

**Mindfulness Meditation Training and Self-Referential Processing
in Social Anxiety Disorder: Behavioral and Neural Effects**

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Abstract

Objective: This study examined the effects of Mindfulness–Based Stress Reduction (MBSR) on the brain-behavior mechanisms of self-referential processing (SRP) in patients with social anxiety disorder (SAD).

Methods: Sixteen patients underwent functional magnetic resonance imaging while encoding self-referential, valence, and orthographic features of social trait adjectives. Post-MBSR, 14 patients completed neuroimaging.

Results: Compared to baseline, MBSR completers showed (a) increased self-esteem and decreased anxiety, (b) increased positive and decreased negative self-endorsement, (c) increased activity in a brain network related to attention regulation, and (d) reduced activity in brain systems implicated in conceptual-linguistic self-view.

Conclusions: MBSR-related changes in maladaptive or distorted social self-view in adults diagnosed with SAD may be related to modulation of conceptual self-processing and attention regulation. Self-referential processing may serve as a functional bio-behavioral target to measure the effects of mindfulness training.

Introduction

Social anxiety disorder (SAD) is a common and frequently debilitating condition characterized by intense fear of evaluation in social or performance situations (Jefferys, 1997; Kessler, McGonagle, Zhao, Nelson, Hughes, Eshleman, Wittchen, & Kendler, 1994). SAD has an early onset (Otto, Pollack, Maki, Gould, Worthington, Smoller, & Rosenbaum, 2001), and regularly precedes other anxiety, mood, and substance abuse/dependence disorders (Lampe, Slade, Issakidis, & Andrews, 2003; Matza, Revicki, Davidson, & Stewart, 2003).

SAD is associated with significant distress and functional impairment in both work and social domains (Lochner, Mogotsi, du Toit, Kaminer, Niehaus, & Stein, 2003; Rapee, 1995; Schneier, Heckelman, Garfinkel, Campeas, Fallon, Gitow, Street, Del Bene, & Liebowitz, 1994), and typically persists unless treated (Clark & Wells, 1995). The early onset of SAD magnifies its impact, including increased school dropout (Van Ameringen, Allgulander, Bandelow, Greist, Hollander, Montgomery, Nutt, Okasha, Pollack, Stein, & Swinson, 2003), poor social integration, and increased co-morbid psychopathology (Lampe et al., 2003; Matza et al., 2003; Randall, Thomas, & Thevos, 2001).

Self-Referential Processing in Social Anxiety Disorder

Cognitive models of social anxiety (Clark & McManus, 2002; Clark & Wells, 1995; Rapee & Heimberg, 1997) suggest that during social situations several psychological processes characterize SAD, including fear of negative evaluation, maladaptive cognitions regarding self (e.g., as socially incompetent) and others (e.g., as critical judges), and an exaggerated self-focus. Self-

referential processing (SRP) is heightened during social and performance situations in patients with SAD (Spurr & Stopa, 2002). Exaggerated SRP in patients with SAD distorts interpretations of social cues and maintains social fears (Bogels & Mansell, 2004). SRP is thought to contribute to (a) negative emotional reactivity, (b) deficits in cognitive regulation of emotion and (c) interference with interpersonal functioning. Thus, clinical interventions that influence SRP may modulate a core mechanism related to SAD.

MBSR and Self-Referential Processing

Mindfulness meditation, as taught in Mindfulness-based Stress Reduction (MBSR), involves the cultivation of present moment focus without distorted evaluation (Kabat-Zinn, 1990). Mindfulness practice is conceptualized as directly reducing the habitual tendency to automatically engage in and react to evaluative mental states (Teasdale, Segal, Williams, Ridgeway, Soulsby, & Lau, 2000).

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). One mechanism by which MBSR produces these reductions in clinical symptoms is through its effect on SRP, including reduction in negative self-rumination (Ramel, Goldin, Carmona, & McQuaid, 2004) and enhancement of experiential and visceral modes of SRP (Farb, Segal, Mayberg, Bean, McKeon, Fatima, & Anderson, 2007).

MBSR and SAD

It is believed that mindfulness training may diminish SRP in patients with SAD, specifically reducing habitual tendencies to engage in hypercritical social

self-view (self-evaluation), and to react in an exaggerated manner to beliefs about how others might view oneself (other-evaluation). Thus, for patients with SAD, mindfulness training may lead to a shift from cognitive distortions of the social self in SAD towards a more adaptive (i.e., less distorted) mode of SRP.

Although the proposed mechanisms of MBSR appear to match the self-other evaluative distortions at the core of SAD, to date, there have been only three studies that have examined the effect of mindfulness training as a clinical intervention for SAD. Patients with generalized SAD treated with either 8-week MBSR or 12-week cognitive-behavioral group therapy (CBGT) showed equivalent improvement on mood, functionality, and quality of life, however, clinician- and patient-rated measures of social anxiety indicated greater effectiveness of CBGT compared to MBSR (Koszycki, Benger, Shlik, & Bradwejn, 2007). Online delivery of MBSR was found to reduce shyness, anxiety and social anxiety (Arana, 2006). An intervention that combined mindfulness and task concentration training reduced fear of negative evaluation and self-ideal discrepancy (Bogels, Sijbers, & Voncken, 2006).

Thus, there is preliminary evidence that mindfulness training may impact self-processing and reduce social anxiety. An important gap in the literature, however, is the lack of an understanding of how MBSR impacts the neural bases of self-referential processes.

SRP, Neural Circuitry, and MBSR

Neuroimaging investigations using different stimulus presentations, including judgments of visually presented trait adjectives (Kelley, Macrae,

Wyland, Caglar, Inati, & Heatherton, 2002), aurally presented statements (Johnson, Baxter, Wilder, Pipe, Heiserman, & Prigatano, 2002), or mental reflection on self-traits (Kjaer, Nowak, & Lou, 2002), have identified a brain network associated with SRP. A recent meta-analysis of neuroimaging investigations has identified three cortical midline brain regions that are reliably activated as a network during SRP: ventral medial prefrontal cortex (VMPFC), dorsal medial prefrontal cortex (DMPFC), and a region spanning posterior cingulate cortex (PCC) and precuneus (Northoff, Heinzl, de Greck, Bermpohl, Dobrowolny, & Panksepp, 2006).

The selective engagement of this SRP-related brain network has been demonstrated for self versus situational focus (Ochsner, Ray, Cooper, Robertson, Chopra, Gabrieli, & Gross, 2004) and for self versus perspective taking (D'Argembeau, Ruby, Collette, Degueldre, Balteau, Luxen, Maquet, & Salmon, 2007). The SRP-related brain network has been shown to vary with ratings of self-relatedness of stimuli recorded post-fMRI (Phan, Taylor, Welsh, Ho, Britton, & Liberzon, 2004), and may be valence-independent (Fossati, Hevenor, Graham, Grady, Keightley, Craik, & Mayberg, 2003).

An investigation of the effect of MBSR on the neural substrates of SRP (Farb et al., 2007) found that a narrative self-focus, characterized as a language-mediated conceptual-analytic mode of evaluation, resulted in activation of midline cortical regions implicated in conceptual self-representation (ventral and dorsal MPFC, PCC) and language processing (left inferior frontal gyrus, middle temporal gyrus). When cued to engage in an experiential self-focus,

characterized as non-goal oriented, present-moment engagement with the contents of one's thoughts, feelings and body state, MBSR-trained participants had decreased brain responses implicated in conceptual self-representation and emotional reactivity (left dorsal amygdala), and increased right lateralized brain responses linked to cognitive control (dorsal and ventrolateral PFC), visceral (posterior insular cortex, somatosensory cortex) and attention (inferior parietal lobule) (Gusnard, Akbudak, Shulman, & Raichle, 2001). This study, however, did not examine changes in neural responses from pre- to post-MBSR training, behavioral ratings of self-endorsement of traits, and differential positive and negative valence related neural responses.

The Present Study

To investigate the effect of mindfulness training on the neural basis of self-processing in patients with SAD, the present study used fMRI to examine MBSR-related changes in clinical symptoms as well as behavioral and neural measures of self-processing. Clinically, we expected the MBSR would reduce symptoms of anxiety and depression. On the SRP task, we expected mindfulness training would increase positive and decrease negative self-view as indexed by changes from pre- to post-MBSR in self-endorsement of social traits. Neurally, our analyses focused on a SRP-related network of cortical midline structures (ventral and dorsal MPFC, PCC). We expected MBSR would result in reduced narrative/conceptual self-focus (i.e., midline cortical neural responses) and increased experiential self-focus (i.e., somatosensory and visceral neural responses) during both positive and negative SRP.

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), depressive (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 a battery of questionnaires and, in a separate session, the fMRI SRP task. Prior to MR scanning, patients were instructed on the SRP task with six practice trials for each of the three trial types using word stimuli not presented during the fMRI task. Stimuli were presented visually with E-Prime software on a PC. Patients with SAD were scanned again after completion of a standard MBSR course.

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 several MBSR courses in medical and academic settings.

Self-Referential Processing Task

The SRP task is based on the self-referential encoding task (Derry & Kuiper, 1981) which is considered an information processing measure of self-endorsement of self-schema. Stimuli consisted of 25 positive and 25 negative social trait adjectives from the Affective Norms of Emotion Words database (Bradley & Lang, 1999), balanced (all $P_s > .51$) on word frequency (positive adjectives=40.5, negative adjectives=33.6), arousal (positive adjectives=5.54, negative adjectives=5.43), valence (deviation from neutral: positive adjectives=2.66, negative adjectives=2.58), and number of letters (positive adjectives=6.9, negative adjectives=7.2).

In a single functional run (9 minutes, 54 seconds), each of the 25 positive and 25 negative adjectives was presented three times, once in each of three conditions: self-referential (self-descriptive or not), the target experiment condition, and two control conditions: valence identification (positive or negative affective meaning) and case identification (upper or lower case). Each of the six conditions (three instructions by two valences) included five blocks of five adjective stimuli. Each block was comprised of a fixation, question (one of three questions: "Describes ME?", "POSITIVE valence?", or "UPPER case?"), and five adjectives of the same valence presented one at a time for 3s each (Figure 1).

Stimulus order was determined by a pseudo-random block sequence with no more than two blocks of the same condition in a row and a random sequence of words and upper/lower case within each block. Participants pressed one of two buttons to indicate whether or not a word was self-descriptive (i.e., self-endorsement), positively valenced, or in uppercase letters. Behavioral responses were made using a custom button box and recorded using Eprime software during the scan.

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. 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= .8594² x 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. 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 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 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. A Time (Baseline, post-MBSR) \times Word Valence (negative, positive) repeated measures ANOVA resulted in a significant interaction of Time by Word Valence on self-endorsement, $F(1,14)=19.91$, $p < .001$, $\eta_p^2 = .60$. Follow-up paired t-tests showed that from baseline to post-MBSR patients had reduced negative, $t(1,14)=3.39$, $p < .005$, and increased positive, $t(1,14)=4.04$, $p < .005$, self-endorsement (Figure 2).

Baseline Neural Results. At baseline, a one-sample t-test of the contrast of positive SRP versus positive case yielded greater BOLD responses for

positive SRP in brain regions implicated in self-processing (medial and dorsomedial PFC, medial precuneus), language processing (left ventrolateral PFC, posterior superior temporal gyrus), memory (parahippocampal gyrus), and visual processing (fusiform, cuneus, lingual gyri) (Table 2, Figure 3A and B).

For the baseline contrast of negative SRP versus negative case, a one-sample t-test yielded greater BOLD responses for negative SRP in brain regions implicated in self-processing (medial and dorsomedial PFC, posterior cingulate), language processing (left ventrolateral PFC), affective processing (subgenual ACC), and visual processing (fusiform gyrus, lingual gyrus) (Table 3, Figure 3C and D).

Post-MBSR Neural Results. We conducted paired t-tests to examine changes from pre- to post-MBSR for the contrast of positive SRP versus positive case and of negative SRP versus negative case. For positive SRP, there was evidence of decreased BOLD responses in brain regions related to self-processing (dorsomedial and medial PFC) and language processing (left inferior frontal gyrus) (Table 4, Figure 4A). Negative SRP versus negative case processing resulted in increased brain responses in visual attention (left inferior parietal lobule and medial precuneus) (Table 4, Figure 4B).

Discussion

The goal of this study was to investigate the effects of MBSR training on behavioral and neural bases of self-referential processing in patients with SAD. Mindfulness training was hypothesized to reduce symptoms of anxiety and

depression, distorted social self-views, and activity in midline brain activations linked to a narrative/conceptual mode of self-referential processing.

Clinical Symptoms

MBSR resulted in moderate reduction of symptoms of social anxiety, depression, rumination, state anxiety, as well as increased self-esteem. These findings replicate previous findings in both healthy adults and clinical samples (Bishop, 2002) and preliminary evidence of clinical improvement in patients with SAD (Arana, 2006; Koszycki et al., 2007). While MBSR reduced social anxiety symptoms (Cohen's $d=1.0$), it did not match the effect of cognitive-behavioral therapy (cognitive restructuring plus exposure; Cohen's $d=1.8$) and pharmacological interventions (Cohen's $d=1.5$) on social anxiety symptoms (Fedoroff & Taylor, 2001). However, a direct comparison of the longer-term impact of these three clinical interventions for SAD has not been conducted.

Self-Referential Processing

MBSR resulted in decreased negative and increased positive self-views on the SRP task. This suggests that training in the mindfulness meditation skills may influence habitual distorted social self-views that are deeply entrenched in SAD. MBSR emphasizes cultivating an equanimous perspective towards mental and visceral experience. This perspective is described as a non-evaluative moment-to-moment awareness and a non-judgmental meta-cognitive orientation.

Being able to shift from evaluative to non-evaluative awareness is a psychological skill that may be related to reductions in negative self-focused rumination. Decreased self-focused attention may account for the adaptive shift

in social self-view in patients with SAD during MBSR. Changes in negative self-focused attention have been shown to vary as a function of social anxiety symptom reduction during from pre- to post-exposure therapy (Hofmann, 2000). This pattern of results indicates that a modulation of both cognitive content (i.e., self-focused thoughts) and cognitive processes (i.e., attention and interpretative biases) may be core mechanisms underlying the effectiveness of psychosocial interventions for SAD.

Neural Bases of SRP

Baseline neural results demonstrate that both positive and negative SRP in patients with SAD yielded robust activation of self-processing midline cortical brain regions (Northoff et al., 2006) and language processing areas (Iacoboni & Wilson, 2006). The apparent greater BOLD response for positive SRP compared to negative SRP may be due to either greater arousal for the positive SRP and/or to reactivity to the negative social traits during the case condition thereby resulting in a smaller difference in BOLD response in the contrast of negative SRP versus case. The similar pattern during positive and negative SRP at baseline in patients with SAD indicates that they automatically rely on a specific form of self-focus that recruits brain systems related to a language-mediated conceptual-analytic mode of evaluation (Farb et al., 2007).

Mindfulness Effects on Neural Bases of SRP

Behavioral ratings (i.e., self-endorsement) and neural responses during negative and positive SRP changed in opposite directions from pre- to post-MBSR. Thus, patients with SAD endorsed fewer negative social traits yet

showed increased neural responses during negative SRP in brain regions implicated in attentional allocation (left inferior parietal lobule and medial precuneus) (Fan, McCandliss, Fossella, Flombaum, & Posner, 2005). This overlaps with findings from Farb and colleagues who found evidence of increased sensory and attentional brain systems in adults with mixed anxiety and depression symptoms after MBSR for experiential versus narrative/conceptual self-focus (Farb et al., 2007). Enhanced activation of attentional networks during negative self-processing may be related to greater attentional engagement towards negative social traits as habitual automatic avoidance diminishes with mindfulness training (Allen, Chambers, & Knight, 2006).

For positive SRP, MBSR resulted in increased self-endorsement of positive social traits and decreased neural responses linked to self-referential and language processing. Similar to the Farb et al. study, the observed changes in neural patterns indicates that MBSR resulted in a shift away from the narrative/conceptual self-focus observed robustly at baseline. This suggests that mindfulness training reduces the prepotent conceptual-linguistic mode of self-processing, and thus generates the possibility of utilizing other modes of self-processing. There was not, however, evidence of increased viscerosomatic activation indicative of embodied experiential self-focus. This may be due to specific features of social anxiety, including an exaggerated habitual tendency to experience interoceptive somatic indicators of anxiety (Edelmann & Baker, 2002) that trigger negative self-perception and self-beliefs (Wells & Papageorgiou, 2001). Thus, unlike the increase in embodied experiential self-focus observed in

healthy adults who completed MBSR in the Farb et al study, decreased emphasis on viscerosomatic interoceptive processes may be clinically beneficial in patients with SAD.

One of the potential effects of MBSR is a reduction in the habitual tendency to engage in a narrative/conceptual mode of self-processing. In terms of neural processes, this suggests that the default narrative/conceptual mode may be reduced (ventromedial PFC, dorsomedial PFC, and posterior cingulate/precuneus) while other types of self-processing that rely less on conceptual-linguistic-narrative modalities are more easily accessed. If the prepotent response in adults with SAD is enhanced negative self-view with concomitant diminished positive self-view, then a training that reduces the habit of distorted conceptual self-view could very well result in increased positive self-endorsement together with decreased neural activity in brain systems that support conceptual self-view.

Clinical Implications

These results provide initial support for a specific neural mechanism of change related to mindfulness training for social anxiety. Furthermore, this study provides brain-behavioral evidence for the cognitive model of social anxiety, specifically, abnormal behavioral and neural patterns of self-processing in SAD. Importantly, MBSR resulted in changes in both positive and negative self-view, both of which have been shown to be aberrant in patients with SAD (Weeks, Heimberg, Rodebaugh, & Norton, 2007) Clinical intervention studies might consider how baseline SRP may moderate treatment adherence, and how

changes in SRP may predict treatment outcome status or mediate changes in social anxiety symptom severity, emotional reactivity and affective dysregulation.

Limitations and Directions for Future Research

This study is limited by the lack of a control group or active comparison clinical intervention that would help delineate more clearly how SRP is modified by MBSR. Future research with control groups will be necessary in order to address potential factors that might be contributing to changes in self-view such as practice effects and habituation to the scanner environment. 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 SRP.

There is need for better behavioral and neural assessment of different modes of SRP, including narrative/conceptual, experiential, as well as other forms. This study examined only experimenter-selected positive and negative social trait adjectives. Patient-generated stimuli may result in more robust brain-behavioral responses in patients with SAD. This would provide a more ecologically valid test of the effects of clinical interventions on SRP.

In the present study, it was not possible to examine temporal dynamics of participants' responses because word stimuli were presented for only 3s each. Use of longer stimulus durations may allow for examination of sustained cognitive processes (e.g., negative rumination) and differential temporal features of BOLD responses in SRP midline structures.

Finally, the MBSR course was offered by the primary investigator of this study and thus the course instructor was not blind to the study outcome measures. Future studies will benefit from having different individuals serve as the research investigator and the course instructor.

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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±9.7 | 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: Positive Self > Case

| Brain Regions | BA | x y z ^a | % Signal Change | Vol (voxels) | t- value |
|---|----|--------------------|-----------------------|-----------------|-------------|
| Positive Self | | | | | |
| <u>Frontal Cortex</u> | | | | | |
| Medial PFC 2 | 10 | 0 45 56 | .53 | 862 | 3.60 |
| R Dorsolateral PFC 8 | 46 | 48 21 22 | .14 | 24 | 3.87 |
| Dorsomedial PFC | | | | | |
| L Inferior Frontal Gyrus 3 | 47 | -52 25 -5 | .44 | 264 | 5.89 |
| R Inferior Frontal Gyrus 5 | 47 | 48 25 -12 | .26 | 132 | 3.43 |
| Middle Cingulate Cortex 14 | 23 | 0 -13 32 | .16 | 12 | 3.42 |
| L Middle Frontal Gyrus 16 | 6 | -38 11 50 | .11 | 8 | 3.63 |
| L Middle Frontal Gyrus 17 | 6 | -45 11 46 | .15 | 7 | 3.47 |
| L Middle Frontal Gyrus 17 | 6 | -48 4 53 | .30 | 7 | 3.58 |
| <u>Temporal Cortex</u> | | | | | |
| L posterior Superior Temporal Gyrus 7 | 22 | -52 -27 1 | .14 | 26 | 3.52 |
| R posterior Superior Temporal Gyrus 11 | 22 | 48 -27 5 | .13 | 15 | 3.39 |
| L Anterior Temporal Pole 10 | 38 | -48 14 -30 | .16 | 18 | 3.38 |
| R Anterior Temporal Pole 21 | 38 | 41 21 -30 | .14 | 4 | 3.83 |
| <u>Parietal Cortex</u> | | | | | |
| Medial Precuneus 13 | 7 | 0 -72 36 | .22 | 12 | 3.38 |
| <u>Occipital Cortex</u> | | | | | |
| Bilateral Fusiform, Lingual Gyrus, Declive 1 | 19 | 24 -86 -19 | .42 | 946 | 4.15 |
| L Fusiform Gyrus 6 | 19 | -38 -75 -16 | .20 | 36 | 3.95 |
| R Cuneus 25 | 18 | 14 -92 12 | .10 | 4 | 4.42 |
| <u>Subcortical</u> | | | | | |
| Thalamus 4 | | -3 -13 15 | .26 | 241 | 4.47 |
| Tonsil 9 | | -3 -51 -30 | .12 | 23 | 4.15 |
| L Declive 12 | | -45 -65 -19 | .22 | 14 | 3.30 |
| R Declive 15 | | 34 -61 -19 | .18 | 9 | 3.73 |
| R Lentiform Nuclues 20 | | 17 -6 8 | .07 | 5 | 3.40 |
| L Parahippocampal gyrus 24 | | -21 -20 -9 | .14 | 4 | 3.48 |
| Case none | | | | | |

Note. t-value threshold ≥ 3.29 , 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, R=right

^aTalairach and Tournoux coordinates of maximum BOLD signal intensity voxel

Table 3

Baseline BOLD Responses: Negative Self > Case

| Brain Regions | BA | x y z ^a | % Signal Change | Vol (voxels) | t- value |
|--------------------------------|-----|--------------------|-----------------------|-----------------|-------------|
| <u>Negative Self</u> | | | | | |
| <u>Frontal Cortex</u> | | | | | |
| Medial PFC 3 | 9 | -10 62 32 | .49 | 529 | 3.56 |
| Medial PFC 9 | 10 | -3 66 19 | .29 | 244 | 3.98 |
| Dorsomedial PFC 7 | 6,8 | -3 18 63 | .51 | 285 | 3.37 |
| Dorsomedial PFC 5 | 8 | -7 28 60 | .42 | 326 | 4.22 |
| Dorsomedial PFC 2 | 8 | -7 52 46 | .55 | 1547 | 3.67 |
| Dorsomedial PFC 10 | 8 | -3 25 50 | .31 | 204 | 3.36 |
| L Inferior Frontal Gyrus 6 | 47 | -55 21 -2 | .38 | 285 | 3.85 |
| Posterior Cingulate 4 | 29 | -3 -48 8 | .33 | 326 | 3.42 |
| R Subgenual ACC 11 | 25 | 13 11 -9 | .17 | 163 | 3.52 |
| <u>Occipital Cortex</u> | | | | | |
| R Fusiform Gyrus 1 | 19 | 41 -72 -19 | .39 | 1913 | 3.59 |
| R Lingual Gyrus 12 | 18 | 3 -96 -9 | .26 | 163 | 3.60 |
| <u>Subcortical</u> | | | | | |
| Declive 8 | | 7 -82 -19 | .26 | 244 | 3.47 |
| <u>Case</u> none | | | | | |

Note. t-value threshold ≥ 3.29 , 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

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

Table 4

Changes in BOLD Responses from Baseline to Post-MBSR

| Brain Regions | BA | x y z ^a | % Signal Change | Vol (voxels) | t- value |
|---------------------------------------|----|--------------------|-----------------------|-----------------|-------------|
| <u>Baseline > Post-MBSR</u> | | | | | |
| <u>Positive Self</u> | | | | | |
| <u>Frontal Cortex</u> | | | | | |
| Medial PFC | 10 | 7 66 5 | -.33 | 7 | 3.83 |
| Medial PFC | 10 | 10 62 22 | -.22 | 4 | 3.35 |
| Dorsomedial PFC | 8 | -3 28 46 | -.35 | 6 | 3.23 |
| L Inferior Frontal Gyrus | 47 | -45 25 -2 | -.30 | 8 | 3.65 |
| L Inferior Frontal Gyrus | 45 | -52 21 8 | -.23 | 5 | 4.13 |
| <u>Subcortical</u> | | | | | |
| R Uvula | | 34 -79 -26 | -.32 | 5 | 3.65 |
| <u>Post-MBSR > Baseline</u> | | | | | |
| <u>Negative Self</u> | | | | | |
| L Inferior Parietal Lobule | 40 | -45 -51 50 | .35 | 4 | 3.02 |
| Medial Precuneus | 7 | 0 -68 46 | .29 | 4 | 2.97 |

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. Experimental design. Each block consists of (a) an asterisk fixation, (b) instruction question to cue self-referential, valence, or orthographic processing, and (c) a set of five different target words of a single valence.

Figure 2. Percent self-endorsement for negative and positive social trait words pre- and post-MBSR. Error bars = SEM. ** $P < .005$

Figure 3. Baseline self-referential processing BOLD responses for positive SRP in A. medial prefrontal cortex and B. ventrolateral prefrontal cortex, and negative SRP in C. medial prefrontal cortex and D. ventrolateral prefrontal cortex.

Figure 4. Changes in BOLD responses for self-referential processing from pre- to post-MBSR. A. Decreased BOLD response during positive self-referential processing vs. positive case: 1=medial PFC (coordinates of peak BOLD response: 7 66 5 and 10 62 22), 2=dorsomedial PFC (-3 28 46), 3=left ventrolateral PFC (-52 21 8), 4=left ventrolateral PFC (-45 25 -2), and B. increased BOLD response during negative self-referential processing, 5=left inferior parietal lobule (-45 -51 50), and 6=medial precuneus (0 -68 46).

Figure 1

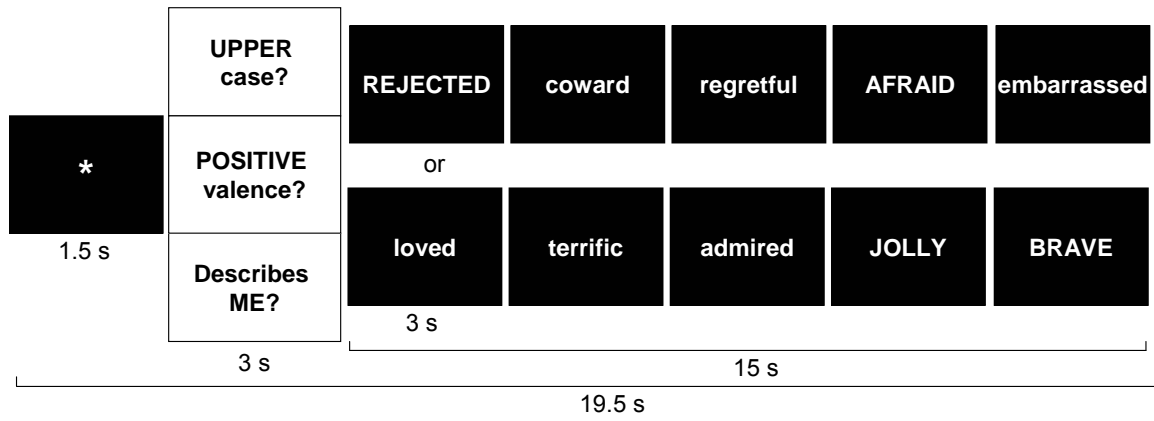


Figure 2

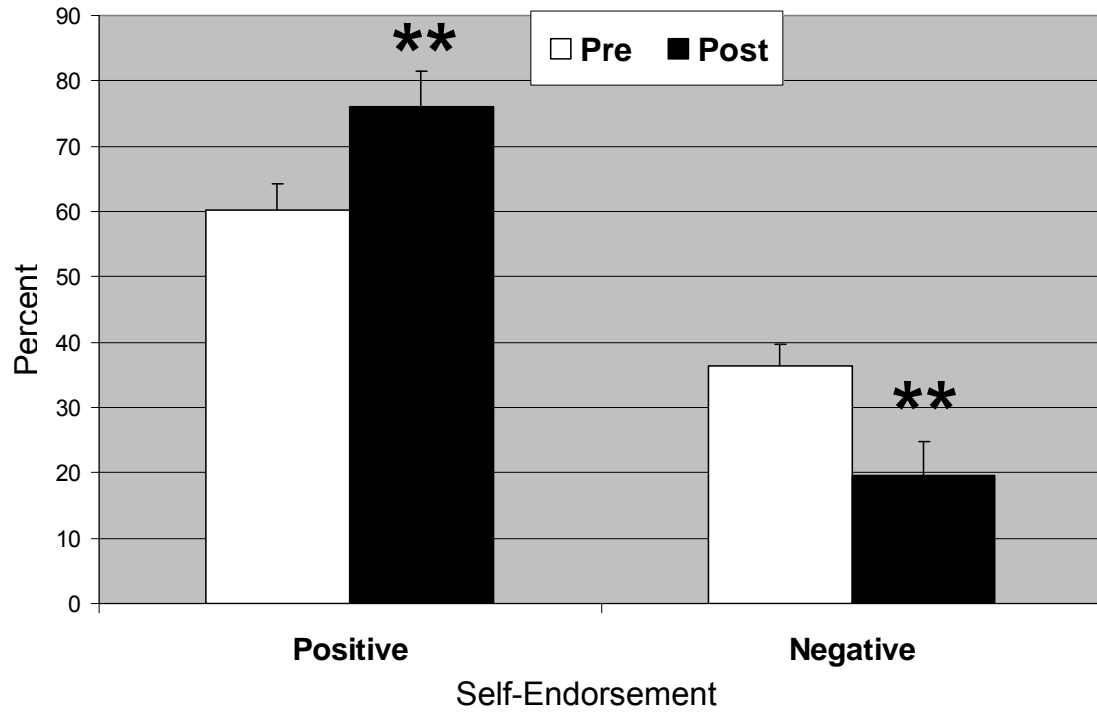


Figure 3

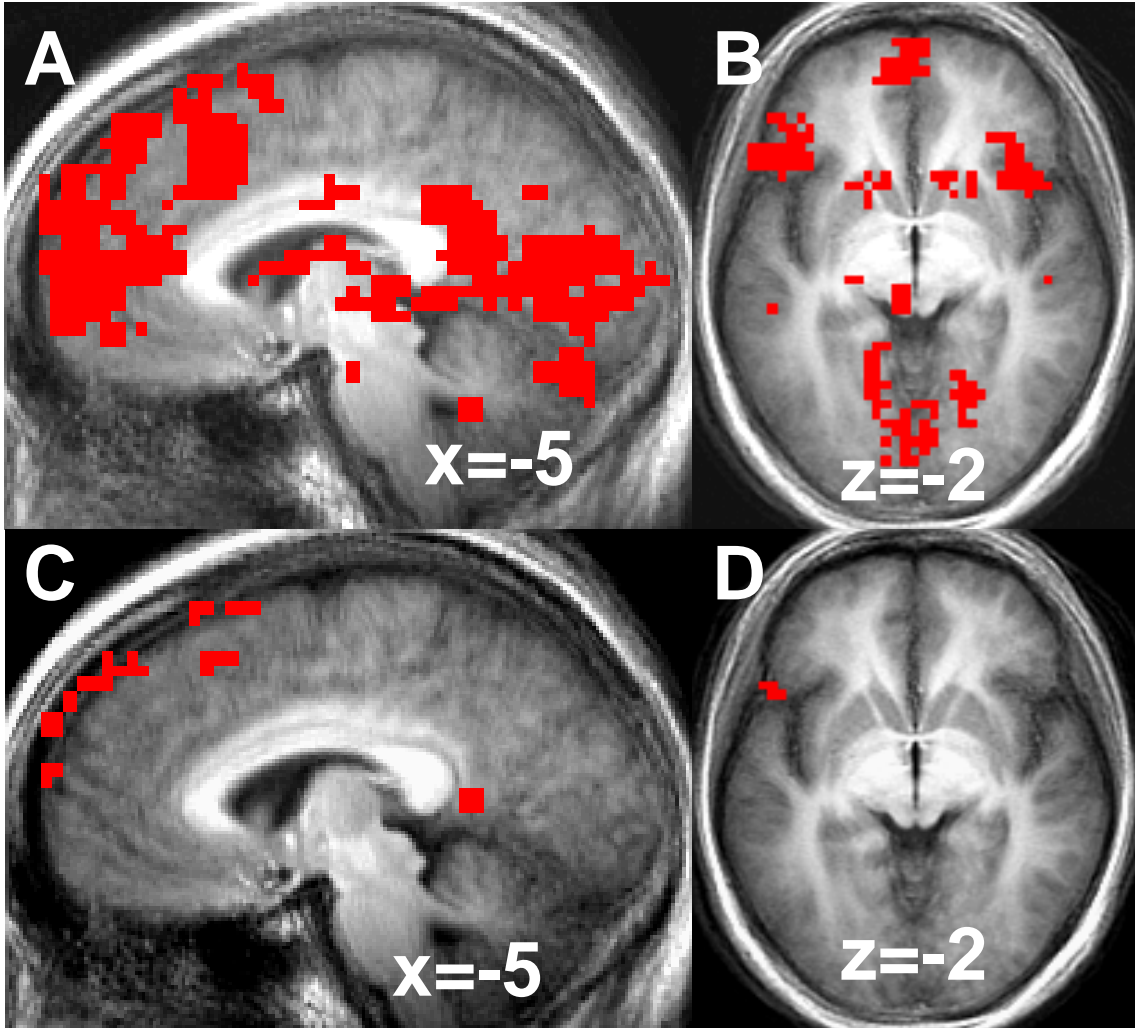


Figure 4

