

Electrocortical evidence for vigilance-avoidance in Generalized Anxiety Disorder

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Abstract

Both exaggerated and attenuated responses to emotional stimuli have been documented in Generalized Anxiety Disorder (GAD). Event-related potentials are well-suited for examining the time-course of neural activity during emotional processing; early components (e.g., the P1) appear to index relatively automatic attention to emotional stimuli, whereas later positivities (e.g., the late positive potential or LPP) index dynamic allocation of attention to emotional stimuli. Twenty-one individuals with GAD and 25 healthy controls (HC) passively viewed emotional and neutral images while ERPs were recorded. An enhanced P1 for unpleasant compared to neutral images was larger in GAD. In addition, the increased LPP to unpleasant compared to neutral images was diminished in the GAD group. These data provide evidence for early hypervigilance for emotional stimuli, followed by failure to engage in elaborative processing, in GAD.

Descriptors: Generalized Anxiety Disorder, Attention, Emotion, Event-related potentials

Generalized Anxiety Disorder (GAD) is a pervasive and often chronic disorder affecting between 4% to 7% of the population (Brawman-Mintzer & Lydiard, 1996; Kessler et al., 1994; Kessler & Wittchen, 2002). GAD is associated with increased health care utilization (Blazer, Hughes, George, Swartz, & Boyer, 1991; Judd et al., 1998; Kessler & Wittchen, 2002) and costs (Greenberg, Sisitsky, & Kessler, 2001), as well as significant social, academic, and vocational impairment (Blazer et al., 1991; Judd et al., 1998; Kessler & Wittchen, 2002; Wittchen, Zhao, Kessler, Eaton, & Ballenger, 1996). Despite its significant public health impact, GAD is not well understood, and the pathophysiology of the disorder is relatively understudied (Dugas, 2000; Mennin, Heimberg, Turk, & Fresco, 2002).

Abnormal allocation of attention to emotional material is thought to play a central role in GAD (Mennin, Heimberg, Turk, & Fresco, 2005; Mennin, Holaway, Fresco, Moore, & Heimberg, 2007; Mogg & Bradley, 2005; Mogg, Bradley, Millar, & White, 1995). For instance, there is ample evidence that individuals with anxiety disorders in general (Bar-Haim et al., 2007; Mogg & Bradley, 1998; Williams, Watts, MacLeod, & Mathews, 1997), and GAD in particular (see, e.g., Mogg & Bradley, 2005, for a review), are characterized by rapid and facilitated attention to threatening stimuli (Bradley, Mogg, Falla, & Hamilton, 1998; Broadbent & Broadbent, 1988; MacNamara & Hajcak, 2010; Mogg et al., 2000), and attentional biases to masked and unattended threatening stimuli (Bishop, Duncan, & Lawrence, 2004; Fox, 1996). However, fMRI research has not consistently found

differences in limbic reactivity to affective stimuli in GAD compared to control groups (Blair et al., 2008; Monk et al., 2006; Whalen et al., 2008).

Neuroimaging research in this area may be complicated by evidence suggesting that response to emotional stimuli in anxiety disorders can change rapidly over the course of stimulus presentation: following early and rapid hypervigilance, anxious individuals may be characterized by reduced processing of threatening stimuli at later stages (Holmes, Nielsen, & Green, 2008; Koster et al., 2006; Mogg, Bradley, Miles, & Dixon, 2004; Mühlberger et al., 2009). For example, anxious individuals (Mogg, Mathews, & Weinman, 1987; Nugent & Mineka, 1994), including GAD patients (Becker, Roth, Andrich, & Margraf, 1999; Mogg et al., 1987), tend not to show an explicit recall bias for threatening information, and in some instances may demonstrate poorer memory for threatening stimuli (Watts, Sharrock, & Tresize, 1986), suggesting that, while initial attention to emotional material may be enhanced, encoding of this information is not facilitated. Further evidence suggesting early increased processing followed by attentional disengagement in anxious individuals also comes from eye-tracking studies (Pflugshaupt et al., 2005; Rohner, 2002; Wieser, Pauli, Weyers, Alpers, & Mühlberger, 2009), fMRI paradigms using cued threat images (Nitschke et al., 2009), and finally ERP research (Holmes et al., 2008; Mueller et al., 2008; Mühlberger et al., 2009). Collectively, these results suggest that attention to emotional stimuli in anxiety disorders might be best understood in terms of rapid orienting and increased response to emotionally salient material, followed by diminished processing at later stages (e.g., vigilance-avoidance; Mogg et al., 1987, 2004). However, despite conceptual appeal, empirical support for this pattern has not yet emerged in a clinical GAD sample.

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Importantly, these data suggest that shifting patterns of attention toward emotional stimuli in GAD might occur on the order of milliseconds following stimulus presentation. The majority of studies attempting to document this have utilized behavioral tasks such as a modified dot probe. Within anxious populations that do not include GAD, research utilizing the dot probe paradigm has variously found (a) no evidence of *either* vigilance or avoidance (Amir, Elias, Klumpp, & Przeworski, 2003; Horenstein & Segui, 1997), (b) evidence for vigilance alone (e.g., Bradley et al., 1998; Mansell, Ehlers, Clark, & Chen, 2002; Mogg, Bradley, De Bono, & Painter, 1997), or (c) evidence for *both* vigilance and avoidance (e.g., Mogg et al., 2004). To our knowledge, there are no published studies demonstrating vigilance-avoidance biases in GAD using the dot probe task.

One explanation for such inconsistencies across dot probe studies is that behavioral measures alone may not be an ideal measure of attentional allocation. Post-perceptual processes may present an inescapable confound (e.g., motor responding, decision-making), and clinical samples in particular often produce highly variable reaction time data (Mogg & Bradley, 2005). In addition, even the most temporally specific dot-probe task provides snapshots of attention in 500-ms increments; it is ill-suited to provide continuous measures of attention *over time*, and it is difficult to specify *which* attentional processes drive the observed effects—shorter reaction times to targets following emotional stimuli might be the result of either rapid orienting to emotional stimuli or difficulty disengaging attention from those stimuli (Fox, Russo, Bowles, & Dutton, 2001; Fox, Russo, & Dutton, 2002; Yiend & Mathews, 2001).

Because of their excellent temporal resolution, event-related potentials (ERPs) might therefore be a particularly useful tool for providing a dynamic portrait of neural activity as it unfolds over time during emotional processing. In particular, several components of the ERP are sensitive to the emotional content of stimuli during passive viewing, and are larger for emotional (both pleasant and unpleasant) compared to neutral images (Foti, Hajcak, & Dien, 2009; see Hajcak, Weinberg, MacNamara, & Foti, 2010, for a review). Earlier components (e.g., 100–300 ms) have been utilized to index relatively obligatory visual processing of emotional stimuli (Foti et al., 2009; Schupp, Junghöfer, Weike, & Hamm, 2004). For example, the P1—a secondary visual cortical response subject to feedback from higher-order areas—presents as an occipitally maximal positive deflection of the ERP waveform, and peaks between 100–130 ms following picture onset (Foxe & Simpson, 2002; Hajcak, Weinberg, MacNamara, & Foti, 2010; Luck, Heinze, Mangun, & Hillyard, 1990; Vogel & Luck, 2000). The P1 is frequently observed to be larger for emotional compared to neutral images (Holmes et al., 2008; Mueller et al., 2008; Mühlberger et al., 2009), though emotional pictures specifically modulate the centrally-maximal negative end of a dipole active in the time-window of the P1 (Foti et al., 2009).

Later positivities, meanwhile, may indicate more deliberate processing based on the elaborated meaning of stimuli (Foti & Hajcak, 2008; Hajcak, Moser, & Simons, 2006; Hajcak & Nieuwenhuis, 2006; MacNamara, Foti, & Hajcak, 2009). For example, the Late Positive Potential (LPP), a central-parietal positive slow modulation of the ERP, is larger in amplitude to both unpleasant and pleasant compared to neutral stimuli (Cuthbert, Schupp, Bradley, Birbaumer, & Lang, 2000; Radilova, 1982; see Hajcak, Weinberg, MacNamara, & Foti, 2010, for a review). The LPP is observed as early as 250 ms post-stimulus onset and continues for the duration of the stimulus presentation (Codisotti,

Ferrari, & Bradley, 2006; Foti et al., 2009; Schupp et al., 2000), and as much as 1,000 ms after stimulus offset (Hajcak, MacNamara, & Olvet, 2010; Hajcak & Olvet, 2008). However, the LPP is also useful as an online index of flexible attentional engagement (Dunning & Hajcak, 2009; Foti & Hajcak, 2008; MacNamara et al., 2009). The magnitude of the LPP has also been linked to differences in state (MacNamara & Hajcak, 2009, 2010) and trait anxiety (Holmes et al., 2008; Moser, Huppert, Duval, & Simons, 2008; Mühlberger et al., 2009). Collectively, these data suggest that the amplitude of the LPP reflects dynamic attentional engagement with emotional stimuli; moreover, the ability of the LPP to track changes in attention to threat on the order of milliseconds and over a sustained period of time, as well as its sensitivity to individual differences in anxiety, makes it an ideal marker for the measurement of elaborative processing of emotional material in GAD.

The current study aims to capitalize on the excellent temporal resolution of ERPs to examine the time course of emotional response in GAD by measuring neural activation over time in a passive picture viewing paradigm. Based on previous research (Holmes et al., 2008; Mühlberger et al., 2009), it was hypothesized that, compared to non-anxious controls, individuals with GAD would demonstrate facilitated early visual processing of unpleasant images, as indicated by *increased* magnitude of early components such as the P1; and subsequently engage in decreased elaborative processing in response to unpleasant content, as indicated by *decreasing* magnitude of the LPP. By including pleasant pictures, we also examined whether this pattern of neural activity in GAD would be specific to aversive stimuli, or would be evident in response to highly arousing stimuli more generally (e.g., Becker, Rinck, Margraf, & Roth, 2001).

Method

Participant Recruitment and Screening

Participants were recruited from the community via electronic advertisements, and were phone screened prior to their arrival in order to rule out current anti-depressant medication usage and history of traumatic brain injury or systemic or neurological illness. In addition, the phone screen consisted of a modified version of the Mini-International Neuropsychiatric Interview (MINI; Sheehan et al., 1998), a brief semi-structured diagnostic interview designed to screen for 17 Axis I disorders. Based on their responses to the phone screening, participants who were either (a) likely to meet criteria for current GAD and no other current Axis I diagnoses or (b) unlikely to meet criteria for any Axis I diagnoses, past or present, were invited to come to the lab.

Once in the lab, all participants were administered the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders (DSM) fourth edition (SCID-I; Spitzer, Williams, Gibbon, & First, 1992) prior to electroencephalographic (EEG) recording. The SCID-I is a well-validated semi-structured interview that provides a framework upon which to make DSM-IV Axis I diagnoses. The SCID was administered by one of three master's-level clinicians. For each group, 5 diagnostic interviews were recorded for inter-rater reliability assessment; all 10 diagnoses were confirmed by a clinical psychologist (GH).

Participants

A total of 21 participants (18 female) who met diagnostic criteria for GAD participated in the study, along with 25 participants (16

Table 1. Demographic and Clinical Characteristics of Healthy Comparison and Generalized Anxiety Disorder Subjects

	Characteristic	Healthy controls (<i>N</i> = 25)		Generalized Anxiety Disorder (<i>N</i> = 21)		<i>p</i>	
		<i>N</i>	%	<i>N</i>	%		
Gender	Female	16	64	17	81	$\chi^2(1) = 2.51$.11
Ethnicity	Caucasian	12	48	15	67	$\chi^2(3) = 5.17$.16
	African-American	1	4	2	10		
	Asian/Asian-American	8	32	3	10		
	Hispanic/Latino	4	16	1	5		
Demographics	Mean		<i>SD</i>	Mean	<i>SD</i>	<i>t</i> (43) = .18	.86
	Age	29.96	9.45	30.6	13.86		
Past diagnoses	Years of education	15.28	1.72	14.90	2.00	<i>t</i> (43) = .69	.50
	Major depressive disorder	0	–	8	38		
Mood and Anxiety Symptom Questionnaire	Panic disorder	0	–	2	9		
	Anorexia	0	–	1	4		
	Social phobia	0	–	1	4		
	Substance abuse	0	–	1	4		
	No past disorder	25	100	8	38		
Mood and Anxiety Symptom Questionnaire	General distress (anxiety)	14.16	4.08	24.72	5.24	<i>t</i> (41) = 7.43	<.001
	General depression)	17.00	6.79	26.78	6.05	<i>t</i> (41) = 4.87	<.001
	Anxious arousal	19.21	3.23	26.28	5.56	<i>t</i> (41) = 5.18	<.001
	Anhedonic depression	43.36	13.25	63.94	9.35	<i>t</i> (41) = 4.82	<.001

female) who did not meet criteria for any Axis I disorder. Fifteen (2 male) of these were the same GAD participants and 15 (2 male) were the same control participants from MacNamara and Hajcak (2010). Demographic information is presented in Table 1. In the present study, one female GAD was excluded from analysis due to poor quality recordings. All participants were paid \$80.00 for their participation in the study.

Visual Stimuli

Though a number of previous studies have utilized emotional faces to examine attentional biases in anxiety disorders (Holmes et al., 2008; Mühlberger et al., 2009; Mueller et al., 2008), there is some evidence that faces are relatively weak elicitors of emotional response (Britton, Taylor, Sudheimer, & Liberzon, 2006; Holmes et al., 2008). One hundred and thirty-five images were therefore selected from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 2005). Normative ratings (Lang et al., 2005) indicated that the 45 unpleasant pictures were less pleasant (valence $M = 1.90$, $SD = .68$) than the 45 neutral pictures ($M = 5.03$, $SD = .31$) which were less pleasant than the 45 pleasant pictures ($M = 7.19$, $SD = .50$; higher numbers indicate more pleasant ratings). Unpleasant ($M = 6.26$, $SD = .71$) and pleasant ($M = 5.38$, $SD = .93$) images were more emotionally arousing than neutral images ($M = 2.98$, $SD = .54$; higher numbers indicate higher arousal). Specific images used in the study are listed in the Appendix.

All visual stimuli were presented on a Pentium D computer, using Presentation software (Neurobehavioral Systems, Inc., Albany, CA). Prior to each trial, participants viewed a white fixation cross on a black background. Each picture was displayed in color at 48.26 cm, the full size of the monitor. Participants were seated approximately 60.96 cm from the screen and the images occupied about 40° of visual angle horizontally and vertically.

Procedure

Subsequent to verbal instructions indicating that they would be passively viewing pictures of varying emotional quality, partici-

pants were seated and EEG sensors were attached. All GAD and healthy control (HC) participants performed multiple tasks during the experiment; results from other tasks are reported elsewhere (MacNamara & Hajcak, 2010; Weinberg & Hajcak, in press a). The order of the tasks was counterbalanced across subjects to avoid confounds presented by engagement in multiple tasks. For the current study, participants viewed three blocks of images, with each block consisting of pleasant-only, unpleasant-only, and neutral-only images. The order of the blocks was random across subjects, and between each block, participants were given a short break. Within each block, the order of picture presentation was random for each participant, and each image was presented twice; blocks lasted approximately 5 min each. Each image was presented for 1,500 ms (e.g., Mogg et al., 2004), with fixed 2-s intervals between image presentations.

EEG Recording and Data Processing

Continuous EEG recordings were collected using an elastic cap and the ActiveTwo BioSemi system (BioSemi, Amsterdam, Netherlands). Thirty-two electrode sites were used, based on the 10/20 system, as well as two electrodes on the right and left mastoids. Electrooculogram (EOG) generated from eye movements and eyeblinks was recorded using four facial electrodes: horizontal eye movements were measured via two electrodes located approximately 1 cm outside the outer edge of the right and left eyes. Vertical eye movements and blinks were measured via two electrodes placed approximately 1 cm above and below the right eye. The EEG signal was pre-amplified at the electrode to improve the signal-to-noise ratio and amplified with a gain of $\times 16$ by a BioSemi ActiveTwo system (BioSemi). The data were digitized at 24-bit resolution with a sampling rate of 1024 Hz using a low-pass fifth order sinc filter with a half-power cutoff of 204.8 Hz. Each active electrode was measured online with respect to a common mode sense (CMS) active electrode producing a monopolar (non-differential) channel. Offline, all data were re-referenced to the average of the left and right mastoids, and band-pass filtered with low and high cutoffs of 0.1 and 30 Hz,

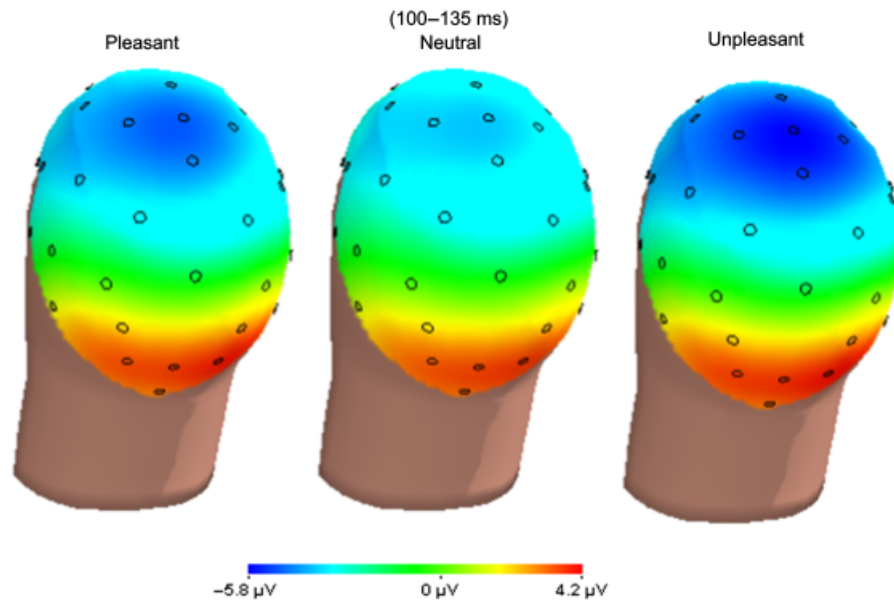


Figure 1. Topographic maps depicting voltages (in μV) from the whole sample for pleasant, neutral, and unpleasant images between 100–135 ms.

respectively; eye-blink and ocular corrections were conducted per Gratton, Coles, and Donchin (1983).

A semi-automatic procedure was employed to detect and reject artifacts. The criteria applied were a voltage step of more than $50.0 \mu\text{V}$ between sample points, a voltage difference of $300.0 \mu\text{V}$ within a trial, and a maximum voltage difference of less than $0.50 \mu\text{V}$ within 100-ms intervals. These intervals were rejected from individual channels in each trial. Visual inspection of the data was then conducted to detect and reject any remaining artifacts. After artifact rejection, there was no significant difference ($t(43) = 1.54$, $p = .13$) in the number of trials entered for the GAD ($M = 253.95$, $SD = 30.31$) or HC groups ($M = 263.68$, $SD = 8.42$).

The EEG was segmented for each trial beginning 200 ms prior to picture onset and continuing for 1,700 ms (i.e., the entire duration of picture presentation). For each trial, a baseline of the average activity in a 200-ms window prior to picture onset was subtracted from every data point. ERPs were constructed by separately averaging epochs in 3 blocks (pleasant, neutral, and unpleasant). Based on both previous literature and visual inspection of the ERP averages, we focused on the early P1 and the LPP in order to examine the time-course of electrocortical activity in response to complex emotional stimuli. Consistent with previous work, the P1 was positive at occipital sites and negative at more central sites for all picture types. Figure 1 displays topographic maps representing the voltage distributions for responses to pleasant, neutral, and unpleasant images in the time-window of the P1 (100–135 ms) for all subjects. Consistent with previous principal components analysis (PCA) research, emotional stimuli in the current study appeared to selectively increase the centro-parietal negative pole of the P1 (e.g., Foti et al., 2009).¹ Because the present study was concerned with processes of emotional differentiation, the P1 was scored at centro-parietal sites where emotional differentiation appears maximal.

Previous research has demonstrated that the LPP is also maximal at these sites (Foti & Hajcak, 2008; Foti et al., 2009;

Hajcak et al., 2009), and visual inspection of grand averages (collapsing across groups) confirmed that this was also the case in the current sample; therefore, an average of activity at four centro-parietal sites (Pz, Cz, CP1, & CP2) was created for both the P1 and the LPP. The P1 was scored as the average activity between 100 and 135 ms. Important information about the time course of emotional responding may be reflected in different windows of the LPP (Foti & Hajcak, 2008; Foti et al., 2009; MacNamara et al., 2009; Weinberg & Hajcak, 2010); in the present study the LPP was evaluated in two windows following stimulus onset: 400–1,000 ms (early window) and 1,000–1,500 ms (late window).

All statistical analyses were conducted using SPSS (Version 15.0) General Linear Model software, with Greenhouse-Geisser correction applied to p values associated with multiple-df, repeated measures comparisons when necessitated by violation of the assumption of sphericity. In order to evaluate differences in emotional responding between groups, as indexed by the P1 and LPP, three 3 (picture type: pleasant, neutral, unpleasant) \times 2 (group: GAD and HC) mixed-model analyses of variance (ANOVAs) were conducted. When appropriate, *post-hoc* interaction contrasts were conducted; in particular, difference scores were computed (pleasant minus neutral; unpleasant minus neutral) and compared between the two groups. Finally, Pearson's correlations were utilized to examine the relationship between electrocortical responses in each of the three time windows.

Results

P1

Grand average stimulus-locked ERPs recorded at Pz, Cz, CP1, & CP2 elicited by pleasant, neutral, and unpleasant pictures are presented in Figure 2 for the control (top) and GAD (bottom) groups. Figure 3 presents topographic maps for HC (top) and GAD (bottom) groups, depicting voltage differences (in μV) for pleasant minus neutral images, and unpleasant minus neutral images after picture onset in the time-range of the P1 (left), early

¹Statistical analyses at an occipital site (Oz) confirm that there is no significant emotional modulation of the positive end of the dipole (3-level repeated-measures ANOVA; pleasant, neutral, unpleasant; $F(2,88) < 1$).

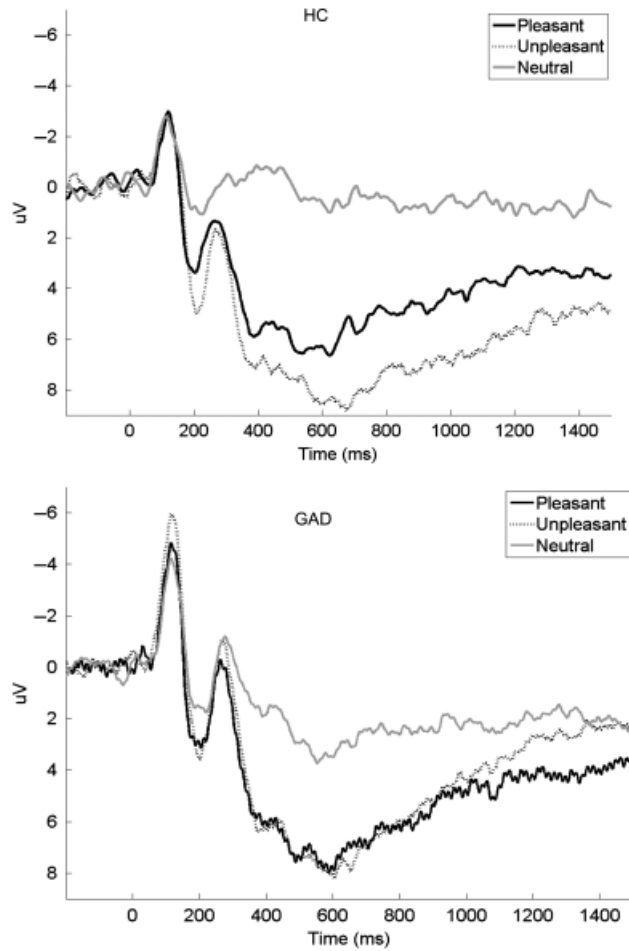


Figure 2. Stimulus-locked ERPs averaged at four centro-parietal sites (Pz, Cz, CP1, & CP2) for HC (top) and GAD (bottom) for pleasant, neutral, and unpleasant images; stimulus presentation occurred at 0 ms.

LPP (middle), and later LPP (right). As indicated in Figures 2 and 3, the affective modulation of the negative pole of the P1 peaked between 100 and 135 ms and was maximal over centro-parietal sites. The P1 appeared larger (more negative) for both pleasant and unpleasant compared to neutral images, but only in the GAD group. Figure 4 presents difference scores for unpleasant minus neutral images (left) and pleasant minus neutral images (right) in the time window of the P1. Mean P1 area measures for both groups are presented in Table 2. Confirming the impressions from Figures 2 and 3, the P1 varied as a function of picture content ($F(2,86) = 4.00, p < .05; \eta_p^2 = .09$; Greenhouse-Geisser $\epsilon = .98$), but not group ($F(1,43) < 1; \eta_p^2 = .01$); the main effect of picture type was qualified by a significant interaction with group ($F(2,86) = 3.79, p < .05; \eta_p^2 = .08$). *Post-hoc* interaction contrasts confirmed that the difference between unpleasant and neutral images was smaller in the HC group ($M = -.08, SD = 1.81$) than GAD group ($M = -1.60, SD = 2.10; t(43) = 2.60, p < .01$). A similar trend-level effect was evident for pleasant pictures when comparing the difference between pleasant and neutral images in the HC group ($M = .31, SD = 1.57$) to the GAD group ($M = -1.00, SD = 2.66; t(43) = 2.07, p = .05$).²

²*Post-hoc* between-group comparisons indicated that the GAD and control groups did not differ significantly in their response to pleasant

LPP (Early Window)

As indicated in Figures 2 and 3, the LPP was maximal over centro-parietal sites in both groups around 600 ms, and was evident as a sustained positivity throughout the duration of emotional picture presentation. The LPP appeared larger (more positive) for both pleasant and unpleasant images compared to neutral; moreover, the differentiation between emotional and neutral pictures appeared *larger* in the HC compared to the GAD group. Figure 4 presents difference scores for unpleasant minus neutral images (left) and pleasant minus neutral images (right) in the time window of the early LPP. Mean LPP area measures for both groups are presented in Table 2. Confirming the impressions from Figures 2 and 3, the LPP differed as a function of picture content ($F(2,86) = 89.09, p < .001; \eta_p^2 = .67$; Greenhouse-Geisser $\epsilon = .83$), but not as a function of group ($F(1,43) < 1; \eta_p^2 = .001$). As with the P1, there was a significant interaction between picture type and group ($F(2,86) = 4.84, p < .01; \eta_p^2 = .10$). *Post-hoc* interaction contrasts indicated that the difference between unpleasant and neutral images was larger in the HC group ($M = 7.00, SD = 3.57$) than in the GAD group ($M = 4.29, SD = 3.51; t(43) = 2.55, p < .05$). This was also true when comparing the difference between pleasant and neutral images in the HC ($M = 5.28, SD = 2.39$) and the GAD group ($M = 3.47, SD = 3.20; t(43) = 2.18, p < .05$).³

LPP (Late Window)

In the late window, the LPP again differed as a function of picture content ($F(2,86) = 22.83, p < .001; \eta_p^2 = .35$; Greenhouse-Geisser $\epsilon = .96$), but not as a function of group ($F(1,43) < 1; \eta_p^2 = .00$). As with the early LPP, there was a significant interaction between picture type and group ($F(2,86) = 5.84, p < .001; \eta_p^2 = .12$). *Post-hoc* interaction contrasts once again confirmed that the difference between unpleasant and neutral images was larger in the HC group ($M = 5.22, SD = 3.01$) than in the GAD group ($M = 1.63, SD = 4.44; t(43) = 3.22, p < .01$). However, unlike the early LPP, the difference between pleasant and neutral images was not significantly different in the HC group ($M = 3.29, SD = 2.74$) and the GAD group ($M = 1.94, SD = 4.65; t(43) = 1.22, p = .23$).⁴

Relationship Between Components

Finally, in order to determine if greater *early* neural activity was associated with decreased *later* neural activity, Pearson's correlations were conducted between the magnitude of the negative pole of the P1, early LPP, and late LPP within each group. Within the GAD group, the magnitude of the negative pole of the P1 was strongly positively associated with the LPP in both the late and early windows (significant r s ranged from .49 to .79), such that a larger (more negative) P1 was associated with an attenuated (less positive) LPP. This effect was evident across picture types; the P1 elicited by pleasant pictures was associated with the LPP elicited by pleasant, neutral, and unpleasant images

($t(43) = 1.07, p = .29$), neutral ($t(43) = .17, p = .87$), or unpleasant ($t(43) = 1.32, p = .19$) images in the time window of the P1.

³*Post-hoc* between-group comparisons indicated that the GAD did not differ from the control group in their response to pleasant ($t(43) = .05, p = .96$), neutral ($t(43) = 1.27, p = .21$), or unpleasant ($t(43) = .66, p = .51$) images in the time window of the early LPP.

⁴*Post-hoc* between-group comparisons indicated that the GAD did not differ from the control group in their response to pleasant ($t(43) = .12, p = .91$), neutral ($t(43) = .99, p = .33$), or unpleasant ($t(43) = 1.72, p = .09$) images in the time window of the late LPP.

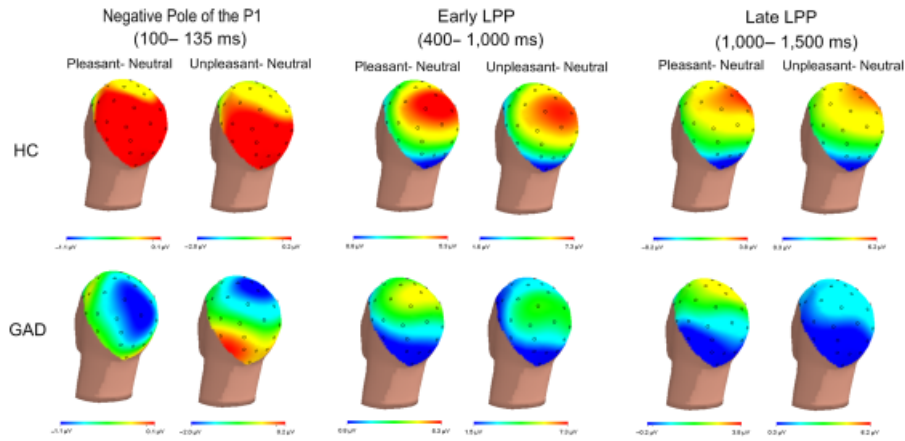


Figure 3. Topographic maps depicting voltage differences (in μV) for HC (top) and GAD (bottom) for pleasant minus neutral images and unpleasant minus neutral images, between 100–135 ms (left), 400–1,000 ms (middle), and 1,000–1,500 ms (right) following picture onset. Note that the GAD and HC groups have the same scale, although different scales are used for each contrast type and each component.

alike. In all cases, a smaller LPP was predicted by a larger (i.e., more negative) P1. However, within each ERP component, responses to picture types were also highly correlated (r s ranged from .65 to .93), making it difficult to isolate unique associations within picture types. In the control group, there were no significant associations between the magnitude of the P1 and the LPP in either time window, though the correlations between picture types within each component were significant (r s ranged from .51 to .91).

Discussion

By examining the time-course of neural activity in response to emotional pictures in a clinical GAD sample, the present study provides evidence of enhanced early processing of emotional material followed by diminished elaborative engagement. In the time-range of the P1 (i.e., within the first 150 ms after picture presentation), individuals with GAD demonstrated greater neural activity to aversive compared to neutral images. However, this early hypervigilance was followed by a reduction in the emotional modulation of the LPP: relative to the control group, individuals with GAD demonstrated decreased differentiation

between unpleasant and neutral pictures that was evident throughout the remainder of picture presentation. Further, in the GAD group alone, early perceptual hyperactivity was related to subsequently decreased attention to emotional stimuli, as reflected by the significant association between the P1 and the two time windows of the LPP.

This pattern of electrocortical response is consistent with previous research in individuals high on trait anxiety (Holmes et al., 2008; Mühlberger et al., 2009), which has been interpreted in light of a “vigilance-avoidance” model of attentional deployment in the anxiety disorders (Mogg et al., 2004; Mogg et al., 1987). Early perceptual hyperactivity, followed by later attentional disengagement from emotional content, might play an important role in the development and maintenance of GAD, as greater vigilance could result in increased likelihood of detecting threat. On the other hand, failure to engage in elaborative processing (i.e., avoidance) precludes prolonged exposure and habituation to the feared stimuli (Borkovec, 1979; Foa et al., 1983; Foa & Kozak, 1986), thereby preventing increased cognitive and somatic processing of the fear-relevant stimuli, which is crucial for modifying fear representations (Foa & Kozak, 1986).

One potential mechanism for the observed differences in the ERP waveform is suggested by evidence from our lab indicating

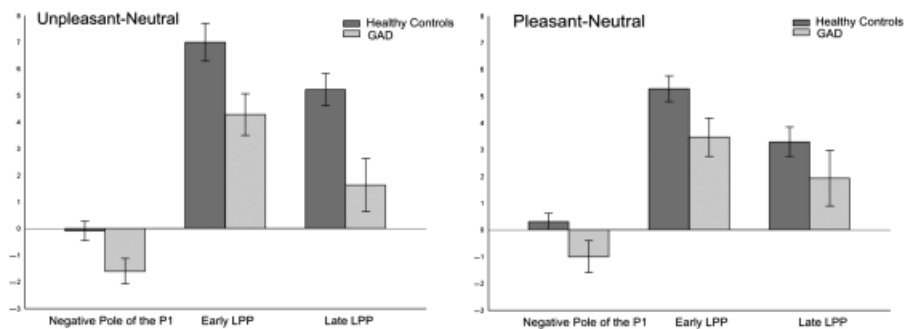


Figure 4. Graphs depicting difference scores between unpleasant and neutral images (left) and pleasant and neutral images (right), for GAD and HC participants (bars denote standard errors). Evidence for early hypervigilance is to the left in the unpleasant minus neutral graph, as indicated by the large negative deflection in the time-window of the P1 elicited by unpleasant images in GAD subjects. In the same graph, evidence for decreased elaborative processing is to the right, as indicated by the diminished LPP to unpleasant images in both the early and late windows in GAD subjects. A similar pattern is presented on the right, for pleasant minus neutral images.

Table 2. Mean ERP Area Measures (μV) for the P1, and the Early (300–1,000 ms) and Late (1000–1,500 ms) LPP (SDs in parentheses)

Picture type	P1		Early LPP		Late LPP	
	GAD	HC	GAD	HC	GAD	HC
Pleasant	– 3.88 (3.35)	– 2.75 (3.71)	5.66 (4.45)	5.73 (4.24)	3.80 (4.09)	3.67(3.87)
Neutral	– 2.88 (3.79)	– 3.06 (3.27)	2.19 (5.36)	.44 (3.88)	1.87 (6.33)	.37 (3.63)
Unpleasant	– 4.483 (3.41)	– 3.14 (3.28)	6.48 (4.95)	7.44 (4.75)	3.50 (4.13)	5.59 (4.01)
Pleasant minus Neutral	– 1.00 (2.66)	.31 (1.57)	3.47 (3.20)*	5.28 (2.39)*	1.94 (4.65)	3.29 (2.74)
Unpleasant minus Neutral	– 1.60 (2.10)*	– .08 (1.82)*	4.29 (3.51)*	6.99 (3.57)*	1.63 (4.45)*	5.22 (3.01)*

* $p < .05$ in a between-groups comparison. No between-group comparisons were significant for direct comparisons of pleasant, neutral, and unpleasant images in any time window.

that the LPP indexes the flexible and dynamic allocation of attention to emotional content. For instance, instructing participants to attend to less aversive portions of threatening images (e.g., pebbles surrounding a corpse, rather than the corpse's face) results in a decrease in LPP magnitude (Dunning & Hajcak, 2009; Hajcak et al., 2009), as does reappraisal and manipulating the meaning of emotional images (Foti & Hajcak, 2008; Hajcak & Nieuwenhuis, 2006; MacNamara et al., 2009). Individuals with GAD might, therefore, engage in the deliberate deployment of visual attention to less threatening portions of the screen, or regulate their emotional experience through worry and other forms of cognitive avoidance (e.g., Mennin et al., 2002, 2005; Salters-Pedneault, Roemer, Tull, Rucker, & Mennin, 2006). It is not clear from the present study whether the GAD participants were engaging in either of these strategies intentionally, though both are potential mechanisms that deserve further investigation. Nevertheless, ERPs appear to be a promising neural marker for examining attention to emotional stimuli in GAD that might not be captured by behavioral measures like the dot-probe task or by measures of neural activity that rely on the sluggish hemodynamic response (i.e., fMRI).

While the LPP elicited by unpleasant images was diminished in the GAD group, particularly in the later window, these subjects also exhibited a numerically *larger* response to neutral images, suggesting that the diminished differentiation of neutral and emotional stimuli is driven by a combination of increased activity to neutral images and decreased activity to unpleasant images. Similarly reduced *differentiation* has been demonstrated in individuals high in trait anxiety (Mühlberger et al., 2009). Given previous evidence that individuals with GAD interpret neutral and ambiguous stimuli as more threatening than non-anxious controls (Butler & Mathews, 1983; Hazlett-Stevens & Borkovec, 2004; Mathews, Richards, & Eysenck, 1989), it stands to reason that unambiguously threatening stimuli might be avoided, but neutral and ambiguous stimuli demand increased processing and attention in GAD. It may indeed be the case that the observed attenuation of emotional modulation in the GAD group is driven by two separate effects; increased processing of neutral material and attenuated attentional engagement with threatening images. Future studies should include self-report measures assessing subjective threat and arousal levels, as well as electrocortical response to specific picture subtypes (e.g., Weinberg & Hajcak, in press b) to further explore the possibility that the reduced modulation by emotional material may be driven by a specific content of emotional and neutral images.

It is also worth noting that in the time window of the P1 there was a trend towards significant differences between the GAD and HC groups for pleasant compared to neutral trials, and this effect

reached significance in the time-window of the early LPP. This is perhaps not surprising in light of increasing evidence that anxiety disorders might be associated with heightened vigilance for both unpleasant *and* pleasant emotional material (Becker et al., 2001; Bradley, Mogg, White, Groom, & De Bono, 1999; Chen, Ehlers, Clark, & Mansell, 2002; Mansell, Clark, Ehlers, & Chen, 1999; Martin, Williams, & Clark, 1991; Vassilopoulos, 2004). It is interesting that the observed pattern appeared more robust for unpleasant images—which could be due to the fact that the aversive stimuli in this study were slightly more arousing. Nevertheless, the current data suggest that abnormal processing of emotional stimuli in GAD may not be specific to threatening stimuli.

Studies in our lab have also found relationships between *enhanced* LPP magnitude to unpleasant images and anxiety (MacNamara & Hajcak, 2009) in one instance utilizing 30 of the same subjects as the present study (MacNamara & Hajcak, 2010). These results, however, were obtained during a speeded response task, in which stimuli were presented briefly (i.e., 250 ms). Tasks necessitating a rapid response to briefly presented images may not permit attentional avoidance; indeed, individuals with GAD may reflexively process the content of threatening stimuli in such contexts (Koster et al., 2006). In the present study, the type of upcoming image was completely predictable. Because anxious apprehension plays an important role in GAD, and because there is evidence for anticipatory activation of the amygdala prior to cued stimuli in GAD (Nitschke et al., 2009), it could be important to examine ERPs in a paradigm in which picture type is randomly determined. The blocked nature of the current design may have facilitated early vigilance, as well as later diminished processing. Overall, further examination of task effects on ERP responses to emotional stimuli in GAD will be necessary.

Finally, there is also evidence suggesting decreased processing of emotional stimuli in major depressive disorder (MDD; Allen, Trinder, & Brennan, 1999; Dichter & Tomarken, 2008; Dichter, Tomarken, Shelton, & Sutton, 2004; Rottenberg, Gross, & Gotlib, 2005; Rottenberg, Kasch, Gross, & Gotlib, 2002; Sloan, Strauss, & Wisner, 2001). Consistent with these data, we have previously documented a decreased LPP among individuals with MDD—although we did not find any evidence for abnormalities in earlier ERPs (Foti, Olvet, Klein, & Hajcak, 2010). This raises the possibility that decreased elaborative processing of threat stimuli is a common factor between MDD and GAD, whereas early vigilance is unique to GAD (e.g., Mogg & Bradley, 2005). That is, reductions in the LPP may be common to both GAD and MDD, whereas an enhanced P1 may be specific to GAD. Given the high rates of comorbidity of GAD and MDD (Brown, Chorpita, & Barlow, 1998; Kessler et al., 1996), as well as

evidence for shared vulnerability factors between the two disorders, (Kendler, Neale, Kessler, Heath, & Eaves, 1992), closer examination of these attentional processes within and between

the two diagnostic groups—at the level of diagnosis and symptom—may be essential in clarifying their relationship to one another.

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APPENDIX

Pleasant Images

7282, 7291, 7482, 7481, 7488, 7350, 7402, 7450, 7400, 7260, 7460, 7289, 7330, 7270, 7430, 1441, 1463, 1710, 1750, 1920, 2040, 2070, 2071, 2080, 2091, 2150, 2165, 2340, 2345, 2550, 4608, 4650, 4652, 4658, 4659, 4660, 4664, 4670, 4676, 4680, 4687, 4689, 4690, 4694, 4695

Neutral Images

7000, 7002, 7004, 7006, 7010, 7025, 7034, 7035, 7040, 7041, 7056, 7090, 7100, 7150, 7175, 2102, 2190, 2191, 2200, 2214, 2280, 2305, 2357, 2381, 2383, 2385, 2393, 2512, 2570, 7550,

5390, 5471, 5510, 5530, 5531, 5731, 5740, 7490, 7491, 7500, 7546, 7547, 7590, 7595, 7700

Unpleasant Images

2730, 2981, 7380, 9008, 9040, 9140, 9181, 9300, 9301, 9320, 9373, 9561, 9570, 9571, 9830, 1120, 1300, 1301, 1930, 2811, 3530, 6250, 6312, 6313, 6315, 6370, 6550, 6560, 6571, 9425, 3015, 3016, 3030, 3051, 3101, 3102, 3110, 3120, 3140, 3168, 3170, 3190, 3261, 3266, 3400