



Neural time course of threat-related attentional bias and interference in panic and obsessive–compulsive disorders



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ABSTRACT

Attentional biases to threat are considered central to anxiety disorders, however physiological evidence of their nature and time course is lacking. Event-related potentials (ERPs) characterized sensory and cognitive changes while 20 outpatients with panic disorder (PD), 20 with obsessive–compulsive disorder (OCD), and 20 healthy controls (HCs) responded to the color (emotional Stroop task) or meaning of threatening and neutral stimuli. ERPs indicated larger P1 amplitude and longer N1 latency in OCD, and shorter P1 latency in PD, to threatening (versus neutral) stimuli, across instructions to attend to, or ignore, threat content. Emotional Stroop interference correlated with phobic anxiety and was significant in PD. Participants with emotional Stroop interference had augmented P1 and P3 amplitudes to threat (versus neutral) stimuli when color-naming. The results suggest early attentional biases to threat in both disorders, with disorder-specific characteristics. ERPs supported preferential early attentional capture and cognitive elaboration hypotheses of emotional Stroop interference.

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1. Introduction

The clinical presentation of anxiety disorders includes cognitive, affective, somatic and behavioral changes (APA, 2000; Zacharko, Koszycki, Mendella, & Bradwejn, 1995). Cognitive alterations include a focus on thought content related to danger (Rachman, 2007; Tata, Leibowitz, Prunty, Cameron, & Pickering, 1996), and sensitivity to threat-related cues in the environment (MacLeod, 2004). Attentional biases to threat appear to be causally related to clinical anxiety (MacLeod, 2004). They predict, for example, cortisol reactivity to stress, which may present a vulnerability to anxiety disorders (Fox, Cahill, & Zougkou, 2010). Threat-related biases are therefore implicated as central to the etiology and maintenance of anxiety disorders (Williams, Mathews, & MacLeod, 1996).

Over three decades, many studies have investigated threat-related biases in clinical and healthy populations, mostly relying on indirect measures such as reaction time (RT) impairment in secondary tasks when threat stimuli are present. RT studies have limitations in that they only allow for the study of biases accompanied by measurable behavioral changes, whereas attentional biases can occur independently of behavioral interference (e.g.

Thomas, Johnstone, & Gonsalvez, 2007; van den Heuvel et al., 2005). RT studies also provide little information about the relative involvement of sensory versus cognitive processes in threat-related biases. The nature and timing of anomalies is of theoretical and clinical importance (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van Ijzendoorn, 2007), as distinctions may guide treatments. Recently, neuroimaging studies have advanced our understanding of brain regions activated during threat processing in anxious and healthy participants, however neuroimaging studies also lack the temporal resolution to localize biases to specific information-processing stages. Additionally, RT and imaging studies indicate that brain and behavioral responses to phobic stimuli differ between obsessive–compulsive and other disorders (van den Heuvel et al., 2005), however these differences remain incompletely understood and controversial (Moritz et al., 2004).

1.1. Imaging studies of threat processing

A key laboratory method for investigating threat-related biases is the emotional Stroop task. In this task, slower RTs when naming ink-color of threat versus neutral words are interpreted to indicate the presence of attentional biases, however usually no direct measure of attention is employed. Relatively recently, neuroimaging studies have shown that emotional Stroop tasks activate the affective (“rostral”) subdivision of the anterior cingulate cortex (Bush, Luu, & Posner, 2000; Whalen et al., 1998). In healthy

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individuals, reduced amygdala activity has been noted when color-naming threat words, which may indicate appropriate regulation of responses to irrelevant threats (Compton et al., 2003). Because behavioral interference is typically absent in healthy participants (Bishop, 2007; Whalen et al., 1998), however, clinical comparisons are needed.

In an fMRI study of the emotional Stroop task (van den Heuvel et al., 2005), PD participants were slower to color-name panic-related words, correlating with increased activation of the right amygdala. Participants with OCD were unimpaired when color-naming OCD related words, but showed increased bilateral amygdala activation relative to HCs, and increased right amygdala activation compared to patients with PD. These effects were interpreted to indicate attentional biases to disorder-specific stimuli in OCD and PD (van den Heuvel et al., 2005). Additionally, OCD imaging studies show increased activation in orbitofrontal–subcortical, limbic and occipital regions during symptom provocation (Adler et al., 2000; Breiter & Rauch, 1996; Chen, Xie, Han, Cui, & Zhang, 2004; Nakao et al., 2005; Rauch, Savage, Alpert, Fischman, & Jenike, 1997; van den Heuvel et al., 2004), indicating heightened neural responses to phobic stimuli.

Despite improved understanding of the brain regions involved in emotional biases and emotional Stroop interference, imaging and RT studies have yet to clearly determine the time course and nature of information-processing mechanisms contributing to emotional Stroop interference. These could include facilitated sensory capture (Mogg, Bradley, De Bono, & Painter, 1997), delayed disengagement (Fox, Russo, Bowles, & Dutton, 2001), effortful avoidance or cognitive elaboration of threat stimuli (Bar-Haim et al., 2007; Kyrios & Iob, 1998). Alternatively, both early, automatic biases towards threat followed by avoidance of threatening stimuli during more strategic stages of processing (or vigilance-avoidance patterns) have been proposed (Bar-Haim et al., 2007; Mogg, Bradley, De Bono, & Painter, 1997; Williams, Watts, MacLeod, & Mathews, 1997). Additionally, while all interpretations of emotional Stroop interference imply that primary processes (such as preferential processing or avoidance of threat) lead to secondary effects (delayed color naming), most studies offer no direct evidence of the primary processes. Emerging anxiety treatments are able to target early, automatic biases to threat (Cisler & Koster, 2010) in addition to well established treatments such as cognitive-behavioral therapy which target more strategic processes. A greater understanding of the nature and timing of biases may help to refine treatments.

1.2. ERP studies of threat processing in clinical anxiety

Event-related potentials' (ERPs') exquisite temporal resolution and sensitivity to emotional processing provide a means to directly measure neural activity associated with threat processing and interference. ERP components occurring relatively early (e.g. the P1, N1 and P2 components) primarily reflect neural activity during sensory processing, whereas those occurring later (e.g. the N2, P3 components and late positive potentials or LPPs) reflect neural activity expended during higher-level cognition including inhibitory and memory-updating processes (Duncan-Johnson & Donchin, 1982; Kok, 2001; Picton, 1992). ERPs are sensitive to both the extent (amplitude) and speed (latency) of processing during sensory and cognitive stages, and can therefore potentially differentiate between hypotheses about the mechanisms underlying emotional Stroop interference. For example, P1 amplitude increases with attention to visual stimuli, with recruitment of extrastriate neurons to visual processing (Carretié et al., 2009; Hopfinger & Mangun, 2001; Martinez et al., 1999; Smith, Cacioppo, Larsen, & Chartrand, 2003), hence can provide a measure of the intensity and speed of sensory processing of threat versus neutral stimuli. Additionally, P3 amplitude is increased to meaningful or

emotionally salient stimuli and is decreased to stimuli when participants are attending to another task, like reading a book (Kok, 2001). ERPs can therefore offer insight into primary processes involved in attention to threat and their relationship to secondary interference.

ERP research examining attention to phobic stimuli in clinical anxiety is currently scant. People with social phobia displayed enhanced right hemisphere N170, an ERP component linked to face processing, in the absence of behavioral effects, indicating anomalies in the early visual processing of angry faces (Kolassa & Miltner, 2006). Additionally, individuals with spider phobias had larger parietal P300 amplitudes to spiders in a pictorial emotional Stroop task, indicating enhanced attention during central cognitive stages. In a visual dot probe task, socially phobic participants had potentiated P1 amplitudes to angry-neutral versus happy-neutral face-pairs and decreased P1 amplitudes to probes replacing emotional faces, taken to indicate hypervigilance-avoidance patterns of attention (Mueller et al., 2009). While these studies have provided additional information about attentional biases to threat in anxiety, pictorial stimuli do not reliably induce RT interference (Kindt & Brosschot, 1999; Kolassa & Miltner, 2006; Kolassa, Musial, Mohr, Trippe, & Miltner, 2005; Lavy, van den Hout, & Arntz, 1993; Mueller et al., 2009), hence these studies have not determined the mechanisms mediating emotional Stroop interference.

There is evidence that emotional content influences ERPs to words during early time windows such as the P1 time window (80–120 ms; Bayer, Sommer, & Schacht, 2012; Bernat, Bunce, & Shevrin, 2001; Junghöfer, Bradley, Elbert, & Lang, 2001; Li, Zinbarg, & Paller, 2007; Scott, O'Donnell, Leuthold, & Sereno, 2009), and that involuntary attention allocation in the visual cortex is not limited to pictorial stimuli, but can occur for word stimuli which have only arbitrary relationships between their visual features and corresponding meaning (Bayer et al., 2012; Ortigue et al., 2004; Rabovsky, Sommer, & Abdel Rahman, 2011). While such effects occur earlier than serial models of language processing would predict, there are proposals that word emotional valence detection may precede and facilitate lexical access (Conrad, Recio, & Jacobs, 2011) and that semantic features can influence sensory processing in the extrastriate cortex (Rabovsky et al., 2011). Alternatively, nonlinguistic mechanisms may contribute to early emotion effects, such as feature detection or associative learning processes that do not depend on lexical access (Bayer et al., 2012).

Only one study has examined ERPs associated with color-naming emotional words in clinical anxiety (post traumatic stress disorder; Metzger, Orr, Lasko, McNally, & Pittman, 1997). While ERPs did not reveal the source of emotional Stroop interference, only the P3 component was analyzed, leaving the possibility that earlier or later effects were overlooked. The small sample size ($n=9$) may also have limited the power to detect differences.

1.3. ERPs during traditional Stroop tasks

Numerous ERP studies have examined interference effects in traditional (non-emotional) Stroop tasks. These involve enhanced fronto-central or broad negativity 350–500 ms possibly indexing conflict (Liotti, Woldorff, Perez III, & Mayberg, 2000), and a sustained negativity over lateral frontal areas and greater positivity centro-parietally, possibly reflecting additional processing of word meaning (Liotti et al., 2000; West, 2003). Emotional and traditional Stroop tasks, however, differ on important dimensions. Only traditional Stroop tasks evoke direct conflict between stimulus dimensions (e.g. the word red appearing in blue font), and neural changes during emotional Stroop tasks are likely indexing emotional salience and interference rather than conflict (Algom, Chajut, & Lev, 2004), necessitating separate investigations.

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