Reduced Dorsal Anterior Cingulate Cortical Activity During Emotional Regulation and Top-Down Attentional Control in Generalized Social Phobia, Generalized Anxiety Disorder, and Comorbid Generalized Social Phobia/Generalized Anxiety Disorder

Karina S. Blair, Marilla Geraci, Bruce W. Smith, Nick Hollon, Jeffrey DeVido, Marcela Otero, James R. Blair, and Daniel S. Pine

Background: Generalized social phobia (GSP) and generalized anxiety disorder (GAD) are both associated with emotion dysregulation. Research implicates dorsal anterior cingulate cortex in both explicit emotion regulation (EER) and top-down attentional control (TAC). Although studies have examined these processes in GSP or GAD, no work compares findings across the two disorders or examines functioning in cases comorbid for both disorders (GSP/GAD). Here we compare the neural correlates of EER and TAC in GSP, GAD, and GSP/GAD.

Methods: Medication-free adults with GSP (EER $n = 19$; TAC $n = 18$), GAD (EER $n = 17$; TAC $n = 17$), GSP/GAD (EER $n = 17$; TAC $n = 15$), and no psychopathology (EER $n = 18$; TAC $n = 18$) participated. During EER, individuals alternatively viewed and upregulated and downregulated responses to emotional pictures. During TAC, they performed an emotional Stroop task.

Results: For both tasks, significant group $\times$ condition interactions emerged in dorsal anterior cingulate cortex and parietal cortices. Healthy adults showed significantly increased recruitment during emotion regulation, relative to emotion-picture viewing. GAD, GSP, and GSP/GAD subjects showed no such increases, with all groups differing from healthy adults but not from each other. Evidence of emotion-related disorder-specificity emerged in medial prefrontal cortex and amygdala. This disorder-specific responding varied as a function of emotion content but not emotion-regulatory demands.

Conclusions: GSP and GAD both involve reduced capacity for engaging emotion-regulation brain networks, whether explicitly or via TAC. A reduced ability to recruit regions implicated in top-down attention might represent a general risk factor for anxiety disorders.

Key Words: Anterior cingulate cortex, emotion regulation, generalized anxiety, imaging, social anxiety, top-down attentional control

Generalized social phobia (GSP) and generalized anxiety disorder (GAD) are two highly disabling, frequently comorbid conditions (1). GSP involves anxiety to social situations, whereas GAD involves excessive worry, often involving both social and non-social themes. Although some imaging suggests that similar neural architecture underlies these two disorders (e.g., Martin *et al.* [2]), few directly compare them. Many imaging studies examine GSP, fewer examine GAD, and none directly compare the two in their noncomorbid state. This study directly compares GSP, GAD, and comorbid GSP/GAD.

Clinical data indicate impaired emotional regulation in both GSP and GAD (e.g., Mennin *et al.* [3] and McClure and Pine [4]). Accordingly, GSP/GAD comorbidity might reflect shared dysfunction in brain regions supporting emotion regulation. However, emotional regulation is a broad term that subsumes a range of cognitive processes (5). Within this range, it has been argued that emotional regulation can engage two sets of control processes—based in dorsal and ventral brain systems—that are differentially affected across the mood and anxiety disorders (6,7).

The first type of emotion regulation involves ventral prefrontal systems that represent emotional value and select actions on the basis of these representations. Altering the strength of reinforcement-valence representations might, through reciprocal mechanisms with systems such as the amygdala, reduce emotional responses. Similarly, ventral anterior cingulate cortex (ACC) might specifically support conflict adaptation, a form of emotional regulation (8). These forms of emotional regulation have received minimal attention with respect to GAD and GSP (however, see Etkin *et al.* [8]) and will not be the focus of this article.

The second type involves dorsal prefrontal cortex (both medial and lateral regions). Attention control represents one vital function of these systems, the priming of relevant representations at the expense of irrelevant ones, thereby resolving representational competition (9). Arguably, such control processes can be recruited explicitly within cognitive reappraisal paradigms, where subjects willfully attempt to alter stimulus representations by priming nonemotional features (10). These processes also might be recruited implicitly through attention distraction paradigms (11–13), where the reduction of emotional responding occurs "... without monitoring ... without insight and awareness" (page 401 in Gyurak *et al.* [5]).

The process of cognitive reappraisal recruits lateral and dorsomedial frontal cortices, dorsal anterior cingulate cortex (dACC), and infe-

From the National Institute of Mental Health (KSB, MG, NH, JD, MO, JRB, DSP), National Institutes of Health, Department of Health and Human Services, Bethesda, Maryland; and the Department of Psychology (BS), University of New Mexico, Albuquerque, New Mexico.

Address correspondence to Karina S. Blair, Ph.D., National Institute of Mental Health, National Institutes of Health, Department of Health and Human Services, 15K North Drive, Rm 115A, MSC 2670, Bethesda, MD 20892-2670; E-mail: peschark@mail.nih.gov.

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Table 1. Subject Characteristics

	GSP	GSP/GAD	GAD	HC	p^a
EER, *n*	19	17	17	18	
TAC, *n*	18	15	17	18	
Age					
EER	29.4 (8.70)	35.7 (9.54)	36.1 (11.75)	33.4 (9.65)	ns
TAC	31.8 (9.10)	33.5 (10.57)	34.9 (10.93)	30.4 (6.86)	ns
Gender					
EER	10 F/8 M	12 F/5 M	13 F/4 M	10 F/8 M	ns
TAC	8 F/10 M	10 F/5 M	10 F/7 M	9 F/9 M	ns
IQ					
EER	123.6 (9.36)	116.7 (12.88)	119.9 (9.20)	116.0 (10.56)	ns
TAC	118.5 (11.98)	118.1 (14.14)	119.1 (9.34)	118.5 (11.90)	ns
LSAS-SR					
EER	73.2 (24.52)	67.4 (20.10)	45.7 (18.23)	16.8 (10.23)	<.001
TAC	75.8 (22.79)	68.7 (20.34)	42.3 (17.31)	15.3 (12.26)	<.001
BAI					
EER	8.6 (7.05)	12.0 (7.12)	12.2 (7.34)	2.3 (2.02)	<.001
TAC	8.8 (6.25)	13.3 (6.18)	11.6 (6.73)	1.1 (1.37)	<.001
STAI-T					
EER	49.1 (9.91)	48.6 (9.12)	49.1 (5.0)	—	ns
TAC	50.8 (10.14)	47.5 (10.63)	44.9 (9.40)	—	ns
IDS					
EER	16.7 (9.85)	23.7 (5.92)	16.9 (7.91)	3.7 (4.79)	<.001
TAC	15.5 (8.27)	24.4 (6.72)	19.1 (7.03)	3.7 (4.96)	<.001

Values given as *n* (SD).

BAI, Beck's Anxiety Inventory; EER, explicit emotion regulation; GAD, generalized anxiety disorder; GSP, generalized social phobia; HC, healthy comparison individuals; IDS, Inventory of Depressive Symptomatology; LSAS-SR, Liebowitz Social Anxiety Scale-Self Rated; ns, nonsignificant; STAI-T, Spielberger Trait-State Inventory—Part Trait; TAC, top-down attentional control.

[a] *p* values refer to the omnibus group tests.

rior parietal cortex (6) (see Kalisch for reviews [14]). Distraction paradigms also recruit these systems (13,15). Patients with GSP show reduced dACC engagement during explicit emotional downregulation of social emotional stimuli (16,17). However, a recent study found that a mixed anxiety-prone group, including patients with GSP or GAD, showed increased ventral and dACC during explicit emotion regulation (EER), relative to low-anxiety comparison individuals (18).

In short, decreased dACC recruitment occurs in GSP during explicit emotional regulation, at least with social stimuli. However, no study examines explicit emotional regulation in GAD, nor do studies examine recruitment of dACC and associated lateral fronto-parietal regions implicated in attentional control. Such recruitment is where emotional responses are implicitly regulated through task-related top-down attention. If patients with GSP, GAD, and GSP/GAD show general dysfunction in regions implicated in top-down attentional control (TAC) (i.e., lateral frontal, ACC, and parietal regions), one would expect all three patient groups to show reduced recruitment as a function of task demands independent of stimulus valence. In contrast, or additionally, we might see group × condition × emotion interactions. Pessoa (19) has argued that increased amygdala response to emotional stimuli interferes with the recruitment of regions implicated in related top-down attention control, and if patients show heightened amygdala responses to negative stimuli specifically, this response might be associated with disrupted recruitment of regions involved in top-down attention control. The current study tests these hypotheses.

Methods and Materials

Subjects

Four different patient groups participated in the study: patients with GSP only ($n = 19$ on the EER task, $n = 18$ on the TAC task), patients with GAD only ($n = 17$ on both tasks), patients with comorbid GSP/GAD ($n = 17$ on EER task, $n = 15$ on TAC task), and healthy comparison (HC) individuals ($n = 18$ on both tasks). Scanning sessions for the subjects completing both tasks were separated by at least 2 weeks. Table 1 shows that subjects were well-matched on demographic data but differed on symptom ratings.

Subjects were explicitly recruited to suffer from particular types of anxiety to facilitate direct comparisons among groups. Thus, patients with GSP could only meet criteria for GSP, subjects with GAD only met criteria for GAD, and subjects with comorbid GSP/GAD only met criteria for GSP and GAD, on the basis of the Structural Clinical interview for DSM-IV Axis I disorders (20) and a confirmatory clinical interview. No patient had any other current Axis I diagnosis; all were medication-free for at least 6 months. The HCs had no psychiatric illness. All subjects were in good physical health and were recruited from National Institute of Mental Health Institutional Review Board-approved fliers and advertisements.

Tasks

For subjects receiving both tasks, task order was counter-balanced both across subjects and across groups.

EER

Procedures followed those used in prior research on EER through reappraisal (e.g., [10,21]). Subjects viewed 30 positive and 30 negative International Affective Picture System pictures. As in prior studies, neutral pictures were not used to minimize confusion. Each picture was viewed three times, where subjects were asked to simply view the pictures, to reappraise them by thinking about them in a way that would make their content more positive (i.e., downregulating a negative image; upregulating a positive image),

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