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Original Research Article

Brief Self-Compassion Training Alters Neural Responses to Evoked Pain for Chronic Low Back Pain: A Pilot Study

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Abstract

Objective. Self-compassion meditation, which involves compassion toward the self in moments of suffering, shows promise for improving pain-related functioning, but its underlying mechanisms are unknown. This longitudinal, exploratory pilot study investigated the effects of a brief (eight contact hours, two weeks of home practice) self-compassion training on pain-related brain processing in chronic low back pain (cLBP). **Methods**. We evaluated functional magnetic resonance imaging (fMRI) response to evoked pressure pain and its anticipation during a self-compassionate state and compared altered brain responses following training with changes on self-reported measures of self-compassion (Self-Compassion Scale [SCS]), interoceptive awareness (Multidimensional Assessment of Interoceptive Awareness [MAIA]), and clinical pain intensity. **Results.** In a sample of participants with cLBP ($N = 20$ total, $N = 14$ with complete longitudinal data) who underwent self-compassion training, we observed reduced clinical pain intensity and disability ($P < 0.01$) and increased trait self-compassion and interoceptive awareness (all $P < 0.05$) following training. Evoked pressure pain response in the right temporo-parietal junction (TPJ) was reduced following training, and decreases were associated with reduced clinical pain intensity. Further, increased fMRI responses to pain anticipation were observed in the right dorsolateral prefrontal cortex (dlPFC) and ventral posterior cingulate cortex (vPCC), and these increases were associated with mean post-training changes in SCS scores and scores from the body listening subscale of the MAIA. **Discussion**. These findings, though exploratory and lacking comparison with a control condition, suggest that self-compassion training supports regulation of pain through the involvement of self-referential (vPCC), salience-processing (TPJ), and emotion regulatory (dlPFC) brain areas. The results also suggest that self-compassion could be an important target in the psychotherapeutic treatment of cLBP, although further studies using controlled experimental designs are needed to determine the specificity of these effects.

Key Words: Temporo-Parietal Junction; Pain Anticipation; Posterior Cingulate Cortex; Cuff Pressure Pain; Self-Compassion; Mindfulness

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Introduction

Chronic low back pain (cLBP) is among the most common and debilitating public health problems worldwide, affecting 10–20% of adults [1] and causing severe interference with psychological and social functioning [2]. There has recently been increased interest in nonpharmacological treatments for this condition, including interventions focused on mindfulness, which is defined as nonjudgmental awareness and acceptance toward inner experiences and physical sensations [3]. Mindfulness-based interventions (MBIs) have shown promise for reducing chronic pain [4] and additionally appear to increase quality of life, coping skills, and psychological functioning in chronic pain sufferers, including in cLBP [5, 6].

The efficacy of MBIs for treating chronic pain may be mediated in part by their effects on interoceptive awareness, particularly awareness of painful sensations. Because chronic pain disorders are characterized by altered bodily representations, including reduced interoceptive capacities [7, 8], mindfulness-based treatments, which emphasize close attention to sensations within the body [9], may prove particularly beneficial. In addition to increased body awareness, self-compassion—the skill of being kind toward oneself in moments of suffering [10]—may be an important component of MBIs for chronic pain. The eight-week Mindful Self-Compassion (MSC) training program is currently among the most popular MBIs in the United States [11], and self-compassion has been proposed as a key mediator of outcomes in MBIs [12]. In community samples, MSC trainings have been shown to improve psychological functioning and life satisfaction, in addition to reducing levels of negative affect [13–15].

In patients with chronic pain, self-compassion is emerging as a valuable skill: Several studies indicate that self-compassion is predictive of positive affect and negatively associated with pain-specific disability in this population [16–18]. Self-compassion training may hold particular promise for the treatment of chronic pain because it targets heightened self-critical tendencies that are frequently observed in this population [19]. In addition, individuals with chronic pain may struggle with the regulation of negative emotions [20], which could potentially be addressed through instruction in self-compassion skills [21]. Chronic pain is also associated with increased rates of early life psychological trauma [22], and self-compassion may be well suited to addressing trauma as it helps individuals to rework dysfunctional narratives about past distressing events and cultivate kindness toward themselves with respect to these events [23]. Training studies on self-compassion are still scarce, but two pilot studies to date suggested that training in loving-kindness meditation, a form of compassion-based meditation that includes training in kindness toward the self, can significantly reduce symptoms of pain and negative affect in cLBP patients [24, 25].

Despite emerging evidence that self-compassion may be useful for treating chronic pain, no studies to date have examined the neurobiological substrates of self-compassion before and after training in this population. Further, if, as currently hypothesized, self-compassion is an important component in MBI mechanisms of action, then even short trainings may impact pain-related functioning and the neural encoding of pain during a self-compassionate state. This exploratory pilot study addresses this gap by investigating the effects of a brief self-compassion training on neural responses to evoked pain in patients with cLBP. Patients were enrolled in a short self-compassion training, where they were provided with meditation techniques to enhance self-compassion in moments of pain. Before and after the intervention, brain responses to a painful mechanical stimulus were examined using functional magnetic resonance imaging (fMRI), and patients completed measures related to pain, pain-specific disability, interoceptive awareness, and psychological functioning. We hypothesized that following the intervention, patients would show reduced pain and pain-related disability, in addition to increases on measures of self-compassion and interoceptive awareness. We also hypothesized that following training, pain-evoked brain responses would be altered in the default-mode network (e.g., posterior cingulate cortex) and salience-processing (e.g., insula) brain regions, both of which have been implicated in chronic pain disorders [26, 27]. Additionally, the default-mode network appears to be an important neural substrate of self-referential processing in the context of mindfulness practice [28–30], and both the default-mode network and insular brain regions show altered patterns of activity following mindfulness-based interventions [31]. Activation of the insula has also been previously observed during an experimentally induced self-compassionate state [32]. Finally, we hypothesized that these changes to brain activation following training would be related to decreased chronic pain intensity and increased trait self-compassion and interoceptive awareness.

Methods

This longitudinal neuroimaging study evaluated cLBP patients at baseline and following a brief, two-visit self-compassion training (Figure 1A). Before and after the intervention, brain responses to evoked pain and pain anticipation were assessed using fMRI.

Patients

Twenty (N = 20) patients (13 female, 7 male) with a mean age (SD) of 40.15 (12.56) years meeting Quebec Task Force Classification System categories I–II (unlikely to exhibit stenosis, mechanical instability or significant

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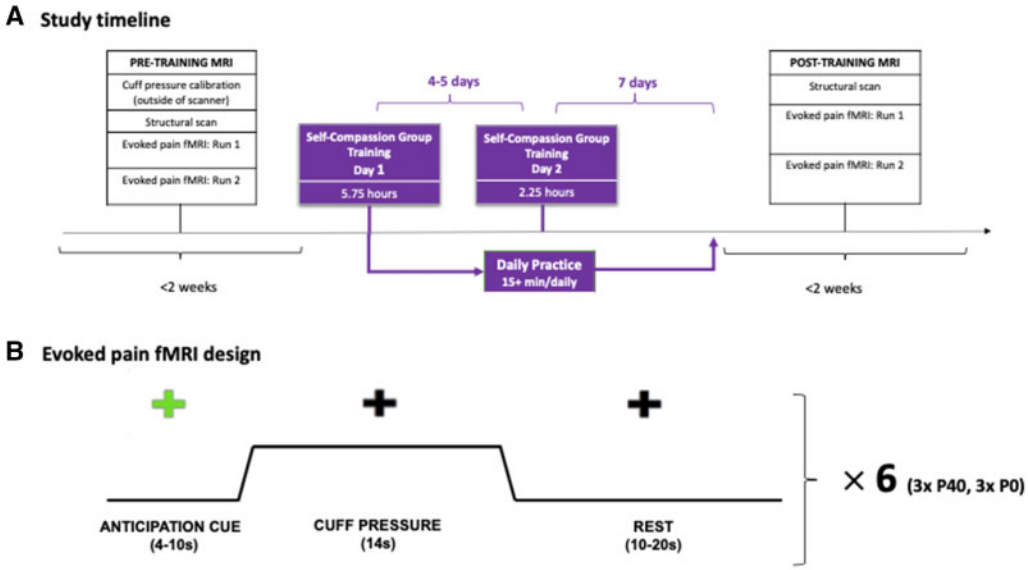

Figure 1. A) Study timeline. B) Experimental design of the cuff pain functional magnetic resonance imaging scan run. Each patient received a total of six cuff pressures over their left lower leg, pseudorandomized in order. Three pressures were tailored to elicit a pain rating of 40/100 (P40), and three were tailored to be nonpainful (P0, 30 mmHg). A cross projected to the subject's visual field , jittered in duration, signaled anticipated onset of cuff pressure.

nerve root involvement) [33] were recruited through flyers and advertisements placed in pain clinics and other locations in the Boston metropolitan area. Eighteen of these patients were included in pretraining fMRI analyses, and 14 were included in longitudinal fMRI comparisons (see *Brain Responses During Evoked Cuff Pain and Pain Anticipation*). The protocol was approved by the Human Research Committee of Partners Healthcare and Massachusetts General Hospital. Patient clinical and demographic characteristics at pretraining are provided in Table 1. Most patients reported either no prior experience with meditation (35%) or fewer than 10 total hours of prior meditation experience (30%) (see the Supplementary Data for more information), and none reported prior experience with self-compassion meditation. No patients reported a history of back surgery. Information about use of medications at the time of study enrollment is also provided in the Supplementary Data. No patients reported changing their medication regimens while enrolled in the study.

All patients completed prescreening over the phone to determine eligibility, at which time they were assessed for the following inclusion criteria: age 21–65; fluency in English; reporting any low back pain for at least six months; average clinical pain rating ≥3 out of 10 on the 11-point LBP intensity scale for the two weeks before enrollment, as determined during phone prescreening; prior health care–seeking behavior (e.g., evaluation by a physician or other health care provider such as a physical therapist or acupuncturist); right-handedness. In addition, patients were excluded from participating if they routinely used opioids ≥60 mg morphine equivalents or planned to change medication or nonpharmacological therapy regimens during or within two months before the study. Patients were also excluded from participating if they met any of the following criteria: conditions that would impede participation in self-compassion meditation (e.g., psychosis); severe and unstable medical conditions that would heighten potential for adverse outcomes; an active substance use disorder in the past six months; contraindications to MRI scanning; history of neurological disease or injury.

Table 1. Demographics and clinical characteristics for all subjects who enrolled in the study (N = 20)

	Mean (SD)
Demographics	
Age, y	40.15 (12.56)
Clinical characteristics	
Duration of pain, y since onset	10.66 (8.98)
PCS	16.16 (8.80)
PROMIS-29, normalized T-scores	
Anxiety	56.19 (8.66)
Depression	53.43 (6.00)
Fatigue	53.83 (2.90)
Pain interference	58.61 (7.69)
Physical functioning	29.23 (5.04)
Sleep disturbance	57.21 (9.60)
Social roles and activities	39.94 (6.41)

PCS = Pain Catastrophizing Scale; PROMIS-29 = Patient-Reported Outcomes Measurement Information System-29.

Information and Screening Visit

An information and screening visit was conducted at either the Athinoula A. Martinos Center for Biomedical Imaging (Martinos Center), Massachusetts General Hospital in Boston, Massachusetts, or the Center for Mindfulness and

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Compassion (CMC) at Cambridge Health Alliance in Somerville, Massachusetts. Patients were provided with detailed information about the study intervention and practice requirements, and a practice commitment interview was conducted to ensure that they could commit to at least 15 minutes of daily compassion-based meditation practice during the intervention. All patients provided written informed consent before participating in any study procedures.

Study Visits

At the pretraining MRI scan visit, all patients first underwent a brief calibration procedure to determine appropriate stimulus intensities for the evoked pain fMRI scan run. Patients were instructed in the use of a 0–100 pain intensity rating scale, and a 13.5-cm-wide Velcro-adjusted pressure cuff connected to a Hokanson rapid cuff inflator was placed over the gastrocnemius muscle on the left lower leg, 3 cm beneath the patella. Calibration was performed using the method of limits, with an ascending series of 10-second pressures delivered in increments of 15 mmHg until patients reported a pain intensity rating of 40/100 (P40). A target rating of 40/100 was selected based on prior research using a moderate but tolerable level of cuff pressure pain (40–50/100) to successfully elicit nociceptive brain responses [34–37]. For pressure control, a very low pressure intended to elicit no pain (30 mmHg; P0) was also tested to ensure that patients did not find it painful. The P40 pressure was then delivered again while patients were lying inside of the scanner and recalibrated if necessary before the MRI procedures (see *Evoked Pain fMRI Scan,* below). Following self-compassion training, subjects completed a second fMRI scan visit during which the cuff pressures were matched to the first scan (identical pressures for P40 and P0). None of the subjects included in fMRI analysis required the P40/P0 pressure values used at their pretraining scan to be adjusted at the post-training scan.

In addition, within one week before and after the intervention, patients completed the following questionnaires using REDCap electronic data capture tools hosted through Partners Healthcare [38]: Multidimensional Assessment of Interoceptive Awareness (MAIA) [39]; Pain Catastrophizing Scale (PCS) [40]; Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29) [41], including the clinical low back pain intensity item (0–10); Roland-Morris Low Back Pain and Disability Questionnaire (RMQ) [42]; Self-Compassion Scale (SCS) [43]. At their post-treatment visit, subjects were also asked to evaluate the program and their expectations about its impact on their daily lives using the Credibility/Expectancy Questionnaire (CEQ) [44].

Self-Compassion Training

Self-compassion (SC) training was administered by two licensed clinical psychologists (CG, SP) with extensive professional experience administering self-compassion interventions and was conducted at CMC. Patients completed two intensive group trainings over the course of two weeks: the first 5.75 hours in length, the second 2.25 hours. The two group trainings were spaced four to five days apart. The training program introduced the theoretical background of self-compassion and its application to various aspects of life, including chronic pain. The training introduced patients to self-compassion meditation, in particular to the practice of loving-kindness meditation toward the self, which was supported by a set of personalized self-compassion phrases. This practice is described as one approach to induce and train a state of self-compassion [14] and is therefore referred to as self-compassion meditation for the purposes of the current study. It was chosen for its expected value for patients and its suitability to be applied during the MRI pain testing procedures. Patients also participated in group discussions and other activities designed to facilitate an embodied sense of self-compassion and improve the ability to apply compassion therapeutically in everyday life (see the Supplementary Data for more detail). At the end of the first group session, patients were asked to continue practicing self-compassion meditation at home for at least 15 minutes daily over the next two weeks, with 20 minutes of daily practice or more suggested, and were provided with guided audio recordings that ranged from 15 to 25 minutes in length to facilitate their practice. Three-minute audio recordings were used before the pain task at the post-training MRI visit to help induce a self-compassionate state throughout the evoked pain task (see the Supplementary Data for more detail). The recordings were a short form of patients' guided home practice meditations and reminded them to be kind and compassionate to themselves in moments of discomfort. Patients logged their daily practice time over the course of the two weeks of the intervention using an online questionnaire that was sent daily using REDCap electronic data capture tools hosted through Partners Healthcare [38].

Evoked Pain fMRI Scan

Brain responses to deep tissue pain were examined using cuff pressure algometry, similarly to previous studies in chronic pain populations [34, 37]. We chose this method because it can assess deep tissue sensitivity without being affected by skin sensitization or desensitization [45] and because it best approximates the deep musculoskeletal pain that is characteristic of chronic myofascial pain disorders such as cLBP [46, 47].

At both pre- and post-training MRI scan sessions, subjects underwent two block-design evoked pain scan runs. At the baseline, pretraining scan, patients were instructed to be kind to themselves during the scan run without any further instructions. At post-training, patients were told to be kind to themselves applying the self-compassion skills that they had learned during the training and practiced at home. In addition, to facilitate a self-

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compassionate state during the post-training scans, a brief (two-minute) audio recording sampled from the home practice materials was played through headphones before (but not during) the evoked pain fMRI runs.

During the fMRI scan runs (Figure 1B), patients viewed a black cross-hair, which turned green to cue anticipation of a subsequent pain block (pain anticipation). This green-cross pain anticipation block was jittered in duration (from four to 10 seconds) so that subjects would not be able to predict when cuff pain would occur. Visual stimuli were presented using validated software (E-Prime 2.0, Psychology Software Tools Inc., Pittsburgh, PA, USA) and a laptop connected to a projector and screen installed inside of the MRI scanner. During each fMRI scan run, a total of six separate cuff pressure stimuli (three P40, three P0), each preceded by the anticipation period and followed by a rest period (jittered in duration, 10–20 seconds), were delivered to the left calf, as in several of our prior studies [34, 36, 37, 48, 49]. The order of pressures was pseudo-randomized but identical across subjects and runs, as follows: P40, P0, P40, P0, P0, P40. After each run, patients were asked to provide retrospective ratings of pain intensity and unpleasantness associated with the painful (P40) stimuli ("on average, on a scale of 0 to 100, where 0 is no pain and 100 is the worst imaginable pain"). Pain intensity ratings were collected following the scan run, rather than during the scan, after each cuff pressure block to avoid distracting patients from entering a self-compassionate state.

MRI data were obtained on a 3.0T Siemens Trio TIM (Siemens Medical, Erlangen, Germany) equipped with a 32-channel head coil at the Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital. T1-weighted structural images were obtained using a three-dimensional (3D) MP-RAGE pulse sequence (TR = 2530 ms, TE = 1.64 ms, flip angle = 7°, FOV = 256 × 256 mm, spatial resolution = 1 × 1 × 1 mm). BOLD functional MRI data (188 volumes/run) were obtained using a gradient echo T2*-weighted pulse sequence with simultaneous multislice (SMS) acquisition for improved spatiotemporal resolution (TR = 1280 ms, TE = 33 ms, flip angle = 65°, matrix = 98 × 98, voxel size = 2 × 2 × 2 mm, 75 axial slices with no gap).

MRI Data Processing and Analysis

MRI data processing was carried out using FSL (FMRIB's Software Library; fsl.fmrib.ox.ac.uk), AFNI (Analysis of Functional NeuroImages; afni.nimh.nih.gov/afni), and Freesurfer (https://surfer.nmr.mgh.harvard.edu/fswiki). Functional data were corrected for head motion (FSL-MCFLIRT) and B_0 inhomogeneities (FSL-TOPUP), skull stripped (FSL-BET), spatially smoothed (Gaussian kernel, FWHM = 5 mm), and temporal high-pass filtered (cutoff = 90 ms) to remove fMRI signal drift. We excluded all fMRI scan runs exhibiting TR-to-TR displacement >2 mm (N = 4 runs between two subjects at pretraining, N = 3 runs between three subjects at post-training). Structural T1-weighted magnetic resonance images were aligned with fMRI data (BBRegister), and functional data were registered to standard MNI space using the FMRIB's Nonlinear Image Registration Tool (FSL-FNIRT).

A first-level, within-subject general linear model (GLM) analysis was performed including separate regressors of interest for pain anticipation, painful cuff pressure (P40), and nonpainful cuff pressure (P0). All regressors were convolved with the canonical double-gamma hemodynamic response function (FSL-FEAT). In addition, head translational and rotational motion re-alignment parameters (FSL-MCFLIRT) were modeled for each subject as regressors of no interest, alongside temporal derivatives for each regressor of interest (P40, P0, pain anticipation). Contrasts evaluated brain response to P40, P0, and the difference between painful and nonpainful cuff pressure (P40-P0). Corresponding first-level parameter estimates and variance maps from each of the two fMRI runs were combined in a second-level analysis using a standard weighted fixed-effects model (FSL-FEAT). The resulting parameter estimates and variance maps were then registered to standard space using the FMRIB's Nonlinear Image Registration Tool (MNI152; FSL-FNIRT). For subjects with only one available run (N = 3, all at the post-training scan), the results of the first-level analysis were similarly registered to standard space (FSL-FNIRT) and included in group analysis, which was performed using FMRIB's local analysis of mixed effects (FLAME1 + 2, cluster-corrected for multiple comparisons, $Z > 2.3$, $P < 0.05$). One-sample group maps were calculated for all regressors of interest (P40, P0, P40-P0) at pretraining (N = 18) and at post-training (N = 14), and results were contrasted between pre- and post-training using a paired *t* test.

An additional exploratory analysis was conducted to examine relationships between changes to task-related brain activation from pre- to post-training and changes on measures of trait self-compassion, interoceptive ability, and clinical pain intensity/disability. Group difference maps between pre- and post-training for P40-P0 and pain anticipation were used to identify regions of interest (ROI), defined as 4-mm-diameter spheres centered at the peak voxel of significant clusters in each map. The average percent signal change for each ROI was then extracted for all subjects for both pre- and post-training scans, and a difference value was calculated (post-training minus pretraining) for each subject. These difference values were then used to investigate associations with clinical/behavioral measures showing significant score changes following training, which were as follows (Table 2): SCS total score, MAIA total score, three MAIA subscales (attention regulation, body listening, self-regulation), low back pain intensity (PROMIS), and RMQ. Associations were also examined between percent signal change difference values for each ROI and total

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Table 2. Pre- and post-training scores on clinical/psychometric measures, compared using two-sample paired *t* tests

	Pretraining (SD)	No. (Pre)	Post-training (SD)	No. (Post)	*t*	*P*	*D*
PROMIS clinical back pain intensity (0–10)	4.15 (1.89)	17	2.89 (1.41)	17	3.53	0.002*	0.55
RMQ (total)	10.44 (4.83)	17	7.28 (4.51)	17	4.63	<0.001*	0.63
MAIA (total)	3.09 (0.46)	15	3.42 (0.62)	15	2.34	0.04*	0.46
Attention regulation	3.18 (0.64)	17	3.62 (0.65)	17	2.43	0.03*	0.67
Body listening	2.65 (0.89)	17	3.21 (1.16)	16	3.62	0.003*	0.54
Emotional awareness	3.73 (0.76)	19	4.17 (0.89)	15	1.91	0.08	0.53
Noticing	3.84 (0.58)	19	3.82 (0.56)	17	0.08	0.94	0.03
Not distracting	1.80 (0.99)	18	2.02 (1.01)	16	0.58	0.57	0.22
Not worrying	2.58 (0.84)	19	2.96 (1.04)	17	1.93	0.07	0.40
Self-regulation	3.25 (0.97)	19	3.83 (0.87)	15	2.36	0.03*	0.64
Trusting	3.19 (1.11)	19	3.73 (1.12)	16	2.09	0.05	0.48
SCS	3.15 (0.81)	18	3.54 (0.94)	15	2.54	0.02*	0.44

Effect sizes were calculated using Cohen's delta (*d*).

MAIA = Multidimensional Assessment of Interoceptive Awareness; RMQ = Roland-Morris Low Back Pain and Disability Questionnaire; SCS = Self-Compassion Scale.

*$P < 0.05$.

amount of meditation practice (minutes) over the course of the intervention. Due to the small sample size and to account for the influence of possible outliers, relationships between changes in brain response and clinical/psychometric measures were assessed using Spearman rank-order correlations, significant at $P < 0.05$.

Results

Course Evaluation and Meditation Practice

No adverse events were noted during the study. Overall ratings of the self-compassion training program were positive, as reflected by scores on the CEQ. On a scale of 0–10, patients provided a mean rating (SD) of 8.59 (2.79) for how logical the course seemed, a mean rating of 7.82 (2.40) for how likely it was to raise their quality of functioning, and a mean rating of 8.76 (2.56) for how likely they were to recommend the course to a friend experiencing similar problems.

The self-reported mean quantity of time spent on meditation practice (home practice) over the course of the study (SD) was 254 minutes (114), with a daily mean (SD) of 18.2 minutes (8.11), consistent with the home practice requirements. Median total and daily minutes of meditation practice were 222 and 15.9 minutes, respectively. Total meditation practice time ranged from 110 to 520 minutes, and daily practice time ranged from 0 to 60 minutes. Mean daily minutes of practice was significantly positively associated with increases in trait self-compassion from pre- to post-training (SCS; $r = 0.56$, $P = 0.04$), but not with increases to interoceptive awareness (MAIA; $r = 0.35$, $P = 0.25$).

Clinical/Psychometric Measures

A series of paired *t* tests were used to investigate changes in clinical and psychometric measures from pre- to post-training, and effect sizes were calculated using Cohen's *d* (Table 2). A total of 19 patients completed at least one pretraining questionnaire, and 17 completed at least one post-training questionnaire. One patient did not complete any questionnaires, but fMRI data were available for group analyses with pretraining data. The sample size (N) includes all subjects who completed a given questionnaire or subscale of a questionnaire (Table 2). Pearson correlations between pretreatment clinical variables indicated that measures of interoceptive awareness as measured by MAIA total and interoceptive awareness as measured by SCS total were significantly positively correlated ($r(13) = 0.65$, $P = 0.01$); no other clinical measures showed significant correlations (Table 3).

At post-training, patients reported significant decreases in low back pain intensity (PROMIS, $P = 0.002$) and Roland-Morris back pain–specific disability ($P < 0.001$) in addition to significantly increased trait self-compassion (SCS total, $P = 0.02$) and interoceptive awareness (MAIA total, $P = 0.04$). Effect sizes for variables showing significant pre–post change ranged from small to medium. For the evoked pain task, ratings of cuff-evoked pain intensity at pre-training (M [SD] = 39.72 [13.08]) did not significantly differ from those at post-training (M [SD] = 36.36 [10.78], $t(13) = 1.26$, $P = 0.23$), nor did ratings of cuff-evoked pain unpleasantness significantly differ between pre-training (M [SD] = 33.36 [18.93]) and post-training (M [SD] = 29.73 [15.18], $t(13) = 0.52$, $P = 0.61$).

Brain Responses During Evoked Cuff Pain and Pain Anticipation

Out of 20 cLBP patients who enrolled in the study, 18 were included in pretraining fMRI analyses (two of the 20 patients who enrolled were excluded from analysis due to excessive head motion on both fMRI scan runs at pretraining). Fourteen were included in longitudinal analyses (of the 18 pretraining patients, one patient

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Table 3. Pearson correlations between pretraining clinical variables

	PROMIS Clinical Back Pain Intensity	RMQ (Total)	MAIA (Total)	SCS (Total)
PROMIS clinical back pain intensity	–	0.44	0.01	−0.22
RMQ (total)	–	–	−0.34	−0.37
MAIA (total)	–	–	–	0.65*
SCS (total)	–	–	–	–

MAIA = Multidimensional Assessment of Interoceptive Awareness; RMQ = Roland-Morris Low Back Pain and Disability Questionnaire; SCS = Self-Compassion Scale.

*$P < 0.05$.

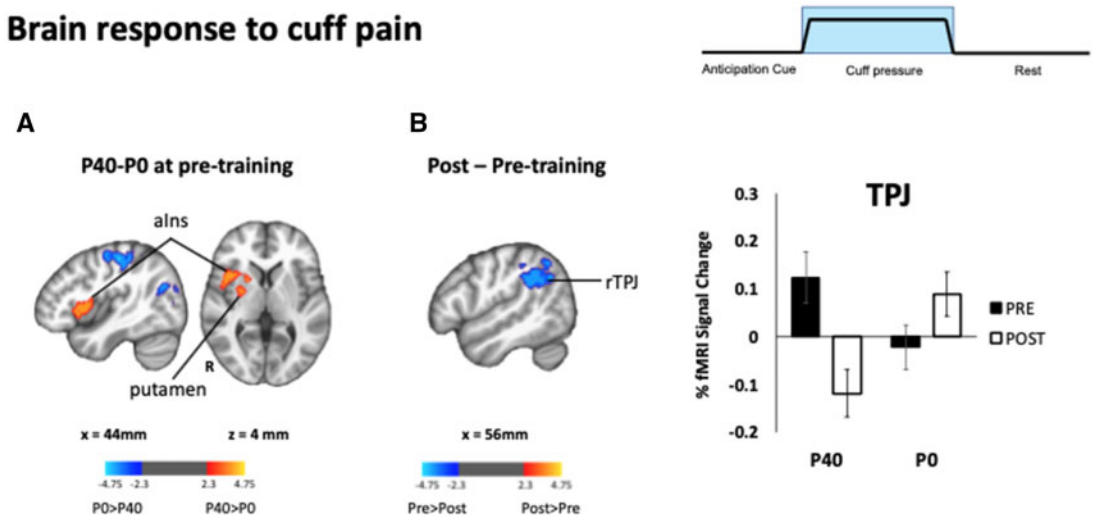

Figure 2. Brain responses to cuff pain pre- and post-training. A) Response to cuff pain (P40-P0) pretraining (N = 18). B) Comparison of post-training with pretraining brain response to cuff pain (P40-P0; post > pre). Error bars represent SEM. aIns = anterior insula; TPJ = temporo-parietal junction.

dropped out of the study before the post-training scan and three did not complete either of the fMRI scan runs at the post-training scan due to discomfort that required early termination of MRI procedures [N = 2] or technical difficulties with experimental equipment [N = 1]). Mean frame displacement values (SD) were 0.52 (0.40) at pre-training and 0.64 (0.42) at post-training; an independent-samples *t* test revealed that this difference was nonsignificant ($t(30) = 0.17$, $P = 0.57$).

Pretraining group maps (Figures 2 and 3) generally demonstrated brain responses to both cuff pain and pain anticipation consistent with our previous studies [34, 36, 37, 48, 49]. Activated regions to left leg cuff pain, controlling for responses to nonpainful stimulation (P40-P0), included right anterior insula/frontal operculum and right putamen. Deactivations (i.e., P40 < P0) to cuff pain were observed in the bilateral precentral and postcentral gyrus (nonleg representations for M1/S1), superior parietal lobule, and occipital cortex. Regions activated during pain anticipation (green cross cue) included the right anterior insula, left secondary somatosensory cortex (S2), left middle temporal gyrus, and bilateral occipital lobe. No significant deactivations were observed to pain anticipation.

Comparison of post- with pretraining brain responses to cuff pain (P40-P0) revealed a significant decrease in activation over the right angular gyrus, including the right temporo-parietal junction (rTPJ; both anterior and posterior regions, with the largest decreases in anterior rTPJ) (Figure 2, Table 4). ROI analysis demonstrated that this post-training decrease in TPJ activation was driven by reduced P40 activation (Figure 2). For pain anticipation, a post-training increase in activation was noted in the right dorsolateral prefrontal cortex (dlPFC) and ventral posterior cingulate cortex (vPCC) (Figure 3, Table 4).

Associations Between Pain and Pain-Anticipatory Brain Responses and Clinical/Psychometric Measures

A significant positive association was observed between post-training change in TPJ response to cuff pain (P40-P0) and post-training change in low back pain intensity (PROMIS; $r = 0.66$, $P = 0.003$, N = 14 pairs) (Figure 4).

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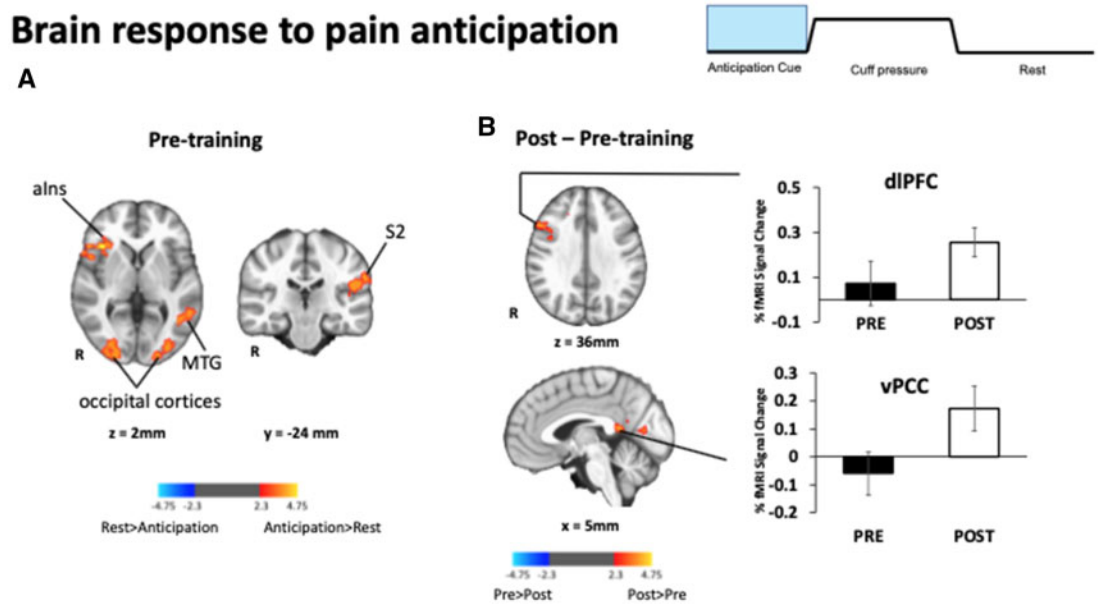

Figure 3. Brain responses to pain cue pre- and post-training. A) Response to the pain cue relative to rest at pretraining (N = 18). B) Comparison of post-training with pretraining brain response to pain cue. Error bars represent SEM. aIns = anterior insula; dlPFC = dorsolateral prefrontal cortex; MTG = medial temporal gyrus; S2 = secondary somatosensory cortex; vPCC = ventral posterior cingulate cortex.

Table 4. Brain areas exhibiting significant changes to activation from pre- to post-training for A) cuff pain (post > pre; P40-P0), B) cuff pain (post < pre; P40-P0), C) pain anticipation (post > pre), and D) pain anticipation (post < pre)

	Side	Size, mm^3	Location (MNI), mm			Z-score		
			X	Y	Z			
A) Post pain > pre pain (P40-P0)						P40-P0	P40-rest	P0-rest
None								
B) Post pain < pre pain (P40-P0)								
TPJ	R	4744	56	−44	30	3.63	3.10	−0.59
C) Post pain anticipation > pre pain anticipation							Anticipation-rest	
Occipital lobe	R	3608	12	−62	14	4.71		
vPCC	R		2	−48	16	3.21		
dlPFC	R	6288	46	8	36	3.74		
D) Post pain anticipation < pre pain anticipation								
None								

vPCC and occipital lobe were part of the same cluster.
dlPFC = dorsolateral prefrontal cortex; TPJ = temporo-parietal junction; vPCC = ventral posterior cingulate cortex.

To account for the influence of a possible outlier in low back pain intensity, we repeated this correlation with the outlier observation removed and found that the association remained ($r = 0.58$, $P = 0.04$). In addition, changes in dlPFC activation during pain anticipation were negatively correlated with change in total SCS score ($r = -0.65$, $P = 0.01$, N = 14 pairs) (Figure 5). Change in vPCC activation during pain anticipation was positively correlated with change in the body listening subscale of the MAIA ($r = 0.66$, $P = 0.01$) (Figure 5). No other ROI showed significant correlation with these clinical/psychometric measures. In addition, no relationship was observed between change in brain response in any ROI examined and changes in total MAIA score or other clinical/behavioral metrics.

Discussion

This exploratory pilot study explored neural responses to evoked pressure pain during a self-compassionate state before and after a brief self-compassion training for cLBP patients. Consistent with our predictions, after training, patients showed significant improvements in self-compassion (SCS scores) and interoceptive awareness (MAIA), as well as clinical pain outcomes (reductions in back pain–specific disability and clinical pain intensity). Perceptions of pain intensity and unpleasantness from the

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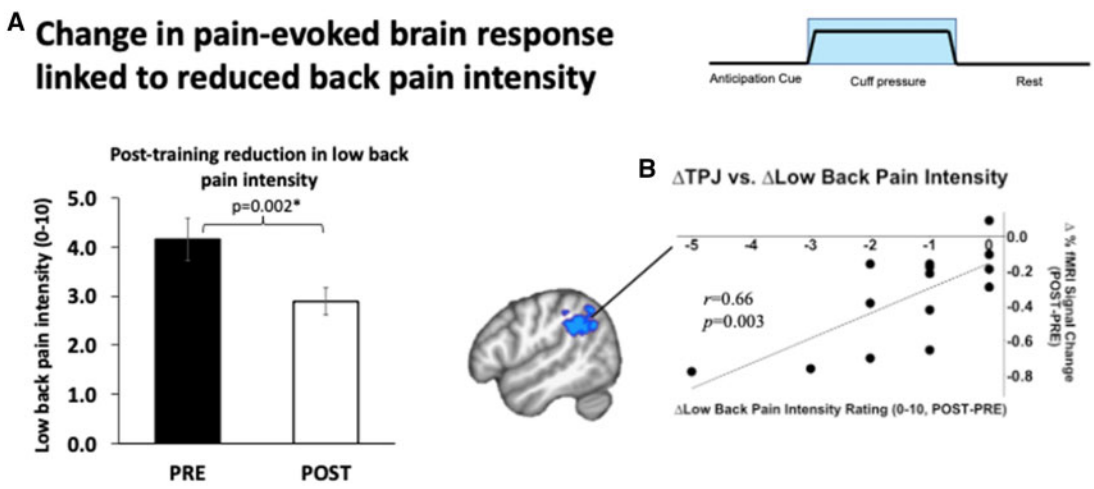

Figure 4. A) Low back pain intensity (PROMIS) was significantly reduced at post-training relative to pretraining ($t = 3.53$, $P = 0.002$, $d = -0.55$). B) A significant positive association was observed between decreases in % functional magnetic resonance imaging signal change to cuff pain and decreases in low back pain intensity (N = 14) from pre- to post-training. Error bars represent SEM. rTPJ = right temporo-parietal junction.

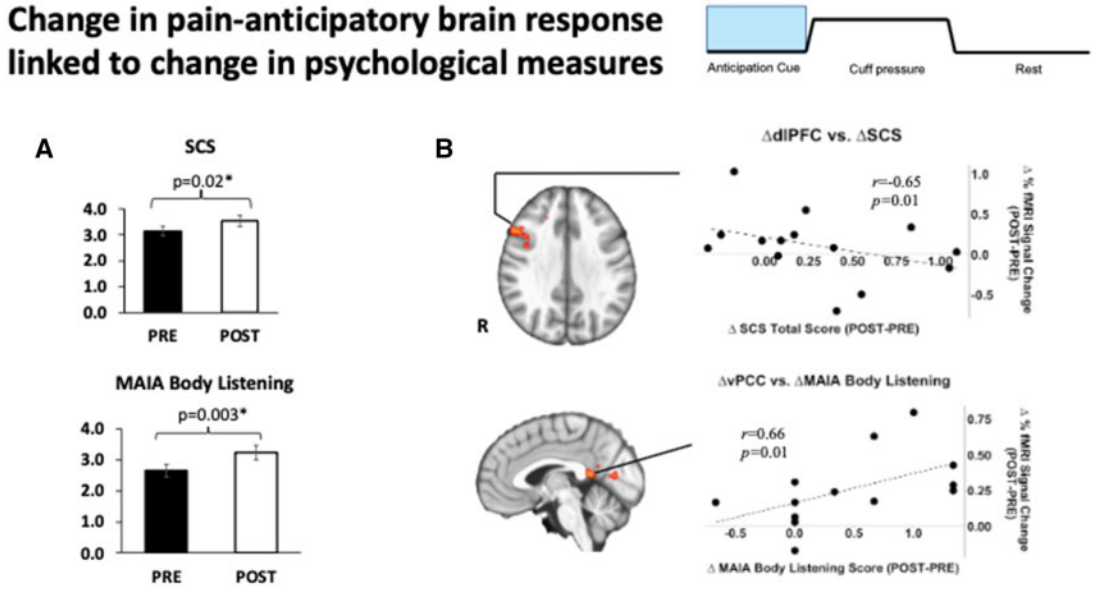

Figure 5.. A) Scores on the Self-Compassion Scale (SCS) and body listening subscale of the Multidimensional Assessment of Interoceptive Awareness (MAIA) increased significantly from pre- to post-training. B) A significant negative association was observed between % functional magnetic resonance imaging (fMRI) signal change to pain anticipation in the right dlPFC and increases in SCS total score (N = 13) and % fMRI signal change to anticipation in vPCC and increases in the body listening subscale of the MAIA. Error bars represent SEM. dlPFC = dorsolateral prefrontal cortex; vPCC = ventral posterior cingulate cortex.

pressure stimulus did not differ between pre- and post-training scans. However, neuroimaging results indicated a decrease in experimental pain-evoked activity in the right TPJ from pre- to post-training, with greater decreases of activity in this area associated with greater improvements (i.e., decreases) in clinical pain intensity. Moreover, during pain anticipation, brain responses in the right dlPFC and vPCC were higher post-training. Increased pain anticipation response in vPCC was associated with increased body listening (MAIA subscale), while greater dlPFC response was negatively associated with increased self-compassion scores (SCS). Our study induced a self-compassionate state to specifically explore its effects on pain processing, and results suggest that differential recruitment of distinct cortical circuitries supports the brain-based mechanisms by which self-compassion training modulates the pain experience.

Although our findings that such brief self-compassion training reduces pain intensity and disability in cLBP may seem surprising, they are consistent with previous

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reports of brief MBI-induced improvements in clinical and experimental pain processing [24, 25], though they may also highlight additional mechanisms unique to self-compassion. Previous studies have demonstrated reduced cLBP following eight or nine weeks of compassion training; MBIs have also been shown to modulate perceptions of experimental pain in healthy populations [50] including in expert meditators [51]. The medium effect sizes that we observed for postintervention reduction in pain intensity and disability are on par with other psychosocial interventions for chronic pain such as cognitive-behavioral therapy [52] and acceptance-based therapy [53]; however, in this study, self-compassion training was not compared against a waitlist or control intervention. Thus, it remains a possibility that observed decreases in clinical pain intensity and pain-related disability were not entirely specific to self-compassion and could have been partly explained by nonspecific features of the intervention such as increased social support [54]. Further studies using controlled experimental designs are needed to confirm the specificity of effects for improving pain-related functioning.

Our finding that right TPJ (rTPJ) response to evoked pain during a self-compassionate state decreased following training is consistent with evidence that this region encodes aspects of attentional salience during pain [55]. The right anterior TPJ in particular shows functional connections with brain networks involved in attention and salience-related processing, including the insula and midcingulate cortex [56, 57]. In relation to self-compassion meditation, the rTPJ may specifically be involved in the contextual updating of attention [58], that is, maintaining the focus of attention on the self while remaining self-compassionate during pain. However, this decrease in activation may not reflect simple sensory habituation to the stimulus due to reduced salience, as ratings of evoked pain were not significantly reduced from pre- to post-training. Alternatively, the finding of reduced TPJ activation following training could implicate the neural circuitry supporting theory of mind (ToM), defined as the ability to attribute mental states such as beliefs, desires, and emotions to both the self and others [59]. In this domain, rTPJ has been variously proposed to mediate distinctions between "self" and "other" perspectives [60], promote self-awareness [61], and encode spatial perceptions of the self [62] including imagery of the self in pain [63]. Future studies should more explicitly explore whether direct measures of pain-related attentional salience and ToM-related processes are linked to altered activation of this brain region.

Reduced right TPJ response following training correlated strongly with reductions in clinical pain intensity, suggesting that patients who showed the most post-training reduction in TPJ response to deep-tissue experimental pain benefited the most in terms of clinical low back pain reduction. Several studies have reported increased TPJ gray matter in regular meditators [64], further supporting the role that this brain region may play a role in regulating pain perception through mechanisms that underlie both self-compassion and mindfulness more generally, for example, being aware and in the moment with painful experiences.

We also found that default-mode network (DMN) brain regions contribute to altered pain processing in our study. Specifically, increased pain anticipation response in vPCC was associated with increased interoceptive attention (body listening, MAIA). Our results thus suggest that increased attention to bodily sensations following training was linked to stronger activation of vPCC while in a self-compassionate state. Prior studies have indicated that PCC encodes self-location and body ownership [65], suggesting that in the current study, self-compassion training heightened awareness of sensations within the self, consistent with the content of the training. However, recent neuroimaging studies have also linked vPCC to pain catastrophizing, a psychosocial construct including internally directed thoughts such as rumination [66] in chronic pain patients [67], potentially indicating that the training more generally modulated self-directed cognition during the anticipation of pain.

In fact, altered DMN activity has been linked to maladaptive self-directed cognition across a variety of medical conditions, including chronic pain [68, 69]. In particular, chronic pain patients show weaker deactivation (i.e., higher levels of activity) in DMN compared with healthy individuals during tasks that require focused attention [26], and higher levels of rumination about chronic pain are associated with increased functional connectivity within the DMN [70]. Interestingly, posterior TPJ regions, which also showed significant reductions in activation of cuff pain in our study, can be considered DMN nodes [71]. However, vPCC responses during the anticipation of pain increased following self-compassion training and practice, potentially highlighting the differential effects of self-compassion training on self-related processing during the anticipation vs experience of pain. Taken together, our results may indicate that self-compassion training impacts DMN-supported self-referential cognition during both pain and its anticipation.

We also found increased dlPFC response to pain anticipation following training, which may reflect emotion regulation processes. Activation of dlPFC has been linked to cognitive strategies such as reappraisal to attenuate negative affect [72–75] and has also been associated with mindful emotion regulation strategies following meditation training [76–78]. As our training was very brief, it appears possible that the early stages of self-compassion involve the recruitment of such higher cortical regions involved in emotion regulation, potentially presenting a new and clinically valuable skill for patients with chronic pain. However, increased dlPFC activation from pre- to post-training was inversely associated with increased self-compassion (SCS score), suggesting that patients

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who exhibited the least additional recruitment of dlPFC at the post-training scan demonstrated the greatest increase in self-compassion. We propose that while prefrontal mechanisms are important for generating feelings of self-compassion, similar to what has been suggested elsewhere [79, 80], these areas may need to be recruited less broadly, potentially reflecting more efficient recruitment, with greater experience and ease at maintaining a self-compassionate state. Although prefrontal mechanisms are likely important for maintaining states of self-compassion at all levels of expertise, some prior studies have indicated that experienced mindfulness practitioners rely less on lateral PFC activation to maintain a meditative state during pain [81, 82], suggesting that experience with self-compassion could follow a similar pattern. Future longitudinal studies should evaluate if dlPFC recruitment is in fact less necessary as patients become more expert in promoting a self-compassionate state during an episode of pain.

Contrary to our hypotheses, we did not observe any changes to pain-evoked brain responses in the insula or other nociceptive brain regions following training, despite prior research implicating the insula in generating feelings of self-compassion [31] and in mediating pain reductions following MBIs [27, 82]. It is also worth noting that we did not observe any relationships between brain responses to pain or pain anticipation and minutes of home meditation practice during the intervention. While accurately measuring "doses" of meditation practice is a known challenge [83, 84], our small sample size may have also limited power to detect this effect. Future studies using longer interventions and objective markers for home practice are needed to better understand the optimal levels of meditation practice.

This pilot study was primarily limited by its small sample size and lack of a control group against which to compare the effects of self-compassion training. This limits the ability to determine whether observed effects on neural responses to evoked pain were specifically related to increased self-compassion. Further, small sample sizes in fMRI studies significantly impact reproducibility [85], compromise the reliability of predictive models generated from fMRI results [86], and can result in certain biases such as overreporting the number of statistically significant foci [87]. Thus, our neuroimaging results should be interpreted with caution, as future studies, particularly those using controlled experimental designs, will be needed to determine their reliability.

In addition, as this was an exploratory study, the intervention used was significantly briefer than the standard eight-week version of Mindful Self-Compassion courses, on which most prior research (e.g., [14]) has been based. However, even short trainings such as the one examined in the current study are useful for isolating the effects of self-compassion as a mechanism underlying the beneficial effects of MBIs for chronic pain. In addition, some prior research has indicated that even brief meditation trainings can substantially improve pain-related functioning and decrease perceptions of experimental pain [27, 88–90]. Further, some studies have suggested that changes to brain activation associated with short-term meditation practice (e.g., over a few weeks) do not differ dramatically from those observed following longer interventions [91, 92]. However, we also note that some recent evidence suggests a waning effect of mindfulness-based interventions on clinical outcomes over time [93], for example, in terms of quality of life [94]. Thus, as the intervention examined in the current study was brief in duration, it is unclear how strongly its observed effects on pain-related functioning will persist over time. This study was also limited by the fact that the intervention focused on one type of self-compassion meditation (loving-kindness meditation toward the self), which does not encompass all self-compassion strategies introduced in standard eight-week MSC programs. Thus, for some patients, different self-compassion meditation approaches might have been more effective. Larger-scale studies evaluating alternate approaches to training self-compassion, as well as those using randomized controlled designs, are needed to build upon these preliminary findings.

Conclusions

The results of this exploratory pilot study tentatively suggest that improvements in cLBP pain intensity, interoceptive awareness, and trait self-compassion following a brief self-compassion training are related to altered neural evoked pain and pain anticipation processing. The involvement of self-referential DMN (i.e., vPCC) and emotion regulation (i.e., dlPFC) brain areas, as well as the reduced involvement of salience-processing areas (i.e., right TPJ), links differential recruitment of distinct cortical circuitries in supporting brain-based mechanisms of self-compassion regulation of pain. Our results also highlight the possibility that self-compassion may be an important target in the psychotherapeutic treatment of cLBP, thus informing the development of future nonpharmacological treatments for this common and vexing chronic pain disorder.

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Supplementary Data

Supplementary data are available at *Pain Medicine* online.

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