms after picture onset. Differences are shown separately for HC (top row) and GAD (bottom row) participants.

DISCUSSION

In order to more fully examine the nature of attentional biases toward threat among individuals with GAD, ERP, and behavioral measures were recorded following the simultaneous presentation of both neutral and aversive pictures in attended and unattended spatial locations. As in previous work,[17] aversive pictures presented in attended locations

TABLE 1. From top to bottom: mean LPP, percentage of trials on which participants responded correctly and reaction time (and standard deviations) for participants in the HC and GAD groups, for each condition. From left to right: neutral targets and neutral distracters; neutral targets and aversive distracters; aversive targets and neutral distracters; and aversive targets and aversive distracters

		Neutral targets neutral distracters	Neutral targets aversive distracters	Aversive targets neutral distracters	Aversive targets aversive distracters
LPP (μv)	HC	5.58 (8.54)	5.88 (8.54)	6.72 (7.43)	8.42 (7.80)
	GAD	4.02 (4.67)	5.19 (5.17)	7.63 (4.84)	6.28 (4.93)
Correct trials (%)	HC	87.3 (8.0)	85.8 (10.5)	88.1 (9.6)	86.2 (8.6)
	GAD	84.3 (8.9)	80.5 (11.2)	85.6 (9.4)	80.6 (9.2)
Reaction time (ms)	HC	719 (128)	731 (133)	747 (137)	742 (128)
	GAD	790 (165)	802 (179)	795 (177)	796 (163)

TABLE 2. Mean scores (and standard deviations) on each of the four subscales of the MASQ (from left to right): Anxious Arousal; Anhedonic Depression; General Distress–Anxiety Symptoms; and General Distress–Depressive Symptoms, for participants in each of the HC (top row) and GAD (bottom row) groups

	Anxious Arousal	Anhedonic Depression	General Distress–Anxiety Symptoms	General Distress–Depressive Symptoms
HC	19.93 (3.82)	49.40 (13.95)	15.07 (4.91)	17.93 (8.26)
GAD	26.13 (6.08)	62.80 (10.61)	24.33 (5.37)	26.80 (6.16)

elicited increased LPPs across participants. Relative to the HC group, the GAD group had larger LPPs to aversive targets when distracters were neutral. On the other hand, aversive distracters resulted in more errors across both groups,[17] though this effect was larger in the GAD group. Together, these results suggest that behavioral and electrocortical measures might index separate, but complimentary aspects of attentional bias toward threat in GAD.

In particular, individuals with GAD demonstrated greater behavioral interference from aversive *distracters*—work that is consistent with some previous behavioral studies.[40,54] This follows on the suggestion that anxiety may be characterized by an overactive stimulus-driven attentional system, which can result in increased attention to task-irrelevant and aversive stimuli in the environment.[3] It has been suggested that anxiety may broaden attention,[11] resulting in greater attention to threat presented in peripheral locations.[55] Consequently, aversive distracters in the present paradigm may have received prioritized processing—and this effect may be greater among individuals with GAD. Importantly, depressive symptomatology as reported on the MASQ (Anhedonic Depression) was uniquely associated with increased errors for aversive compared to neutral distracters; thus, future work might determine the extent to which dysphoria may contribute to behavioral measures of attentional biases in GAD.[56]

Although aversive distracters increased error rates, these trials were not associated with an increased LPP overall.[17] These data are consistent with previous work indicating that the emotional modulation of the LPP is highly sensitive to manipulations of spatial attention.[17,26–29] In this context, behavioral measures may be relatively less sensitive to manipulations of spatial attention; indeed, previous work has shown that behavioral interference may occur even when aversive stimuli are presented subliminally.[57–60]

In regards to neural measures of attentional bias, aversive pictures in attended locations elicited larger LPPs in GAD compared with control participants—but only when neutral pictures were presented in unattended locations. This difference appeared related specifically to self-reported anxiety across participants: higher scores on the MASQ (General Distress–Anxiety Symptoms) were associated with larger LPPs to aversive compared with neutral targets when distracters were neutral; this effect was not driven by individual differences in depression.

Thus, although both control and GAD participants exhibited larger LPPs to aversive targets, individuals with GAD had larger LPPs than control participants when aversive targets were paired with neutral distracters. One possible explanation of this effect is that individuals with GAD may have perceived neutral distracters as more emotionally salient. That is, although neutral compared to aversive distracters may be associated with decreased reactivity among participants low in anxiety, neutral distracters may receive comparable processing as aversive distracters for participants with GAD. This follows on the suggestion by Mogg and Bradley[5] that anxiety may increase the extent to which individuals perceive even relatively innocuous stimuli as aversive.

On the other hand, the behavioral results suggest that *aversive* distracters had a greater impact on performance for GAD compared to control participants. Therefore, another possibility is that individuals with GAD may have allocated greater processing resources to aversive information in target locations, but *only* when there was relatively little competition for attention from pictures in unattended locations. In other words, participants with GAD may have had insufficient resources to engage in the amplified processing of aversive targets when paired with aversive distracters; when distracters were neutral and commanded less attention, individuals with GAD might have had more processing resources to devote to the threatening nature of aversive targets.

Interestingly, aversive targets did not impact behavioral measures. Several studies have similarly found that ERPs may index processing biases in anxiety even when behavioral responses do not.[16–17,61–64] In fact, previous work suggests that a variety of intermediary factors may determine whether attentional biases impact behavior. For example, work by Derryberry and Reed[65] demonstrated that only anxious individuals with low levels of attentional control exhibited behavioral interference from aversive stimuli. In the context of attentional control theory, anxiety should have a more consistent impact on processing efficiency than processing effectiveness.[3] During the majority of tasks, attentional biases would be expected to increase the resources consumed by the task, whereas behavioral performance might be impacted in some, but not all cases.[3] In terms of the present paradigm, the LPP and behavioral results could be understood in terms of processing *efficiency* and *effectiveness*, respectively. The LPP may provide an index of increased engagement of the stimulus-driven attentional system in anxiety—even when these effects do not modulate task performance. In other words, larger LPPs may suggest greater expenditure of attentional resources on task-irrelevant stimulus dimensions, and therefore, reflect reduced processing efficiency among individuals with GAD. On the other hand, behavioral measures track the effects of decreased attentional control on task execution (i.e., processing effectiveness). Thus, this study, by examining both ERP and behavioral measures, suggests that individuals with GAD are characterized by reduced processing efficiency and decreased processing effectiveness, respectively.

To better understand the mechanisms underlying reduced processing efficiency and effectiveness in GAD, future work may benefit by parsing the contributions of initial orientation, avoidance, disengagement, and set-shifting to attentional biases, as has been initiated in nonclinical samples.[9,10,66] For example, researchers using the dot-probe task have measured reaction times to targets that appear in place of threatening ("threat congruent") versus neutral stimuli ("threat incongruent"), compared with a neutral baseline (when targets replace one of two neutral stimuli) in order to derive indices of initial attention toward and disengagement from threatening stimuli, respectively.[67] Recent results from this work have suggested that anxiety may primarily be characterized difficulty *disengaging from* as opposed to increased *initial attention toward* threatening stimuli.[10,68–70] These paradigms could be extended to individuals with GAD and could be supplemented by measurement of the LPP, which appears to index different facets of attentional bias than behavioral measures. Eye-tracking, especially in the context of longer stimulus presentation, may also be useful in future studies aimed at differentiating attention toward versus disengagement from threatening stimuli in GAD.

In addition to examining the effect of anxiety on attentional bias to external aversive stimuli, future work might also examine attention to *internal* aversive stimuli (e.g., worry) and related consequences for processing efficiency and effectiveness.[3] Worry is a hallmark of GAD, and it is possible that increased attention toward worrying thoughts may have had additive or interactive effects on neural response to external aversive stimuli. Future work could test this hypothesis by measuring levels of worrying thoughts just before task performance, or by manipulating levels of worry experimentally. Some work has been done in this regard—for example, Oathes et al.[71] found that compared with control participants, individuals with GAD exhibited greater posterior gamma activation following a worry manipulation. Interestingly, gamma response at these same sites was also decreased in individuals with GAD following successful treatment.

As suggested by Mennin[72] individuals with GAD may be particularly sensitive to emotional or aversive information, and may benefit from therapy aimed at improving emotion regulation skills. Based on the present results, the LPP and behavioral response could be used to measure initial attention to aversive stimuli, as well as declines in attentional biases toward threat following treatment. Moreover, the emotion regulation skills of individuals with GAD could be evaluated both before and after treatment, using the LPP.[21,32,73–75] Thus, in addition to characterizing potential etiological and maintaining factors in GAD, LPP, and behavioral indices of attentional bias toward threat may eventually prove useful in evaluating treatment progress and outcome in GAD.

REFERENCES

1. Beck A, Emery G. Anxiety Disorders and Phobias: A Cognitive Perspective. New York: Basic Books; 1985.
2. Eysenck M. Anxiety and Cognition: A Unified Theory. Hove: Erlbaum; 1997.
3. Eysenck M, Derakshan N, Santos R, Calvo M. Anxiety and cognitive performance: attentional control theory. Emotion 2007;7:336–353.
4. Mathews A, MacLeod C. Induced processing biases have causal effects on anxiety. Cogn Emotion 2002;16:331–354.
5. Mogg A, Bradley B. A cognitive–motivational analysis of anxiety. Behav Res Ther 1998;36:809–848.
6. Williams J, Watts F, MacLeod C, Mathews A. Cognitive Psychol Emotional Disorders. Chichester: Wiley; 1997.
7. MacLeod C, Mathews A, Tata P. Attentional bias in emotional disorders. J Abnorm Psychol 1986;95:15–20.
8. Bar-Haim Y, Lamy D, Pergamin L, et al. Threat-related attentional bias in anxious and nonanxious individuals: a meta-analytic study. Psychol Bull 2007;133:1–24.
9. Bradley B, Mogg K, Falla S, Hamilton L. Attentional bias for threatening facial expressions in anxiety: manipulation of stimulus duration. Cogn Emotion 1998;12:737–753.
10. Fox E, Russo R, Bowles R, Dutton K. Do threatening stimuli draw or hold visual attention in subclinical anxiety? J Exp Psychol 2001;130:681–700.
11. Eysenck M. Anxiety: The Cognitive Perspective. Hove: Erlbaum; 1992.
12. Bishop S, Duncan J, Lawrence A. State Anxiety Modulation of the Amygdala Response to Unattended Threat-Related Stimuli. J Neurosci 2004;24:10364–10368.
13. Bishop S, Jenkins R, Lawrence A. Neural processing of fearful faces: effects of anxiety are gated by perceptual capacity limitations. Cereb Cortex 2007;17:1595–1603.
14. Broadbent D, Broadbent M. Anxiety and attentional bias: state and trait. Cogn Emotion 1988;2:165–183.
15. MacLeod C, Mathews A. Anxiety and the allocation of attention to threat. Q J Exp Psychol A 1988;40:653–670.
16. Bar-Haim Y, Lamy D, Glickman S. Attentional bias in anxiety: a behavioral and ERP study. Brain Cogn 2005;59: 11–22.
17. MacNamara A, Hajcak G. Anxiety and spatial attention moderate the electrocortical response to aversive pictures. Neuropsychologia 2009;47:2975–2980.
18. Lang P, Bradley M, Cuthbert B. International affective picture system (IAPS): affective ratings of pictures and instruction manual. Technical Report A-6. University of Florida, Gainesville, FL, 2005.
19. Cuthbert B, Schupp H, Bradley M, et al. Brain potentials in affective picture processing: covariation with autonomic arousal and affective report. Biol Psychol 2000;52:95–111.
20. Dillon D, Cooper J, Grent-'t-Jong T, et al. Dissociation of event-related potentials indexing arousal and semantic cohesion during emotional word encoding. Brain Cogn 2006; 62:43–57.
21. Foti D, Hajcak G. Deconstructing reappraisal: descriptions preceding arousing pictures modulates the subsequent neural response. J Cogn Neurosci 2008;20:977–988.
22. Hajcak G, Dunning J, Foti D. Neural response to emotional pictures is unaffected by concurrent task difficulty: An event-related potential study. Behav Neurosci 2007;121: 1156–1162.
23. Hajcak G, Olvet D. The persistence of attention to emotion: brain potentials during and after picture presentation. Emotion 2008;8:250–255.
24. Pastor M, Bradley M, Löw A, et al. Affective picture perception: emotion, context, and the late positive potential. Brain Res 2008;1189:145–151.

25. Schupp H, Cuthbert B, Bradley M, et al. Affective picture processing: the late positive potential is modulated by motivational relevance. Psychophysiology 2000;37:257–261.
26. Dunning J, Hajcak G. See no evil: directing visual attention within unpleasant images modulates the electrocortical response. Psychophysiology 2009;46:28–33.
27. Eimer M, Holmes A, McGlone F. The role of spatial attention in the processing of facial expression: an ERP study of rapid brain responses to six basic emotions. Cogn Affect Behav Neurosci 2003;3:97–110.
28. Hajcak G, Dunning J, Foti D. Motivated and controlled attention to emotion: time-course of the late positive potential. Clin Neurophysiol 2009;120:505–510.
29. Holmes A, Vuilleumier P, Eimer M. The processing of emotional facial expression is gated by spatial attention: evidence from event-related brain potentials. Cogn Brain Res 2003;16: 174–184.
30. Mathews A, Mackintosh B, Fulcher E. Cognitive biases in anxiety and attention to threat. Trends Cogn Sci 1997;1:340–345.
31. Codispoti M, Ferrari V, Bradley M. Repetition and event-related potentials: distinguishing early and late processes in affective picture perception. J Cogn Neurosci 2007;19:577–586.
32. MacNamara A, Foti D, Hajcak G. Tell me about it: neural activity elicited by emotional stimuli and preceding descriptions. Emotion 2009;9:531–543.
33. Derakshan N, Eysenck M. Anxiety, processing efficiency, and cognitive performance: new developments from attentional control theory. Eur Psychol 2009;14:168–176.
34. Kessler R, DuPont R, Berglund P, Wittchen H. Impairment in pure and comorbid generalized anxiety disorder and major depression at 12 months in two national surveys. Am J Psychiatry 1999;156:1915–1923.
35. Kessler R, Rubinow D, Holmes C, et al. The epidemiology of DSM-III-R bipolar I disorder in a general population survey. Psychol Med 1997;27:1079–1089.
36. Wittchen H-U, Carter R, Pfister H, et al. Disabilities and quality of life in pure and comorbid generalized anxiety disorder and major depression in a national survey. Int Clin Psychopharmacol 2000;15:319–328.
37. Borkovec T, Ruscio A. Psychotherapy for generalized anxiety disorder. J Clin Psychiatry 2001;62:37–45.
38. Fisher P, Durham R. Recovery rates in generalized anxiety disorder following psychological therapy: an analysis of clinically significant change in the STAI-T across outcome studies since 1990. Psychol Med 1999;29:1425–1434.
39. Behar E, DiMarco I, Hekler E, et al. Current theoretical models of generalized anxiety disorder (GAD): conceptual review and treatment implications. J Anxiety Disord 2009;23: 1011–1023.
40. Bradley B, Mogg K, White J, et al. Attentional bias for emotional faces in generalized anxiety disorder. Br J Clin Psychol 1999;38: 267–278.
41. Mogg K, Millar N, Bradley B. Biases in eye movements to threatening facial expressions in generalized anxiety disorder and depressive disorder. J Abnorm Psychol 2000;109: 695–704.
42. Rinck M, Becker E, Kellermann J, Roth W. Selective attention in anxiety: distraction and enhancement in visual search. Depress Anxiety 2003;18:18–28.
43. Freeman D, Garety P, Phillips M. The examination of hypervigilance for external threat in individuals with generalized anxiety disorder and individuals with persecutory delusions using visual scan paths. Q J Exp Psychol A 2000;53A:549–567.
44. Monk C, Nelson E, McClure E, et al. Ventrolateral prefrontal cortex activation and attentional bias in response to angry faces in adolescents with generalized anxiety disorder. Am J Psychiatry 2006;163:1091–1097.
45. Whalen P, Johnstone T, Somerville L, et al. A functional magnetic resonance imaging predictor of treatment response to venlafaxine in generalized anxiety disorder. Biol Psychiatry 2008; 63:858–863.
46. First M, Spitzer R, Gibbon M, Williams J. Structured Clinical Interview for DSM-IV Axis I Disorders—Non-patient edition (SCID-I/NP). New York: Biometric Research Department; 1995.
47. Neurobehavioral Systems, Inc. Albany, CA.
48. Watson D, Clark L. The Mood and Anxiety Symptom Questionnaire. Iowa City, IA: University of Iowa; 1991.
49. Watson D, McKee Walker L. The long-term stability and predictive validity of trait measures of affect. J Pers Soc Psychol 1996;70:567–577.
50. BioSemi. Amsterdam, Netherlands.
51. Brain Products. Gilching, Germany.
52. Gratton G, Coles M, Donchin E. A new method for off-line removal of ocular artifact. Electroencephalogr Clin Neurophysiol 1983;55:468–484.
53. Foti D, Hajcak G, Dien J. Differentiating neural responses to emotional pictures: evidence from temporal-spatial PCA. Psychophysiol 2009;46:521–530.
54. Taghavi M, Neshat-Doost H, Moradi A, et al. Biases in visual attention in children and adolescents with clinical anxiety and mixed anxiety-depression. J Abnorm Child Psychol 1999;27:215–223.
55. Keogh E, French C. The effect of trait anxiety and mood manipulation on the breadth of attention. Eur J Pers 1999;13:209–223.
56. Bradley B, Mogg K, Lee S. Attentional biases for negative information in induced and naturally occurring dysphoria. Behav Res Ther 1997;35:911–927.
57. MacLeod C, Rutherford E. Anxiety and the selective processing of emotional information: mediating roles of awareness, trait and state variables and personal relevance of stimulus materials. Behav Res Ther 1992;30:479–491.
58. MacLeod C, Hagan R. Individual differences in the selective processing of threatening information, and emotional responses to a stressful life event. Behav Res Ther 1992;30:151–161.
59. Mogg K, Bradley B, Williams R, Mathews A. Subliminal processing of emotional information in anxiety and depression. J Abnorm Psychol 1993;102:304–311.
60. van den Hout M, Tenney N, Huygens K, et al. Responding to subliminal threat cues is related to trait anxiety and emotional vulnerability: a successful replication of Macleod and Hagan (1992). Behav Res Ther 1995;33:451–454.
61. Hajcak G, Franklin M, Foa E, Simons R. Increased error-related brain activity in pediatric obsessive-compulsive disorder before and after treatment. Am J Psychiatry 2008;165:116–123.
62. Hajcak G, McDonald N, Simons R. Anxiety and error-related brain activity. Biol Psychol 2003;64:77–90.
63. Hajcak G, Simons R. Error-related brain activity in obsessive-compulsive undergraduates. Psychiatry Res 2002;110:63–72.
64. Moser J, Hajcak G, Huppert J, et al. Interpretation bias in social anxiety as detected by event-related brain potentials. Emotion 2008;8:693–700.
65. Derryberry D, Reed M. Anxiety-related attentional biases and their regulation by attentional control. J Abnorm Psychol 2002;111:225–236.
66. Mogg K, Bradley B, Miles F, Dixon R. Time course of attentional bias for threat scenes: Testing the vigilance-avoidance hypothesis. Cogn Emotion 2004;18:689–700.

67. Koster E, Crombez G, Verschuere B, De Houwer J. Selective attention to threat in the dot probe paradigm: differentiating vigilance and difficulty to disengage. Behav Res Ther 2004;42:1183–1192.
68. Koster E, Crombez G, Verschuere B, De Houwer J. Attention to threat in anxiety-prone individuals: mechanisms underlying attentional bias. Cogn Ther Res 2006;30:635–643.
69. Yiend J, Mathews A. Anxiety and attention to threatening pictures. Q J Exp Psychol 2001;54:665–681.
70. Fox E, Russo R, Dutton K. Attentional bias for threat: evidence for delayed disengagement from emotional faces. Cogn Emotion 2002;16:355–379.
71. Oathes D, Ray W, Yamasaki A, et al. Worry, generalized anxiety disorder, and emotion: Evidence from the EEG gamma band. Biol Psychol 2008;79:165–170.
72. Mennin D. Emotion regulation therapy for generalized anxiety disorder. Clin Psychol Psychother 2004;11:17–29.
73. Moser J, Hajcak G, Bukay E, Simons R. Intentional modulation of emotional responding to unpleasant pictures: an ERP study. Psychophysiology 2006;43:292–296.
74. Krompinger J, Moser J, Simons R. Modulations of the electrophysiological response to pleasant stimuli by cognitive reappraisal. Emotion 2008;8:132–137.
75. Hajcak G, Nieuwenhuis S. Reappraisal modulates the electrocortical response to unpleasant pictures. Cogn Affect Behav Neurosci 2006;6:291–297.