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Relationships among attention networks and physiological responding to threat

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ABSTRACT

Although researchers have long hypothesized a relationship between attention and anxiety, theoretical and empirical accounts of this relationship have conflicted. We attempted to resolve these conflicts by examining relationships of attentional abilities with responding to predictable and unpredictable threat – related but distinct motivational process implicated in a number of anxiety disorders. Eighty-one individuals completed a behavioral task assessing efficiency of three components of attention – alerting, orienting, and executive control (Attention Network Test - Revised). We also assessed startle responding during anticipation of both predictable, imminent threat (of mild electric shock) and unpredictable contextual threat. Faster alerting and slower disengaging from non-emotional attention cues were related to heightened responding to unpredictable threat, whereas poorer executive control of attention was related to heightened responding to predictable threat. This double dissociation helps to integrate models of attention and anxiety and may be informative for treatment development.

1. Introduction

Researchers have long posited a relationship between attention and anxiety (e.g., Daly, Vangelisti, & Lawrence, 1989; Masters & Johnson, 1970; Wine, 1971). Although a large literature indicates that anxiety is associated with biased attention towards emotional (i.e., threat-related) stimuli (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007), it is not clear whether and in what way anxiety is related to general attention to non-emotional stimuli. Better characterizing the latter relationship has the potential to improve our understanding of anxiety disorder etiology and has implications for treatments such as attention bias modification and cognitive remediation.

One prominent model posits that attention consists of three processes – alerting, orienting, and attentional control – subserved by separable but interacting brain networks (Petersen & Posner, 2012; Posner & Petersen, 1990). *Alerting* consists of vigilance and response readiness – either tonic (i.e., sustained over long periods) or phasic (i.e., a temporary increase in readiness in response to a warning signal). The alerting network consists of the locus coeruleus and its noradrenergic projections to widespread cortical and subcortical regions (Fan, McCandliss, Fossella, Flombaum, & Posner, 2005; Marrocco, Witte, & Davidson, 1994; Petersen & Posner, 2012). *Orienting* consists of selection or prioritization of some sensory inputs over others for processing. Orienting includes both *engaging* attention with selected input and *disengaging* from previously attended input. Engaging is subserved by a dorsal orienting network including superior parietal lobule and frontal eye fields, whereas disengaging is subserved by a ventral orienting network including temporoparietal junction and middle and inferior frontal gyri (Corbetta & Shulman, 2002; Petersen & Posner, 2012). Finally, *attentional control* (or *executive control of attention*) is the effortful process of allocating attention in the face of competing or conflicting demands, such as when a habitual, automatic, or otherwise dominant response to a stimulus must be withheld to

Abbreviations: 5HTTLPR, serotonin transporter-linked polymorphic region; ACC, anterior cingulate cortex; ANT-R, Attention Network Test – Revised; BNST, bed nucleus of the stria terminalis; CD, countdown; CeA, central amygdala; COMT, catechol-*O*-methyltransferase; dlPFC, dorsolateral prefrontal cortex; IFG, inferior frontal gyrus; ISI, interstimulus interval; IUS, Intolerance of Uncertainty Scale; NPU task, No Shock-Predictable-Unpredictable task; vmPFC, ventromedial prefrontal cortex.

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attend to an alternative stimulus. This component of attention is closely linked to emotion regulation and other self-regulatory abilities (Posner & Rothbart, 2013; Zelazo & Cunningham, 2007). Attentional control is subserved by cingulo-opercular and frontoparietal networks, in which the anterior cingulate cortex (ACC) and dorsolateral prefrontal cortex (dlPFC), respectively, play key roles (Matsumoto & Tanaka, 2004; Petersen & Posner, 2012).

Most research on attention and anxiety has examined differences in how anxious people attend to threat-related or other emotional stimuli – a form of emotional or "hot" cognition (Metcalfe & Mischel, 1999). This research indicates that individuals with anxiety disorders or high trait anxiety demonstrate biased attention towards threat cues, particularly when these cues are presented briefly or subliminally (Bar-Haim et al., 2007; Mathews & MacLeod, 2005). This bias may result from facilitated engaging with threat, impaired disengaging from threat, or both (Armstrong & Olatunji, 2012; Yiend, 2010).

These findings are most frequently interpreted as indicating that, because anxious individuals are preoccupied with threat, their attention systems prioritize threat cues for faster and longer processing. However, attention bias findings could also reflect that anxiety is associated with broader differences in how attention networks function, even in processing non-emotional stimuli (Bishop, 2009). That is, anxious individuals may engage with threat cues more quickly and dwell on them for longer not only because these cues are more salient for them, but also because they attend more quickly to or disengage more slowly form *all* salient cues, regardless of emotional content. Anxious individuals may also have diminished ability to inhibit automatic attention towards salient cues (i.e., diminished attentional control). Indeed, the relationship between anxiety and biased attention to threat is more pronounced in individuals with low self-reported attentional control (Bardeen & Orcutt, 2011; Derryberry & Reed, 2002). In line with these possibilities, several more recent theories propose relationships between anxiety and aspects of general, non-emotional, or "cold" attention. These theories also specify how anxiety is related to different attention networks, whereas the tasks used in "hot" attention bias studies generally cannot cleanly separate effects due to alerting, orienting, and attentional control.

These theories are broadly consistent in predicting that trait anxiety is associated with abnormalities in attentional control, but differ in their predictions regarding orienting and alerting. Specifically, Eysenck and colleagues' attentional control theory (Eysenck & Derakshan, 2011; Eysenck, Derakshan, Santos, & Calvo, 2007) posits that trait anxiety causes less efficient attentional shifting (i.e., orienting) and distractor inhibition (i.e., attentional control) as processing demands increase. Bishop (2009), based on Lavie's (2000, 2005) load theory of selective attention, also maintains that anxiety is associated with poorer attentional control, but during conditions of *low* perceptual load. Sylvester et al. (2012) propose that anxiety is associated with increased functioning of the cingulo-opercular network and reduced functioning of the fronto-parietal network (both associated with executive control of attention), as well as increased functioning of the ventral attention network (associated with orienting and stimulus-driven alerting). According to their account, anxious individuals detect and orient towards task-irrelevant stimuli more easily due to overactivity of the ventral attention network. They are also less able to inhibit these alerting and orienting responses due to dysfunction in executive control networks. Thus, all three of these models predict that individuals high in anxiety will demonstrate poorer attentional control. Their predictions regarding anxiety's relationship with orienting are more divergent: Eysenck's model predicts poorer orienting, Sylvester's predicts enhanced orienting and alerting, and Bishop makes no prediction.

Consistent with these predictions, a number of studies have reported that trait anxiety and anxiety disorders are associated with lower self-reported attentional control (Armstrong, Zald, & Olatunji, 2011; Reinholdt-Dunne, Mogg, & Bradley, 2013) and less efficient performance on behavioral measures of attentional control (Bishop, 2009; Pacheco-Unguetti, Acosta, Callejas, & Lupianez, 2010; Pacheco-Unguetti, Acosta, Marqués, & Lupiáñez, 2011). However, this relationship has not been universally observed. Some studies have reported that trait anxiety or related constructs (e.g., behavioral inhibition) are *not* associated with attentional control, and have instead reported relationships with orienting (Garner, Attwood, Baldwin, & Munafò, 2012; Moriya & Tanno, 2009; Tull, Maack, Viana, & Gratz, 2012) or alerting (Dennis, Chen, & McCandliss, 2008; Garner et al., 2012).

All of these studies examined relationships of attention with self-reported anxiety or similar traits. This raises two potential explanations for the inconsistency of findings. First, trait anxiety and related concepts are broad, heterogeneous constructs; it may be that different subcomponents of trait anxiety are related to attention in different ways, producing inconsistencies in the literature. Focusing on more specific affective processes that underlie broad trait anxiety may clarify this issue. Second, cognition and self-report are relatively distal levels of analysis, making it difficult to consistently find relationships between them (Kendler, 2005; Lilienfeld, 2007). More robust relationships may be found by examining constructs at a level of analysis more proximal to cognition, such as psychophysiology.

To address both of these concerns, the present study examined two well-validated motivational processes underlying broad trait anxiety – sensitivity to predictable, certain, imminent harm (often labeled "fear"), and sensitivity to unpredictable, uncertain, contextual threat (often labeled "anxiety," Barlow, 2000; Davis, 2006; Davis, Walker, Miles, & Grillon, 2010; Gray & McNaughton, 2000; Grillon, 2002). These processes are often assessed by measuring eye blink acoustic startle response during anticipation of cued (i.e., predictable) and uncued (i.e., unpredictable) aversive stimuli, respectively (Schmitz & Grillon, 2012). Phasic responding to predictable threat cues is subserved by a circuit including the medial central amygdala (CeA) and projecting primarily to the hypothalamus and brainstem nuclei. Tonic responding to unpredictable threat contexts is subserved by a circuit including the lateral bed nucleus of the stria terminalis (BNST) and lateral CeA (Alvarez, Chen, Bodurka, Kaplan, & Grillon, 2011; Davis, 2006; Davis et al., 2010; Somerville et al., 2013).

In addition to their unique neuroanatomical correlates, the discriminant validity of these processes is supported by their differential response to pharmacological challenge (Grillon et al., 2015; Grillon et al., 2006; Moberg & Curtin, 2009) and differential familial/genetic associations (Nelson et al., 2013; Sarapas et al., 2012). Most importantly, the two processes have discriminant validity for different forms of psychopathology. Exaggerated responding to predictable threat has been associated with specific phobia (McTeague, Lang, Wangelin, Laplante, & Bradley, 2012) and suicidality (Ballard et al., 2014), whereas exaggerated responding to unpredictable threat is associated with posttraumatic stress disorder (Grillon et al., 2009). Given their unique physiological mechanisms and clinical correlates, examination of these two motivational processes may clarify whether different aspects of attention are related to different psychopathology-related processes and outcomes. Indeed, several lines of evidence suggest that predictable vs. unpredictable threat responding may be differentially related to components of attention.

First, the processes are relevant to situations with somewhat different cognitive demands. Unpredictably threatening contexts require sustained vigilance for potential danger and the ability to rapidly detect and orient towards danger when it appears.