

The modification of attentional bias to emotional information: A review of the techniques, mechanisms, and relevance to emotional disorders

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A negative bias in the deployment of attention to emotional stimuli is commonly found in both anxiety and depression. Recent work has highlighted that such biases are causally related to emotional vulnerability, suggesting that interventions that ameliorate them may be therapeutic. Here, we review the evidence that attentional bias can be modified using both pharmacological and psychological interventions. We highlight the behavioral and neuroimaging studies that suggest that these interventions impact upon attention via alteration of distinct neural mechanisms. Specifically, pharmacological interventions appear to influence the initial deployment of attention via an effect on the amygdala-based stimulus appraisal system, whereas psychological interventions influence attention at later time points and may alter activity in the lateral prefrontal cortex. Finally, we suggest a conceptual framework that embraces both pharmacological and psychological approaches and consider the possible implications of this work for future research and treatment development.

A wealth of data from behavioral, neuroimaging, pharmacological, and genetic studies has served to highlight the centrality of attentional processes in our understanding of anxiety and depression. Aberrant deployment of attention, particularly in relation to emotional information, occupies a pivotal position in many of the contemporary models of these disorders in which it is considered a causally relevant, proximal illness process. This view suggests that interventions that modify the habitual deployment of attention to emotional information should impact upon illness expression. In the present article, we will review the evidence that emotional attention may be modified in both experimental and clinical settings. In doing so, we will highlight the data that demonstrate that this modification may be achieved by targeting at least two distinct control mechanisms. Finally, we will consider the implications of this work, particularly with regard to future research and treatment development.

What Evidence Links Abnormalities of Emotional Attention and the Emotional Disorders?

Both depression and anxiety have been associated with biases in the processing of emotional information; patients with these disorders habitually interpret, attend to, and/or remember information in a more negative manner than do nonclinical control participants (Mathews & MacLeod, 2005). Cognitive theorists suggest that these habits of thought are causal factors in the etiology and maintenance of the disorders (Beck, 1976; Mathews & Mackintosh, 1998; Mathews & MacLeod, 2005; Mogg & Brad-

ley, 1998; Williams, Watts, MacLeod, & Mathews, 1997). Anxiety has particularly been associated with a tendency to attend to threatening information—a phenomenon that has been termed *negative attentional bias* (see Figure 1 for a summary of the tasks commonly used to assess attentional bias; Fox, Russo, & Georgiou, 2005; MacLeod, Campbell, Rutherford, & Wilson, 2004; Mathews & MacLeod, 1985; Williams, Mathews, & MacLeod, 1996). Recent work, much of it discussed in the body of this article, has employed simple computer-based tasks in order to induce attentional biases in nonclinical populations (for reviews, see MacLeod, Koster, & Fox, 2009; Mathews & MacLeod, 2002). Critically for psychopathology, these studies provide direct support for a causal role of attention in anxiety by demonstrating that inducing a negative attentional bias can lead to symptoms of anxiety in non-clinical participants.

In depression, the most consistent cognitive abnormalities were initially described in measures of memory (Gilboa-Schechtman, Erhard-Weiss, & Jeczemien, 2002; Mathews & MacLeod, 2005; Ridout, Astell, Reid, Glen, & O'Carroll, 2003; Williams et al., 1997); however, there has been increasing interest in the possibility that attentional biases may exist in this disorder as well. Specifically, depression has been shown to be associated with a tendency to attend to the spatial location of negative words (Bradley, Mogg, & Lee, 1997; Donaldson, Lam, & Mathews, 2007; Mogg, Bradley, & Williams, 1995) and faces (Gotlib, Kasch, et al., 2004; Gotlib, Krasnoperova, Yue, & Joormann, 2004; Joormann & Gotlib, 2007; Leyman, De Raedt, Schacht, & Koster, 2007). Negative at-

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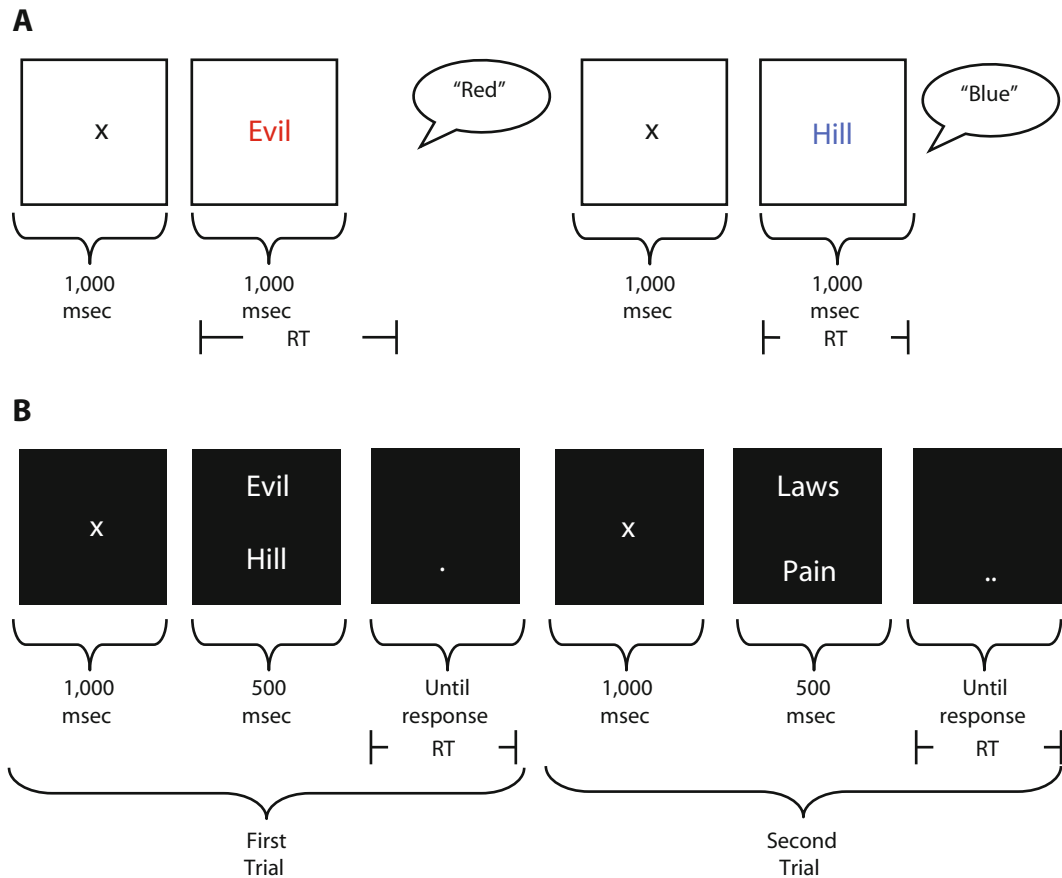


Figure 1. Behavioral methods of assessing emotional attention. Example trials from the two most common behavioral paradigms used to assess attentional function: the emotional Stroop (A) and visual probe (B) tasks. Behavioral tasks such as these are often the preferred method of assessing cognition, since they do not rely on the self-report of internal states, which is notoriously unreliable (Nisbett & Wilson, 1977). During standard emotional Stroop tasks (A), participants are required to ignore the emotional content of a word stimulus while reporting its font color, the rationale being that the emotional aspect of the stimulus interferes with the required behavior and, therefore, lengthens reaction times. The demonstration of a specific lengthening of reaction times to emotional stimuli is argued to show that more processing resources (i.e., attention) have been captured by the stimuli (Williams, Mathews, & MacLeod, 1996), although this interpretation has been disputed (Algom, Chajut, & Lev, 2004; Larsen, Mercer, & Balota, 2006). Emotional Stroop tasks are insensitive to the timing of attentional effects; instead, they provide a general indication that task interference has occurred at some point. The one exception to this is when masked stimuli are presented; in this case, the relevant stimulus is briefly presented and is followed by a nonemotional mask that prevents explicit identification of the stimulus. In such cases, it seems reasonable to assume that early stimulus appraisal processes lead to the task interference. Controversy in the interpretation of Stroop data has led to the increased popularity of visual probe tasks (B). On the basis of paradigms developed by Posner and colleagues (Posner & Petersen, 1990), these have been argued to provide a purer estimate of spatial attention. The most common variety of this task involves the brief presentation of emotional and neutral stimuli, followed by a probe, to which the participant must respond, in the location of one of the stimuli (MacLeod, Mathews, & Tata, 1986). It is assumed that reaction time is improved if attention is focused at the location in which the probe appears—that is, if the stimulus previously found at that location has captured attention. An estimate of attentional bias for emotional stimuli is calculated by comparing reaction times when the probe is found at the location of an emotional stimulus with those when it is found elsewhere. An advantage of visual probe tasks is that they provide information on the temporal characteristics of attention; specifically, they have been described as providing an estimate of attentional deployment at the time the probe is presented (Cooper & Langton, 2006).

tentional biases are also demonstrable in previously depressed, currently euthymic patients (Joormann & Gotlib, 2007), lending support to the proposal that they are involved in the vulnerability to depression rather than solely reflecting a state marker or symptom of the illness.

Although depression and anxiety have both been associated with attentional bias toward negative stimuli, there are differences in how this bias manifests between

the disorders. Most obviously, there appears to be a variation in how long a stimulus must be presented before the bias becomes evident; whereas anxiety is associated with an attentional bias that occurs from 10 to 500 msec after stimulus presentation, in depression the bias seems to occur between 500 and 1,000 msec (Gotlib, Kasch, et al., 2004). These timing effects are consistent with dual-process accounts of brain organization that describe the

existence of two distinct information-processing streams: an automatic stream that processes information in a rapid but inflexible manner and a strategic stream that provides slower, more flexible processing (see Carver, Johnson, & Joormann, 2008, for a recent review of dual-process models relevant to the emotional disorders). It has been suggested (Mathews & MacLeod, 2005) that anxiety is associated with abnormalities in the early, automatic processing of information and depression with abnormalities in later processing stages. In terms of attentional function, this may be reflected by abnormalities of the initial engagement of attention in anxiety, with difficulties in disengaging attention being characteristic of depression (Leyman et al., 2007; see also De Raedt & Koster, 2010). Despite the differences seen in experimental paradigms, it is notable that individuals very often experience both anxious and depressive symptoms concurrently (Maser & Cloninger, 1990; Mineka, Watson, & Clark, 1998) and that there is a large overlap in the evidence-based treatments for these disorders (NICE, 2004, 2007). Thus, although there are some differences in the expression of attentional biases in anxiety and depression, there remains a strong possibility that these disorders share at least some pathological processes.

In summary, there is evidence that a tendency to preferentially attend to negative information is a feature of both anxiety and depression. Differences in the timing of the attentional biases found in depression and anxiety can be accounted for by dual-process models that postulate the existence of temporally separable attention control processes.

What Processes Control Emotional Attention?

The control of attention to emotional information is often conceptualized within a biased competition framework (Bishop, 2007; Desimone & Duncan, 1995; Mathews & Mackintosh, 1998; Vuilleumier, 2005). Broadly, this suggests that the deployment of attention is influenced by biasing signals that act to encourage the focus of attention toward or away from particular stimuli. Two neural systems have been implicated in generating signals of particular relevance to emotional stimuli. A bottom-up amygdala-based system generates a signal that reflects the perceived salience of stimuli (Adolphs, Tranel, Damasio, & Damasio, 1995; Davis & Whalen, 2001) and is thought to cause attention to be directed toward those stimuli. The anterior cingulate cortex (ACC) and lateral prefrontal cortex (IPFC) are considered to be part of a top-down control system that is involved in detecting and resolving processing conflict, with the result that attention may be maintained on relevant stimuli, even in the presence of distraction (Bishop, Duncan, Brett, & Lawrence, 2004; MacDonald, Cohen, Stenger, & Carter, 2000). These neuroanatomical models predict that the negative attentional biases characteristic of emotional disorder may arise from perturbation of either of these systems. Supporting this contention, experimental studies have reported increased amygdala activity to negative stimuli in both depression (Fales et al., 2008; Fu et al., 2004; Sheline et al., 2001; Siegle, Steinhauer, Thase, Stenger, & Carter, 2002) and anxiety (Bishop, Duncan, & Lawrence, 2004; Schneider et al., 1999; Shin, Rauch, &

Pitman, 2006; Straube, Mentzel, & Miltner, 2006; Tillfors, Furmark, Marteinsdottir, & Fredrikson, 2002), whereas frontal activation to the same stimuli has been found to be decreased in both disorders (Bishop, Duncan, et al., 2004; Fales et al., 2008; Mayberg et al., 1999; Shin et al., 2001; although see also Straube et al., 2006; Tillfors et al., 2002). A notable discrepancy arises when these data are compared with those in the behavioral literature; whereas differences in the temporal characteristics of the biases associated with anxiety and depression are evident when assessed behaviorally (see above), neuroimaging studies do not seem to reliably differentiate the disorders. This may be due to constraints on the temporal resolution of functional imaging techniques or to the fact that neuroimaging studies have tended to simply present emotional stimuli without manipulating participants' attention (see Bishop, Duncan, et al., 2004, for an example of a study in which attention was manipulated). Such manipulations allow the effects of attention to be isolated from those due simply to the emotional properties of a stimulus. Nevertheless, the temporal specificity of the attentional effect demonstrated in the behavioral studies of anxiety versus depression remains unexplained by current neuroimaging data.

A further consideration when neuroimaging data are interpreted is that the biasing signals that influence attention seem to have *direction* as well as *magnitude*. For example, whereas depressed patients show decreased activity in the ACC during anticipation of loss, they show *increased* activation during anticipation of gain (Knutson, Bhanji, Cooney, Atlas, & Gotlib, 2008). Similarly, amygdala activity is increased in response to positive stimuli in extroverted participants, as well as to negative stimuli in anxious individuals (Canli, Sivers, Whitfield, Gotlib, & Gabrieli, 2002). These findings suggest that, rather than solely arising from an absolute alteration of function (e.g., decreased attentional control), emotional disorders may also reflect alterations in the valence of information to which the systems preferentially react (e.g., decreased attentional control for negative information and increased control for positive). Accordingly, the interventions reviewed in this article that alter attention to emotional information may be understood as altering this preference, rather than fundamentally changing the efficacy of the system.

Generally, however, the neuroimaging data complement the behavioral findings, in that the most commonly reported neuroimaging abnormalities in the emotional disorders would be expected to lead to negative attentional biases. These abnormalities—increased amygdala and decreased frontal activation in response to attended negative stimuli—are evident in both depression and anxiety and lead to the prediction that interventions that alter the function of either one or both of these systems will influence emotional attention and, in turn, current anxious and depressive symptomatology.

Can the Effects of Treatment on Cognition Be Disentangled From the Effects of Mood?

The interpretation of studies in which the effects of treatments on cognition are investigated can, paradoxically,

cally, be hampered when the treatment is effective. The problem is particularly acute in studies of clinical populations, in which treatments are expected to improve clinical state. These studies inevitably compare groups that differ on two accounts: exposure to treatment (e.g., administration of an antidepressant vs. a placebo) and current levels of psychopathology (e.g., mood). Although such studies are essential when one is examining the effects of a treatment on the relevant population, it is difficult to be certain whether any differences observed in behavior or neural activity reflect the direct action of the intervention or are general effects of clinical status. The influence of this confounding factor can be reduced by studying nonclinical populations, who generally do not experience profound changes of mood and who can, thus, provide important complementary data to the clinical studies. Since the critical issue in the present article concerns the mechanisms by which treatments may work, we will consider both studies of clinical populations and those solely involving nonclinical participants.

Pharmacological Methods of Modulating Attention to Emotional Information

Neurochemical probes have been used to examine how neurotransmitter function may modulate attentional bias in both healthy volunteers and patients. One key strategy has been to see whether biases apparent in depression and anxiety can be mimicked by depletion of the neurochemicals known to be involved in these disorders.

Tryptophan depletion. The synthesis of serotonin in the brain is dependent on the availability of its precursor amino acid, tryptophan, from plasma. Acute administration of an amino acid mixture that selectively lacks tryptophan is effective in decreasing the availability of tryptophan to the brain through processes of increased protein synthesis (lowering plasma tryptophan levels) and increased competition for transport across the blood-brain barrier (Reilly, McTavish, & Young, 1997). Tryptophan depletion (TD) transiently lowers mood in recovered depressed patients, although there is no consistent effect on mood in healthy volunteers (Ruhe, Mason, & Schene, 2007). Recently, however, TD has been used as an experimental tool for examining the role of serotonin in the processing of emotional information in healthy volunteers (Booij, Van der Does, & Riedel, 2003). That TD is seen to affect cognition in nonclinical participants without altering mood suggests that cognitive measures, such as the attentional tasks examined in this article, provide a more proximal or, at least, more sensitive marker of the effects of this intervention than do mood measures. A number of studies (see Table 1) have suggested that reduction of serotonergic function using TD increases the interference associated with negative words in emotional Stroop tasks, both in never depressed populations (Evers, van der Veen, Jolles, Deutz, & Schmitt, 2006) and in previously depressed ones (Hayward, Goodwin, Cowen, & Harmer, 2005; Munafò, Hayward, & Harmer, 2006). Interestingly, a study in which participants took tryptophan supplementation, an intervention predicted to increase serotonergic function, suggested that attention toward negative words

was decreased in females (Murphy, Longhitano, Ayres, Cowen, & Harmer, 2006). However, other studies have produced inconsistent results. First, in previously depressed participants, TD was found to slow responses in the emotional Stroop task to positive words, suggesting increased attentional interference from these positive cues (Booij et al., 2005). A further study showed no effect of TD on a visual-probe task involving threat-related words (Merens, Booij, Haffmans, & Van der Does, 2008). Thus, although TD demonstrably influences the processing of emotional information, there is a degree of inconsistency to this effect.

Two neuroimaging studies have investigated the effects of TD on tasks in which emotional valence was manipulated, although neither explicitly manipulated attention. Both reported increased amygdala activation in response to negative stimuli following TD, although this effect was qualified by participant characteristics, which may explain some of the variance in the behavioral data. Thus, in a nonclinical sample, TD increased amygdala activity to fearful versus happy faces, but only in those with high scores on the behavioral inhibition subscale of the BIS/BAS measure (Carver & White, 1994; Cools et al., 2005). Similarly, a second study reported increased amygdala activation following TD in a group of healthy women, but only those with a family history of depression (van der Veen, Evers, Deutz, & Schmitt, 2007).

Taken as a whole, these findings suggest that TD increases attention to negative emotional information and that its effect is associated with alteration of amygdala function; however, as has been noted with nonattentional measures of cognition (Robinson, Cools, Crockett, & Sahakian, in press), this effect is qualified by individual differences in the participants.

Antidepressant administration. An alternative strategy in the investigation of the effects of neurotransmitter function on attentional bias is to characterize the effects of the pharmacological treatments of the emotional disorders. Serotonergic function can be potentiated using antidepressant medications that specifically block the reuptake of serotonin from the synapse, a strategy recommended in the treatment of both depression and anxiety (NICE, 2004, 2007; Nutt, 2002). A number of experimental studies have assessed the influence of these serotonergic antidepressants on emotional attention in nonclinical groups (see Table 1). A single dose of the antidepressant citalopram was associated with an increased bias toward positive words in a visual-probe task (Browning, Reid, Cowen, Goodwin, & Harmer, 2007), whereas 7 days of citalopram decreased attention to briefly presented fearful faces, an effect not seen with the norepinephric antidepressant reboxetine (Murphy, Yiend, Lester, Cowen, & Harmer, 2009). As was predicted and contrary to the effects of TD, serotonergic antidepressants decreased amygdala activation to negative stimuli in both clinical (Fu et al., 2004; Sheline et al., 2001) and nonclinical (Arce, Simmons, Lovero, Stein, & Paulus, 2008; Del-Ben et al., 2005; Harmer, Mackay, Reid, Cowen, & Goodwin, 2006; Murphy, Norbury, O'Sullivan, Cowen, & Harmer, 2009) populations. There is less evidence that antidepress-

Table 1
Studies That Have Reported the Effects of Pharmacological Manipulations on Measures of Attention to Emotional Information

Study	Intervention	Population Studied ^a	Attentional Task	Type and Duration of Stimulus	Duration of Stimulus ^b	Result	Notes
Evers, van der Veen, Jolles, Deutz, & Schmitt (2006)	Tryptophan depletion	Nonclinical females ($n = 19$, using a within-subjects design)	Emotional Stroop	Positive, negative, and neutral words	200 msec	Increased interference of negative words after tryptophan depletion	Result derived from error rate; no effect for reaction time
Booij et al. (2005)	Tryptophan depletion	Patients in complete or partial remission from depression who were still taking SSRI medication ($n = 20$, using a within-subjects design)	Emotional Stroop	Positive, negative, and neutral words	Up to 1,500 msec	Increased interference from positive words	Complex experimental design with participants completing cognitive tests on four separate occasions
Hayward, Goodwin, Cowen, & Harmer (2005)	Tryptophan depletion	Patients ($n = 24$) with a history of depression who no longer met diagnostic criteria and healthy controls ($n = 24$)	Emotional Stroop	Negative and neutral words	400 msec	Increased interference from negative words	Effect seen in both clinical and control groups; counting version of the emotional Stroop task used
Munafò, Hayward, & Harmer (2006)	Tryptophan depletion	Patients with previous depression who were on antidepressant medication ($n = 24$) or no medication ($n = 24$) and nonclinical controls ($n = 24$)	Emotional Stroop	Negative and neutral words	Unmasked (until response) or masked (14 msec) conditions	Increased interference from negative words in both masked and unmasked conditions	Effect seen only in previously depressed group who were still taking medication
Merens, Booij, Hafmans, & Van der Does (2008)	Tryptophan depletion	Patients ($n = 16$, using a within-subjects design) in complete or partial remission from depression, who were still taking antidepressant medication	Visual probe	Neutral vs. threat words and depression relevant vs. positive words.	500 msec	No significant effects	
Murphy, Longhitano, Ayres, Cowen, & Harmer (2006)	Tryptophan supplementation	Nonclinical females ($n = 19$ per group)	Visual probe	Positive, negative, and neutral words	Unmasked (500 msec) and masked (14 msec) conditions	Decreased attention to negative words in unmasked condition	Result derived from error rate; no effect for males
Browning, Reid, Cowen, Goodwin, & Harmer (2007)	Single dose of citalopram or placebo	Nonclinical group ($n = 15$ per group)	Visual probe	Positive, negative, and neutral words	Unmasked (500 msec) and masked (14 msec) conditions	Increased attention to positive words in both masked and unmasked conditions	
Murphy, Yiend, Lester, Cowen, & Harmer (2009)	Seven days of citalopram, reboxetine, or placebo	Nonclinical group ($n = 14$ per group)	Visual probe	Happy, fearful, or neutral facial expressions	Unmasked (100 msec) and masked (16 msec) conditions	Citalopram reduced attention to fearful face in unmasked condition.	Effect seen only for citalopram; no effect of reboxetine
Putman, Hermans, Koppeschaar, van Schijndel, & van Honk (2007)	Cortisol or placebo	Nonclinical males ($n = 20$, using a within-subjects design)	Emotional Stroop	Fearful or neutral facial expressions	Masked (14 msec) presentation	Decreased interference from fearful faces	
van Honk, Peper, & Schutter (2005)	Testosterone or placebo	Nonclinical females ($n = 16$, using a within-subjects design)	Emotional Stroop	Fearful, happy, or neutral facial expression	Masked (14 msec) presentation	Decreased interference from fearful faces	No effect on happy faces; no mention of the effect of trial order in relevant analysis
Murphy, Downham, Cowen, & Harmer (2008)	Diazepam or placebo	Nonclinical volunteers ($n = 12$ per group)	Visual probe	Fearful, happy, or neutral facial expression	Unmasked (100 msec) or masked (14 msec) presentation	Increased attention toward happy in masked condition	Authors argue that increased attention toward happy is similar to decreased negative bias, as in the relevant trials, happy and neutral stimuli are presented together, and the neutral stimuli are relatively more threatening.

^aUnless otherwise stated, studies used a between-subjects design. ^bCertain task designs (see Figure 1) allow inference as to the timing of the temporal effects of an intervention on attention. In studies that employ such a design and report significant findings, the relevant duration is presented in boldface.

sants alter activity in frontal control regions; two studies reported such an effect (Fales et al., 2009; Kennedy et al., 2001), although both of these involved clinical populations, indicating that the findings may have been secondary to improved clinical status, rather than a treatment effect. An event-related potential (ERP) study has examined the effects of citalopram and reboxetine on the processing of emotional information in healthy volunteers (Kerestes et al., 2009). The high temporal acuity of ERP allowed the authors to demonstrate that both antidepressants influenced processing relatively shortly after stimulus presentation (250 msec), with the effect being found in a component of the ERP known to be sensitive to spatial attention (Eimer, Holmes, & McGlone, 2003). The neuroimaging findings are thus consistent with an initial effect of antidepressants on the amygdala, with alteration of frontal control regions occurring later on in treatment and potentially reflecting improvement in clinical status. Interestingly, a single study has demonstrated that reboxetine also reduces amygdala activity to negative stimuli (Norbury, Mackay, Cowen, Goodwin, & Harmer, 2007), despite apparently having no effect on spatial attention to threat (Murphy, Yiend, et al., 2009). A possible explanation of this discrepancy is provided by recent models of norepinephric function that suggest that it acts specifically as a temporal filter in the control of attention (Aston-Jones & Cohen, 2005). Thus, the behavioral effects of norepinephric manipulation may best be assessed using measures of the deployment of attention in time, rather than in space. De Martino, Strange, and Dolan (2008) reported a series of three studies that examined the influence of the beta-blocker propranolol and reboxetine on an emotional version of the attentional blink task, which specifically assesses the deployment of attention in time. The authors reported a generally deleterious effect of propranolol on attentional function, in that it caused poorer task performance regardless of stimuli salience. Reboxetine was found to improve task performance, although only on trials involving negative emotional stimuli. No positive stimuli were used in the study, limiting conclusions as to the specificity of reboxetine's effect, although they would be in keeping with its effect on attention being primarily evident in the temporal domain.

Together, these studies indicate that serotonergic antidepressants alter attention to emotional information by encouraging a relatively more positive bias. Again, these effects are associated with an effect of the medication on amygdala function.

Alternative pharmacological strategies. On the basis of clinical findings suggesting that acute administration of glucocorticoids reduces the symptoms of post-traumatic stress disorder (Schelling, Roozendaal, & De Quervain, 2004), Putman, Hermans, Koppeschaar, van Schijndel, and van Honk (2007) used an emotional Stroop task to demonstrate that a single dose of the glucocorticoid cortisol reduced interference from masked negative stimuli (fearful faces) in healthy men. The same group had previously reported a similar effect when a single dose of testosterone, which has antidepressant activity (Pope, Cohane, Kanayama, Siegel, & Hudson, 2003), was

administered to females (van Honk, Peper, & Schutter, 2005). Lastly, a single dose of the benzodiazepine diazepam, which has acute anxiolytic effects, has been found to increase attentional bias toward masked happy faces in a nonclinical population (Murphy, Downham, Cowen, & Harmer, 2008), with a complementary effect of reduced amygdala activation to emotional stimuli being reported for another benzodiazepine, lorazepam (Paulus, Feinstein, Castillo, Simmons, & Stein, 2005). Thus, a diverse range of medications, all of which have antidepressant or anxiolytic activity, have been found to reduce negative or increase positive attentional bias.

Summary. A number of pharmacological interventions have been shown to alter attention to emotional stimuli. Taken as a whole, the behavioral data suggest that interventions that improve anxiety or depression (tryptophan supplementation, antidepressant medication, steroids, benzodiazepines) tend to result in attention's being directed away from negative and toward positive stimuli. TD, which leads to a worsening of symptoms in vulnerable individuals, tends to have the opposite effect on attention. As can be seen in Table 1, the majority of these effects are seen early on in the deployment of attention, with a number of studies demonstrating an effect with masked stimuli. The timing of the attentional effects suggests that these interventions alter the function of the bottom-up stimulus appraisal system, a conclusion supported by neuroimaging studies in which altered amygdala activity in response to negative stimuli was the most common finding.

Psychological Methods of Modulating Attention to Emotional Information

Cognitive behavioral therapy (CBT) is a complex psychological intervention that has been developed specifically to change the patterns of thinking and behavior that impact on how individuals interact with the environment and their resulting emotional states (Hollon, Stewart, & Strunk, 2006). CBT has been recommended as a first-line treatment for both depression and anxiety (NICE, 2004, 2007). A single study examining the effect of CBT on attentional function in anxiety disorder suggested that it reduces the negative attentional bias found pretreatment (Mathews, Mogg, Kentish, & Eysenck, 1995). However, as was discussed above, such a finding may be attributed to nonspecific effects of clinical status, rather than being regarded as necessarily a direct effect of treatment. Unfortunately, the complexity and variability of CBT can limit the extent to which it may be applied in controlled experimental trials. Perhaps because CBT is difficult to administer in experimental studies, there has been an increasing interest in developing simpler cognitive tasks that target the key hypothesized emotional processes and lend themselves to controlled experimentation. Although many of these tasks involve the explicit and effortful control of emotion (McRae et al., 2010; Ochsner & Gross, 2005; Phan et al., 2005), a number of techniques have been developed recently to specifically alter the habitual deployment of attention to emotional information (Dandeneau, Baldwin, Baccus, Sakellaropoulou, & Pruessner, 2007;

Table 2
Studies That Have Reported the Effects of Psychological Manipulations on Measures of Attention to Emotional Information

Study	Intervention	Population Studied ^a	Attentional Task	Type of Stimulus	Duration of Stimulus ^b	Result	Notes
Mathews, Mogg, Kentish, & Eysenck (1995)	Seven-session group CBT for anxiety management	Patients with GAD ($n = 24$) were compared with nonclinical controls ($n = 23$) both before and after treatment	Emotional Stroop and visual search	Negative and neutral words	Until response	Borderline significant reduction of negative attentional bias in the anxious group, using emotional Stroop ($p = .06$) and visual search ($p = .07$)	Emotional Stroop task used cards rather than computer to present stimuli.
MacLeod, Rutherford, Campbell, Ebsworthy, & Holker (2002)	Single session of attend-threat or avoid-threat training	Nonclinical ($n = 32$ per group)	Visual probe	Negative and neutral words	Unmasked (500 msec) and masked (20 msec)	Training influenced attention in unmasked condition	Two studies performed, both demonstrating similar effect
Hazen, Vasey, & Schmidt (2008)	Five sessions of avoid-threat or sham attentional training	Nonclinical ($n = 12$ per group) sample with high score on worry scale (includes participants who would meet diagnostic criteria for GAD)	Visual probe	Negative and neutral words	500 msec	Avoid-threat training reduced attention to negative words	
Eldara, Ricona, & Bar-Haim (2008)	Single session of attend-threat or avoid-threat attentional training	Nonclinical ($n = 13$ per group) children 7–12 years of age	Visual probe	Angry and neutral faces	700 msec	Attend-threat training influenced attention	This effect significant only for the faces used in training itself; no generalization to novel faces
Wadlinger & Isaacowitz (2008)	Single session of attend-positive or avoid-positive training	Nonclinical volunteers (approx. $n = 22$ per group)	Eye tracking	Positive and neutral words	8,000 msec	Positive training caused decreased fixation on negative areas of images.	Attentional training with visual probe type
Li, Tan, Qian, & Liu (2008)	Seven sessions of daily avoid-threat/attend-happy or sham training	Nonclinical volunteers with high score on a social anxiety scale ($n = 12$ per group)	Visual probe	Threatening and happy faces	500 msec	Active training caused significant decrease in negative bias.	Significant differences in measures of anxiety between groups at end of training may confound interpretation of attentional effects. The negative pictures were selected as being “threatening” rather than displaying a specific emotion. Since the threatening pictures were paired with positive pictures, these results could also be interpreted as showing an increase in positive attentional bias.

Table 2 (Continued)

Study	Intervention	Population Studied ^a	Attentional Task	Type of Stimulus	Duration of Stimulus ^b	Result	Notes
See, MacLeod, & Bridle (2009)	Fourteen sessions of daily avoid-threat or sham training	Nonclinical volunteers (approx. $n = 19$ per group)	Visual probe	Negative and neutral words	500 msec	Avoid-threat training caused significant decrease in negative bias.	Significant differences in trait and state anxiety between groups at end of training may confound interpretation of attentional effects.
Amir, Beard, Burns, & Bomyea (2009)	Eight sessions of avoid-threat or sham training over 4 weeks	Patients with GAD (approx. $n = 14$ per group)	Visual probe	Negative and neutral words	500 msec	Avoid-threat training caused significant decrease in negative bias.	Significant differences in trait and state anxiety between groups at end of training may confound interpretation of attentional effects.
Wells & Beevers (in press)	Four sessions of avoid-threat or sham training over 2 weeks	Nonclinical volunteers with BDI > 8 ($n = 17$ per group)	Visual probe	Negative and neutral faces and pictures	Faces were presented for 3,000 msec, pictures for 4,500 msec	Avoid-threat training caused significant decrease in negative bias.	Significant differences in depressive symptomatology between groups at end of training may confound interpretation of attentional effects. The stimuli were presented for an unusually long time.
Dandeneau, Baldwin, Baccus, Sakellariopoulou, & Pruessner (2007)	Single session of positive visual search or control training	Nonclinical group ($n = 76/147$ per study in two studies). For analysis, the groups were further divided into high and low self-esteem (see note).	Emotional Stroop (Study 2a) and visual probe (Study 2b)	Negative, positive, and neutral words (Stroop task); happy, angry, and neutral faces (visual probe task)	For Stroop task, 1,200 msec; for visual probe task, 500 msec	Positive training caused decreased interference from negative words and increased interference from positive words during the Stroop task. Positive training reduced attention to angry faces in visual probe task but did not affect attention to happy faces.	A significant effect of training was found only in those with low self-esteem. The influence of self-esteem was assessed by splitting groups using a median split in Study 1 and by adding self-esteem as a regressor in Study 2. A variety of statistical techniques were used to analyze behavioral responses in the separate studies. Stimuli were presented for 3,400 msec during the visual search training.
Dandeneau & Baldwin (2004)	Single session of positive visual search or control training	Nonclinical group ($n = 49$ in total). For analysis, the groups were further divided into high and low self-esteem by a median split.	Emotional Stroop	Negative, positive, and neutral words	1,200 msec	Trend-level results suggest training decreased interference from negative words.	

Note—BDI, Beck Depression Inventory; CBT, cognitive behavioral therapy; GAD, generalized anxiety disorder. ^aUnless otherwise stated, studies used a between-subjects design. ^bCertain task designs (see Figure 1) allow inference as to the timing of the temporal effects of an intervention on attention. In studies that employ such a design and report significant findings, the relevant duration is presented in boldface.

MacLeod, Rutherford, Campbell, Ebsworthy, & Holker, 2002). The most commonly used technique (e.g., MacLeod et al., 2002) employs a variant of the visual probe task (see Figure 1) in which the location of the probe is constrained such that it always replaces the neutral (for *avoid-threat* training) or negative (for *attend-threat* training) word. The task involves many experimental trials, over the course of which participants learn to direct attention toward the type of stimuli that predict the probe location; for example, if the probe always replaces negative stimuli, participants develop the habit of attending to negative stimuli generally (a negative attentional bias). Importantly, there is increasing evidence that using such tasks to encourage a positive attentional bias (avoid-threat training) in clinical populations results in improvement in symptoms (Amir, Beard, Burns, & Bomyea, 2009; Dandaneau et al., 2007; Eldara, Ricono, & Bar-Haim, 2008; Hazen, Vasey, & Schmidt, 2008; Schmidt, Richey, Buckner, & Timpano, 2009). Concerns about the generalizability and duration of these training effects have, to some extent, been countered by preliminary evidence that the beneficial effects on anxiety symptoms persist for at least 4 months after training (Schmidt et al., 2009). A number of studies have assessed the effects of these so-called *attentional training/attentional bias modification* tasks on measures of emotional attention (see Table 2) in both clinical and nonclinical populations. Generally, the tasks are seen to influence attention in the manner expected, although, as can be seen from Table 2, they have only been shown to influence attention to those unmasked stimuli presented for 500 msec or longer. A caveat to this observation is that the training tasks themselves generally involve a version of the visual probe task in which stimuli are presented for 500 msec, raising the possibility that earlier effects on attention might be observed if the training task was altered to present stimuli for a shorter time. However, the published data to date differ from those involving pharmacological manipulations in which effects are reported during earlier stages of information processing. If this behavioral observation is valid, it suggests that cognitive training tasks and pharmacological interventions may alter distinct mechanisms of attentional control, a hypothesis that has previously been raised by a number of authors (DeRubeis, Siegle, & Hollon, 2008; Harmer, 2008). We recently completed a neuroimaging study that tested this view; the effect of attentional training in healthy volunteers was assessed (Browning, Holmes, Murphy, Goodwin, & Harmer, in press), using an fMRI paradigm that varied both emotion and attention (Pessoa, Padmala, & Morland, 2005). The study indicated a significant effect of the training on activity in the IPFC and rostral ACC, with no effects demonstrable in the amygdala. In keeping with their role in mediating attentional control, activity in the IPFC and ACC was increased specifically when participants' attention was directed in the direction opposite to that encouraged by the training task—that is, when the need for control was high. Interestingly, a number of studies have suggested that the explicit reappraisal of emotion is mediated by changes in similar areas (McRae

et al., 2010; Ochsner & Gross, 2005; Phan et al., 2005). When considered together with the neuroimaging studies reviewed above, in which pharmacological manipulation was seen to alter amygdala activity, these results support the conclusion that cognitive and pharmacological interventions may target distinct processes in the control of emotional attention.

Summary. Cognitive training tasks (also known as cognitive bias modification tasks) have been shown to alter both attention to emotional information and clinical status in a predictable manner, although further studies deploying the experimental tasks in clinical populations are needed. The extant results suggest that this effect occurs later in the deployment of attention than that found with pharmacological manipulations, raising the possibility that different attentional control mechanisms are targeted.

Synthesis

A variety of techniques have been shown to alter emotional attention in clinical and nonclinical populations. Across all of these methodologies, interventions that improve anxiety and depression also cause attention to be preferentially deployed away from negative and toward positive information. The greatest amount of data is available for the pharmacological manipulation of the serotonergic system and for the use of cognitive attention training tasks. Characterization of the attentional effects of these interventions, using both behavioral and neuroimaging outcomes, suggests that they target different components of the attentional control system. Specifically, pharmacological modifications appear to alter the initial deployment of attention, via an effect on the amygdala-based appraisal system, whereas cognitive training interventions may influence attention some time later, possibly via an effect on frontal control regions.

Implications for treatment. Current evidence supports the efficacy of serotonergic antidepressants in the treatment of both anxiety and depression. Attentional training interventions have initial evidence suggesting efficacy in anxiety (MacLeod et al., 2009) but have yet to be applied to depressed groups (although a single positive study has been reported in a nonclinical dysphoric group; Wells & Beevers, in press). However, in real-world situations, the ability of either pharmacological or cognitive treatments to induce remission is, at best, moderate (e.g., DeRubeis et al., 2005, reported remission rates of 40%–50%). A number of studies have examined the combination of psychotherapy and antidepressant medication with mixed results (Foa, Franklin, & Moser, 2002; Furukawa, Watanabe, & Churchill, 2007; Pampallona, Bollini, Tibaldi, Kupelnick, & Munizza, 2004); however, all of these studies have used complex psychotherapeutic interventions, rather than procedures designed to target specific cognitive systems, such as attentional training. An intriguing possibility raised by the observation that antidepressant medication and cognitive training influence distinct information-processing stages is that, if combined, their effects on attention may be additive. If true, this would predict that concurrent

administration of both interventions in a clinical setting would improve efficacy over either on its own. However, this prediction rests on the untested assumption that the two interventions combine additively. As an alternative, it is conceivable that the learning that underlies the cognitive training task depends on an intact emotional signal provided by the amygdala; that is, in order to train attention to emotional stimuli, the participant must be able to detect the emotional content of the stimulus. If detecting this signal depends on amygdala function, antidepressant treatment, which can interfere with this function, may block the effects of training. A study in which the effects of the combination of these interventions on attentional function were gauged would be relatively simple to design, allowing the competing hypotheses to be tested. Lastly, it is worth noting that a number of alternative augmentation strategies exist that may bolster the effects of attentional training. In particular, D-cycloserine, a partial NMDA agonist, has been shown to facilitate learning, with early studies suggesting that it may be therapeutically useful when combined with psychotherapy (Norberg, Krystal, & Tolin, 2008; Wilhelm et al., 2008). It has yet to be demonstrated that this agent can augment the acquisition of attentional habits, but were this to be the case, it would seem reasonable to hypothesize that it would increase the efficacy of training.

Are these results relevant to depression? A quick appraisal of the studies summarized in Tables 1 and 2 demonstrates that both pharmacological and psychological manipulations of attention have been assessed using relatively brief stimulus presentations, with all but one of the studies presenting stimuli for 700 msec or less. Consequently, it may be easier to argue that these findings are relevant to anxiety, which is associated with perturbations of early attentional deployment, than that they are relevant to depression, which is associated with later effects (Mathews & MacLeod, 2005). Indeed, the single study that employed longer presentation times (Wells & Beavers, in press) presented stimuli for a much longer duration than that reported in the depression studies. It is not necessarily the case that there are no effects at the latencies typically reported for depression; rather, the studies that would assess these effects have yet to be performed or published. If the modification of attention is, indeed, relevant to the treatment of depression, it would be expected that both pharmacological and cognitive interventions would alter attention when measured at 1,000 msec. In addition, as has been suggested by the anxiety literature, reduction of the negative attentional bias measured at 1,000 msec, using a training paradigm, would be predicted to improve the symptoms of depression.

Future directions. Although we have focused on using measures of emotional attention to dissect the effects of clinical and experimental interventions, the same measures may also be sensitive to individual differences in genetic risk. For example, the long allele of the promoter region of the serotonin transporter gene (5-HTTLPR), which may confer resistance to emotional disorders (Munafò et al., 2009), has recently been found to be associated with a positive attentional bias (Fox, Ridgewell, &

Ashwin, 2009). Alterations in measures of attentional bias may thus provide a proxy marker by which both risk factors and treatment can be compared, within subgroups of patients and, ultimately, within a single individual. The identification of intermediate processes, such as attentional bias, which are believed to play a key role in the transition of risk to illness and treatment to response, is an essential first step in tailoring treatments to individual patients. An interesting initial approach to this issue would be to assess the interaction between genotype and attentional modification. Specifically, do particular genotypes increase or decrease the effects of antidepressants and cognitive training on attention?

Conclusion

In the present review, we have argued that the alteration of attentional bias (assessed using both behavioral and neuroimaging outcomes) is a sensitive, proximal measure of treatment effect for the emotional disorders. We have demonstrated that both pharmacological and cognitive interventions are able to alter attentional biases and that they seem to do so via distinct mechanisms. Future work needs to compare these manipulations directly, using similar outcome measures to understand to what extent they have similar and distinct actions. By unifying our understanding of evidence-based pharmacological and psychological treatments of emotional disorders, recent advances in cognitive-emotional science provide a guiding framework by which such treatments can be rationally combined and developed. This exciting approach offers a theoretically based, clinically informed opportunity to improve treatment efficacy.

AUTHOR NOTE

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