Cognitive load and emotional processing in Generalized Anxiety Disorder: Electrocortical evidence for increased distractibility

Annmarie MacNamara and Greg Hajcak Proudfit
Stony Brook University

Abstract

Generalized Anxiety Disorder (GAD) may be characterized by emotion regulation deficits attributable to an imbalance between top-down (i.e., goal-driven) and bottom-up (i.e., stimulus-driven) attention. In prior work, these attentional processes were examined by presenting unpleasant and neutral pictures within a working memory paradigm. The late positive potential (LPP) measured attention toward task-irrelevant pictures. Results from this prior work showed that working memory load reduced the LPP across participants; however, this effect was attenuated for individuals with greater self-reported state anxiety, suggesting reduced top-down control. In the current study, the same paradigm was used with 106 medication-free, female participants – 71 with GAD and 35 without GAD. Unpleasant pictures elicited larger LPPs, and working memory load reduced the picture-elicited LPP. Compared to healthy controls, participants with GAD showed large LPPs to unpleasant pictures presented under high working memory load. Self-reported symptoms of anhedonic depression were related to a reduced effect of working memory load on the LPP elicited by neutral pictures. These results indicate that individuals with GAD show less flexible modulation of attention when confronted with unpleasant stimuli. Furthermore, among those with GAD, anhedonic depression may broaden attentional deficits to neutral distracters.

Keywords

GAD; ERP; late positive potential; working memory load; attentional control

Generalized Anxiety Disorder (GAD) is a chronic condition characterized by intrusive negative cognitions, perseverative worry, physical tension and difficulty sleeping (Association, 2013). Lifetime prevalence rates for GAD are estimated at nearly 6% (Kessler, Berglund, Demler, Jin, & Walters, 2005) and GAD significantly and negatively impacts public health (Kessler, 2000; Wittchen, 2002). However, despite the suffering and costs associated with GAD, it remains under-researched compared to other anxiety disorders (Boschen, 2008; Dugas, Anderson, Deschenes, & Donegan, 2010), and treatment response for GAD is significantly lower than other anxiety disorders (Borkovec & Ruscio, 2001;
Fisher & Durham, 1999). A better understanding of the mechanisms underlying GAD is needed to improve treatment outcomes (Behar, DiMarco, Hekler, Mohlman, & Staples, 2009).

Recent work suggests that emotion regulation deficits contribute to the development and maintenance of GAD (Mennin, 2004; Roemer et al., 2009). Specifically, individuals with GAD appear impaired in their ability to monitor, understand and modulate emotions - especially when they are simultaneously engaged in goal-directed behavior (Mennin, Heimberg, Turk, & Fresco, 2002; Salters-Pedneault, Roemer, Tull, Rucker, & Mennin, 2006). One mechanism that might explain these impairments in GAD is deficient attentional control, which refers to the balance of top-down (i.e., goal-driven) and bottom-up (i.e., stimulus-driven) attention (Eysenck, Derakshan, Santos, & Calvo, 2007).

Poor attentional control in anxiety may reflect abnormal modulation of emotional processing by the prefrontal cortex. To test this idea, Bishop and colleagues examined blood oxygen level dependent (BOLD) response while participants performed a demanding task, in which unpleasant and neutral distracter stimuli were presented. Results showed that state levels of anxiety were associated with reduced recruitment of the prefrontal cortex (i.e., the dorsolateral prefrontal cortex - dlPFC; Bishop, Duncan, Brett, & Lawrence, 2004) – and, in another study – with less task-related modulation of amygdala activity in response to unpleasant distracters (Bishop, Duncan, & Lawrence, 2004). These results support the notion that anxiety may impair the recruitment of prefrontal regions and reduce filtering of negative, task-irrelevant information.

In addition to hemodynamic measures, electroencephalography (EEG) can be useful in assessing emotional processing in anxiety (MacNamara, Kappenman, Black, Bress, & Hajcak, 2013). For instance, the late positive potential (LPP) is a positive-going waveform that is evident centroparietally around 350 ms after stimulus onset and is larger for emotional than non-emotional stimuli (Cuthbert, Schupp, Bradley, Birbaumer, & Lang, 2000; Foti, Hajcak, & Dien, 2009; Hajcak & Olvet, 2008; Hajcak, Weinberg, MacNamara, & Foti, 2011; Schupp et al., 2000). In addition to being larger for more emotionally arousing stimuli (Cuthbert et al., 2000; Weinberg & Hajcak, 2010), the LPP is larger for personally relevant stimuli, such as pictures of one’s own relatives or one’s own name (Grasso & Simons, 2011; Tacikowski & Nowicka, 2010; Vico, Guerra, Robles, Vila, & Anllo-Vento, 2010). The LPP is also sensitive to willful attempts at emotion regulation: the LPP is smaller when participants are asked to reduce their emotional response to pictures (Hajcak, MacNamara, & Olvet, 2010; Hajcak & Nieuwenhuis, 2006; Parvaz, MacNamara, Goldstein, & Hajcak, 2012). Therefore, the LPP appears to be sensitive to both bottom-up and top-down modulations of stimulus salience.

Like other neural measures of emotion-processing, the LPP is reduced during demanding tasks. For example, MacNamara and colleagues (2011) employed a working memory task known to activate the dlPFC (Manoach et al., 1997). In the retention interval of this task, participants viewed task-irrelevant unpleasant and neutral pictures. Although unpleasant pictures elicited larger LPPs than neutral pictures, the LPP was also smaller under high than low working memory load trials; MacNamara and colleagues suggested that increased
functional activation of the dlPFC during working memory reduced the processing of task-
irrelevant pictures (see also Hajcak, Anderson, et al., 2010; MacNamara, Schmidt, Zelinsky,
& Hajcak, 2012). Moreover, MacNamara and colleagues (2011) found that the effect of
working memory load on the LPP was reduced for participants with higher self-reported
state anxiety. As state anxiety increased, there was less differentiation between the LPP
elicited by pictures presented under high than low working memory load. Thus, MacNamara
and colleagues' (2011) results suggest that the LPP might be used to index anxiety-related
deficits in attentional control (see also MacNamara & Hajcak, 2009; MacNamara & Hajcak,
2010).

Although it is conceivable that difficulties in attentional control may characterize multiple
anxiety disorders, evidence suggests that deficits in attentional control are particularly
relevant to GAD (e.g., Armstrong, Zald, & Olatunji, 2011). Therefore, the current study set
out to extend prior work conducted in a non-clinical sample (MacNamara et al., 2011) to
GAD. Across participants, unpleasant pictures were expected to elicit larger LPPs than
neutral pictures, and high-load trials were expected to elicit smaller LPPs than low-load
trials (MacNamara et al., 2011; MacNamara et al., 2012). In addition, individuals with GAD
were expected to demonstrate less working memory load modulation of the LPP than
controls (MacNamara et al., 2011), especially for trials with unpleasant pictures (Bishop,
Duncan, Brett, et al., 2004; Williams, Mathews, & MacLeod, 1996). Moreover, it was
expected that this effect would be attributable to larger LPPs on high-load unpleasant trials
for individuals with GAD, which would indicate difficulties filtering unpleasant information
under high cognitive load specifically (Eysenck et al., 2007). In line with previous work,
differences in working memory performance (i.e., accuracy) between groups were not
expected (Eysenck et al., 2007; MacNamara et al., 2011). Given that depression is highly
comorbid with GAD, yet may be characterized by different emotional processing deficits
(e.g., Bradley, Mogg, Millar, & White, 1995; Mogg & Bradley, 2005), the current study
oversampled GAD in order to permit examination of the impact of comorbid depression.

Method

Participants

Recruitment—Data was collected from a total of 106 participants who were recruited
using advertisements placed in the Long Island section of the internet site,
www.craigslist.org, around the Stony Brook University campus, and in Stony Brook
University's weekly campus announcements. Potential participants were invited to the lab
after an initial phone-screen, which used a modified version of the Mini-International
Neuropsychiatric Interview (Sheehan et al., 1998). The study was approved by the Stony
Brook University Institutional Review Board (IRB), and participants were paid $20/hr for
their time.

Inclusion and exclusion criteria—Because prevalence rates for GAD are higher in
women than they are in men (Carter, Wittchen, Pfister, & Kessler, 2001), and to reduce
sample heterogeneity, the sample was limited to females aged 18-55 years (in line with prior
work, e.g., Gotlib, Krasnoperova, Yue, & Joormann, 2004; Ray et al., 2009). Thirty-five
adult healthy controls (HC) and 71 adults with DSM-IV GAD participated in the study. Diagnoses were made using the Structured Clinical Interview for DSM-IV (SCID-I/NP, First, Spitzer, Gibbon, & Williams, 1995) to assess for past and present psychological disorders. Individuals in the HC group were required to be free from all past or present Axis I diagnoses. Exclusion criteria in the GAD group were: a lifetime history of psychotic or bipolar disorders; current or recent (i.e., < 6 months ago) obsessive-compulsive, social anxiety, panic, posttraumatic stress or eating disorder as well as substance abuse/dependence. Participants with dysthymia or comorbid major depression were included if the onset of GAD was prior to that of depression (Etkin, Prater, Schatzberg, Menon, & Greicius, 2009). In the GAD group, comorbid current Axis I disorders included: major depression (n = 28), specific phobia (n = 17) and dysthymia (n = 13). Additional exclusion criteria for all participants included the use of psychiatric medications (including, but not limited to medications for anxiety or depression) within 2 months prior to the time of testing, a history of head trauma, or systemic or neurological illness. Diagnostic assessments were made by three Master’s level clinicians who were trained using SCID-I videos, and who received supervision and feedback from the senior author (GHP). Using eight interviews from each of these clinicians, kappa coefficients for anxiety and depressive diagnoses and were found to be quite high (e.g., .88 to .92).

Materials

Participants performed high-load and low-load working memory trials interspersed with task-irrelevant neutral and unpleasant pictures (MacNamara et al., 2011). A total of 120 pictures (60 neutral; 60 unpleasant) from the International Affective Picture System (Lang, Bradley, & Cuthbert, 2005) were used. Working memory load was varied by asking participants to memorize 6 letters (high-load) or 2 letters (low-load). Letter strings were the same as those used by MacNamara and colleagues (2011), and were comprised of 60 2-consonant strings and 60 6-consonant strings (Ashcraft & Kirk, 2001). The task was presented using Presentation software (Neurobehavioral Systems); pictures were centered, presented in color and filled the screen (which measured 48.26 cm, diagonally). Participants were seated approximately 60 cm from the screen and the images occupied about 40° of visual angle horizontally and vertically.

The Mood and Anxiety Symptom Questionnaire (MASQ; Watson & Clark, 1991; Watson & McKee Walker, 1996) was used to measure symptoms of anxiety and depression continuously. Scores were derived using the 62-item MASQ, a 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 over the

---

1The IAPS pictures used were unpleasant (1052, 1201, 1202, 1300, 1302, 2120, 2130, 2811, 3001, 3053, 3059, 3060, 3068, 3100, 3181, 3266, 3350, 3500, 6243, 6260, 6263, 6315, 6350, 6510, 6520, 6520, 6530, 6540, 6550, 6562, 6570, 6821, 6825, 6832, 9042, 9050, 9075, 9163, 9250, 9252, 9253, 9265, 9265, 9403, 9405, 9410, 9413, 9414, 9420, 9427, 9432, 9433, 9582, 9584, 9599, 9635.1, 9902, 9910, 9911, 9920, 9921) and neutral (2026, 2038, 2039, 2104, 2107, 2230, 2384, 2385, 2396, 2397, 2400, 2411, 2446, 2480, 2493, 2494, 2512, 2516, 2745.1, 2840, 5120, 5500, 5534, 6150, 7003, 7006, 7009, 7014, 7018, 7019, 7020, 7026, 7030, 7032, 7033, 7055, 7037, 7038, 7041, 7059, 7060, 7080, 7110, 7130, 7140, 7180, 7217, 7224, 7234, 7493, 7496, 7512, 7547, 7550, 7700, 7705, 7710, 7920, 7950).
past week using a 5-point scale ranging from not at all to extremely; higher ratings indicate increased levels of anxiety and depression. The decision to collect MASQ data was made after data collection had begun; MASQ scores were missing from the first 6 HCs and 13 individuals with GAD.

**Task**

A full description and figure depicting the task are available in MacNamara and colleagues (2011). Participants were told that their task was to memorize the letters presented at the beginning of each trial and that they would be asked to recall these letters at the end of each trial (Ashcraft & Kirk, 2001; MacNamara et al., 2011). Participants were instructed to keep their eyes on the screen throughout the entire trial. Each trial began with the presentation of a 2- or 6-letter string (Ashcraft & Kirk, 2001) that was displayed for 5,000 ms. Next, a white fixation cross was presented on a black background for a random interval ranging between 500 and 1,000 ms; this was followed by a unpleasant or neutral picture presented for 2,000 ms. Following picture offset, participants used the keyboard to enter the letters in the same order as they had been displayed at the beginning of the trial. Participants used the backspace key to correct any mistakes, and the trial ended when they pressed the ‘Enter’ key. To deter participants from using finger placement on the keyboard as a memory aid, participants were instructed to use just one finger to enter the letters, and to keep their hands on their lap during the trial (MacNamara et al., 2011; MacNamara et al., 2012). The inter-trial interval varied randomly between 2,000 and 2,500 ms, during which time a white fixation cross was centrally displayed on a black background.

Each participant saw all pictures and all letter strings exactly once. The pairing of pictures and letter strings was pseudorandom; there were 30 trials in which a 2-letter string was followed by a neutral picture (low-load neutral), 30 trials on which a 2-letter string was followed by an unpleasant picture (low-load unpleasant), 30 trials on which a 6-letter string was followed by a neutral picture (high-load neutral), and 30 trials on which a 6-letter string was followed by an unpleasant picture (high-load unpleasant). Trial-types were intermixed and the order of these trials was completely random. At the end of the experiment, participants completed the MASQ.

**Electroencephalographic recording**

Continuous EEG was recorded using an elastic cap and the ActiveTwo BioSemi system (BioSemi, Amsterdam, Netherlands). Thirty-four electrode sites (standard 32 channel setup, as well as FCz and Iz) were used, based on the 10/20 system; in addition, electrodes were placed on the left and right mastoids. The electrooculogram (EOG) generated from eyeblinks and eye movements was recorded from four facial electrodes - 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 using two electrodes, placed approximately 1 cm beyond the outer edge of each eye. The EEG signal was pre-amplified at the electrode to improve the signal-to-noise ratio. The data was digitized at a 24-bit resolution with a Least Significant Bit (LSB) value of 31.25 nV and a sampling rate of 1024 Hz, using a low-pass fifth order sinc filter with a -3dB cutoff point at 208 Hz. The voltage from each active electrode was referenced online, with respect to a
common mode sense (CMS) active electrode producing a monopolar (i.e., non-differential) channel.

**Data reduction and analysis**

Analyses were performed using Brain Vision Analyzer software (Brain Products, Gilching, Germany). Data were re-referenced offline, to the average of the two mastoids, and band-pass filtered with low and high cutoffs of 0.01 and 30 Hz, respectively. Following the segmentation of data (see below), eye blink and ocular corrections were made according to the method developed by Miller, Gratton and Yee (1988). Artifact analysis was used to identify a voltage step of more than 50.0 μV between sample points, a voltage difference of 300.0 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, and data from individual channels containing artifacts were rejected on a trial-by-trial basis. Six participants (3 HC, 3 GAD) were excluded from the ERP analyses because of poor quality data. The mean number of trial segments included in the statistical analyses after artifact rejection was as follows: low-load neutral – HC \( M = 28.5 \ \text{SD} = 2.2 \), GAD, \( M = 28.2 \ \text{SD} = 2.2 \); low-load unpleasant – HC \( M = 29.0 \ \text{SD} = 1.3 \), GAD \( M = 27.9 \ \text{SD} = 2.3 \); high-load neutral – HC \( M = 28.8 \ \text{SD} = 2.0 \), GAD \( M = 28.2 \ \text{SD} = 2.6 \) and high-load unpleasant – HC \( M = 28.9 \ \text{SD} = 1.8 \), GAD \( M = 28.3 \ \text{SD} = 2.4 \). The number of trial segments remaining after artifact rejection was not affected by condition, group, or their interaction (all \( p < .11 \)).

To examine ERPs, the EEG was segmented for each trial beginning 200 ms prior to picture onset and continuing for 2,200 ms (i.e., the entire 2,000 ms picture presentation duration); baseline correction for each trial used the 200 ms prior to picture onset. The LPP was scored by averaging amplitudes at electrode Pz from 400-2,000 ms after picture onset (Hajcak & Nieuwenhuis, 2006; MacNamara, Post, Kennedy, Rabinak, & Phan, 2013; Moser, Hajcak, Bukay, & Simons, 2006; Williams & Themanson, 2011). Responses to the letter recall task were considered correct if and only if the responses contained the same letters that were presented at the beginning of the trial, entered in the exact order in which they were originally presented. The percentage of correct responses per condition was calculated using the number of correct trials divided by 30 trials per condition. Due to technical errors, behavioral data was not obtained for 3 participants (2 HC, 1 GAD).

A 2 (group: GAD, HC) × 2 (working memory load: low, high) × 2 (picture type: neutral, unpleasant) mixed model repeated measures analysis of variance (ANOVA) was used to examine accuracy data and the LPP. Independent and paired sample \( t \)-tests were used to follow-up significant interactions. Pearson’s correlations were used to determine relationships between brain activity and symptomatology, using difference scores calculated for the effect of working memory load (low-load minus high-load) on the LPP. Because the control group displayed little range on self-report measures of clinical symptomatology, and because the control and GAD groups differed statistically on all MASQ subscales,

---

\[2\] The LPP was also scored in two separate time windows (400-1000 ms, 1000-2000 ms after picture onset) and including the factor “time window” in the overall ANOVA; results were unchanged.

*J Abnorm Psychol.* Author manuscript; available in PMC 2015 August 01.
correlations involving these measures were performed within the GAD group only (Catani, Adenauer, Keil, Aichinger, & Neuner, 2009). Statistical analyses were performed using SPSS (Version 20.0) General Linear Model software.

Results

Participant Characteristics

Table 1 presents clinical characteristics and demographics for the HC and GAD groups, as well as statistical comparisons between groups on these variables. The GAD group reported high levels of anxiety and depression on all four MASQ subscales, compared to the HC group (Table 1). MASQ scores for the GAD group were comparable to those observed in prior work studying community samples with GAD (e.g., MacNamara & Hajcak, 2010), and in other recent work studying anxious and depressed treatment-seeking populations (Boschen & Oei, 2007; Buckby, Yung, Cosgrave, & Killackey, 2007).

Working memory performance

Table 2 presents performance data (i.e., working memory accuracy) and mean LPP amplitudes for each group. As expected, participants recalled more letters on low-load trials than high-load trials ($F(1,101) = 201.51, p < .001, \eta_p^2 = .67$); participants also recalled more letters when trials contained a neutral than unpleasant picture ($F(1,101) = 5.48, p = .02, \eta_p^2 = .05$). Working memory load and picture type interacted ($F(1,101) = 6.01, p = .02, \eta_p^2 = .06$) such that working memory load had a more negative impact on letter recall for trials with unpleasant pictures than it did for trials with neutral pictures. There was no between-groups effect on the LPP and no other significant interactions (all $p$s > .12).

LPP

Unpleasant pictures elicited larger LPPs than neutral pictures ($F(1,98) = 81.42, p < .001, \eta_p^2 = .45$; Table 2, Figures 1 and 2). Working memory load reduced the picture-elicited LPP ($F(1,98) = 36.35, p < .001, \eta_p^2 = .27$). A three-way interaction was observed between working memory load, picture type, and group ($F(1,98) = 5.00, p = .03, \eta_p^2 = .05$; all other $p$s > .22). To examine this interaction, difference scores were created for the effect of working memory load on the picture-elicited LPP (low-load minus high-load; MacNamara et al., 2011), calculated separately for neutral and unpleasant pictures. These difference scores were then compared between groups using independent samples $t$-tests (MacNamara & Hajcak, 2010). The GAD group showed less working memory load moderation of the LPP elicited by unpleasant pictures than did the HC group ($t(98) = 2.16, p = .03$; Figures 1 and 2). Furthermore, this group difference was attributable to larger LPPs on high-load unpleasant trials for the GAD group ($t(98) = 3.15, p = .002$; unpleasant pictures presented on low-load trials, $t(98) = 0.93, p > .35$). No group difference was observed for the effect of working memory load on neutral trials ($t(98) = 0.36, p > .71$).

To examine the influence of comorbid depression, a second orthogonal ANOVA was run within the GAD group (Foti, Kotov, Bromet, & Hajcak, 2012). This second ANOVA contained the following factors: 2 (depression: present, absent) × 2 (working memory load: low, high) × 2 (picture type: neutral, unpleasant), where depression was defined as a
diagnosis of either MDD and/or dysthymia. Main effects of working memory load ($F(1,66) = 17.18$, $p < .001$, $\eta^2_p = .21$; low-load > high-load) and picture type ($F(1,66) = 54.63$, $p < .001$, $\eta^2_p = .45$; unpleasant > neutral) were again observed. However, no interactions or group differences reached significance (all $p$s > .13). Thus, the effect of working memory load on the LPP appeared to be equivalent for individuals with GAD with versus without comorbid depression.

**Correlations**

Within the GAD group, higher scores on the MASQ Anhedonic Depression scale were associated with a smaller effect of working memory load on the LPP elicited by neutral pictures ($r(54) = -.40$, $p = .003$; unpleasant pictures, $r(54) = -.05$, $p > .70$). There were no other significant correlations between MASQ subscales and the LPP (all $p$s > .06).

**Discussion**

Across all participants, unpleasant pictures elicited larger LPPs than neutral pictures; moreover, working memory load reduced accuracy, and attenuated the processing of task-irrelevant stimuli as evidenced by the LPP. These results are consistent with previous studies that examined the impact of working memory load on emotional processing using the LPP (MacNamara et al., 2011; MacNamara et al., 2012). In addition, individuals with GAD evinced reduced load-related modulation of the LPP to unpleasant pictures; specifically, the GAD group had larger LPPs to unpleasant pictures on high-load trials. This effect was not attributable to behavioral differences.

Reduced modulation of the LPP by working memory load in the GAD group provides neural evidence of reduced attentional control in GAD. The results are in line with recent behavioral (Berggren, Koster, & Derakshan, 2012; Berggren, Richards, Taylor, & Derakshan, 2013) and ERP (MacNamara et al., 2011) work that has examined attentional control in non-clinical anxiety. Given specificity to unpleasant pictures, the results observed here also support the notion that GAD may involve increased attention to unpleasant or threatening stimuli (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007; Bradley et al., 1995; Mogg & Bradley, 2005). In recent years, there has been debate regarding the contribution of aberrant bottom-up (i.e., stimulus-driven) versus top-down (e.g., goal-directed) attentional processes on the enhanced processing of unpleasant or threatening stimuli in anxiety (Berggren & Derakshan, 2013; Cisler & Koster, 2010). The current study suggests that GAD is characterized by increased processing of aversive stimuli when cognitive resources are depleted. Put another way, the current results begin to specify the circumstances under which greater attention to unpleasant stimuli is most likely to occur in GAD: high cognitive load may reveal attentional control deficits in GAD that are not evident when executive functions are less taxed (Cornwell et al., 2011; Eysenck et al., 2007).

---

3When correlations were re-run following multiple imputation to account for missing MASQ scores, the same pattern of results was observed.
The current results may suggest novel treatment targets for GAD. For instance, treatments designed to increase attentional control (e.g., Siegle, Ghinassi, & Thase, 2007; Wells, White, & Carter, 1997) or treatments that increase activity in neural regions linked to attentional control (e.g., the dlPFC; Bystritsky, Kerwin, & Feusner, 2009; Pallanti & Silvia, 2009) may be helpful in reducing emotion dysregulation in GAD (also see Mennin, 2004). Relatedly, attentional control may mediate the success of extant treatments for GAD. Along these lines, a recent study found that symptom reduction following cognitive behavioral therapy for anxiety, a gold standard treatment for GAD, was moderated by changes in attentional control (McEvoy & Perini, 2009).

The LPP effects observed in the current study were found in the absence of behavioral differences between groups. According to Eysenck and colleagues, anxiety should have a greater effect on neural measures than behavioral measures because anxious individuals may be able to compensate for the effects of reduced attentional control on behavior (e.g., by trying harder). Along these lines, Fales and colleagues (2008) found that despite an overall and sustained decrease in dlPFC activity, individuals who were more anxious showed increased transient dlPFC activity during a working memory task, suggesting compensatory activity. Still other work has observed altered resting state neural network connectivity in GAD, suggestive of compensatory neural adaptation (Etkin et al., 2009). Therefore, future work may wish to use fMRI or other neural measures with higher spatial resolution in order to better characterize brain regions involved in compensating for attentional control deficits in GAD (Engels et al., 2010; Silton et al., 2011).

In contrast to other ERP work in GAD (e.g., using the error-related negativity; Weinberg, Klein, & Hajcak, 2012), the present results seemed robust to the presence of comorbid depression. That is, load-related modulation of the LPP did not differ for individuals with “pure” GAD versus those with comorbid depression. Attenuated modulation of the LPP might therefore represent a core deficit in GAD that is robust to current depressive symptom severity. Alterations in the LPP might reflect trait-like individual differences related to GAD that are unchanged when individuals enter into, or recover from, depressive episodes (Brown, 2007), though this hypothesis requires examination by tracking patients over time. As the current conclusions regarding specificity to GAD are based on a null effect, they require replication.

Although depression did not appear to impact the main results, increased anhedonic depression within the GAD group was associated with a reduced effect of working memory load on the LPP elicited by neutral pictures. Recent work similarly found that depression was associated with less load-related filtering of task-irrelevant non-emotional stimuli in the visual cortex (Deseilles et al., 2009; Deseilles et al., 2011). Therefore, both the current and prior results suggest that depression may involve deficits in filtering non-emotional, task-irrelevant stimuli. The fact that there was no correlation between self-reported anhedonic depression and modulation of the unpleasant LPP within the GAD group suggests that anhedonic depression did not have explanatory power beyond a diagnosis of GAD for the unpleasant LPP.
Strengths of the current study included the use of a relatively large, “clean” sample (i.e., restrictions on comorbidities and psychiatric medication usage), that facilitated both diagnostic and dimensional approaches to understanding attentional control in GAD and depression. However, a limitation of the current study was the female-only sample. Prior work has found sex differences in the neural processing of emotional stimuli (e.g., the LPP - Syrjänen & Wiens, 2013), including evidence of heightened processing of negative stimuli among females (for a meta-analysis, see Stevens & Hamann, 2012). Therefore, more work will be needed to explicate potential gender differences in the neurobiological correlates of emotion-processing in GAD. Finally, because the current study only included unpleasant and neutral stimuli, it is impossible to be certain that valence, rather than arousal, was the critical factor in the LPP results. Including both pleasant and unpleasant emotional pictures in future studies would help address this limitation.

In conclusion, the current results suggest that individuals with GAD less flexibly modulate attention toward unpleasant stimuli, and that this effect can be traced to deficient control of attention under high cognitive load. The results go beyond prior work (e.g., MacNamara et al., 2011; MacNamara & Hajcak, 2010) in elucidating cognitive components that may contribute to increased distracter processing in GAD and suggest novel candidate treatment targets for GAD. The LPP might provide a useful means of assessing neurobiological “fit” for GAD treatments (e.g., Whalen et al., 2008) aimed at improving attentional control, and tracking treatment progress in this domain.

Acknowledgments

This research was supported in part by a grant from the National Institute of Mental Health, T32MH067631-09 (AM)

References


J Abnorm Psychol. Author manuscript; available in PMC 2015 August 01.


First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JBW. Structured clinical interview for DSM-IV Axis I Disorders – Non-patient edition (SCID-I/NP). New York: Biometric Research Department; 1995.


Watson D., Clark, LA. The Mood and Anxiety Symptom Questionnaire. Iowa City, IA: University of Iowa; 1991.


Figure 1.
Grand-averaged waveforms at electrode Pz, for neutral and unpleasant pictures presented under high and low working memory load, shown separately for healthy controls (left) and individuals with GAD (right).
Figure 2.
The mean LPP for each condition, shown separately for the HC group (left) and the GAD group (right). Error bars represent standard error of the mean.
### Table 1

<table>
<thead>
<tr>
<th>Clinical and demographic characteristics of participants</th>
<th>HC (n = 35)</th>
<th>GAD (n = 71)</th>
<th>Group comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
</tr>
<tr>
<td>Mood and Anxiety Symptom Questionnaire (MASQ)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MASQ Anxious Arousal</td>
<td>19.64</td>
<td>3.76</td>
<td>28.55</td>
</tr>
<tr>
<td>MASQ Anhedonic Depression</td>
<td>54.11</td>
<td>11.01</td>
<td>71.31</td>
</tr>
<tr>
<td>MASQ General Distress – Anxiety Symptoms</td>
<td>15.29</td>
<td>3.61</td>
<td>25.72</td>
</tr>
<tr>
<td>MASQ General Distress – Depressive Symptoms</td>
<td>17.29</td>
<td>3.12</td>
<td>31.90</td>
</tr>
<tr>
<td>Age</td>
<td>23.89</td>
<td>9.12</td>
<td>23.70</td>
</tr>
<tr>
<td>Years of Education</td>
<td>14.72</td>
<td>2.05</td>
<td>15.15</td>
</tr>
<tr>
<td>Global Assessment of Functioning (GAF)</td>
<td>85.29</td>
<td>4.41</td>
<td>59.80</td>
</tr>
<tr>
<td>Employment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>24</td>
<td>69</td>
<td>45</td>
</tr>
<tr>
<td>No</td>
<td>7</td>
<td>20</td>
<td>21</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>14</td>
<td>40</td>
<td>50</td>
</tr>
<tr>
<td>Other</td>
<td>17</td>
<td>49</td>
<td>20</td>
</tr>
</tbody>
</table>

Note. Percentages for employment and ethnicity data sum to < 100 because of missing data.

* \( p < .05; \)

** \( p < .001; \)
### Table 2

Picture-elicited LPP and accuracy data for the letter recall task

<table>
<thead>
<tr>
<th>Load</th>
<th>Picture</th>
<th>HC (n = 32) M</th>
<th>SD</th>
<th>GAD (n = 68) M</th>
<th>SD</th>
<th>HC (n = 33) M</th>
<th>SD</th>
<th>GAD (n = 70) M</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Neutral</td>
<td>2.84</td>
<td>5.37</td>
<td>5.55</td>
<td>6.67</td>
<td>98.08</td>
<td>4.00</td>
<td>96.33</td>
<td>6.91</td>
</tr>
<tr>
<td>Low</td>
<td>Unpleasant</td>
<td>6.88</td>
<td>6.19</td>
<td>10.07</td>
<td>7.34</td>
<td>97.47</td>
<td>5.07</td>
<td>96.86</td>
<td>6.06</td>
</tr>
<tr>
<td>High</td>
<td>Neutral</td>
<td>-.24</td>
<td>6.54</td>
<td>1.99</td>
<td>6.42</td>
<td>69.90</td>
<td>20.50</td>
<td>64.43</td>
<td>22.80</td>
</tr>
<tr>
<td>High</td>
<td>Unpleasant</td>
<td>3.31</td>
<td>5.93</td>
<td>8.03</td>
<td>7.44</td>
<td>65.66</td>
<td>20.79</td>
<td>62.90</td>
<td>24.17</td>
</tr>
</tbody>
</table>