

**Effect of Mindfulness Meditation Training on the Neural Bases
of Emotion Regulation in Social Anxiety Disorder**

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Abstract

Mindfulness meditation is thought to reduce emotional reactivity by modifying attentional processes. Given that social anxiety disorder (SAD) is characterized by emotional and attentional biases as well as distorted negative self-beliefs (NSB), we examined the effects of Mindfulness-Based Stress Reduction (MBSR) on the brain-behavior mechanisms of emotional reactivity and attentional regulation of NSBs in patients with SAD. Sixteen patients underwent functional magnetic resonance imaging (fMRI) while reacting to NSBs and implementing a breath-focused mindful attention form of emotion regulation. Post-MBSR, 14 patients completed neuroimaging assessments. Compared to baseline, MBSR completers showed (a) improvement in anxiety and depression symptoms and self-esteem, (b) decreased negative emotion experience, (c) reduced amygdala activity, and (d) increased activity in brain regions implicated in attention during breath-focused mindful attention regulation. Greater recruitment of attention-related brain networks may be one neuropsychological mechanism through which MBSR reduces avoidance behaviors, improves clinical symptoms, and reduces emotional reactivity to NSBs in adults with SAD.

Introduction

Mindfulness (Pali: sati; Sanskrit: smrti; English: remembering) refers to a quality of attention that infuses the present moment with greater clarity and depth. Mindfulness meditation as trained in the MBSR involves the cultivation of a specific form of attention that is focused on the present moment experience of mental contents and bodily sensations without conceptual elaboration (Kabat-Zinn, 1990).

Research has shown that MBSR diminishes the habitual tendency to emotionally react to and ruminate about transitory thoughts and physical sensations (Ramel, Goldin, Carmona, & McQuaid, 2004; Teasdale, Segal, Williams, Ridgeway, Soulsby, & Lau, 2000). Changes in cognitive forms of such emotion regulation such as attentional deployment have been proposed as a core mechanisms by which MBSR improves clinical symptoms in patients with anxiety and depression disorders (Baer, 2003; Jha, Krompinger, & Baime, 2007).

Emotion Regulation and MBSR

Emotion regulation (ER) refers to a variety of strategies that can be implemented at different points during the emotion-generative process to influence which emotions arise, when and how long they occur, and how these emotions are experienced and expressed (Gross & Thompson, 2007). Distinct forms of ER have their own neural circuitry and temporal features (Goldin, McRae, Ramel, & Gross, 2008). Difficulties with ER have been proposed as an essential feature of mood and anxiety disorders (Campbell-Sills & Barlow, 2007)

and result in neural abnormalities in adults with SAD specifically during social (but not physical) threat (Goldin, Manber, Hakimi, Canli, & Gross, 2009).

The process model of ER (Gross, 1998) proposes five classes of ER strategies, including: situation selection, situation modification, attentional deployment, cognitive change, and response modulation. Mindfulness training has been shown to most directly influence attentional deployment, specifically the ability to exert cognitive control of attentional allocation (Moore & Malinowski, 2009), focused attention (Lutz, Slagter, Dunne, & Davidson, 2008) and orienting to a spatial cue (Jha et al., 2007). The effect of MBSR on attentional deployment in SAD when faced with social anxiety stimuli has not yet been investigated.

Emotion Regulation Deficits and SAD

SAD is a common psychological disturbance with up to 12.1% lifetime prevalence (Kessler, Berglund, Demler, Jin, Merikangas, & Walters, 2005) and is characterized by intense fear of evaluation in social or performance situations (Jefferys, 1997). Cognitive models of social anxiety (Clark & Wells, 1995; Rapee & Heimberg, 1997) highlight the role of attention to both internal threat cues (i.e., negative thoughts, self-beliefs and self-imagery) and external threat stimuli (e.g., harsh facial expressions) as essential to the maintenance of social fear (Schultz & Heimberg, 2008).

Recent electrophysiological studies have demonstrated that adults with SAD demonstrate abnormal attentional processes consisting of early hypervigilance followed by attentional avoidance (i.e., reduced visual processing) of social threat stimuli (Mueller, Hofmann, Santesso, Meuret, Bitran, & Pizzagalli,

2008). Furthermore, adults with SAD have shown diminished recruitment of brain networks implicated in cognitive regulation (dorsolateral PFC, dorsal ACC) and in attention regulation (posterior cingulate/precuneus, inferior parietal lobe, supramarginal gyrus) during cognitive reappraisal of emotional reactivity to social threat (Goldin et al., 2009) and to negative self-beliefs (Goldin, Manber Ball, Werner, Heimberg, & Gross, under review).

MBSR, Emotion Regulation, and SAD

MBSR has been shown to be an effective intervention for reducing the symptoms of stress, depression and anxiety across a wide range of clinical populations (Bishop, 2002). Two studies have examined the effect of MBSR as a clinical intervention for SAD. One study found equivalent improvement in patients with generalized SAD on mood, functionality, and quality of life with either 8-week MBSR or 12-week cognitive-behavioral group therapy (CBGT), but significantly lower scores on clinician- and patient-rated measures of social anxiety for CBGT (Koszycki, Bengner, Shlik, & Bradwejn, 2007). A smaller study using an online version of MBSR found evidence of reductions in shyness, social anxiety, and anxiety (Arana, 2006). Preliminary evidence suggests that MBSR may be effective for SAD. However, no studies have investigated how MBSR modifies the neural bases of attentional emotion regulation specifically when faced with social anxiety-related negative self-beliefs.

The Present Study

To investigate the effect of MBSR training on emotion regulation in patients with SAD, we used fMRI to examine MBSR-related changes in clinical

symptoms as well as behavioral and neural measures of emotional reactivity and regulation. Clinically, we expected the MBSR would reduce symptoms of anxiety and enhance self-esteem in patients with SAD. On the regulation task, we expected that, compared to pre-MBSR measures, MBSR would result in (a) decreased negative emotion after implementing breath-focused mindful attention, (b) decreased brain activity in emotion-related limbic activity (i.e., amygdala), and (c) increased activity in an attention-related brain regions.

Methods

Participants

Participants included 16 (9 females) right-handed patients with SAD who met DSM-IV criteria based on the Anxiety Disorders Interview Schedule–IV (ADIS-IV; (DiNardo, Brown, & Barlow, 1994) for current primary generalized social anxiety disorder. Participants had an average age of 35.2 (SD=11.9), 16.3 (SD=3.5) years of education, and included 8 Anglo-Americans, 5 Asian-Americans, 2 Latino-Americans, and 1 Native American. Comorbid current diagnoses included 3 patients with generalized anxiety disorder, three with specific phobia, and one with panic disorder without agoraphobia. Comorbid past diagnoses included two with obsessive-compulsive disorder, three with dysthymia, and four with past major depressive disorder. All participants provided informed consent in accordance with Stanford University’s Human Subjects Committee guidelines for ethical research. Post-MBSR two patients choose not to participate due to discomfort with MR scanning.

Exclusion Criteria

All participants passed a magnetic resonance scanning safety eligibility screen. Participants were excluded if they reported current use of any psychotropic medication, prior meditation training, any history of neurological or cardiovascular disorders, or met criteria for any current DSM-IV Axis-I psychiatric disorders other than social anxiety, generalized anxiety, agoraphobia, or specific phobia disorders.

Clinical Assessment

Clinical diagnostic assessments were conducted using the ADIS-IV (DiNardo et al., 1994) to diagnose psychiatric disorders. This structured clinical interview is based on the DSM-IV, but has been extended to be more sensitive in differential diagnosis of anxiety disorders. We measured symptoms of social anxiety (Liebowitz Social Anxiety Scale; (Liebowitz, 1987), depression (Beck Depression Inventory-II; (Beck, Steer, & Brown, 1996), rumination (Rumination Style Questionnaire; (Nolen-Hoeksema, 1991), state anxiety (Spielberger State-Trait Anxiety Inventory; (Spielberger, Gorsuch, & Lushene, 1970), and self-esteem (Rosenberg Self-Esteem Scale, (Rosenberg, 1965).

Procedure

Participants were recruited through web-based community listings and referrals from local mental health clinics. Following a phone screen to determine MR eligibility, potential participants were administered a structured clinical diagnostic interview. Eligible patients were administered questionnaires and participated in a brain imaging session. Prior to MR scanning, patients were instructed on the ER task with two practice trials using NSB stimuli not presented

during the fMRI task. Stimuli were presented visually with E-Prime software on a PC. Participants attended a standard MBSR course and were administered all assessments again.

Mindfulness-Based Stress Reduction

MBSR was delivered in an academic setting in a standard format based on the treatment protocol developed by Jon Kabat-Zinn, PhD (Kabat-Zinn, 1990). Participation included 8 weekly 2.5 hours sessions, a half-day retreat, daily home practice based on the audiotapes, and daily monitoring of both formal and informal meditation practices. The course was led by a member of the team (PG) who has led MBSR courses in medical and academic settings for ten years.

Regulation of NSB Task

The regulation task consisted of 18 NSBs (e.g., “I am ashamed of my shyness,” “People always judge me”) and a pseudo-random sequence of two forms of attention regulation: breath-focused mindful attention (9 trials) and distraction-focused attention (9 trials). Each trial consisted of (a) reacting to a NSB for 12s followed by (b) implementation of attention regulation based on a cue to either “Shift attention to the breath” (breath-focused mindful attention) or “Count backwards from 168” (distraction-focused attention) for 12s, and (c) a negative emotion rating (How negative? 1=not at all, 2=slight, 3=moderate, 4=very much) was recorded using Eprime software with a button response pad positioned in the participant’s right hand (3s).

For the sake of clarity and brevity, this paper will only discuss the effects of MSBR on breath-focused mindful attention. There were also six 9s blocks of

asterisk counting randomly inserted throughout the experiment (low-level baseline). Prior to MR scanning, participants were trained on the regulation task with four NSBs not used in the experiment. They were instructed to read repeatedly a single NSB presented in white the middle font against a black background on a screen mounted on the head coil inside the scanner. When a cue appeared above the NSB, participants shifted attention to the physical sensation of their own inhalation and exhalation, or began subtracting by 1s from a three digit number projected above the statement. The regulation task was 9 minutes and 12 seconds (368 time points x 1.5s = 552s) in duration.

Image Acquisition

Imaging was performed on a General Electric 3 Tesla Signa magnet using a custom-built quadrature “dome” elliptical bird cage head coil and a T2*-weighted gradient echo spiral-in/out pulse sequence that used blood oxygenation level-dependent (BOLD) contrast (Glover & Law, 2001). The spiral-in/out sequence results in increased signal-to-noise (Glover & Law, 2001) and has been shown to be effective in recovering BOLD signal in frontal cortex and temporal lobes (Preston, Thomason, Ochsner, Cooper, & Glover, 2004). Head movement was minimized using a bite bar, padding and plungers. During a single run, 368 volumes (each consisting of 22 sequential axial slices) were obtained (TR=1500 ms, TE=30 ms, flip angle=60, FOV=22 cm, frequency encoding=64, single shot, voxel resolution=3.438 mm² x 5 mm). A high-resolution anatomical scan was acquired using a fast spin echo spoiled grass

pulse sequence (voxel resolution= $.8594^2 \times 1.2$ mm; FOV=22 cm, frequency encoding=256).

fMRI Data Preprocessing

Analysis of functional neuroimages (AFNI; (Cox, 1996) was used for preprocessing and statistical analysis. Every volume was examined visually and computationally for MR signal artifacts and outliers related to head movement and magnetic field disturbances. The first four time points in each functional scan were eliminated to account for stabilization of the magnetic field. The optimal base image for realignment and calculation of six motion parameters (three translations and three rotations) was identified empirically based on an automated recursive analysis of the root mean square adjustment for motion correction at each time point. No brain volumes required greater than ± 1.0 mm motion correction in the x, y, or z directions, and there was no evidence of stimulus-correlated motion for any of the six task conditions within- and between-groups. MR signal in each voxel was subjected to a high-pass temporal filter (.011 Hz) to remove low-frequency oscillations and was converted to percent signal change based on the mean MR signal per voxel.

fMRI Statistical Analysis

A multiple regression model was implemented using the AFNI 3dDeconvolve program. The baseline model included parameters to remove variance in each voxel's time series related to mean, linear and quadratic drifts, and the six motion correction parameters. Six reference vectors for each of the six conditions (positive and negative versions of self, valence, and case) were

convolved with a gamma variate model (Cohen, 1997) of the hemodynamic response function to account for the hemodynamic delay to peak BOLD responses. Resultant statistical maps were spatially smoothed with a 4 mm^3 isotropic Gaussian kernel, resampled to 3.438 mm^3 , and converted to Talairach (Talairach & Tournoux, 1988) atlas space. Second-level between-group and paired t-tests were conducted according to a random-effects model. Neural results are reported for the contrast of self versus case processing only in this paper to reduce complexity.

To correct quantitatively for the multiple comparisons, AlphaSim, a Monte Carlo simulation bootstrapping program in the AFNI library, was employed to identify a joint-probability threshold consisting of a voxel-wise threshold of $P < .005$ and minimum cluster-volume threshold $\geq 163 \text{ mm}^3$ ($4 \text{ voxels} \times 3.438 \text{ mm}^3$) that resulted in protection against false positive cluster detection at $P < .01$ in the whole-brain analyses.

Results

Clinical Results

Paired t-tests showed that from baseline to post-MBSR patients had decreased social anxiety, depression, rumination, and state anxiety, as well as increased self-esteem (Table 1).

Behavioral Results

Change from pre- to post-MBSR. Paired t-tests showed that from pre- to post-MBSR patients had no changes in reactivity to NSB, $t(14)=1.21$, ns.

However, as expected, there was a reduction in negative emotion during breath-focused mindful attention from pre- to post-MBSR, $t(14)=3.25$, $p<.01$.

Neural Results

Baseline. At baseline, a one-sample t-test for the contrast of react NSBs versus asterisk counting yielded greater BOLD responses in brain regions implicated in self-referential processing (ventromedial and dorsomedial PFC and PCC/precuneus), emotion (amygdala), dorsal and ventral visual processing (bilateral middle and inferior temporal lobes, cuneus, precuneus, angular gyrus, lingual gyrus, inferior and superior parietal cortex), memory (bilateral PHG). Greater BOLD responses for asterisk counting versus react NSBs included PCC and lingual gyrus (Figure 2 and Table 2).

Change from pre- to post-MBSR. To assess change from pre- to post-MBSR, we contrasted pre- versus post-MBSR responses for breath-focused mindful attention versus react NSBs. This contrast yielded greater BOLD responses for post-MBSR versus pre-MBSR in brain regions implicated in visual attention (inferior and superior parietal lobule, cuneus, precuneus, middle occipital gyrus as well as parahippocampal gyrus). There were no areas of brain activity greater for React versus Breath (Figure 3 and Table 3).

To better understand how MBSR training influences the effect of breath-focused mindful attention on a neural index of emotional reactivity to NSBs, we investigated the BOLD signal time series of the right dorsal amygdala activation observed at baseline in response to react NSB (Figure 4). At baseline, there was a delay of approximately 6 seconds before amygdala activity began to ramp up

towards a peak response at the end of the 12 seconds react NSB component of the block. Compared to pre-MBSR, at post-MBSR patients with SAD demonstrated a significant decrease of right amygdala response prior to the cue to shift attentional focus to the breath.

Discussion

The goal of this study was to investigate the effects of MBSR training for patients with social anxiety disorder on behavioral and neural bases of emotional reactivity and regulation of negative self-beliefs. Mindfulness training was hypothesized to reduce clinical symptoms and negative emotional reactivity to NSBs via reductions in brain activity related to emotion reactivity with increases in attention-related brain networks.

Clinical Measures

MBSR proved effective in improving the clinical symptom profile of social anxiety, depression, rumination, state anxiety and self-esteem in adults with SAD. These findings replicate and extend preliminary reports of symptom reduction in patients with SAD related to mindfulness training (Arana, 2006; Koszycki et al., 2007).

Behavioral Measures

Negative emotion ratings demonstrated that MBSR did enhance the breath-focused mindful attention related down-regulation of emotional reactivity in patients with SAD. This suggests that one of the mechanisms through which mindfulness training alters emotional processes is through explicit enhancement of attention regulation. The lack of change from pre- to post-MBSR in the level of

negative emotion experience during the react NSB condition may be due to overlearned responses (e.g., an automatic tendency to perceive statements about the self as threatening) to NSBs in patients with SAD.

Neural Measures

Baseline neural responses confirmed that reacting to NSBs resulted in activation of the midline cortical regions implicated in self-referential process, including ventromedial PFC, dorsomedial PFC, and posterior cingulate/precuneus (Northoff, Heinzl, de Greck, Bermpohl, Dobrowolny, & Panksepp, 2006), as well as emotion (amygdala) and memory (parahippocampal gyrus) processes.

Compared to pre-MBSR, at post-MBSR there was evidence of increased neural responses in parietal and occipital brain regions involved in attention. This suggests two possible interpretations. First, mindfulness meditation training may have resulted in adults with SAD being more visually engaged in (i.e., less avoidant of) NSBs. Alternatively, greater neural recruitment of attention related brain regions may be due to more refined visualization of the movement of the breath at the nostrils, which also involves better allocation of attention to the task.

Numerous studies have shown exaggerated amygdala response in adults with SAD in response to social anxiety related stimuli including harsh faces (Phan, Fitzgerald, Nathan, & Tancer, 2006; Stein, Goldin, Sareen, Zorrilla, & Brown, 2002) and critical comments (Blair, Geraci, Devido, McCaffrey, Chen, Vythilingam, Ng, Hollon, Jones, Blair, & Pine, 2008). Furthermore, one study has demonstrated that adults with SAD who were classified as responders to either

citalopram medication or cognitive-behavioral group therapy had a reduction in amygdala activity from baseline to post-treatment (Furmark, Tillfors, Marteinsdottir, Fischer, Pissiota, Langstrom, & Fredrikson, 2002). The amygdala BOLD signal time series change from pre- to post-MBSR suggests that mindfulness training may enhance initial emotion reactivity and/or detection of emotional salience of NSBs as suggested by the initial amygdala spike at the post-MBSR assessment. Furthermore, the enhanced initial emotion response indexed by amygdala activity is transient as evidenced by significant decrease in amygdala activity at the end of the react NSB trials well before the onset of the cue to shift attention to the breath. This suggests that MBSR may have facilitated a shift from what was initially an effortful attempt to implement breath-focused mindful attention emotion regulation at pre-MBSR to an automatic shift to breath-focused mindful attentional regulation even before being cued to do so at post-MBSR. This highlights the possibility that one function of meditation training is to change specific aspects of attention regulation from explicit (i.e., more effortful) to an implicit (i.e., more automatic) process.

Clinical Implications

These results demonstrate the mindfulness training as implemented in MBSR may enhance attention processes in the context of negative self-beliefs. This suggests that in patients with SAD who would normally show attentional avoidance of threat stimuli mindfulness training might attenuate avoidance and increase attentional allocation. Thus, MBSR may increase the ability to implement attentional deployment, an early emotion regulation strategy, even

when encountering social threat stimuli. This may be an important mechanism that contributes to the success of exposure therapy for SAD. However, this may also be an outcome of exposure to the contents of attention that is trained explicitly during MBSR.

Limitations and Directions for Future Research

This study is limited by the lack of a control group or active comparison clinical intervention that would provide a basis for making a stronger inference about mindfulness meditation modifies the behavioral and neural substrates of emotion regulation. A randomized clinical trial with at least two groups who undergo two types of stress reduction courses will be necessary to delineate factors that might be contributing to changes in attentional deployment, attention brain networks and specificity of changes in clinical symptoms as well as address other potential confounds such as practice effects and habituation to the MR scanner environment.

A second limitation of this study is that we examined the effect of attentional emotion regulation on a small set of experimenter-selected NSB stimuli. Use of participant-generated NSBs may result in more robust brain-behavioral responses in SAD which could support a more ecologically valid test of the effects of MBSR on emotion regulation.

A third limitation is that this study examined only breath-focused mindful attention. Thus, results cannot be generalized to other forms of mindful attention such as mindful attention of taste, sound, mental states and other bodily sensations. It may be instructive to compare the effects of different clinical

interventions with different mechanisms of change (e.g., cognitive disputation, acceptance, attention training) on the neural bases of mindful attention.

Author Note

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Table 1

Clinical Measures

	Baseline Mean±SD	Post-MBSR Mean±SD	t-test, effect size
LSAS	68.7±21.2	49.3±17.0	4.3***, .59
BDI-II	8.7±9.1	3.4±3.2	2.2*, .27
RSQ	26.4±6.5	19.3±95.7	3.8**, .53
STAI-State	41.5±9.3	29.6±6.4	8.4***, .84
RSE	22.7±4.6	27.2±4.7	3.7*, .51

Note. * $p < .05$, ** $p < .01$, *** $p < .001$; effect size = partial η^2

LSAS=Liebowitz Social Anxiety Inventory, BDI-II=Beck Depression Inventory-II,
RSQ=Rumination Style Questionnaire STAI=Spielberg State Trait Anxiety
Inventory, RSE=Rosenberg Self-Esteem Scale.

Table 2

Baseline BOLD Responses for React to Negative Self-Beliefs versus Asterisk

Counting

Brain Regions	BA	x y z ^a	% Signal Change	Vol (mm ³)	t-value
<u>React > Asterisk</u>					
<u>Frontal Cortex</u>					
Medial PFC 6	10	-6 67 28	.48	15	3.80
Medial PFC 32	10	-3 59 25	.53	4	5.25
Dorsomedial PFC 13	8	0 45 56	.34	8	4.84
Ventromedial PFC 2	10	-7 52 1	.83	30	3.77
Ventromedial PFC 17	10	-3 62 -5	.71	6	5.39
L Superior Frontal Gyrus 4	8	-31 28 53	.28	25	5.37
L Middle Frontal Gyrus 5	6	-31 11 63	.81	24	5.70
R Precentral Gyrus 7	4	48 -10 56	.24	15	3.76
<u>Temporal Cortex</u>					
R Middle Temporal Gyrus 18	21,37	58 -61 5	.58	6	4.02
R Middle Temporal Gyrus 30	39	55 -68 19	.36	4	3.72
R Inferior Temporal Lobe 20	20	45 -3 -30	.21	5	3.78
L Inferior Temporal Lobe 28	37	-58 -55 -5	.27	4	4.19
<u>Parietal Cortex</u>					
Posterior Cingulate 12	30	-3 -48 22	.67	8	4.11
R Inferior Parietal Lobule 25	40	65 -41 25	.55	5	4.66
L Superior Parietal Lobule 19	7	-31 -72 50	.64	6	3.59
<u>Occipital Cortex</u>					
L Superior Occipital Gyrus 1	19	-38 -79 36	.49	133	4.42
R Precuneus 10	19	45 -72 36	.36	12	3.70
R Angular Gyrus 11	39	52 -68 29	.66	9	4.87
R Lingual Gyrus 14	17	10 -96 -5	.92	7	3.77
R Cuneus 16	31	28 -65 12	.84	7	3.58
<u>Subcortical</u>					
R PHG/Amygdala 3	28	14 -17 -16	.39	29	4.14
R PHG 21	34	14 -10 -23	.50	5	4.88
L PHG 8	28	-21 -17 -12	.28	14	4.33
L PHG 9	35	-17 -27 -12	.48	12	4.26
Culmen 27		-3 -37 -23	.28	4	4.97
<u>Asterisk > React</u>					
R Posterior Cingulate Cortex 15	30	14 -55 8	.65	7	7.69
L Lingual Gyrus 22	18	-10 -72 -2	.75	5	4.18
Posterior Cingulate Cortex 23	30	3 -65 12	.73	5	4.32

Note. t-value threshold ≥ 3.69 , voxel $P < 0.005$, minimum cluster volume threshold $\geq 163 \text{ mm}^3$ (4 voxels $\times 3.438 \text{ mm}^3$), cluster $P < 0.01$.

ACC=anterior cingulate cortex, BA=Brodmann area, L=left, PFC=prefrontal cortex, R=right

^a Talairach and Tournoux coordinates of maximum BOLD signal intensity voxel

Table 3

Changes in BOLD Responses from Pre- to Post-MBSR for Breath-Focused

Mindful Attention versus React Negative Self-Beliefs

Brain Regions	BA	x y z ^a	Signal Change	Vol (mm ³)	t-value
<u>Post-MBSR > Baseline</u>					
<u>Breath > React</u>					
<u>Parietal Cortex</u>					
L Inferior Parietal Lobule 3	40	-38 -44 56	.40	16	3.78
R Inferior Parietal Lobule 11	40	55 -34 53	.66	4	3.32
L Superior Parietal Lobule 4	7	-28 -65 46	.61	9	3.45
Precentral Gyrus 5	4	-31 -24 70	.32	9	3.77
<u>Occipital Cortex</u>					
Medial Cuneus 1	18	0 -79 22	.37	65	4.01
L Cuneus 8	17	-17 -75 8	.67	4	4.29
R Cuneus 10	19	28 -85 32	.26	4	3.51
R Middle Occipital Gyrus 2	17	28 -61 8	.64	25	3.22
R Precuneus 6	19	17 -85 39	.39	8	3.48
R Precuneus 9	7	14 -68 36	.37	4	3.39
<u>Subcortical</u>					
R Parahippocampal Gyrus 7		28 -51 1	.41	4	3.36
<u>React > Breath</u>					
<u>none</u>					

Note. t-value threshold ≥ 3.21 , voxel $P < 0.005$, minimum cluster volume threshold $\geq 163 \text{ mm}^3$ (4 voxels $\times 3.438 \text{ mm}^3$), cluster $P < 0.01$.

BA=Brodmann area, L=left, PFC=prefrontal cortex

^a Talairach and Tournoux coordinates of maximum BOLD signal intensity voxel

Figure Captions

Figure 1. Negative emotion experience ratings pre- and post-MBSR.

Ratings for the breath-focused mindful attention blocks were collected during the fMRI task. Ratings for the react NSBs were collected post-fMRI. ** $P < .01$. Error bars = SEM.

Figure 2. Baseline BOLD responses during react NSB versus asterisk

counting. Thresholded at $t \geq 3.69$, voxel $P < .005$, cluster volume $\geq 163 \text{ mm}^3$, cluster $P < .01$.

Figure 3. Greater BOLD responses for post versus pre-MBSR for the

contrast of breath-focused mindful attention versus react NSB. IPL=inferior parietal lobule, MOG=middle occipital gyrus, PHG=parahippocampal gyrus, SPL=superior parietal lobule. Thresholded at $t \geq 3.21$, voxel $P < 0.005$, cluster volume $\geq 163 \text{ mm}^3$, cluster $P < 0.01$.

Figure 4. Right dorsal amygdala BOLD signal time series during reacting

to NSB and breath-focused mindful attention at pre- and post-MBSR. * $P < .05$.

Figure 1

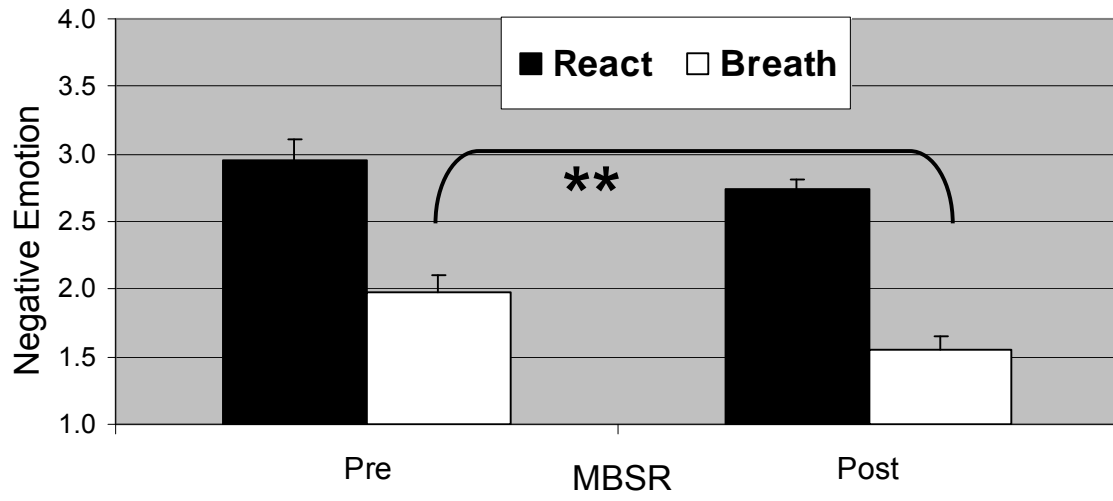


Figure 2

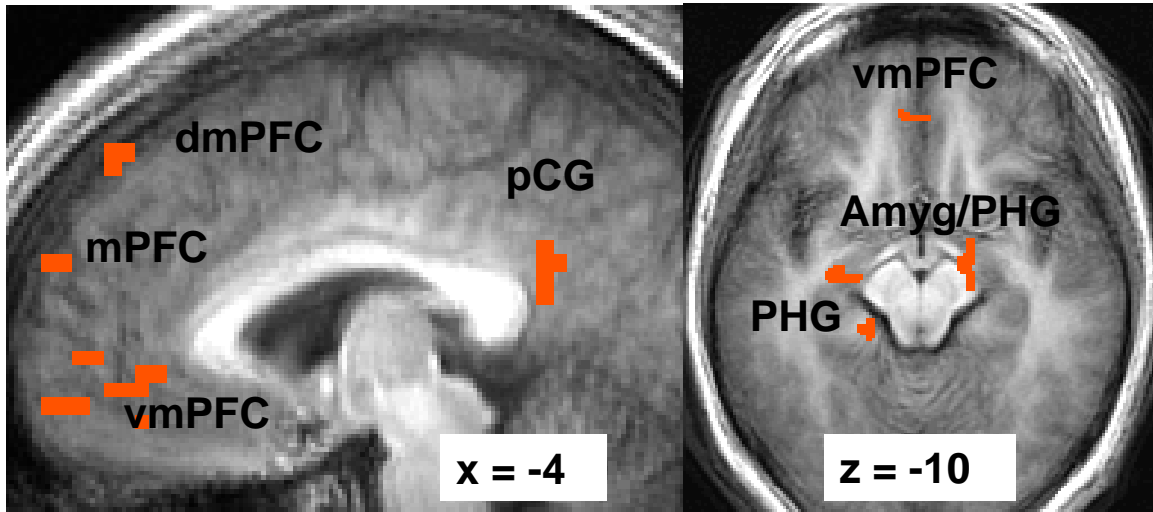


Figure 3

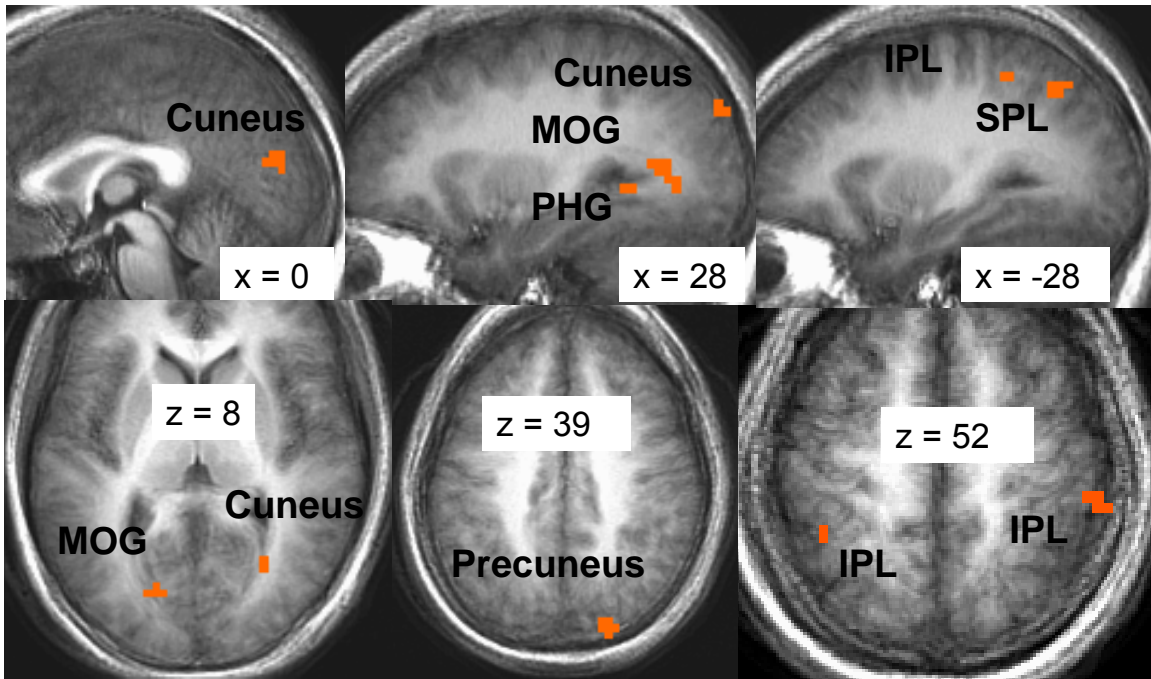
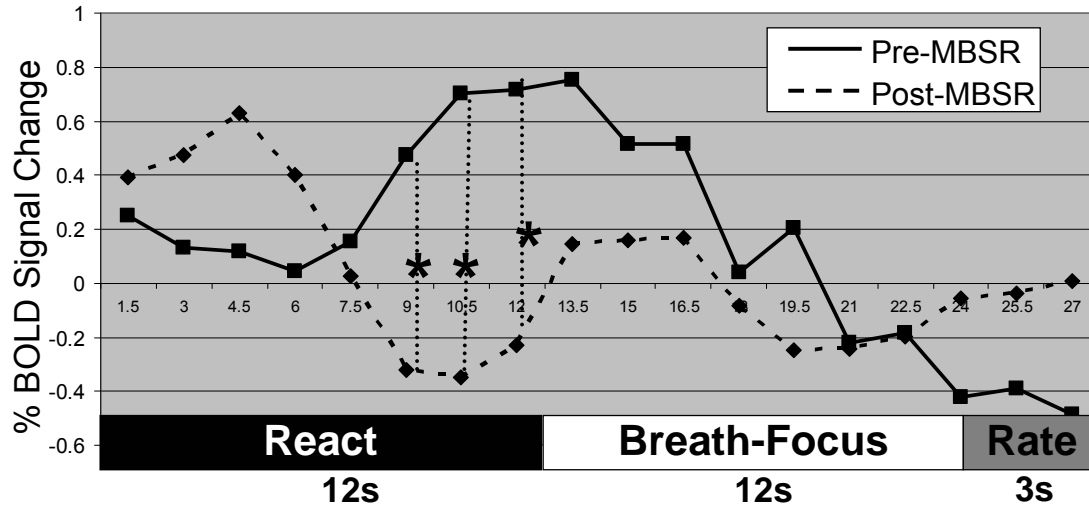


Figure 4



References

- Arana, D. (2006). The practice of mindfulness meditation to alleviate the symptoms of chronic shyness and social anxiety. *Dissertation Abstracts International: Section B: The Sciences and Engineering*, 67, 2822.
- Baer, R. A. (2003). Mindfulness training as a clinical intervention: A conceptual and empirical review. *Clinical Psychology: Science and Practice*, 10, 125-143.
- Beck, A. T., Steer, R. A., & Brown, G. K. (1996). *Beck depression inventory - second edition manual*. San Antonio, TX: The Psychological Corporation.
- Bishop, S. R. (2002). What do we really know about mindfulness-based stress reduction? *Psychosomatic Medicine*, 64, 71-84.
- Blair, K., Geraci, M., Devido, J., McCaffrey, D., Chen, G., Vythilingam, M., et al. (2008). Neural response to self- and other referential praise and criticism in generalized social phobia. *Arch Gen Psychiatry*, 65, 1176-1184.
- Campbell-Sills, L., & Barlow, D. H. (2007). Incorporating emotion regulation into conceptualizations and treatments of anxiety and mood disorders. In J. J. Gross (Ed.), *Handbook of emotion regulation* (pp. 542-559). New York: Guilford.
- Clark, D. M., & Wells, A. (1995). *A cognitive model of social phobia*. New York, NY: Guilford Press.
- Cohen, M. S. (1997). Parametric analysis of fmri data using linear systems methods. *Neuroimage*, 6, 93-103.

- Cox, R. W. (1996). Afni: Software for analysis and visualization of functional magnetic resonance neuroimages. *Computers and Biomedical Research*, 29, 162-173.
- DiNardo, P. A., Brown, T. A., & Barlow, D. H. (1994). *Anxiety disorders interview schedule for dsm-iv: Lifetime version (adis-iv-l)*. New York, NY: Oxford University Press.
- Furmark, T., Tillfors, M., Marteinsdottir, I., Fischer, H., Pissiota, A., Langstrom, B., et al. (2002). Common changes in cerebral blood flow in patients with social phobia treated with citalopram or cognitive-behavioral therapy. *Arch Gen Psychiatry*, 59, 425-433.
- Glover, G. H., & Law, C. S. (2001). Spiral-in/out bold fmri for increased snr and reduced susceptibility artifacts. *Magnetic Resonance in Medicine*, 46, 515-522.
- Goldin, P. R., Manber Ball, T., Werner, K., Heimberg, R. G., & Gross, J. J. (under review). Neural mechanisms of cognitive reappraisal of negative self-beliefs in social anxiety disorder.
- Goldin, P. R., Manber, T., Hakimi, S., Canli, T., & Gross, J. J. (2009). Neural bases of social anxiety disorder: Emotional reactivity and cognitive regulation during social and physical threat. *Arch Gen Psychiatry*, 66, 170-180.
- Goldin, P. R., McRae, K., Ramel, W., & Gross, J. J. (2008). The neural bases of emotion regulation: Reappraisal and suppression of negative emotion. *Biological Psychiatry*, 63, 577-586.

- Gross, J. J. (1998). The emerging field of emotion regulation: An integrative review. *Review of General Psychology*, 2, 271-299.
- Gross, J. J., & Thompson, R. A. (2007). Emotion regulation: Conceptual foundations. In J. J. Gross (Ed.), *Handbook of emotion regulation* (pp. 3-24). New York: Guilford.
- Jefferys, D. (1997). Social phobia: The most common anxiety disorder. *Australian Family Physician*, 26, 1061, 1064-1067.
- Jha, A. P., Krompinger, J., & Baime, M. J. (2007). Mindfulness training modifies subsystems of attention. *Cognitive Affective and Behavioral Neuroscience*, 7, 109-119.
- Kabat-Zinn, J. (1990). *Full catastrophe living: Using the wisdom of your body and mind to face stress, pain, and illness*. New York, N.Y.: Dell Publishing.
- Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of dsm-iv disorders in the national comorbidity survey replication. *Archives of General Psychiatry*, 62, 593-602.
- Koszycki, D., Benger, M., Shlik, J., & Bradwejn, J. (2007). Randomized trial of a meditation-based stress reduction program and cognitive behavior therapy in generalized social anxiety disorder. *Behaviour Research and Therapy*, 45, 2518-2526.
- Liebowitz, M. R. (1987). Social phobia. *Modern Problems in Pharmacopsychiatry*, 22, 141-173.

- Lutz, A., Slagter, H. A., Dunne, J. D., & Davidson, R. J. (2008). Attention regulation and monitoring in meditation. *Trends Cogn Sci*, 12, 163-169.
- Moore, A., & Malinowski, P. (2009). Meditation, mindfulness and cognitive flexibility. *Conscious and Cognition*, 18, 176-186.
- Mueller, E. M., Hofmann, S. G., Santesso, D. L., Meuret, A. E., Bitran, S., & Pizzagalli, D. A. (2008). Electrophysiological evidence of attentional biases in social anxiety disorder. *Psychological Medicine*, 1-12.
- Nolen-Hoeksema, S. (1991). Responses to depression and their effects on the duration of depressive episodes. *Journal of Abnormal Psychology*, 100, 569-582.
- Northoff, G., Heinzl, A., de Greck, M., Bermpohl, F., Dobrowolny, H., & Panksepp, J. (2006). Self-referential processing in our brain-a meta-analysis of imaging studies on the self. *Neuroimage*, 31, 440-457.
- Phan, K. L., Fitzgerald, D. A., Nathan, P. J., & Tancer, M. E. (2006). Association between amygdala hyperactivity to harsh faces and severity of social anxiety in generalized social phobia. *Biol Psychiatry*, 59, 424-429.
- Preston, A. R., Thomason, M. E., Ochsner, K. N., Cooper, J. C., & Glover, G. H. (2004). Comparison of spiral-in/out and spiral-out bold fmri at 1.5 and 3 t. *Neuroimage*, 21, 291-301.
- Ramel, W., Goldin, P. R., Carmona, P. E., & McQuaid, J. R. (2004). The effects of mindfulness meditation on cognitive processes and affect in patients with past depression. *Cognitive Therapy and Research*, 28, 433.

Rapee, R. M., & Heimberg, R. G. (1997). A cognitive-behavioral model of anxiety in social phobia. *Behavioral Research and Therapy*, 35, 741-756.

Rosenberg, M. (1965). *Society and the adolescent self-image*. Princeton, NJ: Princeton University Press.

Schultz, L. T., & Heimberg, R. G. (2008). Attentional focus in social anxiety disorder: Potential for interactive processes. *Clinical Psychology Review*, 28, 1206-1221.

Spielberger, C. D., Gorsuch, R. L., & Lushene, R. E. (1970). *Manual for the state-trait anxiety inventory*. Palo Alto, CA: Consulting Psychologists Press.

Stein, M. B., Goldin, P. R., Sareen, J., Zorrilla, L. T., & Brown, G. G. (2002). Increased amygdala activation to angry and contemptuous faces in generalized social phobia. *Arch Gen Psychiatry*, 59, 1027-1034.

Talairach, J., & Tournoux, P. (1988). *Co-planar stereotaxic atlas of the human brain*. New York: Thieme.

Teasdale, J. T., Segal, Z. V., Williams, J. M. G., Ridgeway, V. A., Soulsby, J. M., & Lau, M. A. (2000). Prevention of relapse/recurrence in major depression by mindfulness-based cognitive therapy. *Journal of Consulting and Clinical Psychology*, 68, 615-623.