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Attentional control and unpleasant stimuli: an event-related potential study in individuals with Generalized Anxiety Disorder and Major Depressive Disorder

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Abstract of the Dissertation

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Theories of attentional control posit that both anxiety and depression should be associated with reduced filtering of task-irrelevant stimuli; reduced attentional control may also underlie an early attentional bias toward unpleasant stimuli that has been observed in individuals with Generalized Anxiety Disorder (GAD). Major Depressive Disorder (MDD), on the other hand, has been less consistently associated such an attentional bias, and individuals with comorbid GAD/MDD often fail to exhibit an attentional bias toward unpleasant stimuli. To determine whether individuals with GAD and those with comorbid GAD/MDD would exhibit reduced attentional control (i.e., difficulty moderating attention to task-irrelevant stimuli), and whether this would vary for unpleasant compared to neutral stimuli or early versus later stages of stimulus processing, the present study employed a working memory task interspersed with the presentation of task-irrelevant unpleasant and neutral pictures. Working memory load activates the dorsolateral prefrontal cortex (DLPFC), a neural region implicated in attentional control, and functional activation of the DLPFC has been shown to reduce the processing of task-irrelevant pictures. As in prior work, the late positive potential (LPP) event-related potential was larger for unpleasant compared to neutral pictures, and working memory load reduced the picture-elicited LPP. Higher working memory load also reduced frontal alpha power, suggesting increased frontal brain activity; moreover, the modulation of left frontal alpha by working memory load predicted reductions in the LPP. In contrast to the control (n = 35) and comorbid (n = 36) groups, individuals with pure GAD (n = 36) failed to show working memory load modulation of the LPP elicited by unpleasant pictures in the middle time window. In the latest time window, individuals in the comorbid group failed to show an effect of working memory load on the LPP elicited by either picture type. Correlational analysis revealed a smaller effect of working memory load on picture-elicited LPPs for individuals with higher self-reported anhedonic depression. The results suggest that reduced attentional control may represent a shared feature of GAD and comorbid GAD/MDD; comorbid MDD may attenuate early attention toward unpleasant stimuli and modulate later, reactive cognitive control mechanisms observed in GAD.

Dedication Page

This dissertation is dedicated to my parents, Carmel O'Sullivan and Stewart Crampton for the curiosity they instilled in me, and to my brother, Joseph Crampton, for his passion for ideas.

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List of Abbreviations

Dorsolateral prefrontal cortex: DLPFC
Electroencephalographic: EEG
Event-related potentials: ERP
Generalized Anxiety Disorder: GAD
Late positive potential: LPP
Major Depressive Disorder: MDD

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Introduction

Generalized Anxiety Disorder (GAD) is a chronic and debilitating condition with a lifetime prevalence rate estimated at 6% (Kessler, Berglund, Demler, Jin, & Walters, 2005). It is associated with significant economic burden, owing to its place as the leading cause of workplace disability in the U.S. (Kessler, 2000) and to increased use of primary care (Wittchen, 2002). Despite its significant public health impact, GAD is not well understood and relatively few studies have been conducted on GAD. For example, GAD is diagnosed nearly four times more often than obsessive compulsive disorder (OCD; Kessler et al., 2005), yet a recent literature search uncovered two to three times as many studies on OCD. Moreover, rates of response to treatment for GAD are significantly lower than for other anxiety disorders (Borkovec & Ruscio, 2001; Fisher & Durham, 1999). A better understanding of the mechanisms underlying GAD is needed if outcomes for the disorder are to be improved (Behar, DiMarco, Hekler, Mohlman, & Staples, 2009).

One factor complicating research on GAD has been high levels of comorbidity with Major Depressive Disorder (MDD). For instance, a recent study found that 39% of individuals with GAD also met criteria for MDD at the time of assessment; lifetime prevalence of MDD increased to 65% four years later and to 74% at eight years (Bruce, Machan, Dyck, & Keller, 2001). Comorbid MDD often onsets after GAD and decreases the likelihood that individuals will recover from GAD (Bruce et al., 2001), making it an important factor in determining clinical course. Despite this, many studies do not control for comorbidity of GAD and MDD and relatively few studies have investigated the ways in which comorbid depression may impact the mechanisms underlying GAD.

In addition to being highly comorbid, GAD and MDD are very similar disorders: they overlap in symptomatology, share a common genetic vulnerability (Kendler, Neale, Kessler, Heath, & Eaves, 1992; Roy, Neale, Pedersen, Mathe, & Kendler, 1995) and both respond to anti-depressants (Gorman, 2002; Rivas-Vazquez, 2001). Because of the similarities between GAD and MDD, there has been a movement to classify GAD in the same category as MDD in upcoming diagnostic systems (Watson, 2005). Yet despite similarities between GAD and MDD, there is evidence to suggest that GAD is a disorder in its own right and should be considered distinct from MDD (Mennin, Heimberg, Fresco, & Ritter, 2008). For instance, GABA/benzodiazepine receptor dysfunction plays a role in GAD but not in MDD (Lydiard & Monnier, 2004). In addition, GAD may be characterized by unique pathological mechanisms such as increased worry (Chelminski & Zimmerman, 2003) and intolerance of uncertainty (i.e., ambiguous situations are perceived as distressing; Dugas, Buhr, & Ladouceur, 2004).

Evidence for shared versus unique mechanisms in GAD and MDD could shed light on the redundancy or distinctiveness of these diagnostic categories. For instance, theories of attentional bias originally postulated that both anxiety and depression should be characterized by increased attention toward unpleasant stimuli. In recent years, however, evidence has accrued which suggests that anxiety and depression may be distinguished by temporal differences in the allocation of attention toward unpleasant stimuli. Specifically, anxiety appears characterized primarily by increased *early* attention to unpleasant stimuli, whereas depression seems characterized by *later*, more elaborative processing of unpleasant stimuli (e.g., Bradley, Mogg, Millar, & White, 1995; Foa, McNally, & Murdock, 1989; MacLeod, Mathews, & Tata, 1986;

McCabe & Gotlib, 1995; Mogg, Bradley, Williams, & Mathews, 1993; Mogg, Mathews, & Weinman, 1987). Such findings argue for a mechanistic distinction between GAD and MDD.

Building on attentional bias work, the attentional control literature (e.g., Eysenck, Derakshan, Santos, & Calvo, 2007; Mayberg et al., 1999) has attempted to account for abnormalities in *controlled* attentional processes that may also underlie anxiety and depression. Attentional control refers to the extent to which individuals are successful in directing attention away from certain stimuli and toward other stimuli, and these theories have sought to understand anxiety and depression in terms of disruptions to the balance of involuntary and voluntary attention. Attentional control theories may offer a more complete account of attention to emotional stimuli in anxiety and depression - however, there are gaps in this literature. For instance, attentional control theories have not sought to differentiate between attentional control deficits in anxiety versus depression. Moreover, few studies have been conducted on clinically anxious individuals, and the time-course of attention control deficits in anxiety and depression has not been examined. Given evidence from the attentional bias literature, one possibility is that GAD may be characterized primarily by *early* deficits in attentional control that are specific to unpleasant stimuli, whereas MDD might be associated with non-affective deficits in attentional control that are evident *later* on during stimulus presentation – though this possibility has not been tested.

If a mechanistic difference between GAD and MDD lies in the temporal course of attentional deployment, then temporally-sensitive measures of attention are potentially important in helping to understand differences and similarities underlying the disorders. To date, most of the research on anxiety and depression has used behavioral measures, such as response time. For instance, in the dot-probe task, individuals typically view two pictures presented on either side of fixation (e.g., to the left and right). One of these pictures is usually emotional (e.g., an unpleasant picture) and the other picture is neutral. After picture offset, a target (e.g., a dot) appears in place of one or the other pictures, and participants are asked to respond to this target as quickly and as accurately as possible. Faster response times to targets that appear in place of unpleasant compared to neutral pictures are taken to indicate an attentional bias toward unpleasant stimuli, because it is assumed that participants were attending to the unpleasant stimuli just before target onset. Response times on tasks such as this have been widely used in research on attention in anxiety and depression. Unfortunately, such response times can only provide a "snapshot" of attentional allocation at a single point in time and are therefore relatively ineffective at characterizing temporal differences in attention (particularly when images are onscreen long enough for participants to shift attention from one image to the next). Continuous measures such as electroencephalographic (EEG) event-related potentials (ERPs), on the other hand, can index attentional allocation on a millisecond by millisecond basis and can capture shifts in attention that occur throughout the stimulus presentation duration. Moreover, ERPs can provide an index of attention that is relatively free from the influence of other processes, such as decision making and motor response, which may confound behavioral measures. In addition, ERPs can be recorded alone or in conjunction with behavioral measures. For these reasons, ERPs are particularly well-suited to an examination of mechanistic differences between GAD and MDD.

The goals of the proposed project were threefold. One aim was to extend prior work conducted in non-clinically anxious individuals (MacNamara, Ferri, & Hajcak, 2011) in order to determine whether GAD is characterized by decreased attentional control, and whether reduced

attentional control would be specific to unpleasant compared to neutral pictures. A second aim was to clarify shared and distinct facets of GAD and MDD. If a comorbid diagnosis of MDD were to affect attentional processes in GAD (e.g., the timing or affective nature of attentional control deficits), then this would suggest a mechanistic distinction between the disorders. A third aim was to observe how attentional abnormalities in GAD and comorbid GAD/MDD might correspond to behavioral outcomes, continuous measures of symptomatology and an EEG measure of reduced prefrontal brain activation (alpha).

Attentional bias models

Although attending to unpleasant or threatening stimuli might be considered adaptive in certain circumstances (e.g., when walking through a dangerous neighborhood at night), anxious and depressed individuals may vastly overestimate the extent of unpleasant stimuli in the environment. Continually attending to unpleasant stimuli may induce chronic arousal, behavioral interference and fatigue among other symptoms. In addition, increased attention toward unpleasant stimuli might serve to *maintain* cognitive biases in anxiety and depression. For example, excessive attention toward unpleasant stimuli could lead a person to perceive more unpleasant stimuli, thereby confirming the expectation that the world is an unsafe and unfriendly place (a vicious cycle).

Beginning in the 1970s and 1980s, Beck (1976) and Bower (1981) suggested that a cognitive bias toward negative material predisposed individuals to develop anxiety or depression. Moreover, negative mood states were thought to maintain an attentional bias toward negative information once a disorder had developed. Importantly, both Beck (1976) and Bower (1981) predicted that anxiety and depression would be characterized by the permeation of mood-congruent cognitive biases at every stage of stimulus processing (e.g., perception, attention and memory), and indeed, initial evidence supported this notion. For example, anxiety was associated with faster responses to targets that replaced unpleasant compared to neutral stimuli on the dot-probe task (MacLeod et al., 1986) and depression was associated with facilitated memory for unpleasant stimuli (see Blaney, 1986 for a review; Clark & Teasdale, 1982; Mathews & Bradle, 1983).

While these early models provided a useful framework from which to begin to understand emotion-cognition interactions in anxiety and depression, Beck's (1976) and Bower's (1981) theories were unable to accommodate empirical findings that began to emerge in the late 1980's and 1990's. Specifically, anxiety did not seem to be associated with enhanced memory for threatening material (e.g., Foa et al., 1989; Mogg et al., 1987) and depression did not appear to be associated with early attentional biases for unpleasant information (e.g., Bradley et al., 1995; MacLeod et al., 1986; McCabe & Gotlib, 1995; Mogg et al., 1993). Therefore, the *time course* of cognitive biases appeared important in characterizing anxiety and depression, and a new theory was needed to explain empirical findings.

Williams and colleagues (Williams, Watts, MacLeod, & Mathews, 1988) provided such a theory when they proposed the "two-stage" theory of emotion processing. This theory distinguished between automatic and strategic biases in attention toward unpleasant stimuli. Anxiety was believed to be associated with the increased early, automatic processing of unpleasant stimuli, known also as hypervigilance. By contrast, depression was believed to be

associated with increased later-onset, more elaborative processing of unpleasant material. Williams and colleagues' (1988) theory fit well with clinical depictions of depression as involving increased *rumination* - the tendency to think passively and repetitively about a negative event once it has occurred (i.e., later on). Indeed, this idea was formalized some years later in *rumination theory*, in which rumination is believed to play a causal role in depression (i.e., by interfering with problem-solving and decreasing social support; Nolen-Hoeksema, 2004; Nolen-Hoeksema & Davis, 1999; Nolen-Hoeksema, Morrow, & Fredrickson, 1993). William and colleagues' (1988) theory is also compatible with the notion of *vigilance-avoidance* (discussed in more detail below), in which anxious individuals are believed to exhibit increased early attention toward unpleasant stimuli but avoidance of these same stimuli later on (Mogg, Bradley, Miles, & Dixon, 2004).

Although William and colleagues' (1988) theory could account for the empirical literature on attentional bias in pure depression and pure anxiety, it was unable to explain why comorbid depression appears to attenuate early attentional biases normally observed in anxiety. If increased early attention toward unpleasant stimuli plays a *causal* role in anxiety, then *all* anxious individuals – including those comorbid for depression – should exhibit if this bias, yet this does not appear to be the case. For example, Bradley and colleagues found that only individuals with pure GAD and not those with comorbid GAD/MDD exhibited an early attentional bias for unpleasant words on the Stroop task (Bradley et al., 1995). Similarly, Mogg and colleagues found no evidence for a threat-related bias on the Stroop task in individuals with depression, despite high levels of self-reported anxiety in this group (Mogg et al., 1993). Using a dot-probe task, Mogg, Bradley and Williams (1995) also found that only anxious but not depressed individuals exhibited an attentional bias toward subliminally presented unpleasant stimuli, despite high levels of anxiety in both groups. Finally, using eye-tracking, Mogg and colleagues (Mogg, Millar, & Bradley, 2000) found that individuals with GAD looked more rapidly toward angry faces, yet a similar effect was not observed in individuals with MDD, even though 13 of 15 participants in the MDD group were also diagnosed with GAD (Mogg et al., 2000). These results are difficult to reconcile with the notion that an early attentional bias toward negative information plays a causal role in anxiety.

In an attempt to account for the absence of an early attentional bias toward unpleasant stimuli in comorbid anxiety and depression, Mogg and Bradley (1998) proposed the cognitive-motivational model of emotional disorders. This model suggested that both anxiety and depression are characterized by a low threshold for threat-detection. In other words, both anxious and depressed individuals should be more likely to evaluate neutral or mildly unpleasant stimuli as highly unpleasant or threatening. Despite this, an early attentional bias toward unpleasant stimuli is not observed in depression because, according to Mogg and Bradley (1998), depressed individuals are characterized by disruption of a goal-engagement system – a system believed to moderate the strength of behavior directed toward external goals and stimuli. According to Mogg and Bradley (1998), only anxious individuals should allocate increased early processing resources toward unpleasant stimuli because depressed individuals are motivationally disengaged from the environment.

This notion fits broadly with other models of anxiety and depression. For instance, the helplessness-hopelessness model suggests that depression is characterized by a feeling of hopelessness in which engagement with the external world is thought of as futile (e.g., Alloy,

Kelly, Mineka, & Clements, 1990). In a similar vein, the tripartite model suggests that whereas both depression and anxiety are characterized by affective distress and high levels of negative affect, low trait positive affect should be uniquely associated with depression (Watson, Clark, & Carey, 1988). Low positive affect has also been linked to abnormalities in the production of the neurotransmitter dopamine (Heinz, Schmidt, & Reischies, 1994), which is thought to underlie motivation and goal-engagement (e.g., Depue & Iacono, 1989). Finally, low positive affect in depression has been associated with decreased vigilance (Schrijvers et al., 2008) and reduced engagement with the environment (Clark & Watson, 1991). Together, this work converges with Mogg and Bradley's (1998) suggestion that depression may be associated with reduced goal engagement, leading to the absence of an early attentional bias toward unpleasant stimuli, despite a low threshold for the detection of these stimuli.

Evidence in support of attentional bias models

Empirical evidence has corroborated the notion that pure anxiety is distinguished from depression primarily by increased *early* attention toward unpleasant stimuli (e.g., Mathews, 1990; Mogg & Bradley, 1998; Williams et al., 1988). For example, high compared to low trait anxious participants have been found to be faster to detect threatening faces among an array of non-threatening faces (Byrne & Eysenck, 1995). Individuals with high trait anxiety were also found to be faster to detect targets that replaced briefly presented (e.g., 100 ms) unpleasant compared to neutral stimuli on a probe-detection task (Koster, Crombez, Verschuere, Van Damme, & Wiersema, 2006) and similar results have been found in individuals with GAD (Bradley, Mogg, White, Groom, & de Bono, 1999; MacLeod et al., 1986). EEG studies have also supported the notion that anxiety is uniquely associated with increased early attention toward unpleasant material. For example, larger early ERPs to unpleasant stimuli have been observed among anxious individuals in the visual search, visual probe and other paradigms, even when this bias has not been observed in manual response times (e.g., Buodo, Sarlo, & Munafò, 2009; Flykt & Caldara, 2006; Fox, Derakshan, & Shoker, 2008). By contrast, early attentional biases toward unpleasant stimuli have *not* been typically observed in depressed individuals (e.g., MacLeod et al., 1986; Mogg et al., 1993).

Further evidence that anxiety – but not depression - may be associated with increased early attention toward unpleasant stimuli comes from work that has used subliminally presented stimuli (e.g., presentation durations in the range of 14 ms). For example, individuals with high levels of non-clinical anxiety (MacLeod & Rutherford, 1992) and those with GAD (Bradley et al., 1995; Mogg et al., 1993) have been found to exhibit increased interference from subliminally presented unpleasant words on the Stroop task. Using subliminally presented stimuli on the dot-probe task, similar results have been found in high trait-anxious individuals (Bradley, Mogg, & Lee, 1997) and those with GAD (Mogg et al., 1995). Interestingly, these studies found no evidence of increased attention toward subliminally presented unpleasant stimuli among depressed individuals (Bradley et al., 1997; Mogg et al., 1995; Mogg et al., 1993) or those comorbid for GAD and MDD (Bradley et al., 1995). This seems to be the case even when subliminally presented stimuli have been specifically tailored to depression (e.g., words like "sadness", "failure"; see Mathews & MacLeod, 2005 for a review).

Rather than being associated with increased early attention toward unpleasant stimuli, depression may be associated with increased *later* attention toward unpleasant stimuli, in line

with William's and colleagues' (1988) theory and rumination theory (Nolen-Hoeksema, 2004; Nolen-Hoeksema & Davis, 1999; Nolen-Hoeksema et al., 1993). In the lab, evidence of increased later attention to unpleasant stimuli in depression has been found using a variety of paradigms. For example, eye-tracking work suggests that depressed individuals look longer at unpleasant stimuli compared to control participants (Caseras, Garner, Bradley, & Mogg, 2007; Eizenman et al., 2003). Researchers have also used the dot-probe task to examine later attentional biases toward unpleasant stimuli by increasing stimulus presentation durations (e.g., stimuli may be presented for 1000 ms or longer). When participants respond faster to targets that appear in place of unpleasant (compared to neutral) stimuli presented for longer durations, this is taken to indicate increased *later* attention toward unpleasant stimuli because it is assumed that attention is focused on these stimuli during the latter part of stimulus presentation. Unlike when shorter stimulus presentation durations have been used, studies using the dot-probe task with longer stimulus presentation durations *have* found evidence of an attentional bias toward unpleasant stimuli among depressed individuals (Bradley et al., 1997; Gotlib, Krasnoperova, Yue, & Joormann, 2004; Mathews, Ridgeway, & Williamson, 1996). Such results have *not* been found in individuals with GAD (e.g., Gotlib et al., 2004; but see Hankin, Gibb, Abela, & Flory, 2010 for work in non-clinically anxious individuals).

The absence of a later attentional bias toward unpleasant stimuli in anxiety might arise from the *avoidance* of these stimuli later on during stimulus presentation. Although avoidance may reduce distress in the short term, in the long-term, it may contribute to the maintenance of anxious symptomatology and GAD in particular (Borkovec, Alcaine, & Behar, 2004; Borkovec & Roemer, 1995; Mennin, Heimberg, Turk, & Fresco, 2002; Roemer, Salters, Raffa, & Orsillo, 2005). For instance, an individual with GAD might avoid applying for a job because he is fearful of failure, and of the emotional arousal he will experience when filling out an application. In so doing, he will not learn to tolerate emotional arousal and will not have the opportunity to observe that actual outcomes are not always as terrible as imagined (e.g., he might actually get the job!). In other words, avoidance might prevent the extinction of fear because information incompatible with feared consequences is not acquired and used to alter beliefs about feared situations (Foa & Kozak, 1986). Avoidance is also reinforcing because of the reduction in emotional arousal that is experienced when a feared stimulus is avoided. For these reasons, avoidance may play a crucial role in maintaining anxious symptomatology; moreover, the prevention of avoidance may be essential to the effective treatment of GAD (e.g., Borkovec et al., 2004).

Mogg and colleagues (2004) have formalized the notion that anxious individuals initially attend to threatening stimuli and then rapidly disengage from these same stimuli in their theory of vigilance-avoidance (Mogg et al., 2004). Behavioral studies (Koster et al., 2006; Mogg et al., 2004) and EEG studies (e.g., Weinberg & Hajcak, 2011a) have found evidence of vigilance-avoidance among individuals with non-clinical anxiety and GAD. For example, in the Koster and colleagues (2006) study described earlier, highly trait anxious individuals showed increased attention for unpleasant stimuli presented for short durations (i.e., 100 ms); at longer stimulus presentation durations, however (e.g., 500 ms), anxious individuals avoided unpleasant stimuli. These results are in line with the notion that anxious individuals may divert attention away from threatening stimuli later on during stimulus presentation once attentional allocation is under conscious control. Similar results have been found using EEG. For instance, Weinberg and Hajcak (2011a) used a passive viewing task and found that individuals with GAD evinced

enhanced early ERPs (i.e., within the first 150 ms), but attenuated later ERPs (400 ms onwards) for unpleasant compared to neutral stimuli. Thus, individuals with GAD may preferentially allocate *early* but not *late* attention toward unpleasant stimuli.

Attentional control in anxiety and depression

The work described above has focused on *bottom-up* attention toward unpleasant stimuli. Bottom-up attention refers to the idea that certain stimuli are more likely to capture attention because they are naturally motivationally salient; in other words, a person does not need to decide that these stimuli deserve attention. From this perspective, anxious or depressed individuals are predisposed to attend more toward unpleasant stimuli because these stimuli are more salient for them than for other individuals, possibly because of a biological vulnerability or early learning history (Johnson, Kamilaris, Calogero, Gold, & Chrousos, 1996; Logan & Goetsch, 1993).

Top-down attention, by contrast, refers to the goal-directed allocation of attention to stimuli that people decide are important. Efforts to increase top-down attention can be modeled in terms of the heightened activation of task-relevant stimulus representations and the inhibition of competing stimulus representations (e.g., Cohen, Dunbar, & McClelland, 1990). Theories that suggest a role for top-down attention in anxiety and depression propose that not only might unpleasant stimuli be more salient for anxious and depressed individuals - these individuals might also have difficulty directing attention away from task-irrelevant stimuli. In other words, anxiety and depression might be characterized by deficits in attentional *control*, and decreased attentional control might lead to an attentional bias toward unpleasant stimuli. Theories of attentional control build on the attentional bias work by attempting to parse bottom-up and top-down contributions to attentional allocation.

Though the attentional control approach holds promise for a more complete understanding of the mechanisms underlying anxiety and depression, important gaps remain in the literature. For instance, despite decades of research suggesting that anxiety is characterized by increased attention toward unpleasant stimuli, the attentional control literature suggests that attentional control deficits in anxiety should not be specific to unpleasant stimuli. In addition, theories of attentional control have developed separately for anxiety and depression (with a sparser literature for depression), and there has been little crosstalk between these literatures; indeed, issues of comorbidity have not typically been addressed. Finally, attentional control studies have generally been conducted on non-clinically as compared to clinically anxious individuals; leaving it unclear as to whether attentional control deficits manifest differently in clinically anxious populations.

Attentional control in anxiety

Two theories of anxiety that incorporate the notion of top-down attention are Mathews and Mackintosh's (1998) theory and Eysenck and colleagues' attentional control theory (ACT; Eysenck et al., 2007). Both theories represent a subtle yet important shift in the way attentional mechanisms in anxiety are conceptualized. Specifically, these theories suggest that the degree to which unpleasant distracters capture attention in anxiety depends on the balance between top-down and bottom-up attentional systems.

According to ACT, the influence of goal-directed (i.e., top-down) attention is compromised relative to the influence of stimulus-driven (i.e., bottom-up) attention in anxiety (Derakshan & Eysenck, 2009; Eysenck et al., 2007). Several predictions follow. First, attentional biases in anxiety should not be limited to unpleasant stimuli (Eysenck et al., 2007). Rather, anxious individuals should have difficulty inhibiting attention toward all kinds of stimuli. There is some evidence to support this point. For instance, experimentally induced anxiety has been associated with greater behavioral interference on *non-emotional* Stroop tasks (e.g., Pallak, Pittman, Heller, & Munson, 1975). Greater anxiety has also been linked to attentional control difficulties on other tasks using non-emotional stimuli, such as the visual search (Fox, 1994; Moser, Becker, & Moran, 2012; Pacheco-Unguetti, Acosta, Marqués, & Lupiáñez, 2011).

The antisaccade task has also been used to examine the effects of anxiety on attentional control in the context of non-affective stimuli. In this task, a cue is presented to the left or right of fixation and participants are required to fixate on the opposite side of the screen as quickly as possible. Correct responses require overcoming the tendency to fixate the cue. Therefore, faster initial eye movements toward the correct side of the screen are thought to reflect better attentional control. Derakshan and colleagues (Derakshan, Ansari, Hansard, Shoker, & Eysenck, 2009) used an antisaccade task in which the cue was a neutral shape (i.e., an oval). They found that anxious individuals evinced longer saccade latencies than non-anxious individuals, in line with the notion that anxiety involves impaired inhibitory control, even in the context of neutral stimuli. Similar studies were conducted by Garner and colleagues (Garner, Ainsworth, Gould, Gardner, & Baldwin, 2009) and Wieser and colleagues (Wieser, Pauli, & Mühlberger, 2009), who used antisaccade tasks with emotional and neutral cues. These studies found that anxiety increased saccade latency; moreover, anxiety did not interact with cue type to predict saccade latency (Garner et al., 2009; Wieser et al., 2009). That is, anxious individuals were just as slow to saccade away from neutral compared to unpleasant cues. Together, these studies suggest that anxiety may be associated with an overall deficit in attentional control that may not depend on the aversive nature of stimuli (but see, for example, Eysenck & Byrne, 1992).

Importantly, these findings seem at odds with the vast body of literature suggesting that anxiety is fundamentally characterized by an attentional bias toward unpleasant stimuli. Indeed, in a recent meta-analysis, Bar Haim and colleagues (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007) concluded that evidence in support of an attentional bias toward threat in anxiety was so strong that future work should move on to questions concerned with the mechanisms underlying this bias. One possible explanation for the discrepancy between these bodies of work is that studies in support of attentional control theories have not generally examined clinically anxious individuals, who may be more biased toward threatening information than non-clinically anxious individuals (Williams, Mathews, & MacLeod, 1996).

A second prediction of attentional control theories (Eysenck et al., 2007; Mathews & Mackintosh, 1998) is that increased attention toward task-irrelevant stimuli in anxiety should not necessarily affect behavior. This is because anxious individuals may be able to compensate for deficits in attentional control, for example, by expending more effort. When salient stimuli are irrelevant to the task at hand, bottom-up and top-down attention should exert opposing influences on the activation of distracter representation. In other words, bottom-up attention will facilitate the processing of salient distracter stimuli while top-down attention will resist processing these stimuli in order to focus on task-relevant stimuli. Because top-down attention is subject to

conscious control, anxious individuals may be able to overcome the tendency for salient distracters to dominate attentional focus. In line with this prediction, several studies have found that anxious individuals often perform on par with non-anxious individuals, even in tasks requiring the inhibition of attention toward threatening stimuli (Derakshan & Eysenck, 1998; Ikeda, Iwanaga, & Seiwa, 1996; MacNamara & Hajcak, 2009; Naveh-Benjamin, McKeachie, Lin, & Holinger, 1981; Richards, French, Keogh, & Carter, 2000).

Even when behavioral performance is not reduced in anxiety, ACT predicts that anxious individuals will allocate increased processing resources toward task-irrelevant stimuli,. This increased consumption of processing resources can be thought of as the "hidden cost" of anxiety and is referred to as reduced *processing efficiency* (Eysenck et al., 2007). Processing efficiency is reduced when more processing resources are required to complete a task, without an improvement in performance. The notion that anxiety reduces processing efficiency is central to attentional control theories because it reflects the imbalance between bottom-up and top-down attentional systems that is hypothesized to underlie anxiety. Because they do not rely on outward performance, neural measures provide an important means of measuring reduced processing efficiency.

Measuring reduced processing efficiency: hemodynamic indices

Hemodynamic measures such as functional magnetic resonance imaging (fMRI) can be used to index the effects of anxiety on neural activity in particular brain regions, and in so doing, can inform and help validate attentional control theories. For example, an imbalance between bottom-up and top-down attention in anxiety might involve abnormal interactions between the prefrontal cortex and areas of the brain associated with the processing of motivationally salient stimuli (e.g., the amygdala). Several prefrontal regions have been implicated in attentional control, key among them the dorsolateral prefrontal cortex (DLPFC). The DLPFC is believed to maintain stimulus-processing priorities in line with goal-directed behavior (Miller & Cohen, 2001) and has been associated with the successful attenuation of stimulus processing during emotion regulation. For instance, in laboratory paradigms in which participants were asked to reduce unpleasant emotions, activity was shown to increase in the DLPFC and decrease in the amygdala (Hariri, Mattay, Tessitore, Fera, & Weinberger, 2003; Lévesque et al., 2003; Ochsner, Bunge, Gross, & Gabrieli, 2002; Ochsner & Gross, 2005). In other work, activity in the DLPFC was found to be negatively correlated with activity in emotion processing regions during an emotion regulation task, further suggesting a reciprocal relationship between these areas (Banks, Eddy, Angstadt, Nathan, & Phan, 2007). Although it is likely that no direct physiological link exists between the DLPFC and the amygdala, activity in these structures may be related via connections in other neural regions, including in the orbitofrontal cortex (Amaral & Price, 1984; Cavada, 2000; Porrino, Crane, & Goldman Rakic, 1981).

Work using cognitive (i.e., non-affective) tasks has also supported the notion that activity in the DLPFC may be associated with the attenuated processing of emotional stimuli. For example, Van Dillen and colleagues (Van Dillen, Heslenfeld, & Koole, 2009) asked participants to solve difficult and easy math problems while viewing task-irrelevant emotional and neutral pictures. Difficult compared to easy math problems increased activity in the DLPFC and decreased amygdala activity elicited by unpleasant pictures. Working memory tasks are also known to activate the DLPFC (Manoach et al., 1997) and similar results have been found using

these tasks. For example, Erk and colleagues asked participants to perform easy or difficult working memory trials while anticipating (Erk, Abler, & Walter, 2006) or viewing (Erk, Kleczar, & Walter, 2007) task-irrelevant emotional or neutral pictures. Results showed that working memory load increased activity in the DLPFC and reduced activity in the amygdala, in line with the proposal that activity in these regions might be reciprocally related (Drevets & Raichle, 1998).

Of relevance to attentional control theories - if the DLPFC is involved in the top-down regulation of attention toward emotional stimuli, then anxiety might be expected to involve a disruption in the balance of activity between the DLPFC and emotion-processing regions of the brain (particularly during tasks that require inhibition of the processing of task-irrelevant stimuli). To investigate this idea, Bishop and colleagues (Bishop, Duncan, Brett, & Lawrence, 2004) examined prefrontal brain activity while participants performed a demanding task involving unpleasant and neutral distracter stimuli. Participants were required to indicate whether two houses were the same or different while ignoring a pair of fearful or neutral faces presented in a different location on the screen. Both faces within a pair were always either fearful or neutral and the proportion of fearful to neutral distracters varied by block. Results showed that individuals high in state anxiety evinced less recruitment of the DLPFC in response to unpleasant distracters as expectancy of unpleasant distracters was established (i.e., when comparing fear-frequent to fear-infrequent blocks). In another study using a similar task, Bishop and colleagues (Bishop, Duncan, & Lawrence, 2004) found that greater state anxiety was associated with increased amygdala reactivity to fearful distracters. Together, these results suggest that anxiety is characterized by reduced recruitment of neural regions implicated in attentional control (i.e., the DLPFC) and with the increased processing of unpleasant distracters.

Measuring reduced processing efficiency: the late positive potential

In addition to hemodynamic indices, ERPs can be used to provide a highly sensitive index of the processing of unpleasant stimuli and the interactive effects of top-down and bottom-up attention on stimulus processing. The late-positive potential (LPP) is a positive-going, centroparietal, P300-like ERP that begins approximately 300 ms following stimulus onset and is sensitive to the allocation of attention to motivationally-salient stimuli (Schupp et al., 2000). As far as the neural generators of the LPP are concerned, combined ERP-fMRI work has found that the LPP corresponds to increased blood flow in occipital, parietal and inferotemporal regions, suggesting activation in parietal attention networks (Sabatinelli, Lang, Keil, & Bradley, 2007). Likewise, source localization has suggested that the LPP originates in the occipital and posterior parietal cortex (Keil et al., 2002). One possibility is that the LPP results from bidirectional influences between frontal and occipitoparietal cortex (Moratti, Saugar, & Strange, 2011) and downstream contributions from the amygdala could also play a role in the generation of the LPP (Hajcak, MacNamara, & Olvet, 2010; Liu, Huang, McGinnis-Deweese, Keil, & Ding, 2012).

The LPP is larger for emotional compared to neutral pictures and words (Cuthbert, Schupp, Bradley, Birbaumer, & Lang, 2000; Dillon, Cooper, Grent-‘t-Jong, Woldoff, & LaBar, 2006; Foti, Hajcak, & Dien, 2009; Hajcak & Olvet, 2008; Schupp et al., 2000). In addition, the LPP is sensitive to changes in stimulus salience on a more fine-grained level. For instance, the LPP is larger for pictures that are described negatively compared to neutrally (Foti & Hajcak, 2008; MacNamara, Foti, & Hajcak, 2009). In addition, the LPP is larger to food pictures in

participants deprived of food (Stockburger, Schmälzle, Flaisch, Bublatzky, & Schupp, 2009) and to personally salient stimuli such as photographs of one's own relatives or loved ones (Grasso & Simons, 2011; Vico, Guerra, Robles, Vila, & Anllo-Vento, 2010). Therefore, the LPP seems sensitive to categorical differences in picture emotionality and to individual variation in the perceived salience of stimuli.

The LPP is also sensitive to top-down (i.e., goal-directed) effects on stimulus salience. For example, the LPP is smaller when participants are asked to categorize pictures along non-affective compared to affective picture dimensions (e.g., deciding how many people are in an image versus deciding whether a picture is pleasant or unpleasant; Hajcak, Moser, & Simons, 2006). In addition, when participants are asked to respond to certain pictures (targets) while ignoring other pictures (non-targets), the LPP is larger for emotional compared to neutral pictures and for target compared to non-target pictures (Weinberg, Hilgard, Bartholow, & Hajcak, 2012). In sum, the LPP appears to track the influence of goal-directed *and* stimulus-driven attention on stimulus salience.

Because the LPP is sensitive to individual variation in the perceived salience of stimuli, it may also provide a means of measuring anxiety-related increases in the processing of unpleasant or task-irrelevant stimuli. For example, participants in a study by MacNamara and Hajcak (2009) were required to indicate whether pairs of unpleasant or neutral pictures were the same or different, while ignoring unpleasant or neutral pictures presented in another area of the screen. Participants were only asked to respond to the identity/sameness of pictures presented in attended locations, not to the affective nature of these images. In line with previous work, the LPP was only increased for unpleasant compared to neutral pictures presented in spatially attended locations (Dunning & Hajcak, 2009). In addition, emotional modulation of the LPP elicited by these stimuli was larger for participants with greater self-reported state anxiety. In other words, individuals who were more anxious engaged in increased neural processing of unpleasant compared to neutral stimuli, even though the unpleasant nature of pictures was irrelevant to the task at hand. These results suggested reduced processing efficiency among participants with greater state anxiety, because they were more sensitive to the task-irrelevant affective dimension of pictures. In a follow-up study, similar results were found in individuals with GAD (MacNamara & Hajcak, 2010), suggesting that the LPP may also track decreased processing efficiency in clinical anxiety.

Like other neural indices of emotion-processing, the LPP has been found to be sensitive to DLPFC-mediated attentional modulation. For example, Hajcak and colleagues (Hajcak, Anderson, et al., 2010) used epidural stimulators to activate the DLPFC in a group of treatment resistant mood-disordered patients. They found that physiological stimulation of the DLPFC reduced the LPP elicited by unpleasant pictures; moreover, this effect was specific to activation of the DLPFC and was not observed when the frontopolar cortex was stimulated. Therefore, the LPP is reduced in response to activation of the DLPFC, and may track the prefrontally-modulated processing of unpleasant stimuli, even in severely emotionally disordered individuals.

To determine whether *functional* (i.e., task-related) activation of the DLPFC reduces the LPP and how this might vary with anxiety, MacNamara and colleagues (2011) employed a working memory task interspersed with the presentation of unpleasant and neutral pictures. MacNamara and colleagues (2011) asked participants to memorize 2 or 6 letters; this was

followed by the presentation of a unpleasant or neutral picture for 2000 ms; next, participants were required to recall the letters in the same order in which they had been presented at the beginning of the trial. Although DLPFC activation was not *measured* in this study, prior work suggests that DLPFC activation increases linearly with the number of items participants are asked to hold in memory (Manoach et al., 1997). Therefore, the higher working memory load condition can be thought of as involving greater DLPFC activation, compared with the low-load condition. Results showed that, as expected, unpleasant compared to neutral pictures elicited an increased LPP. In addition, the picture-elicited LPP was smaller under high compared to low working memory load. These results suggest that functional activation of the DLPFC reduces the processing of task-irrelevant pictures and that these effects can be indexed using the LPP.

In addition to these main effects, MacNamara and colleagues (2011) also 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 compared to low working memory load. In other words, functional activation of the DLPFC seemed to have less of an effect on picture processing for participants who were more anxious. These results are in line with those reported by Bishop and colleagues (Bishop, Duncan, Brett, et al., 2004; Bishop, Duncan, & Lawrence, 2004), who found that greater state anxiety was associated with decreased DLPFC activity in response to task-irrelevant fearful stimuli. MacNamara and colleagues' (2011) results further suggest that the *LPP* might be used to index anxiety-related deficits in DLPFC-mediated attentional control.

Attentional control in depression

Reduced attentional control in depression tends to have been conceptualized first and foremost in terms of the neural circuitry underlying attentional control. For example, Mayberg's (1997) model provides a neurobiological account of depression that is focused on abnormalities in fronto-limbic brain systems. Abnormalities in ventral areas of the brain, including in the hypothalamic-pituitary-adrenal axis and limbic-paralimbic regions (e.g., the hippocampus, subgenual anterior cingulate and insula) were proposed by Mayberg (1997) to underlie vegetative aspects of depression such as sleep and appetite disturbances. Abnormalities in dorsal areas of the brain, including the DLPFC, the inferior parietal, dorsal anterior cingulate and medial frontal regions were proposed to result in deficits in executive functioning and attentional control in depression. Finally, disruptions in the balance of activity between prefrontal and limbic areas of the brain were suggested to underlie affect regulation deficits observed in depression.

In line with Mayberg's (1997) model, neuroimaging work has identified deficits in prefrontal neural regions in depression; interestingly, these regions are the same regions hypothesized to underlie attentional control difficulties in anxiety (e.g., Bishop, Duncan, Brett, et al., 2004; MacNamara et al., 2011). For example, Siegle and colleagues found increased amygdala activity and decreased DLPFC activity in depressed participants during an affective task and a working memory task, respectively (Siegle, Thompson, Carter, Steinhauer, & Thase, 2007). Studies that have examined resting prefrontal activity have also revealed deficits for depressed individuals. In particular, dorsal regions of the prefrontal cortex, including the DLPFC, dorsomedial PFC (DMPFC) and dorsal ACC have been found to be less active in depressed compared to control participants (Baxter et al., 1989; Bench, Friston, Brown,

Frackowiak, & Dolan, 1993; Martinot et al., 1990). Work examining experimentally induced sadness has found similar results. For example, Mayberg and colleagues (1999) found that following a sad mood induction, healthy individuals evinced increased activity in limbic and paralimbic regions and decreased activity in regions of the prefrontal cortex, including the DLPFC.

Together, these studies suggest that depression may be characterized by *hypofrontality* – i.e., decreased activity in frontal neural regions. This notion is further supported by work showing that successful treatment of depression is associated with increases in prefrontal activity. For example, in the Mayberg and colleagues' (1999) study described above, a second experimental group included individuals who were scanned prior to and following pharmacological treatment for depression. Relative to pre-treatment scans, successfully treated individuals showed increased activity in areas of the prefrontal cortex - including in the DLPFC - and decreased activity in neural regions associated with the processing of emotional stimuli. Similar results have also been found in other studies (e.g., Kennedy et al., 2001; Mayberg et al., 2000). In addition to pharmacological treatments, physiological and behavioral treatments for depression have also been used to increase prefrontal activity. For instance, activation of prefrontal regions using transcranial magnetic stimulation (TMS) or deep brain stimulation has been shown to successfully treat depression (see Nahas, Lorberbaum, Kozel, & George, 2004 for a review). Neurobehavioral treatments that require patients to perform working memory tasks (Siegle, Ghinassi, & Thase, 2007) or directed attention tasks (Wells, 2000) have also been shown to activate the prefrontal cortex and to successfully treat depression (Papageorgiou & Wells, 2000; Siegle, Ghinassi, et al., 2007). Importantly, changes in prefrontal activity, including in the DLPFC, appear to be responsible for these treatment gains (Siegle, Ghinassi, et al., 2007).

Motivation for the current study

A biased competition view of attention (Mathews & Mackintosh, 1998) suggests that the strength of a stimulus' neural representation is determined by a balance of bottom-up and top-down attention. By this logic, an attentional bias toward unpleasant stimuli could result from heightened bottom-up attention toward unpleasant stimuli or from decreased top-down direction of attention away from (task-irrelevant) unpleasant stimuli. Therefore, deficits in attentional control could underlie attentional biases toward unpleasant stimuli observed in anxiety and depression. In line with this notion, Derryberry and Reed (2002) found that an attentional bias toward unpleasant stimuli was observed in anxious individuals reporting low but not high levels of self-reported attentional control. Also, recent work suggests that attentional bias training therapy reduces anxious and depressive symptomatology and increases self-reported attentional control (Bowler et al., 2012). In the attentional bias literature, investigators have not traditionally attempted to parse bottom-up and top-down attentional processes. The attentional control literature has distinguished between these two types of attention, however it has failed to account for decades of attentional bias work suggesting that anxiety-related (and possibly depression-related) attentional control deficits should be specific to unpleasant stimuli and to early or late portions of stimulus presentation (Eysenck & Derakshan, 2011; Eysenck et al., 2007). In addition, the attentional control literature has not investigated how comorbid depression may affect attentional control in anxiety.

The current study aimed to integrate aspects of the attentional bias and attentional control literatures by determining: 1) whether GAD is associated with deficits in attentional control using the LPP, 2) whether these deficits are specific to unpleasant stimuli, 3) whether these deficits are specific to the early portion of stimulus presentation and 4) whether attentional control in GAD is affected by a diagnosis of comorbid depression. To this end, participants with pure GAD, participants with comorbid GAD/MDD and a group of healthy controls performed the same working memory task used by MacNamara and colleagues (2011). In this paradigm, low-load and high-load working memory trials were interspersed with the presentation of task-irrelevant unpleasant and neutral stimuli during the retention period; behavioral measures and EEG were recorded throughout. This task was used because it varies both top-down and bottom-up attention: working memory load was used to vary demands on goal-directed (i.e., top-down) attention and picture type was used to vary salience effects on stimulus-driven (i.e., bottom-up) attention. The LPP elicited by task-irrelevant pictures is sensitive to the influence of both these attentional systems (i.e., emotion-related increases and load-related decreases), and could therefore be used to test the prediction that the balance of bottom-up and top-down attention is disrupted in GAD and comorbid GAD/MDD.

Hypotheses

Behaviorally, it was expected that participants would recall fewer letters on the high-load compared to the low-load trials – i.e., the high-load trials were expected to be more difficult than the low-load trials. Group effects on the number of letters recalled were not expected, in line with the notion that anxiety should affect processing efficiency more consistently than it affects behavioral performance (Eysenck et al., 2007; MacNamara et al., 2011; MacNamara & Hajcak, 2009). In regards to the LPP elicited by task-irrelevant pictures, it was expected that unpleasant compared to neutral pictures would elicit larger LPPs, and high-load compared to low-load trials would elicit smaller LPPs (MacNamara et al., 2011). Based on the idea that both anxiety and depression may be characterized by decreased attentional control and deficient recruitment of the prefrontal cortex (Eysenck et al., 2007; Mayberg et al., 1999), and building on prior work using this task (MacNamara et al., 2011), it was expected that a reduced effect of working memory load on the LPP would be observed in both clinical groups. For individuals with pure GAD, it was hypothesized that the effect of working memory load would be reduced specifically for the LPP elicited by *unpleasant* pictures and only during the *early* portion of picture presentation (i.e., prior to 1000 ms). This would fit with prior work suggesting that anxiety is characterized by increased *early* attention toward unpleasant stimuli (e.g., Mogg et al., 2004). Based on work suggesting that depression may attenuate a threat-related bias normally observed in anxiety (Bradley et al., 1995; Mogg et al., 2000), it hypothesized that attentional control difficulties in the comorbid group would not vary by picture type; in other words, it was expected that a decreased effect of working memory load would be observed for the LPP elicited by both unpleasant *and* neutral pictures in the comorbid group. Working memory load effects on the LPP were also expected to be reduced during both early and later portions of picture presentation for the comorbid group. Together, these results would support the idea that attentional control is disrupted in clinical anxiety, and that an additional diagnosis of MDD may broaden these attentional control deficits to include both early and late portions of stimulus presentation, and both neutral and unpleasant stimuli.

In addition to the LPP, the P1 was measured as an index of early picture processing. The P1 is a positive-going ERP component peaking at occipital sites around 100-130 ms after stimulus onset. It is believed to measure the facilitated processing of salient visual stimuli (Hillyard, Vogel, & Luck, 1998) and may be larger for emotional compared to neutral pictures (Delplanque, Lavoie, Hot, Silvert, & Sequeira, 2004; Hot, Saito, Mandai, Kobayashi, & Sequeira, 2006). Based on recent research which found that emotional modulation of the P1 by unpleasant images may be heightened among participants with GAD (Weinberg & Hajcak, 2011a), the P1 was used as an exploratory measure of early attention toward task-irrelevant stimuli in the current study.

A second exploratory analysis involved measuring oscillatory EEG activity as an index of frontal brain activity during high versus low working memory load. Greater alpha power – i.e., EEG activity in the 8-13 Hz range – has been linked to reduced brain activity and the disengagement of task-relevant brain regions (Gevins, Smith, McEvoy, & Yu, 1997; Pfurtscheller, Stancak, & Neuper, 1996). *Reduced* frontal alpha, therefore, indicates *increased* frontal activity. For example, cognitive reappraisal (which involves reinterpreting the meaning of emotional stimuli) activates prefrontal brain regions (e.g., the DLPFC; Lévesque et al., 2003; Ochsner et al., 2002; Ochsner & Gross, 2005), and has been shown to reduce frontal alpha activity (Parvaz, MacNamara, Goldstein, & Hajcak, 2012). Because cognitive reappraisal and working memory tasks are known to activate the same prefrontal brain regions (i.e., the DLPFC), it was reasoned that in the present study, working memory load might also reduce frontal alpha activity. Moreover, an additional aim was to determine whether a load-related reduction in alpha power (i.e., *increased* frontal activity) might vary by group and whether load-related changes in alpha power might predict changes in the magnitude of the LPP.

Method

Participants

A total of 107 participants: 36 individuals with GAD, 36 individuals with comorbid GAD and MDD and 35 healthy controls (HCs) were recruited from the community. This sample size was determined based on a power analysis of prior work. There is no prior, published work that has examined the LPP in individuals with GAD and comorbid GAD/MDD. However, MacNamara and Hajcak (2010) used the LPP to index attention toward task-relevant and task-irrelevant unpleasant and neutral pictures in GAD and control participants. They identified a 3-way interaction (group X target type X distracter type) for the LPP with a large effect size (d = 1.54). Using this effect size as an estimate for a group X working memory load X picture type modulation of the LPP, with a minimum of 25 participants per group, power was estimated to be greater than .90 for the current project. Participants were recruited using advertisements placed in the Long Island section of internet site, www.craigslist.com, around the Stony Brook University campus, and in Stony Brook University's campus announcements. The study was approved by the Stony Brook University Institutional Review Board (IRB), and participants were paid $75 for their time.

Inclusion and exclusion criteria

Participants calling about the study were initially screened over the phone using the Mini International Neuropsychiatric Interview (M.I.N.I., Sheehan et al., 1998). If deemed eligible during the phone-screening procedure, participants were informed that they were likely to be eligible for the laboratory study, however, they were told that if they were deemed ineligible over the course of a more extensive assessment on the day of the experiment, they would receive pro-rated payment ($25/hr) for their time and the experiment would be discontinued.

Eligible participants were scheduled for an experimental session, which lasted approximately 3 hours. During the course of the experiment, participants performed 3-4 other tasks which were unrelated to the current study; the order of these tasks was counterbalanced with the working memory task, and the results of these other tasks are reported elsewhere. A research assistant blind to group membership performed the EEG setup and guided participants through the task. The working memory paradigm took approximately 30 minutes to complete; therefore, participants' time during the experiment was allocated as follows: clinical interview, 40 min; EEG setup, 20 min; task, 30 min; questionnaires, 20 min; cleanup and payment, 15 min.

At the experimental session, a diagnostic evaluation was conducted by an advanced clinical psychology doctoral student using the Structured Clinical Interview for DSM-IV (SCID-I/NP, First, Spitzer, Gibbon, & Williams, 1995) to assess for past and present psychological disorders. To qualify as a participant in the GAD group, individuals needed to meet criteria for GAD and not for any other Axis I disorder. To qualify as a participant in the comorbid group, individuals met criteria for GAD and MDD and did not meet criteria for any other Axis I disorder. Past Axis I disorders were permitted in both clinical groups, however participants in the GAD group could not have met criteria for a mood disorder within the previous 6 months. Healthy controls did not have any current or past Axis I diagnoses. None of the participants were taking psychotropic medications, currently or 2 months prior and none suffered head injuries or had serious medical conditions. To reduce participant variability, the sample was limited to females aged 18-55 years (in line with prior work, e.g., Gotlib et al., 2004; Ray et al., 2009). Participant demographics are presented in Table 1; groups did not differ on age ($p > .94$) or number of years of education ($p > .19$).

Materials

A total of 120 pictures (60 neutral; 60 unpleasant) from the International Affective Picture System (Lang, Bradley, & Cuthbert, 2005) were used[1]. The task was presented using

[1] The 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, 6530, 6540, 6550, 6562, 6570, 6821, 6825, 6832, 9042, 9050, 9075, 9163, 9250, 9252, 9253, 9265,9265, 9403, 9405, 9410, 9413, 9414, 9420, 9427, 9428, 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, 2441, 2446, 2480, 2493, 2495, 2512, 2516, 2745.1, 2840, 5120, 5500, 5534, 6150, 7003, 7006, 7009, 7014, 7018, 7019, 7020, 7026, 7030, 7032, 7033,

Presentation software (Neurobehavioral Systems); pictures were centered, presented in color and filled the screen (which measured 48.26 cm, diagonally). Letter strings were the same as those used by MacNamara and colleagues (MacNamara et al., 2011), and were comprised of 60 2-consonant strings and 60 6-consonant strings (Ashcraft & Kirk, 2001).

The Mood and Anxiety Symptom Questionnaire (MASQ; Watson & Clark, 1991; Watson & McKee Walker, 1996) was used to measure symptoms of depression and anxiety. Scores were derived using the 62-item MASQ[2], 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 ‘‘during the past week, including today’’ using a 5-point scale ranging from “not at all” to “extremely”; higher ratings indicate increased levels of depression and anxiety.

To investigate self-reported differences in sustained attention toward negative events, the 10-item Ruminative Responses Scale (RRS; Treynor, Gonzalez, & Nolen-Hoeksema, 2003) was used to measure ruminative tendencies among participants. This scale is adapted from the earlier, 22-item RRS and has been specifically designed to remove items that overlapped significantly with depression (Treynor et al., 2003). Participants are asked to indicate the extent to which they engage in a variety of responses when they are “upset—sad, blue, nervous”. Responses are made on a 4-point scale ranging from “never or almost never” to “always or almost always”. There are 5 items that measure a reflective component of rumination (e.g., “Go away by yourself and think about why you feel this way”) and 5 items that measure brooding (e.g., “Think about a recent situation, wishing it had gone better”); higher ratings indicate increased rumination.

To measure the extent to which participants are motivated to avoid negative experiences, the 13-item Distress Aversion (DA) scale from the Measure of Experiential Avoidance Questionnaire (MEAQ; Gámez, Chmielewski, Kotov, Ruggero, & Watson, 2011) was given. The MEAQ has been found to have superior internal consistency and better discriminant validity vis-a-vis neuroticism compared to other measures of avoidance (Gámez et al., 2011). The DA scale is one of the more general scales in the measure (other scales include Behavioral Avoidance, Procrastination and Repression/Denial) and captures negative attitudes toward and evaluations of distress (e.g., “Happiness involves getting rid of negative thoughts”). Responses are made on a 6-point scale ranging from “Strongly Disagree” to “Strongly Agree”; higher ratings indicate increased distress aversion.

7035, 7037, 7038, 7041, 7059,7060, 7080, 7110, 7130, 7140, 7180, 7217, 7224, 7234, 7493, 7496, 7512, 7547, 7550, 7700, 7705, 7710, 7920, 7950).

[2] Participants completed the 90-item version of the MASQ, however, results are reported using the 62-item version (contained within the 90-item version) because it has been deemed to be more parsimonious (Watson et al., 1995). Results did not differ between the 62- and 90-item versions (e.g., no correlations were observed between the General Distress: Mixed Symptoms scale and any other measure).

To measure worry levels, participants completed the 16-item Penn State Worry Questionnaire (PSWQ; Meyer, Miller, Metzger, & Borkovec, 1990), designed to measure the excessiveness, generality and uncontrollability of participants' worry (e.g., "My worries overwhelm me"). Participants respond using a 5-point scale, ranging from "Not at all typical of me" to "Very typical of me" and higher scores indicate greater levels of worry.

Task

Figure 1 depicts a sample trial from the task. Participants performed high-load and low-load working memory trials interspersed with task-irrelevant neutral and unpleasant pictures. 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 asked 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 5000 ms. Next, a white fixation cross was presented on a black background for a random interval ranging between 500-1000 ms; this was followed by a unpleasant or neutral picture presented for 2000 ms. Following picture offset, participants used the keyboard to enter the letters in the same order as they were displayed at the beginning of the trial. Participants used the backspace key to correct any mistakes, and the trial ended when they pressed 'enter'. To deter participants from using finger placement on the keyboard as a memory aid, participants were instructed to use one finger to enter the letters and to keep their hands on their lap during the trial (MacNamara et al., 2011). The inter-trial interval varied randomly between 2000-2500 ms, during which time a white fixation cross was presented on a black background.

Participants were seated approximately 60 cm from the screen and the images occupied about 40° of visual angle horizontally and vertically. Each participant saw all pictures and all letter strings exactly one time. 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, the RRS, the DA scale and the PSWQ; following this, participants were paid for their time. A referral sheet of local psychotheraputic services, including those offered by the university, was made available to interested participants.

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, one electrode was placed on each of 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 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 (non-differential) channel.

Data reduction and analysis

Off-line analyses were performed using Brain Vision Analyzer software (Brain Products, Gilching, Germany). Following EEG segmentation (see below), 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. Eye blink and ocular corrections were made using the method developed by Gratton, Coles and Donchin (1983). 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 was rejected on a trial-to-trial basis. Seven participants (3 HCs, 4 comorbid GAD/MDD) were excluded from the ERP analyses because of poor quality data recordings.

To examine ERPs, the EEG was segmented for each trial beginning 200 ms prior to picture onset and continuing for 2200 ms (i.e., 2000 ms beyond picture onset).; baseline correction for each trial was performed using the 200 ms prior to picture onset. The P1 was scored by averaging amplitudes from 100-130 ms after picture onset at electrode Oz (Hajcak, Weinberg, MacNamara, & Foti, 2011). The LPP was scored by averaging amplitudes at electrode Pz during three time windows: 300-600 ms, 600-1000 ms and 1000-2000 ms after picture onset (Dennis & Hajcak, 2009; Foti et al., 2009).

To evaluate frontal alpha power, data corresponding to the 6000 ms prior to picture presentation on each trial were extracted. This period of time corresponded to 0-500 ms of time preceding letter presentation, the 5000 ms letter presentation period and the variable 500-1000 ms interval that occurred between letter offset and picture onset. Therefore, for all trials, the entire letter presentation period and the entire time between letter offset and leading up to picture onset were evaluated. Spectral power was computed for each 6000 ms segment using a fast Fourier transform (FFT) with a 10% Hanning window, performed on artifact-free, ocularly corrected 1-second segments that were overlapped by 50%. Resulting power (in $\mu V^{2/}$/Hz) in the alpha band (8-13 Hz) was averaged separately across trials for each condition and electrode. Frontal alpha power was evaluated laterally, at electrodes F7 and F8 (Jackson et al., 2003). In addition to the 7 participants excluded from the ERP analyses, one additional participant (from the GAD group) was excluded from the alpha power analysis because of poor quality data recording on electrode F8. Prior to statistical analysis, the distribution of power in each condition was normalized using the natural logarithm (Davidson, Jackson, & Larson, 2000).

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 in each condition. Due to technical errors, behavioral data was not obtained for 4 participants (2 HC, 2 comorbid GAD/MDD).

The ERP and accuracy data were evaluated with a 3 (group: HC, GAD, comorbid) x 2 (working memory load: low, high) x 2 (picture type: neutral, unpleasant) mixed measures analysis of variance (ANOVA); for the LPP, this was performed separately for each time window. Frontal alpha power was evaluated using a 3 (group: HC, GAD, comorbid) x 2 (electrode laterality: left, right) x 2 (working memory load: low, high) mixed measures ANOVA. Independent and paired *t*-tests were used to follow-up significant interactions as appropriate. MASQ symptom scores were used to characterize anxiety and depression levels in each group. An exploratory aim was to determine whether significant effects on the EEG, ERP and behavioral measures (i.e., using difference scores) would vary with each other, or with MASQ symptom scores. Scores on the RRS and PSWQ were used to determine whether increased attention toward pictures later on during stimulus presentation would relate to self-reported rumination or worry. In addition, the DA scale was used to evaluate avoidance tendencies among participants and to determine whether reduced attention toward unpleasant pictures in the later portion of stimulus presentation would relate to self-reported avoidance. Statistical analyses were performed using PASW (Version 18.0) General Linear Model software.

Results

Self-report

Table 1 presents self-report data from participants, shown separately by group and across all participants. Compared with participants from the HC group, participants with GAD and those comorbid for depression and GAD had higher levels of anxiety (HC vs. GAD: Anxious Arousal, $t(54) = 4.60$, $p < .01$; General Distress – Anxiety Symptoms, $t(54) = 5.27$, $p < .01$; HC vs. Comorbid: Anxious Arousal, $t(57) = 6.03$, $p < .01$; General Distress – Anxiety Symptoms, $t(57) = 9.93$, $p < .01$) and depression (HC vs. GAD: Anhedonic Depression, $t(54) = 2.86$, $p < .01$; General Distress – Depressive Symptoms, $t(54) = 4.63$, $p < .01$; HC vs. Comorbid: Anhedonic Depression, $t(57) = 8.48$, $p < .01$; General Distress – Depressive Symptoms, $t(57) = 9.63$, $p < .01$). Comorbid participants also reported higher levels of depression than those with pure GAD (Anhedonic Depression, $t(57) = 3.92$, $p < .01$; General Distress – Depressive Symptoms, $t(57) = 2.93$, $p < .01$); the clinical groups did not differ from each other in self-reported anxiety levels (Anxious Arousal, $t(57) = .05$, $p > .95$; General Distress – Anxiety Symptoms, $t(57) = .54$, $p > .59$). Compared to healthy controls, the clinical participants also reported higher levels of worry (HC vs. GAD: $t(41) = 5.81$, $p < .01$; HC vs. Comorbid: $t(45) = 4.87$, $p < .01$) and rumination (HC vs. GAD: $t(23) = 2.95$, $p < .01$; HC vs. Comorbid: $t(24) = 2.62$, $p < .05$), though they did not differ from control participants in distress aversion (HC vs. GAD: $t(25) = 1.73$, $p > .09$; HC vs. Comorbid: $t(25) = 1.07$, $p > .29$). The clinical groups did not differ from each other in self-reported worry ($t(50) = .73$, $p > .47$), rumination ($t(33) = .39$, $p > .69$) or distress aversion ($t(32) = .71$, $p > .48$).

Working memory performance

Table 2 presents accuracy data for each condition and group. As expected, participants recalled more letters on low-load compared to high-load trials ($F(1,100) = 237.77$, $p < .001$, $\eta_p^2 = .70$). There was also a trend for participants to recall more letters when trials contained a neutral compared to an unpleasant picture ($F(1,100) = 3.77$, $p = .06$, $\eta_p^2 = .04$). Working memory load and picture type interacted ($F(1,100) = 5.56$, $p < .05$, $\eta_p^2 = .05$) such that working memory load had a more negative effect on letter recall for trials on which unpleasant compared to neutral pictures were presented. There were no other significant interactions (all *p*s > .30) and there was no between-groups effect ($p > .38$).

P1

There were no significant main effects or interactions (all *p*s > .26) and there was no overall effect of group ($p > .89$).

LPP

LPP amplitudes for each condition and group are presented in Table 2. Figure 2 depicts picture-locked grand average waveforms at electrode Pz, shown separately for each condition. Figure 3 depicts scalp distributions of voltages for neutral and unpleasant pictures (shown separately), presented on low-load minus high-load trials, shown separately for each time window in which the LPP was scored and for each group.

300-600 ms

Unpleasant compared to neutral pictures elicited larger LPPs ($F(1,97) = 116.83$, $p < .001$, $\eta_p^2 = .55$), as did pictures presented on low-load compared to high-load trials ($F(1,97) = 71.34$, $p < .001$, $\eta_p^2 = .42$). There were no significant interactions (all *p*s > .34). There was a significant effect of group ($F(2,97) = 3.52$, $p < .05$, $\eta_p^2 = .07$): individuals with GAD had larger LPPs than controls ($t(66) = 3.10$, $p < .05$); the comorbid group did not differ from those with GAD ($t(66) = .66$, $p > .50$) nor did they have significantly different LPPs than the controls ($t(62) = 1.73$, $p > .89$).

600-1000 ms

LPPs were larger for unpleasant compared to neutral pictures ($F(1,97) = 128.27$, $p < .001$, $\eta_p^2 = .57$) and for pictures presented on low-load compared to high-load trials ($F(1,97) = 32.60$, $p < .001$, $\eta_p^2 = .25$). Two-way interactions did not reach significance (all *p*s > .30) and there was no overall effect of group ($p > .08$). Group, picture type and working memory load interacted to determine the size of LPPs ($F(2,97) = 39.36$, $p < .05$, $\eta_p^2 = .06$).

This interaction was followed up by a 2 (working memory load: low, high) x 2 (picture type: neutral, unpleasant) repeated measures ANOVA performed separately for each group. Amongst controls, unpleasant compared to neutral pictures elicited larger LPPs ($F(1,31) = 83.27$, $p < .001$, $\eta_p^2 = .73$), as did pictures presented on low-load compared to high-load trials ($F(1,31) = 15.84$, $p < .001$, $\eta_p^2 = .34$); working memory load and picture type did not interact ($p > .21$).

For comorbid individuals, unpleasant compared to neutral pictures elicited larger LPPs ($F(1,31) = 37.16$, $p < .001$, $\eta_p^2 = .54$), as did pictures presented on low-load compared to high-load trials ($F(1,31) = 4.54$, $p < .05$, $\eta_p^2 = .13$); working memory load and picture type did not interact ($p > .30$). Among the GAD group, the LPP was larger for unpleasant compared to neutral pictures ($F(1,35) = 36.19$, $p < .001$, $\eta_p^2 = .51$) as well as for pictures presented on low-load compared to high-load trials ($F(1,35) = 14.99$, $p < .001$, $\eta_p^2 = .30$). Furthermore, working memory load and picture type interacted to determine LPP amplitude for those with GAD ($F(1,35) = 4.15$, $p < .05$, $\eta_p^2 = .11$). Paired *t* tests revealed that for individuals with GAD, working memory load reduced the LPP elicited by neutral ($t(35) = 4.56$, $p < .001$) but not unpleasant pictures ($t(35) = 1.57$, $p > .12$).

1000-2000 ms

Unpleasant compared to neutral pictures ($F(1,97) = 70.27$, $p < .001$, $\eta_p^2 = .23$) and pictures presented on low-load compared to high-load trials ($F(1,97) = 28.78$, $p < .001$, $\eta_p^2 = .30$) elicited larger LPPs in this window. There was no overall effect of group ($F(2,97) = 2.97$, $p > .06$, $\eta_p^2 = .06$). Neither the two-way interaction between group and working memory load ($F(2,97) = 1.90$, $p = .15$, $\eta_p^2 = .04$) nor the three-way interaction between group, working memory load and picture type ($F(2,97) = 2.24$, $p = .11$, $\eta_p^2 = .04$) reached significance. All other interactions also failed to reach significance (*p*s > .49). Based on a-priori predictions, a 2 (working memory load: low, high) x 2 (picture type: neutral, unpleasant) repeated measures ANOVA was performed separately for each group. For the controls, LPPs were larger for unpleasant compared to neutral pictures ($F(1,31) = 50.54$, $p < .001$, $\eta_p^2 = .62$) and for pictures presented on low-load compared to high-load trials ($F(1,31) = 17.89$, $p < .001$, $\eta_p^2 = .37$); working memory load and picture type did not interact for the HCs ($p > .89$). Picture type and working memory load effects were also observed for individuals with GAD (unpleasant > neutral: $F(1,35) = 14.81$, $p < .001$, $\eta_p^2 = .30$; low-load > high-load: $F(1,35) = 14.89$, $p < .001$, $\eta_p^2 = .30$) and picture type and working memory load did not interact for individuals with GAD ($p > .31$). For comorbid individuals, unpleasant compared to neutral pictures elicited larger LPPs ($F(1,31) = 27.77$, $p < .001$, $\eta_p^2 = .47$), however the effect of working memory load was not significant ($p > .17$). Working memory load and picture type did not interact to determine LPP amplitudes for the comorbid group ($p > .44$).

Frontal alpha

Table 2 presents left and right frontal alpha power in low- and high-load conditions for each group. Frontal alpha power was greater (bilaterally) on low-load compared to high-load trials ($F(1,96) = 23.02$, $p < .0001$, $\eta_p^2 = .19$). There was no interaction between group and working memory load ($p > .65$) and other effects did not reach significance (all *p*s > .27).

Correlations

Difference scores for the effect of working memory load and picture type were calculated for LPPs, working memory performance and frontal alpha power (effect of working memory load only). Pearsons correlations were used to determine the extent to which working memory

load and picture type effects related to self-report measures of anxiety and depression and how effects co-varied among measures (e.g., LPP, alpha power and working memory performance).

Figure 4 depicts the association between the effect of working memory load (low-load minus high-load) on left frontal alpha power and the effect of working memory load (low-load minus high-load) on the LPP in the 1000-2000 ms window. As is suggested by the figure, the effect of working memory load on alpha power at left frontal sites was positively correlated with the effect of working memory load on the LPP in the 1000-2000 ms window ($r(99) = .21$, $p < .05$); non-significant trends in the same direction were also observed in the 300-600 ms window ($r(99) = .18$, $p < .08$) and in the 600-1000 ms window ($r(99) = .16$, $p < .12$). The relationship between frontal alpha power and the LPP was specific to difference scores for the two measures; in other words, left frontal alpha power and the LPP were not correlated on trials with low (1000-2000 ms window: $r(99) = .14$, $p > .16$) or high (1000-2000 ms window: $r(99) = .00$, $p > .96$) working memory load. There were no significant correlations between right frontal alpha power and the LPP (all ps > .17), and there were no significant correlations between frontal alpha power and any other measure (i.e., self-report or behavioral; all ps > .17).

Figure 5 depicts associations between self-reported anhedonic depression (scores on the MASQ, Anhedonic Depression) and the low-load minus high-load LPP difference, shown separately in each of the three time windows in which the LPP was scored. As is suggested by the figure, self-reported anhedonic depression was associated with a reduced effect of working memory load on the LPP in all three time windows (300-600 ms: $r(82) = -.24$, $p < .05$; 600-1000 ms: $r(82) = -.22$, $p < .05$; 1000-2000 ms: $r(82) = -.26$, $p < .05$). This effect was driven by larger LPPs on high-load trials (300-600 ms: $r(82) = .20$, $p = .07$; 600-1000 ms: $r(82) = .24$, $p < .05$; 1000-2000 ms: $r(82) = .25$, $p < .05$), rather than smaller LPPs on low-load trials (300-600 ms: $r(82) = .03$, $p > .77$; 600-1000 ms: $r(82) = .06$, $p > .60$; 1000-2000 ms: $r(82) = .09$, $p > .44$). Scores on other self-report measures did not relate to the LPP (all ps > .06)[3].

The effect of picture type on working memory performance was enhanced for participants with greater distress aversion (i.e., participants with higher scores on the DA scale; $r(42) = .30$, $p = .05$). This effect was specific to the performance difference between unpleasant and neutral pictures: in other words, DA scores did not correlate with working memory performance on trials with either unpleasant ($r(42) = -.24$, $p > .12$) or neutral ($r(42) = -.11$, $p > .49$) pictures. There were no other significant correlations between working memory performance and self-report measures (all ps > .12), and there were no significant correlations between working memory performance and the LPP (all ps > .16).

History of depression

To determine whether condition effects on the LPP differed for individuals with GAD with a history of depression ($n = 14$) compared to those without a history of depression ($n = 22$), independent t tests were performed on LPP difference scores for these subgroups. Difference

[3] There was a trend for scores on the MASQ, General Distress – Depressive Symptoms scale to correlate negatively with the low-load minus high-load difference for the 1000-2000 ms LPP ($r(82) = -.21$, $p = .06$) such that greater depression was associated with a smaller effect of working memory load.

scores for the effect of picture type (unpleasant minus neutral) and working memory load (low-load minus high-load) as well as for the effect of working memory load on specific picture types (i.e., load effects calculated separately for neutral and unpleasant pictures) were used. Using these difference scores, effects did not vary between individuals with GAD who did have a history of depression compared to those who did not (all *p*s > .11).

Discussion

The current study aimed to determine whether GAD is characterized by deficits in attentional control, whether these deficits are specific to unpleasant stimuli and whether they are present specifically in the early portion of stimulus presentation. Another aim was to investigate the influence of comorbid MDD on attentional control in GAD. It was hypothesized that the presence of comorbid MDD would lead to broader deficits in attentional control both temporally and in regards to picture type. In addition to these primary aims, the current study sought to understand how attentional control deficits as measured by the LPP would relate to behavioral performance (letter recall). Self-report measures were used to determine whether attentional control deficits would be associated with symptoms of anxiety and depression in a continuous fashion. Exploratory analyses included reduced frontal alpha as a measure of greater frontal brain activity, and the P1 as a measure of early attention toward task-irrelevant pictures.

An effect of working memory load was not observed on the P1 (Morgan, Klein, Boehm, Shapiro, & Linden, 2008; Zanto & Gazzaley, 2009). In line with prior work that has used IAPS pictures, there was also no effect of picture type on the P1 (Foti et al., 2009; Olofsson & Polich, 2007). Prior work suggests that compared to IAPS, emotional faces may more reliably modulate P1 amplitudes (Mühlberger et al., 2009; Mueller et al., 2008), possibly because faces are less pictorially complex than IAPS scenes. Together, these results suggest that, given its early latency, the P1 may be ill-suited to measuring higher-order or visually complex distinctions in stimulus salience.

Across all three time windows of the LPP, unpleasant compared to neutral pictures elicited larger LPPs (Cuthbert et al., 2000; Foti et al., 2009), as did pictures presented on low-load compared to high-load trials (MacNamara et al., 2011). These results replicate prior work and suggest that functional activation of prefrontal brain regions involved in attentional control, including the DLPFC, may reduce the processing of task-irrelevant pictures.

Condition effects did not interact with group in the 300-600 ms window of the LPP, however there was an overall between-groups effect, such that individuals with GAD evinced larger LPPs compared to those in the HC or comorbid groups. The results suggest that individuals with GAD might find all stimuli – even neutral pictures – more engaging than controls, at least during this early portion of picture presentation. One possibility is that anxiety-related somatic arousal results in greater orienting or altering responses early on during stimulus presentation (Bruder et al., 2002). Another possibility is that anxious individuals are predisposed to perceive even non-threatening or mildly threatening stimuli as highly arousing (Mogg & Bradley, 1998). By contrast, depression may blunt reactivity to salient stimuli (Foti, Olvet, Klein,

& Hajcak, 2010; Rottenberg, Gross, & Gotlib, 2005), which could explain why the comorbid group did not evince enhanced LPPs in this time window.

In the 600-1000 ms window of the LPP, main effects of picture type and working memory load were evident for all three groups. However, for the GAD group, working memory load reduced the LPP elicited by neutral, but not unpleasant pictures. Therefore, in this time window, participants with GAD appeared to allocate attention toward task-irrelevant unpleasant pictures in an inflexible manner (i.e., irrespective of task demands). Thus, in the context of unpleasant pictures, individuals with GAD exhibited less top-down moderation of picture processing – i.e., decreased attentional control.

In the 1000-2000 ms window, individuals from the HC and GAD groups evinced effects of picture type and working memory load on the LPP, whereas the comorbid group showed an effect of picture type, but no effect of working memory load. Thus, comorbid individuals appeared to allocate nearly the same amount of attention toward task-irrelevant pictures in the high-load and low-load conditions. The results support the notion that depression may be associated with increased distracter processing, especially later on during stimulus presentation (De Raedt & Koster, 2010). In addition to this group interaction, self-reported anhedonia was associated with a decreased effect of working memory load on the LPP in all three time windows.

Behaviorally, participants recalled more letters on low-load compared to high-load trials and on trials which contained a neutral, compared to an unpleasant picture. These results are in line with prior work which has found that distracting, unpleasant stimuli may compete more for working memory resources, leading to behavioral interference (Weinberg & Hajcak, 2011b; Zanto & Gazzaley, 2009). Also, the negative effect of working memory load on letter recall was stronger when trials contained an unpleasant compared to a neutral picture (MacNamara et al., 2011), suggesting that picture type potentiated working memory load effects on performance. Importantly, there were no group effects on behavior, and no interactions between condition and group.

Correlational analysis revealed that greater self-reported distress aversion was associated with a stronger effect of picture type on letter recall. Distress aversion refers to an individual's desire to avoid stressful or negative experiences and has previously been found to be correlated with self-reported depression and anxiety (Gámez et al., 2011). In the current study, mean levels of distress aversion tended to be higher for GAD compared to HC participants, though differences between groups were not significant. A larger effect of picture type on letter recall for participants high in distress aversion suggests that a desire to avoid negative emotionality, may, paradoxically, increase the extent to which unpleasant stimuli interfere with behavioral performance. These results are in line with prior work which has found that thought blocking (Roemer & Borkovec, 1994; Wegner, Schneider, Carter, & White, 1987) and emotional suppression (Gross & Levenson, 1997) may increase and sustain affective arousal.

Attentional mechanisms underlying GAD

Several studies have suggested that individuals with GAD are characterized by increased early, bottom-up attention toward unpleasant stimuli (e.g., Bradley et al., 1999; MacLeod et al.,

1986). Unlike in some previous work (Weinberg & Hajcak, 2011a), a larger effect of picture type on early ERPs (i.e., the P1) was not observed in the GAD group. Importantly, however, deficits in attentional control (as indexed by the LPP) were observed only for unpleasant and not for neutral pictures, and only in an early portion of picture presentation (600-1000 ms after picture onset).

These results are in line with those obtained by Bishop and colleagues (Bishop, Duncan, & Lawrence, 2004) who used an fMRI paradigm to examine attentional control in the context of threatening and neutral distracters. Participants were required to attend to pairs of faces or houses presented simultaneously above and below or to the left and right of fixation. Face pairs could be either threatening or neutral and face type never varied within a pair (i.e., both images were either threatening or neutral). On each trial, participants were asked to respond to either the face or house pair and indicate whether the images within the pair were the same or different; the other pair of images was irrelevant to the task at hand. Bishop and colleagues (Bishop, Duncan, & Lawrence, 2004) found that for participants with greater self-reported anxiety, there was little effect of task relevance on amygdala activation elicited by threatening faces. Furthermore, in a follow-up study using the same paradigm, Bishop and colleagues (Bishop, Duncan, Brett, et al., 2004) identified a possible mechanism for these effects: participants who were more anxious showed less effective recruitment of the DLPFC in response to threatening distracters. Therefore, anxiety – and GAD in particular - may be characterized by reduced attentional control over the processing of task-irrelevant unpleasant distracters, which might correspond to less DLPFC involvement in the filtering of task-irrelevant stimuli.

In addition to picture-type specificity, deficits in attentional control in the GAD group were temporally specific, occurring only between 600-1000 ms after picture presentation. These results are in line with the notion that GAD is characterized by an early, but not a late attentional bias toward unpleasant stimuli (Bradley et al., 1995; Gotlib et al., 2004; Mogg et al., 1993). For instance, Koster and colleagues (Koster, Verschuere, Crombez, & Van Damme, 2005) used a dot-probe task and presented threatening pictures for 100, 500 and 1250 ms. Results showed that high- versus low-trait-anxious participants only differed in an attentional bias toward threat for the 500 ms presentation condition. Therefore, attentional control may be compromised in GAD relatively early on, yet after initial, more obligatory evaluations of stimulus salience have been made. In line with this notion, Derryberry and Reed (2002) found that among anxious participants, self-reported attentional control deficits moderated attention toward threatening stimuli presented for 500 ms, but not 250 ms.

In contrast to results observed in the 600-1000 ms time window, individuals with GAD *did* show an effect of working memory load on the later portion of the LPP (1000-2000 ms after picture onset). Later portions of the LPP (i.e., 1000 ms onwards) might be especially sensitive to the willful redirection of attention (e.g., Dunning & Hajcak, 2009; Hajcak, Dunning, & Foti, 2009) and might also be sensitive to anxiety-related avoidance of unpleasant stimuli (Weinberg & Hajcak, 2011a). In contrast to prior work that used a passive viewing task (and no working memory load condition), the present study did not find a reduced effect of picture type on the LPP for individuals with GAD during this time window stimuli (Weinberg & Hajcak, 2011a). However, the results suggest that individuals with GAD resumed attentional control over unpleasant pictures during this later time window. In a different task context, it is possible that this resumption of attentional control might be observed as avoidance of unpleasant pictures. For

instance, in the Koster and colleagues' dot-probe study described above (Koster, Verschuere, et al., 2005), highly trait anxious individuals attended away from threatening stimuli in the 1250 ms condition.

Braver and colleagues' (Braver, Gray, & Burgess, 2007) *dual mechanisms of control* theory might also be helpful in interpreting these results. According to Braver and colleagues (Braver et al., 2007), cognitive control can be achieved in one of two ways: proactively or reactively. *Proactive* control is believed to involve the early and sustained representation of task goals, and should be most effective when the environment is predictable, because processing priorities are maintained consistently throughout a task. If initial representations of task goals in working memory are weak, however, individuals may need to employ *reactive* control to deal with unexpected processing conflicts. Reactive control is implemented later on during stimulus processing, and is generally thought to be less effective than proactive control.

Braver and colleagues suggest that anxious individuals are more likely to use reactive control, because of deficits in prefrontal neural regions (Braver et al., 2007). As such, anxious individuals are believed to recruit cognitive control resources on an "as needed" basis, and may require more processing resources to perform on par with controls, because they need to compensate for baseline deficits in attentional control (Osinsky, Gebhardt, Alexander, & Hennig, 2011). For instance, in a recent study, anxious individuals were found to exhibit less sustained lateral PFC activity, but increased transient lateral PFC activity during a working memory task (Fales et al., 2008), suggesting that anxious individuals increased attentional resources on an ad-hoc basis, in order to cope with task demands. In the present study, individuals with GAD may have reacted to initial decrements in attentional control experienced early on during picture presentation by increasing attentional control during the latter portion of picture presentation (from 1000 ms onwards). Future work could inform this hypothesis using fMRI, in order to determine whether a GAD-related resumption of attentional control later on during stimulus presentation is accompanied by increased transient activity in the lateral PFC.

Attentional mechanisms underlying comorbid GAD/MDD

In contrast to the GAD group, attentional control deficits for the comorbid group were not limited to unpleasant stimuli. Instead, results indicated an overall failure of working memory load to modulate the LPP in the 1000-2000 ms window, irrespective of picture type. Some work has suggested that depression, like anxiety, is characterized by increased attention toward unpleasant stimuli (Caseras et al., 2007; Eizenman et al., 2003), however, other work has disputed this (Bradley et al., 1995; MacLeod et al., 1986; Mogg et al., 1993) or has even reported *less* differentiation between unpleasant and neutral pictures in depression (Rottenberg et al., 2005; Rottenberg, Gross, Wilhelm, Najmi, & Gotlib, 2002). Comorbid depression has also been found to attenuate threat-related biases normally observed in anxiety (Bradley et al., 1995; Mogg et al., 2000). Therefore, depression may be associated with an overall deficit in attentional control that predominates over the unpleasant-specific attentional control deficit evident in pure GAD.

In line with this, recent work has suggested that depression is associated with a reduced ability to filter out even non-emotional, task-irrelevant stimuli. For example, Desseilles and colleagues (Desseilles et al., 2009) used an fMRI paradigm in which participants were asked to

respond to centrally presented symbols, while task-irrelevant geometric patterns were presented to the left and right of fixation. Depending on the instructions, the centrally presented task could be more difficult (high-load) or less difficult (low-load). Results showed that cognitive load reduced the processing of task-irrelevant stimuli in the visual cortex across participants; however, depressed individuals showed less load-related modulation of distracter processing (Desseilles et al., 2009). Moreover, across participants, cognitive load was found to increase coupling between frontal and visual cortices, suggesting that these areas worked together to modulate distracter processing when task load was high. Depressed individuals, however, failed to show this increased coupling between prefrontal and visual regions, suggesting that ineffective connectivity might underlie reductions in distracter filtering. Therefore, both the current and prior results suggest that depression may involve non-emotional deficits in the filtering of task-irrelevant stimuli that may be accompanied by less effective engagement of prefrontal regions.

Attentional control deficits in the comorbid group were also specific to the 1000-2000 ms window. These results are in line with work which has found that depressed individuals have difficulty directing attention away from task-irrelevant stimuli during later portions of stimulus presentation (Koster, De Raedt, Goeleven, Franck, & Crombez, 2005). Furthermore, they are in line with work from the neuropsychological literature, which has used non-affective tasks that engage the DLPFC and frontoparietal attention network. This work has reported deficits in sustained attention among depressed individuals (van der Meere, Börger, & van Os, 2007; Weiland-Fiedler et al., 2004). For example, in one study, depressed individuals became less effective in responding to target stimuli over the duration of an experiment which lasted a half-hour (van der Meere et al., 2007). In the present study, comorbid depression may have also reduced individuals' ability to sustain task-related attentional focus over time, though in the current study this was observed as a reduced effect of working memory load on the LPP during the latter portion of each *trial*.

Despite the fact that attentional control deficits in the comorbid group were specific to the 1000-2000 ms window of the LPP, self-reported anhedonic depression was related to a reduced effect of working memory load in all three time windows of the LPP. Anhedonia is a core symptom of depression, and may differentiate depression from anxiety (Watson et al., 1988; Watson & Tellegen, 1985), however the present results suggest that its relationship to attentional control operates in a continuous fashion, cutting across diagnostic boundaries. In prior work, impairments in attentional control associated with anhedonia have been compared to those associated with multitasking (Bredemeier et al., 2011). Therefore, in the present study, anhedonia may have reduced the filtering of task-irrelevant stimuli because, like a competing task, it consumed task-relevant attentional resources. In future work, investigators may wish to focus on specific aspects of depression such as anhedonia, rather than diagnostic categories (which are inherently noisier), in order to obtain a clearer picture of the relationship between depressive characteristics and impairments in attentional control.

Neural mechanisms underlying (decreased) attentional control

The current results suggest that both GAD and comorbid GAD/MDD are associated with deficits in attentional control. Based on prior work, it might be tempting to conclude that such results point to anxiety- and depression-related *reductions* in DLPFC activity (i.e., hypoactivity). However, such conclusions should be drawn with caution, particularly in regards to the present

study, in which DLPFC activation was not measured. Prior research suggests that depending on the type of task, different patterns of prefrontal activity are observed in anxiety and depression. For instance, Bishop and colleagues found evidence of anxiety-related reductions in DLPFC activity during a task requiring the inhibition of attention to threatening distracters (Bishop, Duncan, Brett, et al., 2004). On the other hand, Santos, Wall and Eysenck (2006; cited in Eysenck et al., 2007) reported anxiety-related increases in lateral prefrontal activation during a paradigm that required task switching. In the depression literature, the majority of evidence seems to point to deficits in prefrontal activity (Davidson, Pizzagalli, Nitschke, & Putnam, 2002), although some studies have also reported depression-related increases in PFC activity (Kerestes et al., 2012; Matsuo et al., 2006). Still, other work suggests depression-related reductions in DLPFC activity *and* decreased connectivity between prefrontal and emotion-processing regions of the brain (Desseilles et al., 2009; Siegle, Thompson, et al., 2007). Because of reduced connectivity between these regions, compensatory *increases* in DLPFC activity might even be observed in anxious and depressed individuals, especially when these participants perform on par with controls (Basten, Stelzel, & Fiebach, 2011; Harvey et al., 2005; Kerestes et al., 2012).

While the present study used a task known to activate the DLPFC, other brain regions are also involved in attentional control. For instance, the anterior cingulate cortex (ACC) is believed to work with the DLPFC to implement early and late stage attentional control (Banich, 2009). The rostral ACC (rACC) has been associated with the processing of emotional stimuli, while the dorsal ACC (dACC) has been associated with conflict monitoring in cognitive tasks. Both the rACC and dACC may play a role in alerting the DLPFC to the need for increased attentional control, and in implementing this additional control (Bishop, Duncan, Brett, et al., 2004). Therefore, these regions may also be involved in anxiety- and depression-related attentional control deficits. For instance, Bishop and colleagues (Bishop, Duncan, Brett, et al., 2004) found that not only was activity in the DLPFC attenuated in participants who were more anxious, but rACC activity was also lower, suggesting inefficient signaling between these two regions. On the other hand, Silton and colleagues (Silton et al., 2011) found that depression was characterized by weakened coordination of DLPFC and dACC activity, while anxiety was distinguished by increased dACC activity. Anxiety-related increases in dACC activity also occurred later in time than depression-related DLPFC activity, suggesting that anxious individuals might have been more likely to rely on reactive cognitive control mechanisms (Braver et al., 2007). This work dovetails with the results of the present study, and suggests that depression and anxiety may be characterized by temporally distinct patterns of attentional control. Furthermore, this work emphasizes the need to consider brain *systems*, rather than isolated regions, in identifying the neural underpinnings of attentional control deficits in anxiety and depression.

The present study examined the hypothesis that frontal alpha activity might relate to working memory load. Specifically, it was proposed that greater working memory load might decrease frontal alpha, in line with the notion that alpha activity reflects the inhibition of cortical activity (Gevins et al., 1997; Pfurtscheller et al., 1996). In addition, the present study aimed to determine how frontal alpha might vary between groups and relate to the LPP. As hypothesized, working memory load decreased frontal alpha power during the 6000 ms during letter presentation and leading up to picture onset (Chavanon, Wacker, Leue, & Stemmler, 2007; Gevins et al., 1997). Moreover, greater working memory load modulation of left frontal alpha power during letter presentation predicted greater working memory load modulation of the LPP

during picture presentation. These results corroborate evidence from other studies which has suggested that physical (Hajcak, Anderson, et al., 2010) and task-related (MacNamara et al., 2011; Van Dillen et al., 2009) activation of prefrontal brain regions may reduce the processing of salient, task-irrelevant stimuli. The specificity of LPP-alpha correlations to alpha power in the *left* hemisphere also fits with the purported involvement of the left prefrontal cortex in the encoding of verbal material during memory tasks (Fletcher, Shallice, & Dolan, 2000; Habib, Nyberg, & Tulving, 2003) and with prior work, in which alpha power at left frontal sites was reduced during a cognitive reappraisal task that also attenuated the LPP (Parvaz et al., 2012). Increased activation in the left prefrontal cortex has also been found to be associated with the successful regulation of attention toward unpleasant pictures using fMRI (Goldin, McRae, Ramel, & Gross, 2008). Thus, while *group* effects were not observed for alpha power in the present study, the results are encouraging in that they suggest that reductions in frontal alpha power might provide a means of measuring prefrontal brain activity associated with task-related increases in attentional control and related reductions in the processing of task-irrelevant stimuli.

Conclusions

The current study aimed to determine whether GAD is characterized by attentional control deficits, and to characterize these deficits in terms of their affective nature and timing. Results showed that attentional control deficits were evident in GAD; moreover, these deficits were specific to an early portion of unpleasant picture presentation, in line with decades of research from the attentional bias literature. These results build on prior work by suggesting that affective hypervigilance – frequently observed as an attentional bias toward unpleasant stimuli in behavioral tasks such as the dot-probe - may correspond to early, reduced attentional control in GAD.

Another aim of the study was to shed light on the influence of comorbid depression on attentional control in GAD. Results showed that comorbid GAD/MDD was associated with non-affective deficits in attentional control that occurred in the later portion of stimulus presentation. Thus, the presence of comorbid depression seems to outweigh interactive (i.e., picture type X working memory load) effects observed in pure GAD, resulting in broader deficits in attentional control. These results are in line with prior research suggesting that comorbid depression may attenuate threat-related biases normally observed in anxiety. They further suggest that the inability to sustain attentional control into later portions of stimulus presentation duration may be important in understanding comorbid GAD/MDD. For instance, De Raedt and Koster (2010) suggest that deficits in later-stage, prefrontally-mediated attention might underlie depression-related phenomena such as rumination.

In addition to characterizing attentional control processes in pure GAD and comorbid GAD/MDD, the current study aimed to shed light on some of the shared and unique mechanisms underlying GAD and MDD. The results indicate that both groups – i.e., individuals with pure GAD and those with comorbid GAD/MDD - exhibit reduced attentional control. In line with this, recent work found that both GAD and MDD were characterized by abnormal activity in neural regions associated with emotion-regulation (i.e., ventral-cingulate-amygdalar circuit) on a task requiring the inhibition of attention to distracting stimuli (emotional Stroop; Etkin & Schatzberg, 2011). Such results support a "common-disorder" model, in which GAD and MDD might be considered to have the same etiology. However, both the current study and prior work have also

supported an "independent-factor" model, in which GAD and MDD would be considered to have different underlying mechanisms. For example, Etkin and Schatzberg (2011) also found that, despite similar ventral-cingulate-amygdalar abnormalities, only participants with MDD, and not those with GAD successfully activated a compensatory neural network involving the lateral prefrontal cortex, in order to avoid behavioral interference from *emotional* distracters. In the current study, differences were also found in the timing and affective nature of attentional control deficits for individuals with pure GAD and those comorbid for depression. Thus, while GAD and MDD may share a common deficit in the neural circuitry underlying attentional control, they may differ in terms of affective reactivity (i.e., GAD-related increases in the 300-600 ms LPP and less flexible processing of unpleasant stimuli in the 600-1000 ms window). Rather than conceptualizing GAD and MDD as either distinct or redundant syndromes, the present results highlight the utility of alternative models that may capture both the divergence and overlap between GAD and MDD.

For example, from a functional and temporal perspective, a *causal* model could be used to explain the relationship between GAD and MDD. Evidence in support of such a model includes the fact that GAD often onsets before MDD (Kessler, Walters, & Wittchen, 2004), which suggests that the mechanisms underlying GAD might contribute to the development of depression. In addition, individuals comorbid for GAD and MDD spend the majority of their time not *actively* comorbid (i.e., not meeting full criteria for both disorders concurrently; Brown, 2007). Therefore, attentional and affective mechanisms in GAD may change in a cyclic pattern over time as individuals transition in and out of depressive episodes. Such a model could explain why GAD and MDD may share some features, such as reduced attentional control and not others, such as affective hyper-reactivity (Mennin et al., 2008).

Strengths of the current study include the use of temporally sensitive measures of brain activity and a relatively "clean" sample (i.e., no comorbidities and no psychiatric medication usage), which allowed for the attribution of group differences to the diagnoses of interest rather than to other confounding factors. Weaknesses included a moderately sized sample and an inability to obtain a spatially precise measure of prefrontal brain activity or activity in other brain regions. Future work should aim to extend the present results by using a larger sample size and incorporating fMRI or other neural measures with higher spatial resolution. Future work might also wish to examine attentional control in the context of pleasant stimuli (Kerestes et al., 2012), and to compare attentional control using both affective and non-affective tasks in the same individuals (Siegle, Thompson, et al., 2007). The present results suggest evidence of overlapping yet unique attentional control deficits in GAD and comorbid GAD/MDD; an important area for future research will be to determine whether individuals at risk for GAD or MDD, or those currently in remission for one of these disorders exhibit these attentional abnormalities, in order to assess the state- or trait-nature of attentional control deficits in these individuals over time.

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Table 1
Means (and standard deviations) for self-report measures (top section) and demographics (bottom section), shown separately for each group and across all participants.

	HC *n* = 35		GAD *n* = 36		Comorbid *n* = 36		Overall *n* = 107	
MASQ Anxious Arousal	19.64 (3.76)		28.46 (9.42)		28.58 (6.98)		25.67 (8.17)	
MASQ Anhedonic Depression	54.11 (11.01)		64.39 (15.53)		78.16 (10.75)		65.99 (15.95)	
MASQ General Distress – Anxiety Symptoms	15.29 (3.61)		25.18 (9.26)		26.23 (4.71)		22.37 (7.94)	
MASQ General Distress – Depressive Symptoms	17.29 (3.12)		27.71 (11.49)		35.81 (9.73)		27.24 (8.17)	
DA	40.20 (15.09)		48.41 (9.67)		45.76 (11.84)		45.52 (12.02)	
PSWQ	47.68 (10.56)		65.71 (9.75)		63.57 (11.24)		60.04 (12.88)	
RSS	20.00 (3.78)		25.18 (4.22)		24.61 (4.27)		23.98 (4.51)	
Age	23.89 (9.12)		23.39 (6.04)		23.97 (7.72)		23.75 (7.65)	
Years of Education	14.72 (2.05)		15.56 (2.81)		14.72 (1.63)		15.01 (2.24)	
Ethnicity*	*n*	*%*	*n*	*%*	*n*	*%*	*n*	*%*
Caucasian	12	34.3	23	63.9	20	55.6	55	51.4
Other	17	48.6	12	33.3	13	36.1	42	39.2

* some percentages do not add up to 100% because participants declined to provide ethnicity.

Table 2
Mean (and standard deviations) for alpha power at lateralized frontal sites during the 6000 ms prior to picture onset, LPP amplitudes elicited by pictures 300-600 ms, 600-1000 ms and 1000–2000 ms after picture onset, as well as accuracy data for the letter recall task, presented in each of the four conditions and shown separately for each group and collapsed across group.

			HC	GAD	Comorbid	Overall
	Load	Electrode				
Alpha Power (μv^2/Hz; -6000 ms – 0 ms)	Low	F7	.11 (.11)	.09 (.06)	.10 (.10)	.10 (.09)
	High	F7	.09 (.10)	.08 (.04)	.08 (.08)	.08 (.08)
	Low	F8	.10 (.11)	.09 (.05)	.09 (.07)	.09 (.08)
	High	F8	.08 (.07)	.08 (.06)	.07 (.05)	.08 (.06)
	Load	Picture Type				
LPP (μv; 300-600 ms)	Low	Neutral	1.74 (4.44)	5.33 (5.37)	3.93 (7.17)	3.74 (5.89)
	Low	Unpleasant	6.36 (4.90)	9.30 (6.91)	7.68 (8.07)	7.84 (6.80)
	High	Neutral	-1.91 (5.06)	.86 (5.63)	.92 (6.31)	-.01 (5.78)
	High	Unpleasant	1.48 (5.51)	5.60 (6.06)	4.79 (8.06)	4.02 (6.78)
LPP (μv; 600-1000 ms)	Low	Neutral	2.84 (4.85)	6.03 (5.69)	4.61 (7.63)	4.56 (6.23)
	Low	Unpleasant	9.35 (5.87)	10.86 (7.39)	10.21 (7.68)	10.17 (7.00)
	High	Neutral	-.17 (5.78)	1.55 (5.49)	2.04 (6.96)	1.16 (6.10)
	High	Unpleasant	4.77 (6.46)	9.13 (6.60)	8.61 (7.62)	7.57 (7.10)
LPP (μv; 1000-2000 ms)	Low	Neutral	2.92 (6.24)	6.49 (5.98)	4.84 (8.52)	4.82 (7.05)
	Low	Unpleasant	8.58 (7.08)	9.95 (7.61)	10.08 (7.89)	9.55 (7.49)
	High	Neutral	-.09 (7.50)	1.82 (6.33)	2.68 (8.28)	1.48 (7.38)
	High	Unpleasant	2.81 (6.48)	7.15 (7.39)	9.06 (9.24)	6.37 (8.12)
Accuracy (% Correct)	Low	Neutral	98.08 (4.00)	96.57 (8.14)	96.08 (5.41)	96.89 (6.16)
	Low	Unpleasant	97.47 (5.07)	97.41 (6.38)	96.27 (5.73)	97.06 (5.74)
	High	Neutral	69.90 (20.50)	66.94 (18.78)	61.76 (26.43)	66.18 (22.14)
	High	Unpleasant	65.66 (20.79)	64.81 (21.48)	60.88 (26.91)	63.79 (23.08)

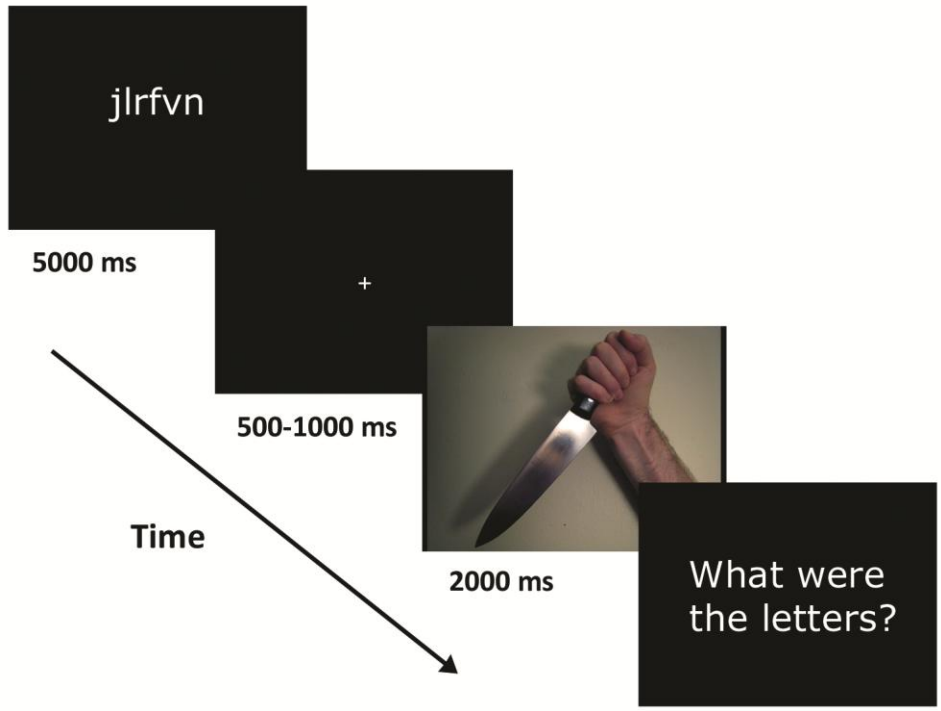

Figure 1. A depiction of a sample trial from the task (from MacNamara et al., 2011). On each trial, participants viewed a 2- or 6-letter string for 5000 ms. This was followed by a fixation cross for 500-1000 ms and then by a neutral or unpleasant picture, presented for 2000 ms. Pictures were irrelevant to the task, however participants were asked to keep their eyes onscreen throughout the duration of each trial. At the end of each trial, participants were asked to recall the letters in the same order in which they were presented at the beginning of the trial. (Font size is not to scale).

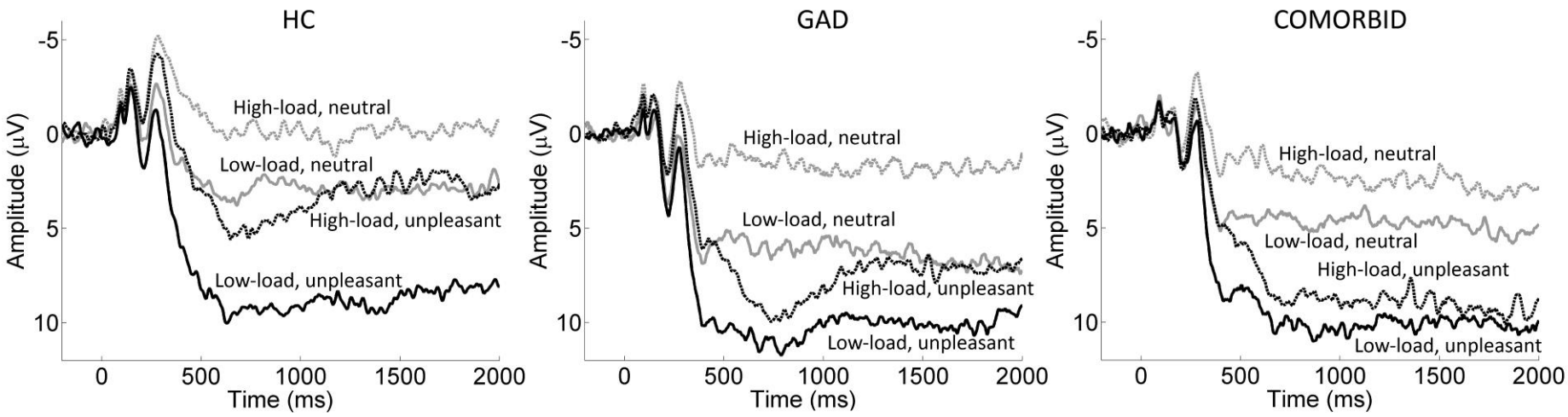

Figure 2. Grand-averaged waveforms at electrode Pz, for neutral and unpleasant pictures presented under high and low working memory load, shown separately for healthy controls (left), individuals with GAD (middle) and individuals comorbid for GAD and MDD (right).

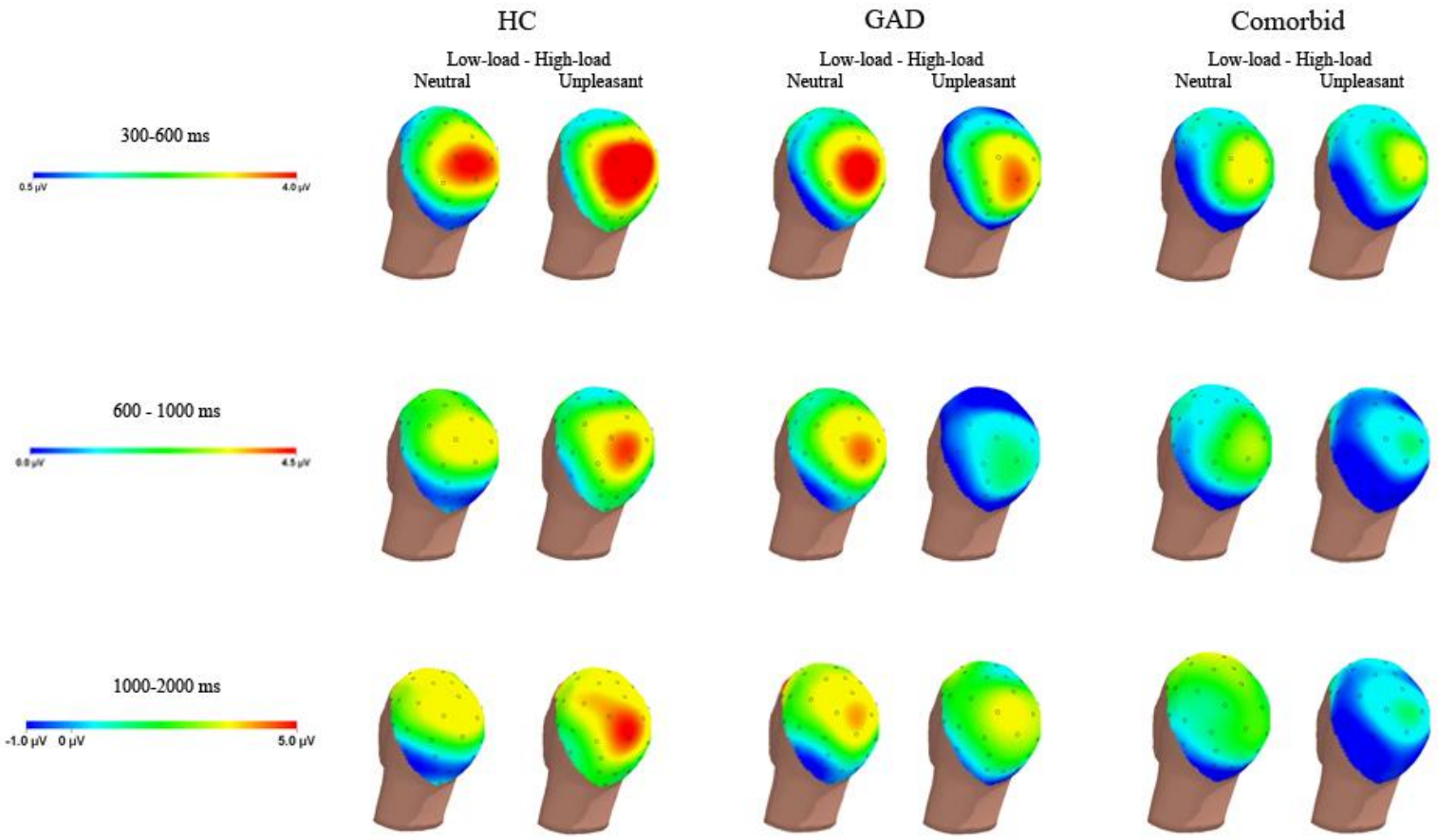

Figure 3. Topographic maps depicting voltage differences for LPP amplitudes elicited on low-load minus high-load trials, shown separately for neutral and unpleasant pictures and for healthy controls (left column), individuals with GAD (middle column) and individuals comorbid for GAD and MDD (right column), for time windows 300-600 ms (top row), 600-1000 ms (middle row) and 1000-2000 ms (bottom row) following picture onset. Note the different scale used for each time window.

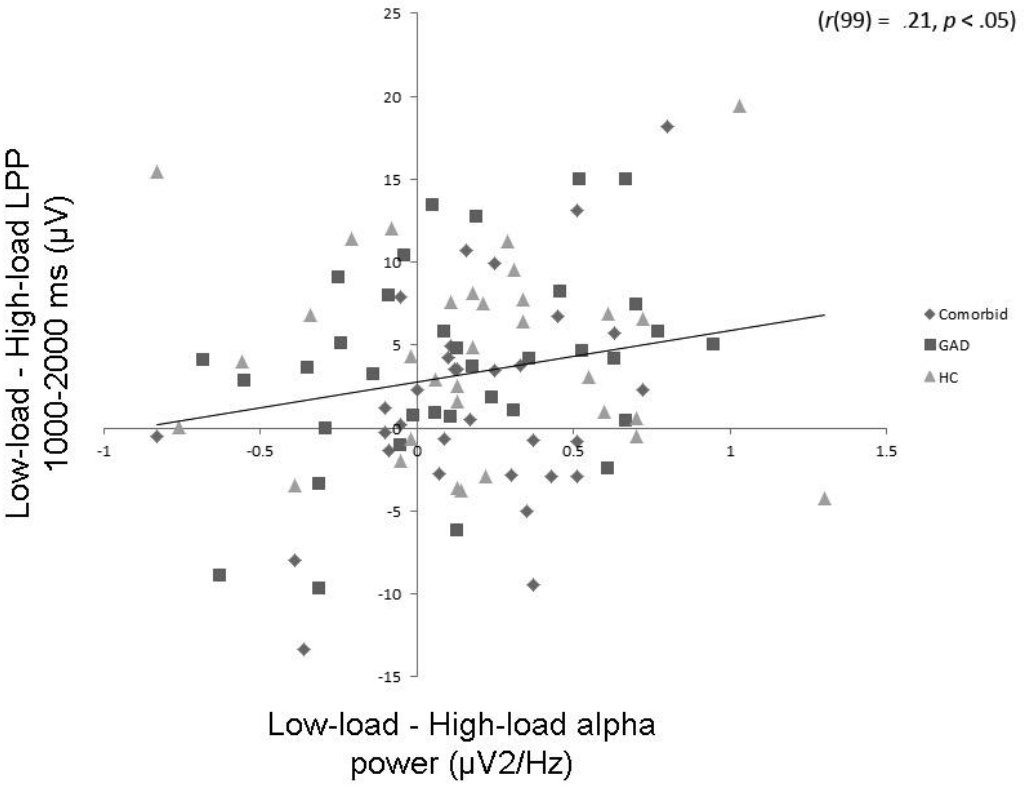

Figure 4. Scatterplot depicting the association between the low-load minus high-load difference for the picture-elicited LPP in the 1000-2000 ms window and the low-load minus high-load difference for alpha power at electrode F7, during the 6000 ms preceding picture onset.

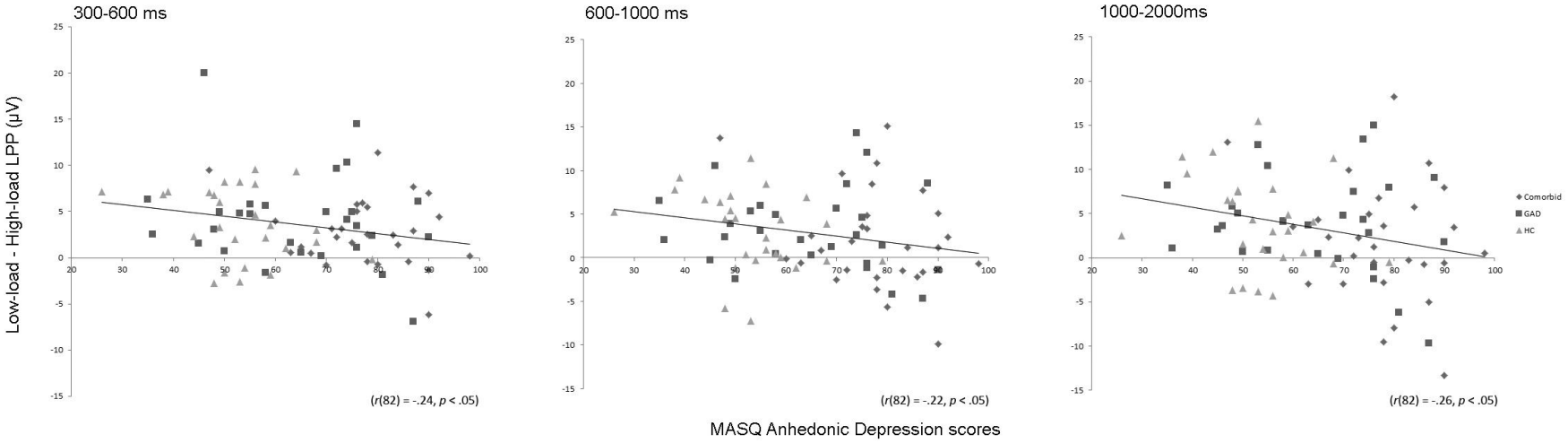

Figure 5. Scatterplots depicting the association between self-reported anhedonic depression (on x axes) and the low-load minus high-load LPP difference (on y axes), shown separately for the 300-600 ms window (left), the 600-1000 ms window (middle) and the 1000-2000 ms window (right).