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Emotion Regulation in Social Anxiety Disorder: Reappraisal and Acceptance of Negative Self-beliefs

Matthew L. Dixon, Craig A. Moodie, Philippe R. Goldin, Norman Farb, Richard G. Heimberg, and James J. Gross

ABSTRACT

BACKGROUND: Social anxiety disorder (SAD) is characterized by negative self-beliefs (NSBs) that are thought to maintain symptom severity—at least in part—by impairing emotion regulation. Few studies to date have investigated the neural basis of emotion regulation during NSBs in SAD. Moreover, different regulation strategies have not been directly compared, leaving open questions about the generality of emotion regulation deficits in SAD.

METHODS: Patients with SAD (n = 113) and healthy control subjects (n = 35) underwent functional magnetic resonance imaging while reacting to NSBs or attempting to downregulate negative emotions occasioned by NSBs using either reappraisal (reinterpreting negative beliefs) or acceptance (nonjudgmentally experiencing thoughts and emotions). Ratings of negative emotion were collected after each trial.

RESULTS: When cued to do so, patients with SAD were able to downregulate negative emotions using both reappraisal and acceptance and demonstrated effective recruitment of frontoparietal regulatory regions. Patients with SAD demonstrated greater activation of default mode network and somatomotor regions for the react versus accept contrast. Both groups demonstrated reductions in frontoparietal and default mode network activation during acceptance relative to reappraisal. Greater SAD symptom severity was associated with lower activation in frontoparietal regions during both regulation conditions.

CONCLUSIONS: There were no group differences in frontoparietal recruitment during two distinct emotion regulation strategies. However, individual differences in symptom severity within the SAD group were associated with frontoparietal regulation–related activation. Patients with SAD were differentiated from control subjects in default mode network recruitment patterns, suggesting that acceptance may be a useful task condition for revealing altered neural activity in SAD.

Keywords: Acceptance, Default mode network, Frontoparietal, Reappraisal, Regulation, Social anxiety

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Social anxiety disorder (SAD) is a pernicious and highly prevalent disorder (12.1% lifetime prevalence) with an early age of onset (1). SAD is characterized by excessive fear of being negatively evaluated by others and acting in ways that will be embarrassing (2). SAD is associated with substantial impairment in job performance and social relationships and frequently precedes the development of other disorders (3,4). Cognitive models propose that a core feature of SAD is negative self-beliefs (NSBs), for example, thinking that one is boring or flawed (5–7). NSBs are deeply ingrained thought patterns that distort incoming social information and trigger excessive emotional reactivity.

Emotion Regulation Deficits in SAD

There is considerable interest in understanding the extent to which emotion regulation deficits contribute to SAD (8–12). Reappraisal is an adaptive regulation strategy that involves reinterpreting the meaning of a stimulus in a way that alters its emotional impact (13). Self-reports reveal less reappraisal success in patients with SAD versus control subjects in some studies, but no group differences in others (14–16). Continuous measures of SAD symptom severity suggest a link between greater symptom burden and reduced reappraisal success (16). When employing reappraisal, healthy individuals engage frontoparietal regions involved in cognitive control and language processing (17,18). These regions somewhat overlap with the frontoparietal control network, as defined by resting-state functional connectivity analyses (19–21). Prior findings have produced mixed results as to whether SAD is associated with altered frontoparietal activation during reappraisal (14–16,22,23), though the therapeutic effects of cognitive behavioral therapy appear to depend on changes in this circuit (24). Thus, additional work is needed to clarify the relationship

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between emotion dysregulation in SAD and potential dysfunction in frontoparietal circuitry.

Beyond reappraisal, the neural signature of other adaptive regulation strategies that mitigate social anxiety is largely unknown. One such strategy is acceptance, a component of mindfulness practice, which has demonstrated efficacy in reducing social anxiety severity (25–27). Acceptance is distinct from reappraisal in that it involves an active willingness to fully experience thoughts, emotions, and sensations in an open and nonjudgmental manner as they change from moment to moment, without attempting to change or avoid them (28–30). Both reappraisal and acceptance are regulatory strategies characterized by the deliberate control of attention to minimize excessive emotional reactivity. There are key differences in how control processes operate, however, with reappraisal relying on the controlled retrieval of semantic information and perspective-taking to alter the interpretation of a stimulus, whereas acceptance involves attentional control to disengage from habitual patterns of cognitive elaboration and reactivity that normally accompany exposure to NSBs. Thus, acceptance is not a passive processing state, but a distinct regulatory strategy. Acceptance and mindfulness-related practices are associated with frontoparietal engagement (31–35). However, acceptance may be somewhat less dependent on frontoparietal executive processes (36) than reappraisal, given that there is no attempt to effortfully alter emotional experience. Additionally, these strategies likely rely on at least partially distinct neural mechanisms, given that reappraisal, but not acceptance, involves linguistic and conceptual processing, perspective-taking, and reasoning—functions that rely on the default mode network (DMN) when self-referential stimuli are involved (37,38). Prior work has reported aberrant recruitment of DMN regions in SAD (39–41); however, it is currently unknown whether patients demonstrate altered DMN activation during reappraisal or acceptance.

Though there is growing interest in comparing the neural bases of reappraisal and acceptance (32,35,42), no study to date has directly compared these strategies in SAD, leaving open questions about the generality of emotion regulation deficits in this disorder. Moreover, conclusions from prior neuroimaging studies of SAD are limited by small sample sizes (typically $<$30 patients). Given the concerns about power in psychological and neuroscientific research, especially neuroimaging (43), it is critical to examine emotion regulation in SAD with larger samples of patients. Finally, few studies have examined emotion regulation in SAD using NSBs [e.g., (16,24)]. Given that NSBs are a core element sustaining negative emotion in this disorder and are a key target for treatment, it is important to examine emotion regulation capacity following NSB exposure. Moreover, DMN regions are highly sensitive to the personal relevance of stimuli and may be overlooked when the neural circuitry of regulation is assessed using stimuli that lack a self-referential component.

Current Study

The current study examined the neural basis of two forms of emotion regulation (reappraisal and acceptance) using ecologically valid stimuli with a large sample of patients with SAD (n = 113) and healthy control subjects (n = 35). Participants were asked to listen to vignettes describing anxiety-inducing social situations followed by NSB statements while brain activity was measured with functional magnetic resonance imaging (fMRI). Within each functional run, participants alternated between blocks of responding to NSBs using reappraisal, acceptance, or a no regulation control condition. We examined 3 main hypotheses: 1) relative to the healthy control group, SAD would be associated with altered recruitment of frontoparietal control regions and DMN self-referential processing regions during reappraisal and acceptance; 2) reappraisal and acceptance would recruit overlapping frontoparietal regions, but differ in reliance on DMN regions involved in self-referential thinking and conceptual processing in both groups; and 3) social anxiety symptom severity and negative emotion ratings would correlate negatively with frontoparietal activation during emotion regulation.

METHODS AND MATERIALS

Participants

Our final sample (Supplemental Table S1) included in data analysis consisted of 113 patients with SAD (mean [SD] age = 32.9 [7.92] years; 61 women) and 35 healthy control subjects (mean [SD] age = 32.1 [8.70] years; 22 women) who provided informed consent in accordance with the Institutional Review Board at Stanford University, passed MRI safety screening, were 22 to 55 years of age, were fluent in English, and were right-handed as assessed by the Edinburgh Handedness Inventory (44). Control subjects had no history of psychiatric disorders. Patients with SAD met criteria for a primary diagnosis of generalized SAD based on the Anxiety Disorders Interview Schedule for DSM-IV: Lifetime version (45). Clinical interviews were conducted by doctoral clinical psychologists and doctoral students in clinical psychology trained on the Anxiety Disorders Interview Schedule for DSM-IV: Lifetime version. Patients met criteria if they endorsed greater than moderate social fear in 5 or more distinct social situations assessed by the Anxiety Disorders Interview Schedule for DSM-IV: Lifetime version. Patients also had a score greater than 60 on the Liebowitz Social Anxiety Scale Self-Report (46,47), the cutoff score for the generalized subtype of SAD as determined by receiver operator characteristics analysis (48). Participants were excluded for comorbid diagnoses of current major depressive disorder, posttraumatic stress disorder, or obsessive-compulsive disorder; use of pharmacotherapy or psychotherapy during the past year; participation in cognitive behavioral therapy for any anxiety disorder during the last 2 years; any previous mindfulness-based stress reduction course; previous participation in long-term meditation retreats; history of regular meditation practice of 10 minutes or more 3 or more times per week; history of neurological disorders or head trauma; cardiovascular disorders, thought disorders, or bipolar disorder; and current substance/alcohol abuse or dependence. Criteria related to meditation allowed us to look at natural (untrained) variation in reappraisal and acceptance efficacy.

NSB Task

The NSB task was programmed using E-prime software (Psychology Software Tools, Sharpsburg, PA). During fMRI scanning, participants were asked to close their eyes and listen to experimenter-constructed social anxiety–related short stories,

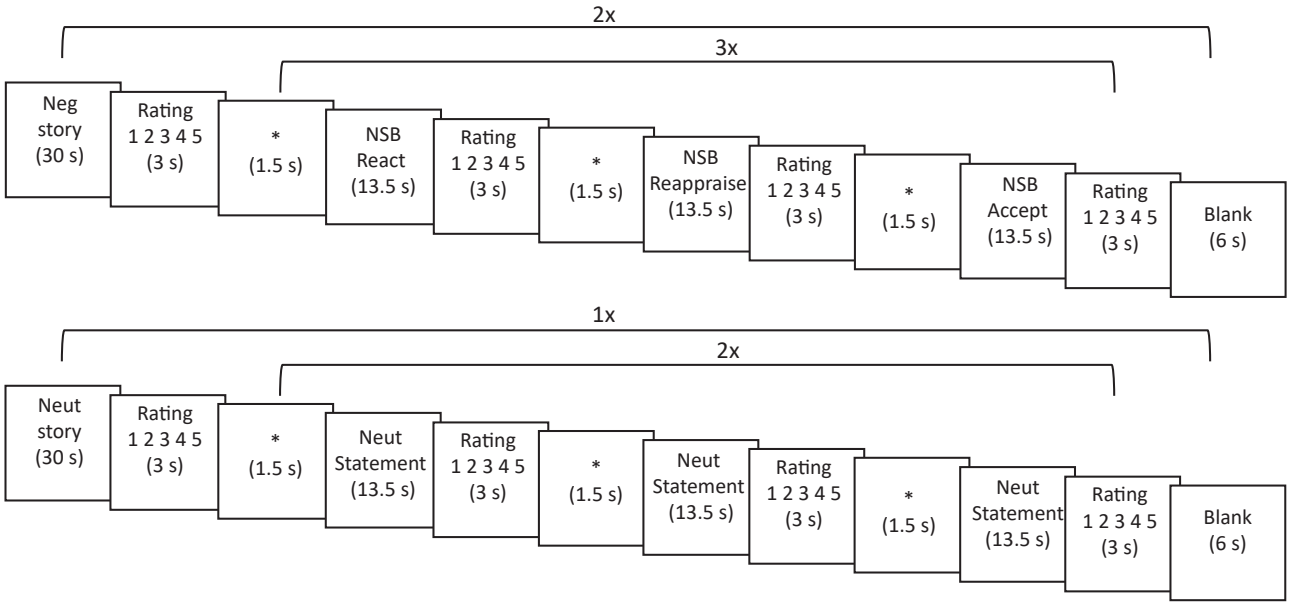

Figure 1. Task structure. There were 3 runs, and each run contained 3 blocks: 2 negative (Neg) blocks followed by a neutral (Neut) block. Within each block, participants listened to a negative or neutral vignette describing a social situation, followed by negative self-belief (NSB) or neutral statements. During NSBs, participants adopted 1 of 3 mindsets (reactivity, reappraisal, or acceptance). Each condition (mindset) was preceded by an asterisk and followed by a negative emotion rating. 1×, 2×, and 3× indicate the number of times a particular event sequence (within the bracket) was repeated.

followed by NSB statements. We fitted each participant with pneumatic headphones over the ears and inside the head coil. We then tested the sound levels with each participant before fMRI scanning to ensure that the human voice stimuli could be heard clearly above the background MRI machine noise. A story might describe a situation in which the participant is having lunch with new acquaintances and they seem bored, and the conversation feels strained. NSBs may include statements such as "Why am I such a bore" or "Why do I do such a bad job on everything" (see Supplemental Appendix for list of statements). Although the statements were experimenter-created rather than ideographic, we use the term NSBs because they were drawn from a small set of statements that are typical of the beliefs in this population, and they are beliefs that are negative and focused on the self. Participants were asked to process the NSBs in 1 of 3 ways: 1) react to the negative statements by reflecting on how the NSB may describe something true about themselves and to let themselves feel the sting of the statements; 2) regulate their reaction by reappraising the meaning of the statements to make the belief less negative (e.g., if the belief was "no one likes me," reappraisal may have involved telling oneself that "this is not always true, some people like me"); or 3) regulate their reaction by accepting their reactions, which involved a nonjudgmental monitoring of thoughts, memories, emotions, and sensations as they appeared and dissolved, without modifying or avoiding them. The react condition provided a comparison condition against which we examined regulation-related activation.

After each story and after each trial (set of NSBs), participants were cued by a tone to open their eyes, view a screen with the numbers 1 2 3 4 5, and provide a rating of their emotional state using a button response pad in the right hand (from 1 = not at all negative, to 3 = moderately negative, to 5 = extremely negative). Ratings were not collected for 3 participants owing to equipment malfunction. Before the task, participants were given instructions and training on the react and regulate strategies. They then verbalized their understanding of the strategies to an experimenter and practiced the strategies while telling the experimenter what they were thinking and doing. They received feedback until they demonstrated effective strategy usage.

There were 3 functional data acquisition runs (Figure 1). Each run included 2 negative blocks and a neutral block. Negative blocks started with presentation of an anxiety-related story (30 seconds), followed by a negative emotion rating (3 seconds), and then 9 trials. Each trial consisted of an asterisk (1.5 seconds) to start the trial, presentation of 2 NSB statements (13.5 seconds), and then a negative emotion rating (3 seconds). Participants adopted one of the strategies visually cued on screen (e.g., REACT) during NSB presentation. Each of the 3 key conditions (react, reappraise, and accept) was repeated 3 times in a pseudorandom order within a negative block. After the 2 negative blocks, there was a neutral block to allow the negative emotion to dissipate. This consisted of a neutral story (15 seconds), a negative emotion rating (3 seconds), and then 6 blocks of neutral statements (13.5 seconds each) that were each preceded by an asterisk and followed by a negative emotion rating. There was a blank period (6 seconds) before the neutral story and at the end of the run. Each negative or neutral story presentation involved a new story. A different set of NSB statements was presented for each condition within a run, with NSB/condition associations counterbalanced across runs. There were 18 trials of each key condition. Each condition was presented for 4.05 minutes of total time (18 trials × 13.5-second duration of NSB statements).

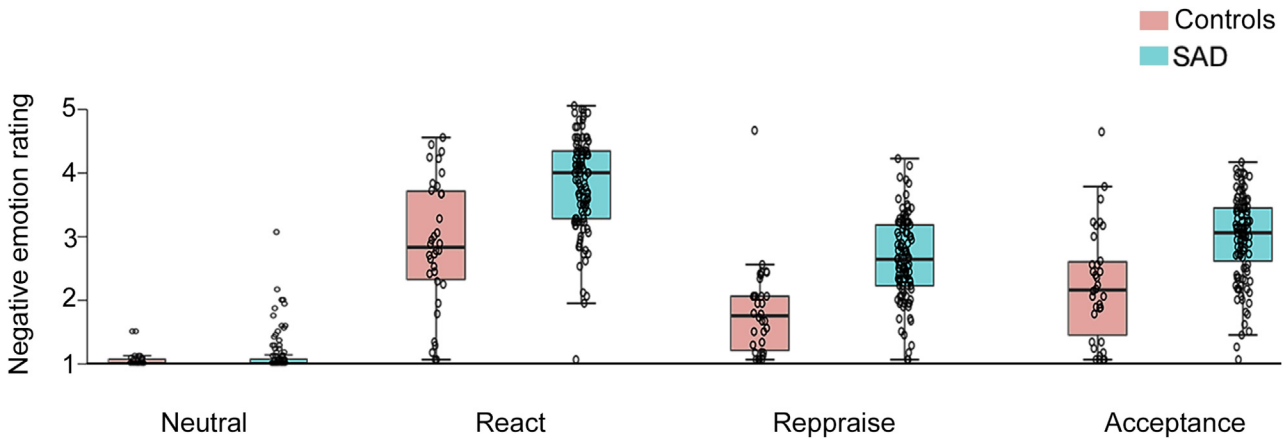

Figure 2. Ratings of negative emotion after each condition. Plots include individual data points with the median (black line), interquartile range (shaded area), and 1.5 × interquartile range (whiskers). SAD, social anxiety disorder. [Figure was created with JASP Version 0.9 computer software (JASP Team, 2018).]

fMRI Data Acquisition and Preprocessing

fMRI data were collected using a GE 3T SIGNA MRI system (GE Healthcare, Waukesha, WI) with a T2*-weighted gradient-echo spiral-in and spiral-out pulse sequence (49) and were motion and slice-time corrected, normalized to Montreal Neurological Institute space, and spatially smoothed using SPM12 (Supplement).

First- and Second-Level Analyses

For each participant, we performed a linear regression using the following regressors: 1) negative stories, 2) react to NSBs, 3) reappraise NSBs, 4) accept NSBs, 5) negative emotion rating, 6) asterisk at the beginning of each trial, 7) neutral stories, 8) neutral belief statements, and 9) blank period at the middle and end of each run. Each regressor was convolved with a canonical hemodynamic response function. The model included regressors of no interest to account for subject motion: 6 parameters from realignment and framewise displacement time course [computed based on Power *et al.* (50)]. Framewise displacement showed a low correlation with the 6 motion parameters (mean r = .15) and was therefore included in the model to account for residual noise. The model included constants to account for between-run differences in mean activation and a high-pass filter (128-second cutoff) to remove low-frequency drifts.

Contrast images (e.g., reappraise > react) were entered into second-level random-effects analyses to assess group-level significance. Controlling for multiple comparisons was achieved through threshold-free cluster enhancement (51), which produces continuous familywise error (FWE)–corrected p values for all voxels (Supplement). Data and analysis code are available at https://github.com/matthewldixon/SAD_Audio.

RESULTS

Preliminary Findings

A 2 (group: SAD vs. control) × 2 (condition: neutral vs. react NSB) analysis of variance revealed a group × condition interaction for negative emotion ratings ($F_{1,143}$ = 27.39, p < .001, η_p^2 = .16) (Figure 2). Negative emotion ratings were similar for patients and control subjects during the neutral condition (t_{143} = 1.42, p = .16, η_p^2 = .014), but significantly higher for patients during the react NSB condition (t_{143} = 5.99, p < .001, η_p^2 = .20). Thus, NSBs triggered strong emotional reactions in all participants, but stronger reactivity in patients with SAD. Patients and control subjects showed a similar reduction in negative emotion during reappraisal compared with react (main effect of condition: $F_{1,143}$ = 240.99, p < .001, η_p^2 = .63; no interaction: F < 1) and during acceptance compared with react (main effect of condition: $F_{1,143}$ = 132.94, p < .001, η_p^2 = .48; no interaction: $F_{1,143}$ = 2.23, p = .14). All participants reported a greater reduction in negative emotion during reappraisal than acceptance (main effect of condition: $F_{1,143}$ = 78.25, p < .001, η_p^2 = .35; no interaction: F < 1). Ratings were similar across repetitions (trials) of each condition (Supplemental Figure S1).

Reappraisal

Across all participants, the reappraise > react contrast revealed extensive activation in frontoparietal regions, including the rostrolateral prefrontal cortex (PFC), inferior frontal sulcus, inferior frontal gyrus (IFG)/middle frontal gyrus, anterior inferior parietal lobule (aIPL), frontal eye fields, midcingulate cortex/supplementary motor area (SMA), and anterior insula (p < .05 FWE corrected) (Figure 3). There was also activation in DMN regions, including the rostromedial PFC (RMPFC) and dorsomedial PFC (DMPFC), posterior cingulate cortex (PCC), posterior IPL (pIPL), temporoparietal junction, superior frontal sulcus, temporal poles, and pregenual anterior cingulate cortex (ACC). Reappraisal was also associated with activation of the somatomotor cortex, caudate, putamen, thalamus, and visual cortex. The react > reappraise contrast revealed activation of the right posterior superior temporal sulcus and retrosplenial cortex (p < .05 FWE corrected) (Figure 3). There were no significant group differences for either contrast.

Acceptance

Across all participants, the only regions showing significant activation at the corrected (p < .05 FWE) statistical threshold

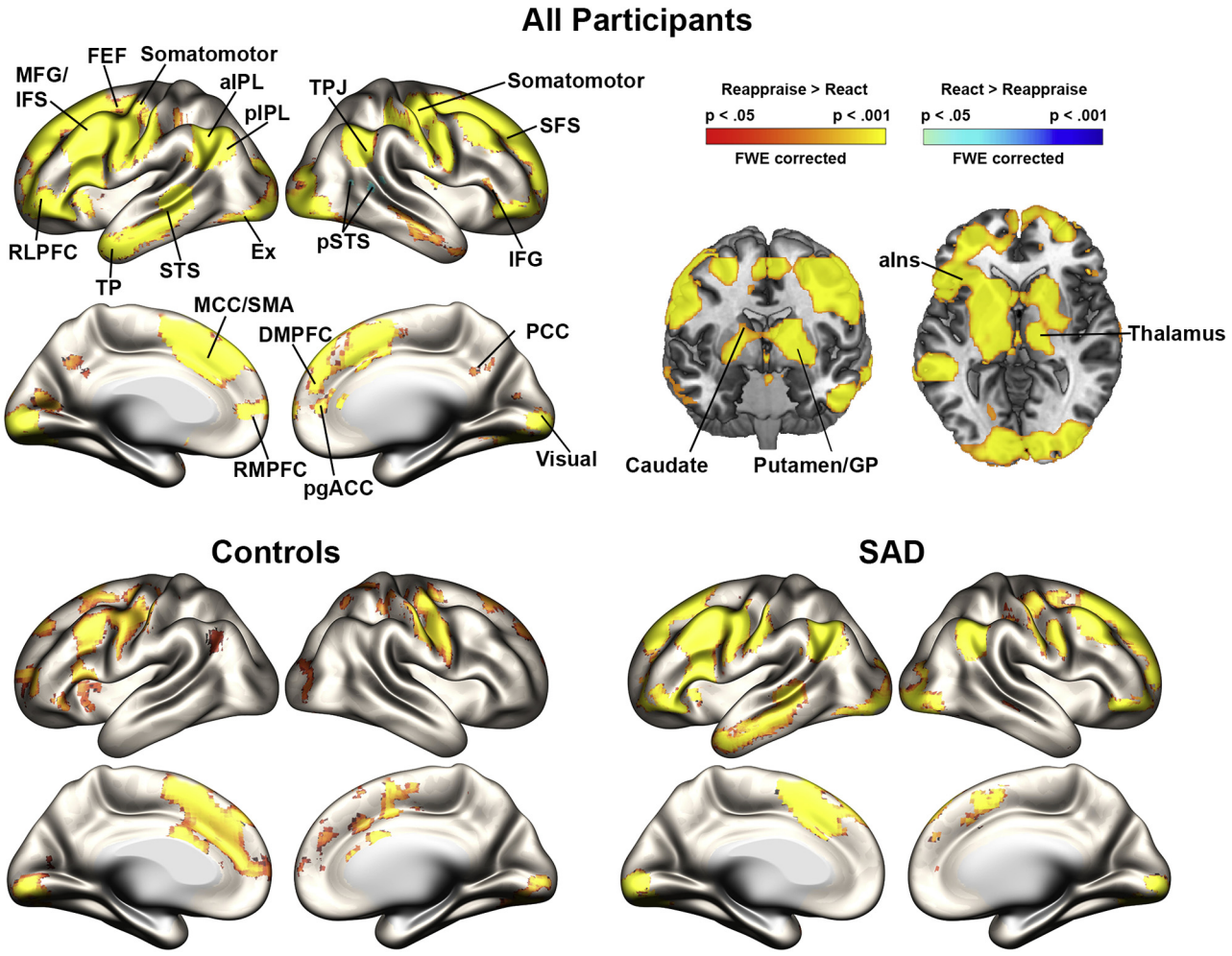

Figure 3. Brain activation for the reappraise vs. react negative self-belief conditions. Warm colors indicate stronger activation during reappraisal; cool colors indicate stronger activation during reactivity. Activation of the retrosplenial cortex during the react condition is not visible on the rendered surface. aIns, anterior insula; aIPL, anterior inferior parietal lobule; DMPFC, dorsomedial prefrontal cortex; Ex, extrastriate cortex; FEF, frontal eye fields; FWE, familywise error; GP, globus pallidus; IFG, inferior frontal gyrus; MCC/SMA, midcingulate cortex/supplementary motor cortex; MFG/IFS, middle frontal gyrus/inferior frontal sulcus; PCC, posterior cingulate cortex; pgACC, pregenual anterior cingulate cortex; pIPL, posterior inferior parietal lobule; pSTS, posterior superior temporal sulcus; RLPFC, rostrolateral prefrontal cortex; RMPFC, rostromedial prefrontal cortex; SAD, social anxiety disorder; SFS, superior frontal sulcus; TP, temporopolar cortex; TPJ, temporoparietal junction.

for the accept > react contrast were the right aIPL and left visual cortex. At a more lenient threshold ($p < .005$ uncorrected), activated voxels were found in several frontoparietal regions (rostrolateral PFC, inferior frontal sulcus, middle frontal gyrus, frontal eye field, anterior midcingulate cortex, posterior middle temporal gyrus) (Figure 4). There were no significant group differences in acceptance-related activation in any regions.

Across all participants, the react > accept contrast revealed activation (at $p < .05$ FWE corrected threshold) in DMN regions (RMPFC, DMPFC, PCC, precuneus, pregenual ACC, pIPL, superior temporal sulcus, temporal poles) as well as the amygdala, bed nucleus of the stria terminalis, medial orbitofrontal cortex (OFC), lateral OFC, subgenual ACC, anterior insula, periaqueductal gray, substantia nigra/ventral tegmental area, caudate, globus pallidus, hypothalamus, retrosplenial cortex, hippocampus, left parahippocampal gyrus, somatomotor cortex, thalamus, cerebellum, and left extrastriate cortex (Figure 4). Consistent with hypothesis 1, there was a robust group difference with the SAD group showing stronger activation for the react > accept contrast in DMN regions (RMPFC, DMPFC, PCC, precuneus, pregenual ACC, pIPL, left superior frontal sulcus) as well as in the right dorsal posterior insula, retrosplenial cortex, right hippocampus, bilateral parahippocampal gyrus, cuneus, lingual gyrus, somatomotor cortex, anterior midcingulate cortex, and SMA ($p < .05$ FWE corrected) (Figure 5 and Supplemental Figure S2).

Reappraisal Versus Acceptance

Consistent with hypothesis 2, across all participants there was greater activation during reappraisal versus acceptance in

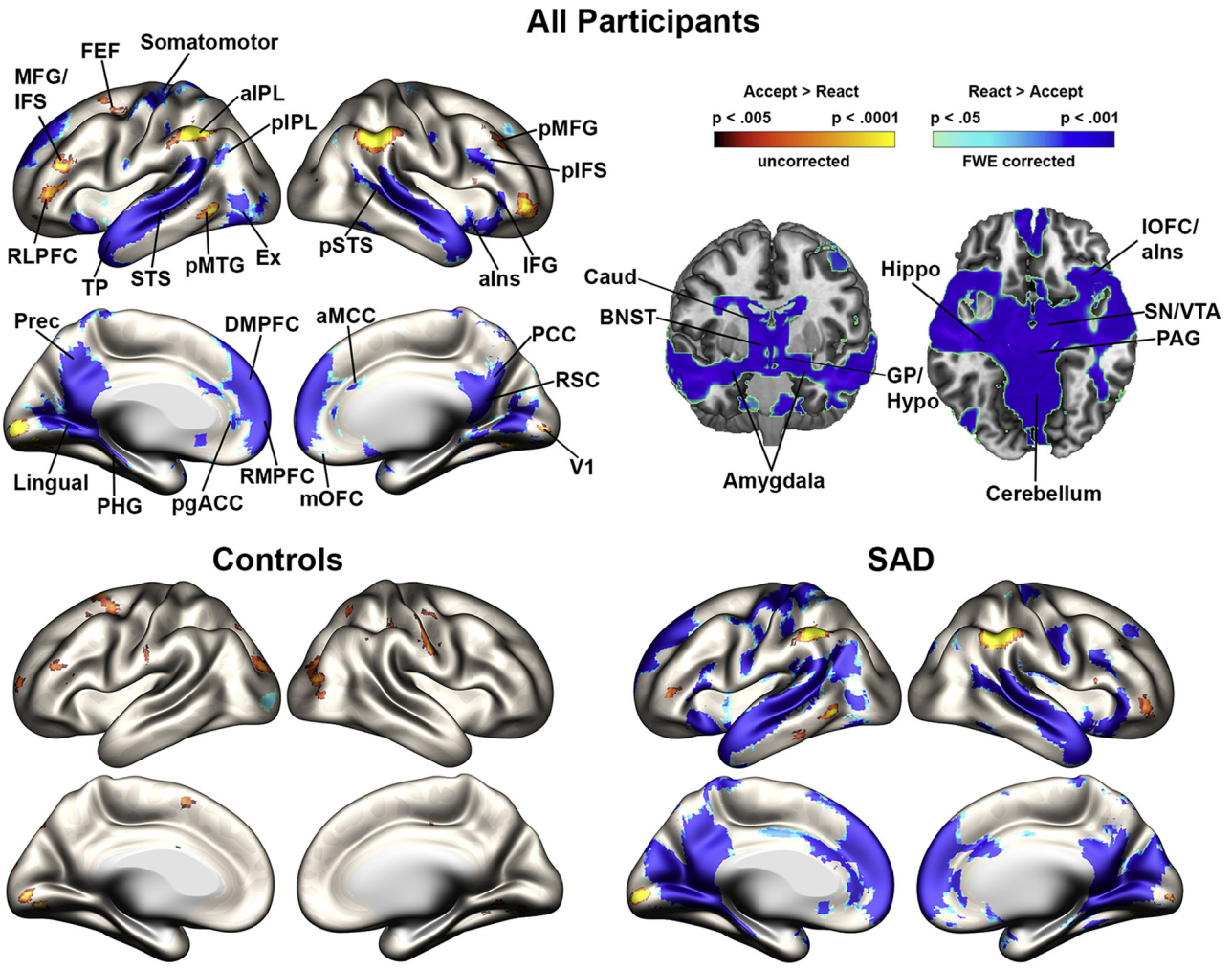

Figure 4. Brain activation for the accept vs. react negative self-belief conditions. Warm colors indicate stronger activation during acceptance; cool colors indicate stronger activation during reactivity. aIns, anterior insula; aIPL, anterior inferior parietal lobule; aMCC, anterior midcingulate cortex; BNST, bed nucleus of the stria terminalis; Caud, caudate; DMPFC, dorsomedial prefrontal cortex; Ex, extrastriate cortex; FEF, frontal eye fields; FWE, familywise error; GP/Hypo, globus pallidus/hypothalamus; Hippo, hippocampus; IFS, inferior frontal sulcus; lOFC, lateral orbitofrontal cortex; MFG/IFG, middle frontal gyrus/inferior frontal sulcus; mOFC, medial orbitofrontal cortex; PAG, periaqueductal gray; PCC, posterior cingulate cortex; pgACC, pregenual anterior cingulate cortex; PHG, parahippocampal gyrus; pIPL, posterior inferior parietal lobule; pMTG, posterior middle temporal gyrus; Prec, precuneus; pSTS, posterior superior temporal sulcus; RLPFC, rostrolateral prefrontal cortex; RMPFC, rostromedial prefrontal cortex; RSC, retrosplenial cortex; SAD, social anxiety disorder; SFS, superior frontal sulcus; SN/VTA, substantia nigra/ventral tegmental area; TP, temporal poles; TPJ, temporoparietal junction.

DMN regions (RMPFC, DMPFC, PCC, pIPL, superior frontal sulcus, precuneus, temporal pole). There was also greater activation in frontoparietal regions (rostrolateral PFC, IFG, aIPL, midcingulate cortex/SMA) as well as in the amygdala, bed nucleus of the stria terminalis, anterior and posterior insula, medial OFC, lateral OFC, periaqueductal gray, substantia nigra/ventral tegmental area, hypothalamus, caudate, putamen, hippocampus, parahippocampal gyrus, retrosplenial cortex, and visual cortices ($p < .05$ FWE corrected) (Figure 6). No regions were more activated in the accept > reappraise contrast. The difference between strategies in control subjects was mainly driven by activation during reappraisal (Supplemental Figure S3). In contrast, the difference between strategies in patients was driven by a combination of activation during reappraisal and less activation during acceptance (Supplemental Figure S3). Although patients demonstrated a more widespread pattern of neural difference across strategies, there were no significant group differences.

Relationship Between Emotion Reports, Social Anxiety Symptom Severity, and Brain Activation

We examined whether the strength of frontoparietal activation during regulation was associated with individual differences in the severity of social anxiety symptoms within the SAD group as measured with the Liebowitz Social Anxiety Scale Self-Report (Supplement). We restricted our analysis to voxels located within an independently defined frontoparietal mask that was finalized before data analysis and based on meta-analyses (Supplement; Supplemental Figure S4) (17,33).

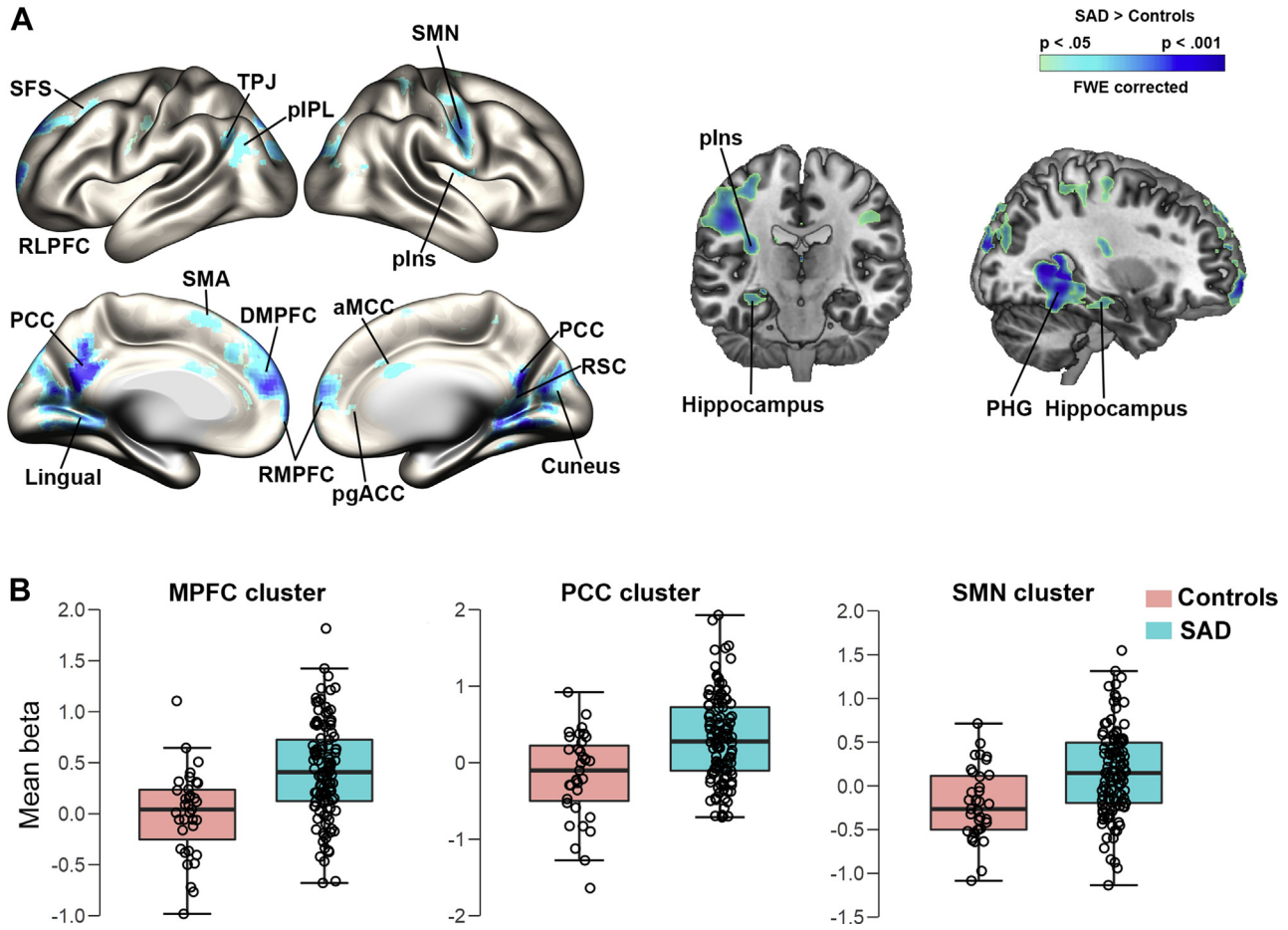

Figure 5. Group difference demonstrating stronger activations in the social anxiety disorder (SAD) group for the react > accept negative self-belief contrast. **(A)** Whole-brain analysis ($p < .05$ familywise error [FWE] corrected) revealing that patients with SAD exhibited stronger activation in default mode network, affective, memory, and somatomotor regions. **(B)** To visualize the results in more detail, we used the MarsBaR toolbox to extract mean β parameter estimates across voxels within each cluster for each participant. The medial prefrontal cortex (MPFC) cluster encompassed the rostromedial prefrontal cortex (RMPFC), dorsomedial prefrontal cortex (DMPFC), and pregenual anterior cingulate cortex (pgACC); the posterior cingulate cortex (PCC) cluster encompassed the PCC, retrosplenial cortex (RSC), parahippocampal gyrus (PHG), cuneus, and lingual gyrus; and the somatomotor network (SMN) cluster encompassed ventral somatosensory and motor cortices. The plots include individual data points with the median (black line), interquartile range (shaded area), and 1.5 × interquartile range (whiskers). aMCC, anterior midcingulate cortex; pIns, posterior insula; pIPL, posterior inferior parietal lobule; SFS, superior frontal sulcus; SMA, supplementary motor area; TPJ, temporoparietal junction. (Figure was created with JASP Version 0.9 computer software [JASP Team, 2018].)

Consistent with hypothesis 3, lower symptom severity was associated with greater activation in several frontoparietal regulatory regions, including the left IFG/anterior insula, left premotor cortex, and left pre-SMA during both reappraisal and acceptance ($p < .005$, voxel extent > 5) (Figure 7). Lower severity was further associated with greater activation of the right mid-DLPFC, right IFG, right anterior midcingulate cortex, right caudate, bilateral IPL, and left middle temporal gyrus during reappraisal and greater activation of the left inferior frontal sulcus and right anterior insula during acceptance ($p < .005$, voxel extent > 5) (Figure 7). Similar results were obtained when using a mask search volume derived from task-related activation in the current study (Supplemental Figure S5). Finally, we performed a parametric modulation analysis to look for neural responses that were negatively associated with trial-by-trial ratings of negative emotion (Supplement). Within the frontoparietal search mask, control subjects versus patients demonstrated a greater negative relationship with task ratings in a small cluster in the left parieto-occipital sulcus (x, y, z = −12, −58, 8; k = 11).

DISCUSSION

The current findings demonstrate the following: 1) no difference between control subjects and patients with SAD in down-modulating negative emotion or activating frontoparietal regions during reappraisal or acceptance; 2) a significant difference between patients and control subjects in DMN and somatomotor activation in the react > accept contrast; 3) greater activation of DMN, frontoparietal, and value-learning regions in both groups during reappraisal compared with acceptance; and 4) heterogeneity within the SAD group, with individuals reporting greater symptom severity exhibiting less frontoparietal engagement during emotion regulation.

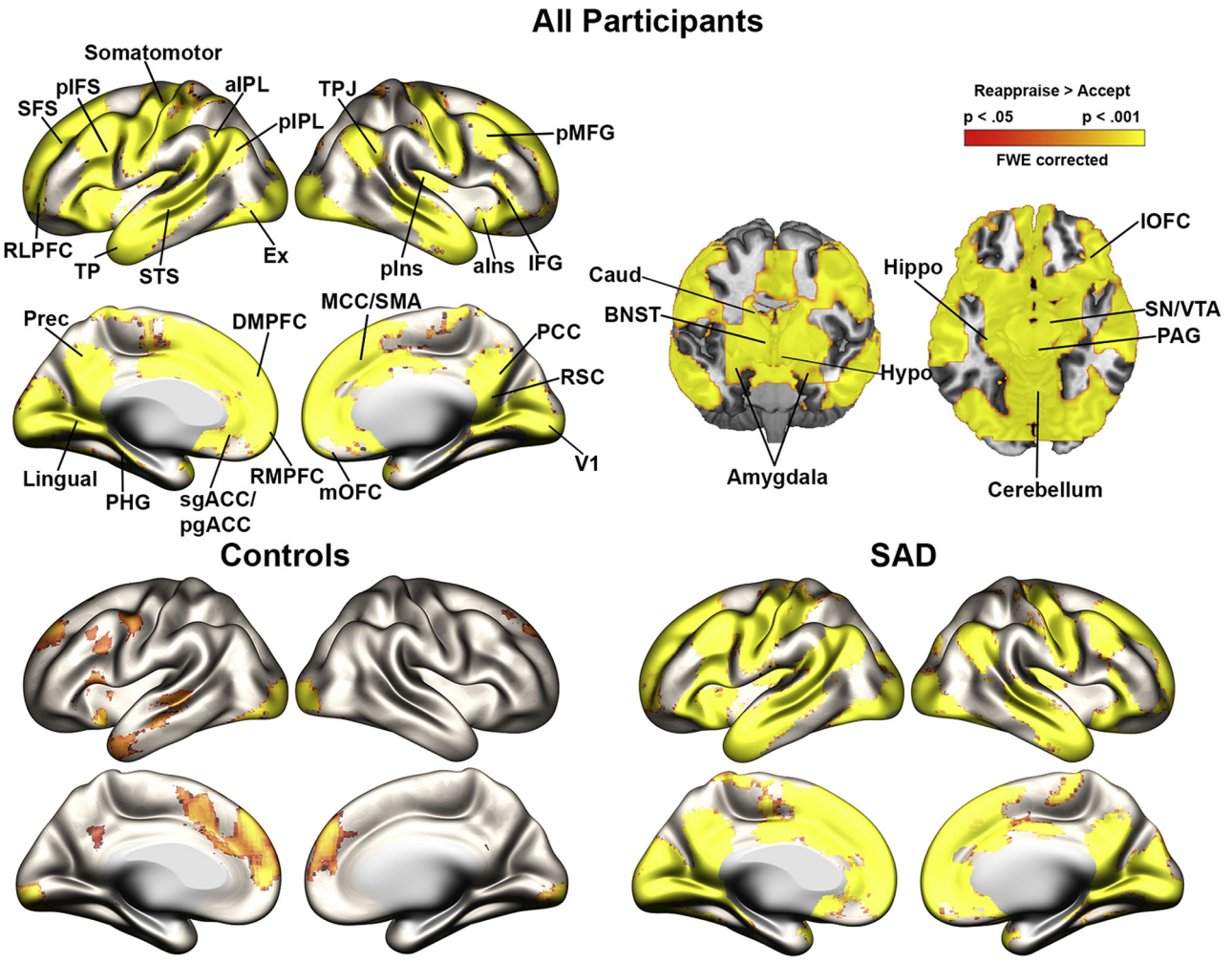

Figure 6. Brain regions showing greater activation for reappraisal than acceptance. aIns, anterior insula; aIPL, anterior inferior parietal lobule; BNST, bed nucleus of the stria terminalis; Caud, caudate; DMPFC, dorsomedial prefrontal cortex; Ex, extrastriate cortex; FWE, familywise error; Hippo, hippocampus; Hypo, hypothalamus; IFG, inferior frontal gyrus; lOFC, lateral orbitofrontal cortex; MCC/SMA, midcingulate cortex/supplementary motor area; mOFC, medial orbitofrontal cortex; PAG, periaqueductal gray; PCC, posterior cingulate cortex; PHG, parahippocampal gyrus; pIFS, posterior inferior frontal sulcus; pIns, posterior insula; pIPL, posterior inferior parietal lobule; pMFG, posterior middle frontal gyrus; Prec, precuneus; pSTS, posterior superior temporal sulcus; RLPFC, rostrolateral prefrontal cortex; RMPFC, rostromedial prefrontal cortex; RSC, retrosplenial cortex; SAD, social anxiety disorder; SFS, superior frontal sulcus; sgACC/pgACC, subgenual/pregenual anterior cingulate cortex; SN/VTA, substantia nigra/ventral tegmental area; TP, temporopolar cortex; TPJ, temporoparietal junction.

Emotion Regulation in SAD

Emotional dysregulation is thought to be an important component of SAD (8–12). The current findings along with other reports (15,16) show that patients with SAD can effectively down-modulate negative emotion when cued to use reappraisal or acceptance. Moreover, patients were able to recruit frontoparietal control regions that support the top-down modulation of cognitive and emotional processes (17,52,53). Prior work has reported mixed results in terms of altered frontoparietal engagement during reappraisal in SAD (14–16,22,23). It is possible that heterogeneity within SAD samples may obscure clear group differences and behaviorally relevant brain activity patterns. In line with this, we found that patients with SAD reporting greater symptom severity demonstrated lower activation in frontoparietal regions during both regulation conditions. These regions included the left IFG, premotor cortex, and pre-SMA that support the active maintenance of task rules (54), controlled retrieval and resolution of conflict between semantic representations (55), and internally directed behavior (56). The severity analysis was restricted to a search mask derived from reliable frontoparietal activation patterns in healthy control subjects during emotion regulation and attentional control tasks. This affords a clear functional interpretation of these results and suggests that difficulty recruiting frontoparietal regulatory regions may be a key factor in the etiology and/or maintenance of severe SAD symptoms.

Our findings further revealed stronger activation of DMN, episodic memory, and somatomotor regions during the react condition relative to the accept condition in patients versus control subjects. Prior work has similarly found that DMN

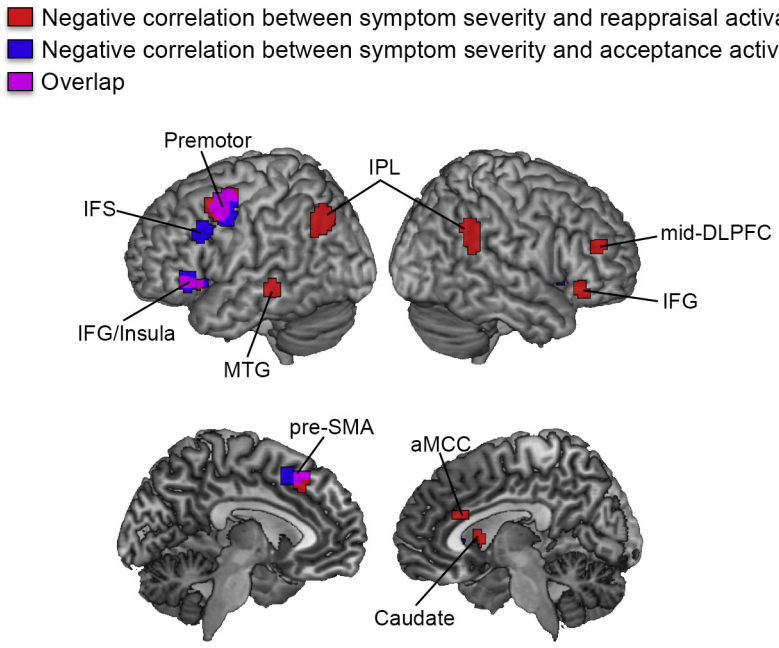

Figure 7. Relationship between regulation-related activation and symptom severity in the social anxiety disorder group. The results were binarized at $p < .005$, voxel extent >5 based on the frontoparietal mask search volume. Greater activation in frontoparietal regulatory regions during reappraise > react and during accept > react was associated with lower symptom severity in the social anxiety disorder group. aMCC, anterior midcingulate cortex; DLPFC, dorsolateral prefrontal cortex; IFG, inferior frontal gyrus; IFS, inferior frontal sulcus; IPL, inferior parietal lobule; MTG, middle temporal gyrus; SMA, supplementary motor area.

activation is lower during acceptance-based task conditions than comparison conditions (31,57). Our task design did not include null events, which could have served as an implicit baseline condition to compare against each condition of interest. As such, it is unclear whether the group difference was driven by altered neural activity in patients during the react condition or during the acceptance condition. In either case, these findings provide compelling evidence that DMN function is altered in SAD. The DMN is involved in reflecting on the self (38) and valuation processes (58) and plays a role in representing the content and valence of self-beliefs (59,60). Our findings are consistent with the idea that disrupted self-referential processing contributes to SAD (5–7) and align with prior observations of altered DMN processing in this disorder (39–41). It is also possible that patients used avoidance instead of, or in addition to, acceptance, given that avoidance is a key feature of all anxiety disorders.

In contrast to acceptance, reappraisal was associated with increased DMN activation in both groups. Although the DMN is not considered to be part of the canonical reappraisal neural circuitry (17), this is likely because most studies have used stimuli that lack self-relevance. The DMN may play a key role in reappraisal when the target is self-beliefs. During reappraisal, coactivation of frontoparietal and DMN regions may support the restructuring of self-beliefs and a lessening of negative valence. Specifically, the DMN may represent the target to be regulated (self-beliefs), while the regulatory mechanisms supported by frontoparietal regions may act on and modify the target. The fact that no group difference was observed during reappraisal suggests that acceptance may be more useful in revealing altered neural activity in the DMN self-referential system in SAD. More broadly, the divergent patterns of DMN engagement during reappraisal and acceptance suggest that this network has a context-dependent relationship with adaptive emotional processing and suggests that lack of DMN variability across different cognitive states may be more indicative of pathology than activation magnitude in any one condition. Greater ability to both upregulate and downregulate the DMN across different conditions may be a sign of psychological flexibility related to self-referential processing. This highlights the value of comparing different regulation strategies in the same study.

The current findings have several implications. First, they suggest that alterations in frontoparietal recruitment in SAD during emotion regulation are not present at the group level (vs. control subjects), but may be revealed when individual differences in severity are examined. Thus, investigating heterogeneity within this disorder may be a fruitful approach. Second, they suggest that altered recruitment of DMN-mediated processes contributes to SAD. One possibility is that altered DMN recruitment reflects excessive negative self-referential processes that trigger elevated reactivity and bias the types of emotion regulation strategies that are selected in everyday life. Healthy individuals are less likely to choose adaptive emotion regulation strategies such as reappraisal when emotional intensity is high (61). Excessive reactivity in patients with SAD could potentially bias choice toward maladaptive strategies, such as rumination and expressive suppression, instead of adaptive strategies, such as reappraisal and acceptance, in daily life (8,9,12,62). A final implication based on the strategy comparison is that reappraisal might require more effort and resources. This makes sense given that reappraisal involves more extensive cognitive processing (e.g., perspective-taking, linguistic processing, selecting an appropriate way to reframe the stimulus, inhibiting an initial response). Moreover, acceptance and mindfulness may not

require much frontoparietal cognitive control–related activation [e.g., (36)].

Limitations and Future Directions

Several limitations should be noted. First, our task focused on the implementation of regulation strategies rather than the choice aspect, which may be important in naturalistic contexts. Comparing strategy selection and implementation in future work could yield important insights. Second, we used experimenter-created, rather than ideographic, NSBs. Whereas this has the benefit of standardization, the statements may not have been evocative for all participants. Third, although it is advantageous to examine a large number of patients, the group contrasts may have been affected by the unequal sample sizes. Importantly, we found similar results when dividing the patients with SAD into smaller groups and comparing each with the control group. Fourth, it is unknown whether our findings will generalize to individuals with comorbidities (e.g., depression). This is an important issue to address in future work. Fifth, participants may have been more effective in implementing reappraisal compared with acceptance, given that the latter may require training to be effectively implemented. Participants' beliefs about success in using each strategy support this point (Supplemental Figure S6). As such, the current study is limited in the conclusions drawn about the acceptance condition. Finally, we focused on only two different emotion regulation strategies. Whereas these strategies are believed to be among the most adaptive, other results could potentially be observed with the inclusion of additional strategies (e.g., distraction).

In summary, group-level comparisons did not reveal a difference in frontoparietal engagement during reappraisal or acceptance, but they did reveal a robust difference in DMN deactivation patterns. Within the SAD group, greater symptom severity was associated with lower frontoparietal recruitment during both emotion regulation conditions. Our findings highlight the utility of examining individual differences and using acceptance as a task condition to reveal neural aberrations in the DMN that distinguish patients with SAD from control participants.

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