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Vigilance in the laboratory predicts avoidance in the real world: A dimensional analysis of neural, behavioral, and ecological momentary data in anxious youth



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ABSTRACT

Vigilance and avoidance of threat are observed in anxious adults during laboratory tasks, and are posited to have real-world clinical relevance, but data are mixed in anxious youth. We propose that vigilanceavoidance patterns will become evident in anxious youth through a focus on individual differences and real-world strategic avoidance. Decreased functional connectivity between the amygdala and prefrontal cortex (PFC) could play a mechanistic role in this link, 78 clinically anxious youth completed a dot-probe task to assess vigilance to threat while undergoing fMRI. Real-world avoidance was assessed using Ecological Momentary Assessment (EMA) of self-reported suppression and distraction during negative life events. Vigilance toward threat was positively associated with EMA distraction and suppression. Functional connectivity between a right amygdala seed region and dorsomedial and right dorsolateral PFC regions was inversely related to EMA distraction. Dorsolateral PFC-amygdalar connectivity statistically mediated the relationship between attentional vigilance and real-world distraction. Findings suggest anxious youth showing attentional vigilance toward threat are more likely to use suppression and distraction to regulate negative emotions. Reduced PFC control over limbic reactivity is a possible neural substrate of this pattern. These findings lend ecological validity to laboratory vigilance assessments and suggest PFC-amygdalar connectivity is a neural mechanism bridging laboratory and naturalistic contexts. © 2016 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND

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1. Introduction

Anxious youth, like anxious adults, display a pattern of vigilant attention toward threat-relevant cues in the laboratory (Bar-Haim et al., 2007). Biased attention toward threat is posited to contribute to the maintenance of anxiety over time (MacLeod et al., 1986), providing persistent opportunities for both physiological reactions and anxiety-promoting beliefs (e.g., the world is full of danger) to be rehearsed. When present in youth, threat vigilance may therefore represent a key mechanism through which life-long trajectories of affective psychopathology (Pine et al., 1998) are initiated and maintained.

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An excessive focus on threat may promote anxious physiological responding and maladaptive cognitions, but clinical manifestations of anxiety are largely characterized by persistent avoidance of threat. Mogg et al. (2004) proposed a vigilance-avoidance model of cognitive bias in anxiety, suggesting that following early attentional vigilance to threat cues, anxious individuals strategically direct attention away from threat in an attempt to decrease anxiety elicited by aversive stimuli (i.e., avoidance is used as an emotion regulation strategy). Avoidant attentional patterns during late stages of stimulus presentation (i.e., >1500 ms post-onset) have been observed in at least some studies of anxious adults (e.g., Bogels and Mansell, 2004)-although avoidance is not strictly confined to late time points in the adult literature, but has also been observed at early time points, particularly when threat severity is strong (Wald et al., 2011; Shechner et al., 2012). In youth, vigilanceavoidance findings are decidedly mixed. While vigilance to threat is relatively well-established in pediatric samples (Bar-Haim et al., 2007)-although there are clear exceptions, e.g., in the fMRI scanner (Monk et al., 2006)-avoidance findings are quite inconsistent,

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ranging from the hypothesized vigilance-avoidance pattern (In-Albon et al., 2010), to avoidance at early timepoints only (Gamble and Rapee, 2009), to early vigilance with no later group differences (Shechner et al., 2013), to consistent attentional patterns across anxious and non-anxious youth at both early and later timepoints (Price et al., 2013). One possibility is that subsets of anxious youth differ in their attentional patterns (Salum et al., 2012); but the vigilance-avoidance hypothesis implies that the same individuals would be prone to both early vigilance and later avoidance. An additional possibility is that attention measured on the time-course of seconds in the laboratory (even at stimulus presentations ≥ 2 s) represents relatively "automatic" (i.e., involuntary, routinized) forms of avoidance (Najmi et al., 2010; Buetti et al., 2012) that may not be fully developed in youth. If this were the case, we might more readily see avoidance in a less automatic form, i.e., deployed as a strategic (i.e., voluntary, effortful) emotion regulation response to real-world stressors. However, previous attentional bias studies have been limited to laboratory assessments of both vigilance and avoidance, leaving this potential pattern uninvestigated.

Ecological Momentary Assessment (EMA) is an ecologically valid method for characterizing emotional reactivity and emotion regulation through repeated in vivo sampling. It entails the gathering of representative real-time data on emotion and behavior in natural environments through the use of signaling devices (Silk et al., 2011). EMA is designed to overcome several limitations of laboratorybased assessments. It accesses emotions experienced in real-world contexts and circumvents memory biases associated with delayed retrospective recall. EMA studies in adults have found that compared to non-anxious individuals, those with social anxiety report higher rates of a specific type of avoidance, experiential avoidance, which is defined as efforts to escape, avoid, alter, or conceal undesirable emotions or thoughts (Kashdan et al., 2013). Conversely, in the only EMA study to date to assess avoidance in anxious youth, anxious and control youth used avoidance with comparable frequency (Tan et al., 2012). A focus on individual differences on an EMA measure of avoidance would enable a direct examination of the hypothesis that laboratory-assessed vigilance in anxious youth is associated with strategic, real-world avoidance. This focus on individual differences may be critical to understanding the role of vigilance in anxiety if, for example, a subset of anxious patients exhibit a high degree of attentional bias, and also show a greater degree of real-world maladaptive avoidance.

Neuroimaging studies have pointed to prefrontal-limbic functional connectivity as a key neural mechanism that is altered during attentional bias tasks in both anxious youth (Price et al., 2014; Monk et al., 2008) and young adults with a childhood history of behavioral inhibition (Hardee et al., 2013). In a previous group comparison of anxious and healthy youth using an overlapping dataset (Price et al., 2014), we reported that anxious youth as a group, particularly the most severely anxious among the clinical sample, were characterized by reduced integration of response across prefrontal (rostrodorsal anterior cingulate) and limbic (hippocampal/parahippocampal) regions during an attentional bias (dot-probe) task. Decreased communication and synchronization between bottom-up limbic regions (reacting to threat) and top-down prefrontal regions (controlling attention) are posited to contribute to anxiety and threat hypervigilance (Bishop, 2008), resulting in reduced capacity to override threat orienting and attentional capture. Because amygdala-prefrontal connectivity subserves both automatic and controlled processing, it may be mechanistically important in both vigilance and avoidance. Specifically, reduced integration in this circuit during threat processing could foster both hyperactive early/automatic responses to threat (vigilance) and overreliance on maladaptive forms of voluntary emotion regulation (e.g., avoidance) in the real world-particularly given that adaptive alternatives for strategic emotion regulation

Table 1

Descriptive characteristics of the sample.

Anxious youth $(n = 78)$	
Age	10.7 (1.4)
Female (%)	56.4
Caucasian (%)	85.9
Head of household education, median	Standard college degree
Household income, median	\$80-90,000
Current diagnosis ^a (%)	
Separation anxiety disorder	20.5
Social phobia	24.4
Generalized anxiety disorder	73.1
Specific phobia	15.4
Major depressive disorder	1.3
Attention deficit/hyperactivity disorder	2.6
Pediatric Anxiety Rating Scale	20.7 (4.6)
EMA suppression use, % of negative events EMA distraction use, % of negative events Mean RT bias	71.8% (29.5%) 43.4% (25.7%) 14.2 (114.9)

Note. Data presented as mean (SD) unless otherwise noted. EMA=Ecological Momentary Assessment; RT=reaction time.

^a Diagnostic groups are partially overlapping due to inclusion of comorbid patients. Primary/principle diagnoses were not designated, meaning that percentages for the 3 diagnostic inclusion groups will not sum to 100.

(e.g., cognitive restructuring) may rely on functional integration within the same circuit (Wager et al., 2008). Current analyses provide novel information regarding the extent to which attentional vigilance and real-world avoidance are linked to one another, and to functional integration within this threat processing circuit.

In summary, the current study assessed individual differences in attentional vigilance, related neural substrates, and real-world use of avoidance as an emotion regulation strategy in a sample of 78 clinically anxious youth. We predicted that (a) greater attentional vigilance in the lab and (b) reduced PFC-amygdalar functional connectivity would be associated with greater real-world engagement in avoidance following a negative event, assessed via EMA. To further understand the extent to which observed neural function might be mechanistically important, we tested whether PFC-amygdalar connectivity statistically mediated the relationship between vigilance and avoidance. While primary analyses and conclusions pertain to the sample of anxious youth, we used available data from a small sample of control youth (n=20) to conduct preliminary explorations of whether observed mechanistic relationships were specific to clinical anxiety or might generalize across the full spectrum of anxious and non-anxious youth.

2. Methods

2.1. Participants

Seventy-eight unmedicated youth (ages 9-14) with DSM-IV diagnoses of Generalized Anxiety Disorder, Separation Anxiety Disorder, and/or Social Phobia were recruited through a larger treatment outcome study (see Table 1 for further details). These three prevalent diagnoses were included to allow investigation of transdiagnostic biobehavioral patterns, a growing priority in psychiatric research (e.g., Research Domain Criteria initiative; Insel et al., 2010). A comparison sample of 20 youth with no lifetime history of DSM-IV-TR disorders also completed all measures (see Table S1a). The larger study was designed to have an uneven allocation due to the primary focus on mechanisms of treatment for pediatric anxiety (treatment outcomes are presented in Silk et al. (in press)). The present analyses therefore focused on the anxious sample, where power was sufficient to permit an individual differences approach. The control sample was used in sensitivity analyses only, allowing us to preliminarily assess the specificity of any observed links to anxious youth.

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