Emotional Context and Error Monitoring in Generalized Anxiety Disorder

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INTRODUCTION

- Generalized anxiety disorder (GAD) is characterized by excessive worry. According to the cognitive avoidance model of GAD (Borkovec, Alcaine, Behar, Heimberg, Turk, & Mennin, 2004), the frequent use of worry serves the function of reducing physiological experiences of anxious arousal. This chronic expenditure of cognitive resources, however, is likely associated with a range of neurocognitive and performance abnormalities, but these remain poorly understood.
- One neurocognitive system that may be dysregulated in GAD is response monitoring (Etkin, Prater, Hoeft, Menon, & Schaftzberg, 2010; Etkin, Prater, Schatzberg, Menon, & Greicius, 2009; Paulesu, Sambugaro, Torti, et al., 2010). For example, Paulesu and colleagues (2010) found that following a worry induction, GAD patients were unable to normalize activation of the anterior cingulate cortex, which underlies response monitoring. This suggests reduced flexibility and sensitivity of the response monitoring system.
- Scalp-recorded event-related potentials have been used to examine response monitoring in GAD. The error-related negativity (ERN) is thought to reflect the relatively early and automatic detection of errors (Falkenstein, Hohnsbein, Hoormann, & Blanke, 1991b), whereas the error positivity (Pe) is thought to index more in-depth error recognition and salience processing (Falkenstein Hoorman, & Blanke, 2000; Nieuwenhuis, Ridderinkhof, Blom, Kok, 2001).
- Studies examining GAD and error-monitoring ERPs primarily document hypermonitoring of errors as measured by larger ERNs to errors, although few of these studies examined GAD as a diagnostic entity (Weinberg, Olvet & Hajcak, 2010; Weinberg, Klein & Hajcak, 2012). In contrast, Xiao and colleagues (2011) failed to find enhanced ERNs in a GAD sample. Findings on the association between GAD and Pe are inconclusive.
- Because emotional stimuli signifying threat or ambiguity heighten anxious arousal (Compton, Carp, Chaddock, Fineman, Quandt, & Ratliff, 2007; Mathews & MacLeod, 1994; Mathews & MacLeod, 2002) the presence of these stimuli may amplify disruptions in error monitoring associated with GAD. This hypothesis has received relatively scant empirical attention (Etkin et al., 2010).
- Nitschke et al. (2009) provide further support for the hypothesis that GAD is associated with inflexible or indiscriminant responses, particularly in emotional contexts. They found greater bilateral dorsal amygdala activation to both aversive and neutral stimuli compared to controls indicating indiscriminant response patterns and a heightened anticipation of negative outcomes.
- If the response monitoring system shows reduced flexibility and sensitivity in GAD, then this might be most clearly indicated by **indiscriminant recruitment of error monitoring**. Accordingly, we tested the novel hypothesis that GAD would be associated with greater ERN and Pe amplitudes to **errors and correct responses**. We predicted that this indiscriminant error monitoring would be amplified in the context of threat-relevant and ambiguous stimuli (angry and neutral faces) relative to a non-emotional condition.

HYPOTHESES

1. Emotional stimuli, particularly threat-relevant faces, will disrupt performance (reduce accuracy) in the GAD versus control group
2. The GAD versus control group will show increased ERN/Pe amplitudes to correct trials, particularly in the threat-relevant angry face condition, suggesting indiscriminant error monitoring.

METHOD

Participants

- Participants were 40 individuals (32 female), aged 18-35 (M = 22.83, SD = 5.44). Nineteen participants met criteria for GAD (16 female; M^{AGE} = 23.37, SD = 6.08) and 21(16 female; M^{AGE} = 22.33, SD = 4.90) were age-matched control participants. All GAD participants were medication free.

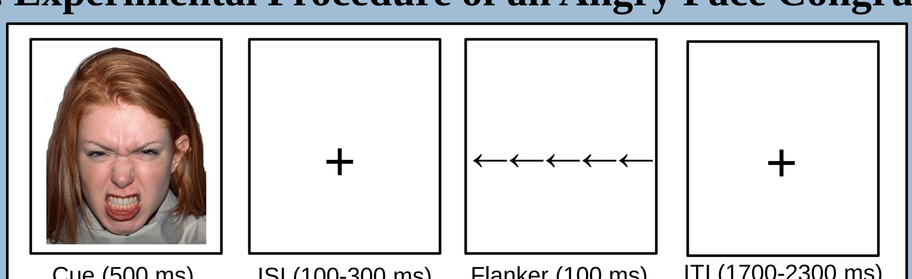
Emotional Faces

- Faces of 16 actors portraying angry and neutral expressions were shown for a total of 32 face stimuli (Tottenham et al., 2009). Each face stimulus was shown 45 times.

Modified Flanker Task

- A modified flanker task was used for this study. This task requires the participant to identify the direction (right or left) of the central arrow that is flanked by either four arrows facing the same direction (congruent trial) or the opposite direction (incongruent trial). In addition, this study used facial primes (angry and neutral) and had no face trials.
- The task was a total of 3 blocks (no face, neutral face, angry face), with 480 trials per block. In order to avoid carryover effects from the angry condition, the order of experimental blocks was not counterbalanced. Two hundred and forty of the trials in each block displayed congruent flankers while 240 trials displayed incongruent flankers. Eighty practice trials preceded the first block with an 80% accuracy score necessary to begin the experimental blocks.
- RTs and accuracy data were recorded. Trials with RTs faster than 200 ms and longer than 800 ms after flanker presentation were excluded from analyses.

Figure 1. Experimental Procedure of an Angry Face Congruent Trial



Generalized Anxiety Disorder

- The **Standard Clinical Interview for DSM Disorders** (SCID-I/P; First, Spitzer, Gibbon, & Williams, 2002) was used to identify participants with elevated anxiety levels who met criteria for Generalized Anxiety Disorder (GAD). The SCID is a semi-structured interview that assesses the presence and severity of DSM-IV defined mental disorders. Participants who met criteria for current GAD (with or without current Major Depressive Disorder or dysthymia) as well as those who did not meet criteria for any anxiety or mood disorders on the SCID were included.

Anxiety Measures

- In addition to the SCID, paper-based questionnaires were given to assess differences in self-reported levels of anxiety and worry for each group. These measures included the Penn State Worry Questionnaire (PSWQ; Meyer, Miller, Metzger, & Borkovec, 1990), Generalized Anxiety Questionnaire (GAD-Q-IV; Newman, Zuellig, Kachin, Constantino, & Cashman, 2002), and the State-Trait Anxiety Inventory (STAI; Spielberger, 1983).
- Independent samples t-tests confirmed that the GAD group had higher scores for **GADQ** [M^{GAD} = 10.18, SD = 1.32 vs. $M^{CONTROL}$ = 4.69, SD = 4.69; $t(38) = -7.48$, $p < .001$], **PSWQ** [M^{GAD} = 63.84, SD = 12.46 vs. $M^{CONTROL}$ = 43.91, SD = 11.50; $t(38) = -5.26$, $p < .001$], **STAI state** [M^{GAD} = 43.26, SD = 13.08 vs. $M^{CONTROL}$ = 33.62, SD = 11.20; $t(38) = -2.51$, $p = .02$], and **STAI trait** [M^{GAD} = 51.68, SD = 9.67 vs. $M^{CONTROL}$ = 39.81, SD = 9.81; $t(38) = -3.85$, $p < .001$].

EEG Recording and Analysis

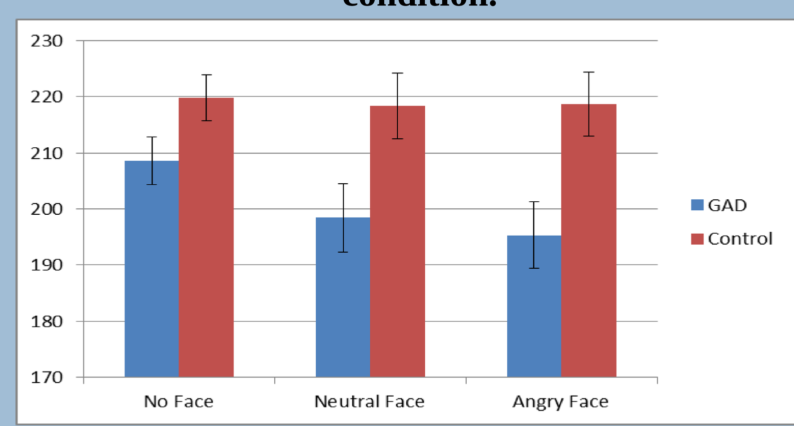
- EEG activity was recorded during the passive viewing and cognitive reappraisal tasks via BioSemi 64 Ag/AgCl scalp electrodes, sampled at 512 Hz and amplified with a band pass of 0.16-100 Hz. Eye movements were monitored by electrooculogram (EOG) signals.
- Using Brain Vision Analyzer, data were referenced offline to the average of the entire scalp and filtered with a low-cutoff frequency of .1 Hz and a high-cutoff frequency of 30 Hz. Stimulus-locked data to faces were segmented into epochs from 200 ms before stimulus presentation to 600 ms after stimulus onset, with a 200 ms baseline correction. Response-locked data were segmented for each trial beginning at 200 ms before each response onset to 1000 ms after stimulus onset. The 200 ms window from -200 ms to 0 ms prior to response onset was used as the baseline.
- Following ocular correction (Gratton & Coles, 1983), artifacts were identified using the following criteria and removed from analyses: data with voltage steps greater than 50 µV, changes within a given segment greater than 300 µV, and activity lower than .5 µV per 100 ms.
- ERPs were quantified as: the N170 was calculated as the mean amplitude between 130 ms and 180 ms at P9 and P10, to measure differences in processing angry and neutral faces. The ERN was calculated as the mean amplitude between 10 ms and 50 ms at FCz. The Pe was calculated as the mean amplitude between 140 ms and 340 ms at Cz.

RESULTS

Hypothesis 1: Threat-relevant faces will disrupt task performance in the GAD versus control group

A 3 (Condition: no, neutral, angry) x 2 (Group: GAD, control) mixed-design factorial ANOVA was conducted for the number of correct responses made on incongruent trials. There was a significant Condition x Group interaction, $F(2, 76) = 3.22$, $p = .046$, $\eta^2 = .08$. Pairwise comparisons revealed that the control group (M = 218.29, SD = 17.47) made significantly more correct responses in the neutral face condition compared to the GAD group (M = 198.42, SD = 34.18), $p = .02$. This same effect was significant in the angry condition ($M^{CONTROL}$ = 218.67, SD = 12.64 vs. M^{GAD} = 195.32, SD = 35.33; $p = .01$). **Thus, disrupted performance was evident in the GAD group for both neutral and angry faces.**

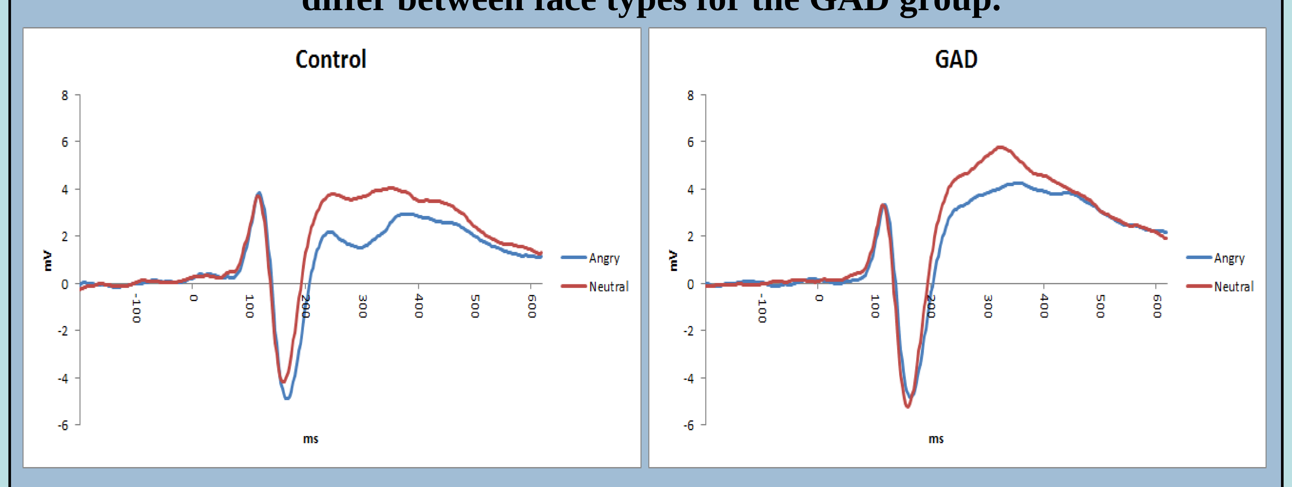
Figure 2. The control group made significantly more correct responses on incongruent trials in the neutral and angry face conditions compared to the GAD group. However, the groups did not perform differently in the no face condition.



N170

Exploratory analyses examined whether the GAD group differed from the control group in the processing of angry and neutral faces. A 2 (Condition: neutral, angry) x 2 (Group: GAD, control) mixed-design factorial ANOVA was conducted for N170 amplitudes. There was a significant Condition x Group interaction, $F(1,38) = 5.70$, $p = .02$, $\eta^2 = .13$. Pairwise comparisons revealed that N170 amplitudes became significantly more negative from the neutral (M = -2.74, SD = 3.39) to the angry (M = -3.43, SD = 3.57) condition for the control group (p = .01). However, the difference between N170 amplitudes in the neutral (M = -3.67, SD = 2.82) and angry (M = -3.52, SD = 2.48) conditions was not significant for the GAD group (p = .54). This suggests that the introduction of both ambiguous and angry faces recruited similar cognitive resources.

Figure 3. In the control group, N170 amplitudes were significantly more negative to angry versus neutral faces (left panel); N170 amplitudes did not differ between face types for the GAD group.



Hypothesis 2: The GAD versus control group will show increased ERN/Pe amplitudes to correct trials, particularly in the threat-relevant angry face condition, suggesting indiscriminant error monitoring.

ERN

First, a 3 (Condition: no, neutral, angry) x 2 (Correctness: correct, incorrect) x 2 (Group: GAD, control) mixed-design factorial ANOVA was conducted for ERN amplitudes. As expected, there was a main effect of Correctness, $F(1,36) = 51.33$, $p < .001$, $\eta^2 = .59$. Overall, pairwise comparisons revealed that ERN amplitudes were significantly more negative on incorrect (M = -4.95, SD = 2.91) versus correct trials (M = -1.74, SD = 2.49), $p < .001$. No other significant effects emerged.

Pe

A 3 (Condition: no, neutral, angry) x 2 (Correctness: correct, incorrect) x 2 (Group: GAD, control) mixed-design factorial ANOVA was conducted for Pe amplitudes. There was a main effect of Condition, $F(2,72) = 3.49$, $p = .04$, $\eta^2 = .09$. Pe amplitudes were significantly larger in the neutral condition (M = 3.65, SD = 3.32) and angry face condition (M = 3.36, SD = 2.92) compared to the no face condition (M = 2.57, SD = 3.10; p = .02 and p = .03, respectively). There was also a main effect of Correctness, $F(1,36) = 28.41$, $p < .001$, $\eta^2 = .44$ showed that, as expected, Pe amplitudes were significantly larger on incorrect (M = 4.73, SD = 3.63) compared to correct trials (M = 1.67, SD = 2.86), $p < .001$.

In addition, the interaction of Correctness x Group was marginally significant, $F(1,36) = 3.47$, $p = .07$, $\eta^2 = .59$.

In order to follow up this trend seen in the Correctness x Group interaction, the neutral and angry face conditions were analyzed separately from the no face condition.

First, a univariate ANOVA for the no face condition was conducted with Pe amplitudes on no face incongruent incorrect trials. Results were not significant, $F(1,36) = .63$, $p = .43$.

Then, a 2 (Condition: neutral, angry) x 2 (Correctness: correct, incorrect) x 2 (Group: GAD, control) mixed-design factorial ANOVA was conducted for Pe amplitudes. There was a significant Correctness x Group interaction, $F(1,36) = 4.30$, $p = .045$, $\eta^2 = .11$. Pairwise comparisons revealed a pattern of elevated Pe amplitudes on correct trials in the GAD group. For correct trials, Pe amplitudes were significantly more positive in the GAD group (M^{GAD} = 3.27, SD = 2.75) compared to the control group ($M^{CONTROL}$ = .81, SD = 2.93), $p = .02$. Additionally, in the control group Pe amplitudes were significantly more positive on incorrect trials (M = 5.08, SD = 3.83) compared to correct trials (M = .81, SD = 2.93), $p < .001$. However, in the GAD group, Pe amplitudes on incorrect trials (M = 4.85, SD = 3.78) were not significantly more positive compared to correct trials (M = 3.27, SD = 2.75), $p = .09$. Between-group differences in Pe amplitudes on incorrect trials did not reach significance.

Figure 4. Pe amplitudes to correct trials were significantly elevated across the neutral and angry face conditions in the GAD versus control group.

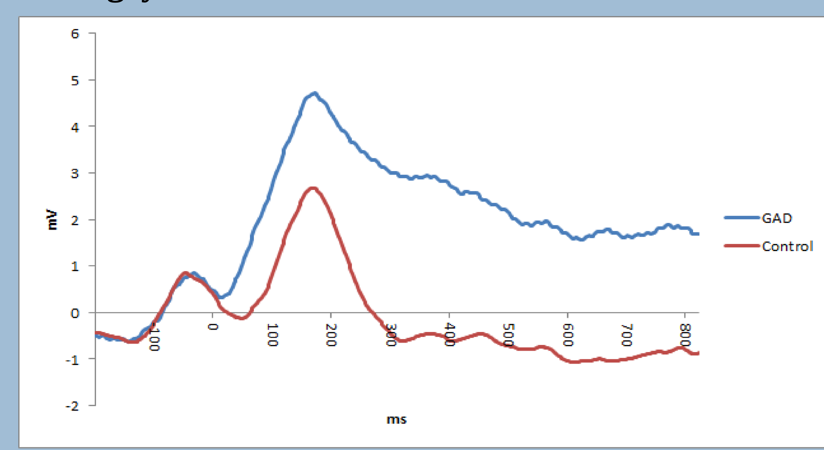
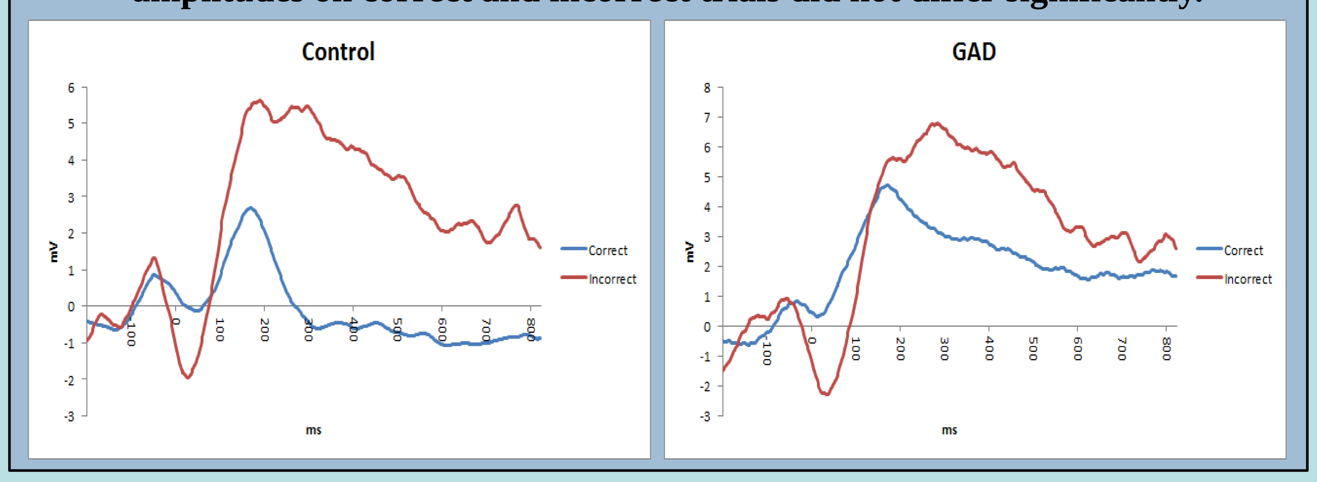


Figure 5. In the control group, the Pe was significantly more positive on incorrect trials compared to correct trials (left panel). In the GAD group, Pe amplitudes on correct and incorrect trials did not differ significantly.



DISCUSSION

- The ERN and Pe were examined in non-emotional, ambiguous, and threat-relevant contexts in order to evaluate disruptions in response monitoring associated with GAD.
- As predicted, neutral and angry faces specifically disrupted performance in the GAD versus control group. The control group made significantly more correct responses on incongruent trials in both the neutral and angry face conditions. Performance did not differ between groups on the no face condition.
- In addition, the GAD versus control group showed blunted sensitivity of ERP responses to angry versus neutral faces, suggesting hyper-responsivity to these social-affective cues. That is, in the control group, N170 amplitudes were significantly more negative on angry face compared to neutral face trials. However, this difference was not significant in the GAD group.
- Consistent with predictions, the GAD versus control group showed increased Pe amplitudes to correct trials across neutral and angry face conditions. This effect was not significant in the no face condition. Furthermore, the Pe was significantly larger on incorrect trials compared to correct trials in the control group but not in the GAD group.
- Contrary to predictions, there were no significant group differences in the ERN.
- Collectively, our findings highlight the impact of emotional context on more elaborate stages of error monitoring in GAD. Our results support other recent ERP findings looking at the P1and LPP in GAD that suggest an early hypervigilance to emotional pictures followed by a failure to adjust and tune responses as content changes (Weinberg & Hajcak, 2011).
- Taken together, the present findings suggest dampened sensitivity to emotional context and hyper-monitoring/reduced discrimination of error monitoring in the GAD group.

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