Neural activations during self-related processing in patients with chronic pain and effects of a brief self-compassion training – A pilot study

Jacqueline Lutz[a,b,1], Michael P. Berry[a,1], Vitaly Napadow[a], Christopher Germer[b], Susan Pollak[b], Paula Gardiner[c], Robert R. Edwards[d], Gaelle Desbordes[a,2], Zev Schuman-Olivier[b,2,*]

[a] Department of Radiology, Harvard Medical School, Martinos Center for Biomedical Imaging, Massachusetts General Hospital, 149 13th St., Charlestown, MA 02129
[b] Department of Psychiatry, Harvard Medical School, Center for Mindfulness and Compassion, Cambridge Health Alliance, 1035 Cambridge Street, Suite 21A, Cambridge, MA 02141
[c] Program for Integrative Medicine and Healthcare Disparities, Boston Medical Center, Boston University School of Medicine, 771 Albany St, Boston, MA 02118
[d] Department of Anesthesiology, Harvard Medical School, Brigham & Women's Hospital, 850 Boylston St., Chestnut Hill, MA 02457

ARTICLE INFO

ABSTRACT

Chronic pain negatively affects psychological functioning including self-perception. Self-compassion may improve self-related functioning in patients with chronic pain but understanding of the neural mechanisms is limited. In this study, twenty patients with chronic low back pain read negative self-related situations and were instructed to be either self-reassuring or self-critical while undergoing fMRI. Patients rated their feelings of self-reassurance and self-criticism during each condition, and brain responses were contrasted with neutral instructions. Trait self-compassion measures (SCS) were also acquired. Brain activations during self-criticism and self-reassurance were localized to prefrontal, self- and emotion-processing areas, such as medial prefrontal cortex, dorsolateral prefrontal cortex (dlPFC), dorsal anterior cingulate cortex and posterior cingulate cortex. Self-reassurance resulted in more widespread and stronger activations relative to self-criticism. Patients then completed a brief self-compassion training (8 contact hours, 2 weeks home practice). Exploratory pre-post comparisons in thirteen patients found that feelings of self-criticism were significantly reduced and brain activations were greater in the anterior insula and prefrontal cortical regions such as dlPFC. Pre-post increases in dlPFC activation correlated with increased self-compassion (SCS), suggesting that early self-compassion skills might primarily target self-criticism via dlPFC upregulation. Future controlled studies on self-compassion training in chronic pain populations should extend these results.

1. Introduction

Chronic pain is a major physical and mental health problem affecting 10%–20% of the adult general population (Meucci et al., 2015). According to the bio-psychological framework, chronic pain can negatively affect social and psychological functioning, which in turn increases suffering from chronic pain (Simons et al., 2014). In particular, the perception of self is an important psychological factor influenced by the frequent or continuous experience of pain (Sutherland and Morley, 2008; Yu et al., 2015). Indeed, negative evaluations of the self in patients with chronic pain have been described in a recent review (Yu et al., 2015) which complements phenomenological work (Osborn and Smith, 1998), pointing to an increase in negative self-

evaluations and shame in patients with chronic pain. Further, self-critical judgment has been found to predict lower quality of life and to increase stress and depression in patients with chronic medical conditions (Pinto-Gouveia et al., 2014). Thus, negative self-evaluation seems to exert a pivotal influence on daily functioning in people with chronic pain (Yu et al., 2015).

The clinical importance of negative self-evaluations has spurred neuroimaging work on the neural correlates of such states: in healthy participants, self-criticism appears to activate cortical midline regions, associated with general self-referential processing and recall of autobiographical information (posterior cingulate areas), along with regulatory prefrontal regions (dorso- and ventrolateral prefrontal cortex) and regions associated with bottom-up emotion processes and

awareness (amygdala, insula) (Brühl et al., 2014; Doerig et al., 2014; Longe et al., 2010). This pattern was found to be consistent in a study comparing depressed, recovered depressed, and healthy control participants; however, participants with higher scores on a self-report measure of perceived criticism showed weaker prefrontal activation during self-criticism (Hooley et al., 2012). Further, a study on mindfulness meditators suggested that skills to manage negative states, such as self-criticism, were associated with stronger dorsolateral and dorsomedial frontal activations, supporting a role for cognitive regulation in self-related emotional processing (Lutz et al., 2016a) and also suggesting that mindfulness training might help manage negative self-evaluations.

For patients with chronic medical conditions, self-compassion in particular can be seen as a potential 'antidote' to negative self-evaluations like self-criticism (Luoma and Platt, 2015; Neff, 2003; Neff et al., 2007). Self-compassion is the skill of being kind and caring towards the self in moments of suffering and is thought to constitute an important mechanism of mindfulness interventions (Kuyken et al., 2010). Importantly, self-compassion appears especially promising for improving psychological functioning in patients suffering from chronic illnesses and pain (Pinto-Gouveia et al., 2014; Purdie and Morley, 2015; Sirois et al., 2015; Wren et al., 2012).

Studies on chronic pain populations have associated *trait self-compassion* with higher positive affect and adaptive coping styles (e.g. acceptance), along with lower negative affect, pain catastrophizing and pain disability (Purdie and Morley, 2015; Sirois et al., 2015; Wren et al., 2012). However, research into *self-compassionate states* and skill development in chronic pain populations is in its infancy. Two pilot studies to date have shown promise for loving-kindness interventions, which include self-compassion exercises, in patients with cLBP, reporting reductions in pain, anger, and psychological distress (Carson, 2005; Chapin et al., 2014).

Despite the promise of targeting self-compassion for improving quality of life and even pain severity in chronic pain, its underlying mechanisms are less well studied, and neural correlates are largely unknown. To date, only a few fMRI studies have investigated aspects of self-compassion. One study presented participants with scenarios of typical negative personal situations and instructed them to imagine being self-reassuring – a proxy for self-compassion – while experiencing these situations (Longe et al., 2010). Similarly to previous studies on compassion towards others, self-compassion was associated with insula activation, potentially representing a soothing, affective component of self-compassion (Hofmann et al., 2011). In addition, self-compassion was associated with ventrolateral prefrontal cortex activity (VLPFC), potentially indicating a component of cognitive reappraisal. Another study reported increased ventromedial prefrontal cortex-amygdala connectivity during social threat in participants with low trait self-compassion, pointing towards increased negative emotional processing (Parrish et al., 2018).

However, no study thus far has assessed neural correlates of self-criticism and self-reassurance in clinical populations, such as in patients with chronic pain. Furthermore, no previously published study has examined whether self-compassion training can alter these activations and how such changes relate to self-reported measures of trait self-compassion.

Using the self-appraisal fMRI task adapted from Longe et al. (2010), the current pilot study attempted to address this gap by 1) assessing affective and neural responses to self-reassurance (as a proxy for self-compassion) and self-criticism in patients with chronic pain, and 2) studying the effects of a brief self-compassion training (8 contact hours, and 2 weeks of at-home training for at least 15 min a day) designed to help induce a state of self-compassion, and potential links between brain activation changes following training and changes in self-report measures related to self-compassion. Consistent with the original self-appraisal task used by Longe et al. (2010), we used self-reassurance as a close proxy for self-compassion as it aligns with the core tenet of self-compassion to be kind, understanding and reassuring to oneself in times of suffering (Neff, 2003).

We expected that self-criticism and self-reassurance during fMRI scanning in patients with chronic pain would show similar activations to those reported in previous studies, mainly comprising emotion regulation (e.g. insula, dlPFC) and self-referential processing (e.g. mPFC, PCC) regions, consistent with the main nodes of the default-mode network (Raichle, 2015). For the self-compassion training, we hypothesized increases in self-compassion (assessed with the trait self-compassion scale, SCS), in addition to increased ratings of self-compassion and decreased ratings of self-criticism during the self-appraisal task after self-compassion training. Based on previous studies examining self-criticism and self-reassurance, we hypothesized that following training, increased activation would be observed in prefrontal regions involved in emotion regulation (e.g., dlPFC) during self-criticism, whereas increased activation would be observed in insular and cortical midline regions (i.e., those implicated in self-referential processes and including anterior cingulate (ACC), dorsomedial prefrontal cortex (dmPFC) and posterior cingulate cortex (PCC), (Northoff, 2004)) during self-compassion.

2. Methods

The present longitudinal neuroimaging study reports data before and after a brief self-compassion training comprising two group training days (8 contact hours) and approximately 2 weeks of home practice. Self-compassion group trainings were run twice during 2017, to allow smaller, focused groups and timely scanning before and after the trainings (Fig. 1). We focus on post-training changes to fMRI brain responses to self-criticism and self-reassurance, alongside changes to self-reported feelings of self-criticism and self-reassurance. Results of an evoked pain experiment, which was also administered as a component of this study, will be reported elsewhere.

Patients

Twenty patients (N = 20, 13 female, 7 male, mean age 40.2 years old) meeting Quebec Task Force Classification System categories I-II
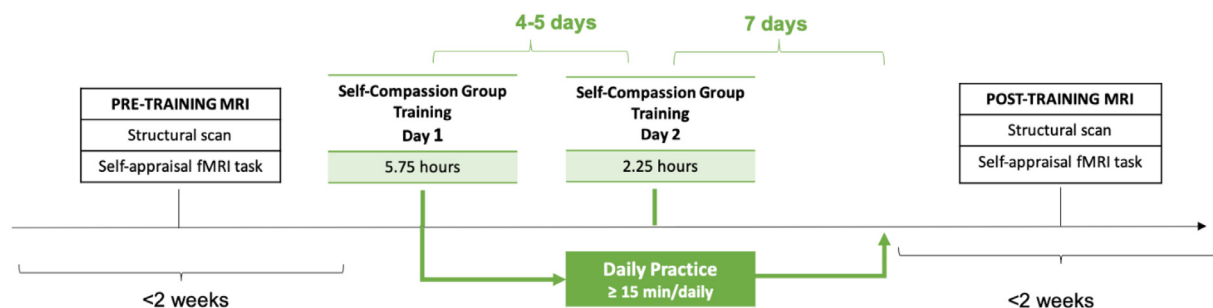

Fig. 1. Study timeline – In person group training sessions were 4–5 days apart. Patients were instructed to complete daily home-practice of at least 15 min/day, and practice duration was assessed daily during the 2 weeks following the group training day 1.

Table 1

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

	Mean (SD)
Demographics	
Age	40.15 (12.56)
Clinical characteristics	
Duration of pain (years since onset)	10.66 (8.98)
PCS[a]	16.16 (8.80)
PROMIS clinical back pain intensity (0–10)[a] PROMIS-29 (normalized T-scores)[a]	4.15 (1.89)
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)

Note: PCS = Pain Catastrophizing Scale; PROMIS-29 = Patient-Reported Outcomes Measurement Information System-29. [a] N = 19.

(unlikely to exhibit stenosis, mechanical instability or significant nerve root involvement (Abenhaim et al., 2003; Loisel et al., 2002) for chronic low back pain (CLBP) were recruited through Clinical Trials listings (https://clinicaltrials.partners.org), a medical records database at Partners Healthcare, and through flyers placed in pain clinics and other locations in the Boston area. The protocol was approved by the Human Research Committee of Partners Healthcare and Massachusetts General Hospital.

Patient clinical and demographic characteristics at pre-training are provided in Table 1.

Most patients reported less than ten total hours of prior meditation experience (see Supplementary Table 1 for more information), and none reported prior experience with self-compassion meditation. Information about medication use at the time of study enrollment is provided in Supplementary Table 2.

All patients completed a phone pre-screening to determine eligibility and were assessed for the following inclusion criteria: aged 21–65; fluency in English; average clinical pain rating greater than or equal to 3/10 on the 11-point LBP intensity scale for the two weeks prior to enrollment; prior healthcare-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 non-pharmacological therapy regimens during or within two months prior to the study. Patients were also excluded from participating if they met any of the following criteria: conditions which would impede participation in self-compassion meditation or impact ability to tolerate a group (e.g., psychosis); severe and unstable medical conditions that would heighten potential for adverse outcomes; an active substance use disorder in the past 6 months; contraindications to MRI scanning; history of neurological disease or injury.

2.1. Information and screening visit

All patients completed an information and screening visit at either the Athinoula A. Martinos Center for Biomedical Imaging (Martinos Center) at Massachusetts General Hospital in Boston, MA or at the Center of Mindfulness and Compassion at Cambridge Health Alliance in Somerville, MA. During this visit, patients were interviewed by study staff to ensure willingness to comply with daily practice requirements related to the training. All patients were also screened for inclusion and exclusion criteria and provided written informed consent prior to participating in any study procedures.

Table 2

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

	Pre-training (SD)	N (pre)	Post-training (SD)	N (post)	t	p	d
FFMQ	3.39 (0.57)	18	3.52 (0.60)	17	1.19	0.25	0.19
SCS	3.15 (0.81)	18	3.54 (0.94)	15	2.54	**0.02***	0.44

2.2. Pre- and post-training assessment visits

Within two weeks before the self-compassion training, patients underwent an MRI scanning visit. Further, they completed clinical/psychometric questionnaires online (REDCap electronic data capture system) consisting of the Five Facet Mindfulness Questionnaire (FFMQ, Baer et al., 2008); the Self-Compassion Scale (SCS, Neff, 2003); the Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29, B. M. Craig et al., 2014), including the clinical pain intensity item (0–10); the Roland-Morris Low Back Pain and Disability Questionnaire (RMQ, Roland, Fairbank, & Bombardier, 2000); and the Pain Catastrophizing Scale (PCS, Sullivan, 1995). Subjects also provided ratings of the self-compassion program using the Course Evaluation Questionnaire (CEQ, Devilly & Borkovec, 2000) at their post-training visit. For the purposes of the current investigation, only score changes on the FFMQ and SCS were considered, as these measures were considered most relevant to the self-appraisal fMRI experiment (details about post-training changes to other measures will be reported elsewhere).

Changes in FFMQ and SCS following self-compassion training are presented in Table 2, including sample sizes for each measure and the results of paired t-tests comparing scores at pre- and post-training. In some cases, patients completed questionnaires only partially, for which instances scores on that measure were not calculated.

2.3. Self-compassion training

Self-compassion training was conducted at the Center for Mindfulness and Compassion at Cambridge Health Alliance, administered by two licensed clinical psychologists (CG, SP). All patients completed two intensive group trainings, constituting eight total hours of contact time, over the course of two weeks. The training provided theoretical background in self-compassion and its application to chronic pain *(see Supplementary Material for more information)*. In particular, patients were introduced to the practice of loving-kindness meditation specifically and exclusively directed towards the self. Loving-kindness towards the self has been described as a key approach to induce and train self-compassion and represents a foundational element of the 8-week Mindful Self-Compassion (MSC) curriculum (Neff and Germer, 2013). We chose to use this meditation technique in collaboration with the developer of the MSC curriculum (CG), specifically for its suitability for a brief training.

Thus, loving kindness towards the self will be referred to as self-compassion meditation for the remainder of this report. After the first group session, patients were asked to continue practicing self-compassion meditation at home for at least 15 min daily over the next two weeks and were provided with guided audio recordings ranging from 15 to 20 min in length. Recordings were intended to support patients' at-home practice. Patients recorded their daily practice minutes using an online questionnaire, sent each day via email using REDCap electronic data capture (Harris et al., 2009) during 2 weeks following the first Group Training Day.

2.4. Self-appraisal fMRI task

A task adapted from Longe et al. (2010) was used to investigate

Table 3

Brain regions showing significant activations or deactivations at pre-training (*n* = 17) to **A.** Self-Criticism > Neutral, **B.** Self-Criticism < Neutral, **C.** Self-Reassurance > Neutral, **D.** Self-Reassurance < Neutral, **E.** Self-Reassurance < Self-Criticism. *Note:* Clusters are numbered by magnitude of the Z-score corresponding to the peak voxel for that cluster.

*Asterisks correspond to the area with the peak voxel (absolute maximum) for a given cluster, all other areas/voxels are local maxima within a cluster.

| | Side | Cluster | Size (mm^3) | Location (MNI, mm) | | | Z-Score | |
				X	Y	Z		
A. Self-Criticism > Neutral								
Frontal Pole*	R	1	11,712	18	54	−4	4.22	
Insula	R	1	11,712	30	24	−2	3.22	
Caudate	R	1	11,712	18	22	6	3.07	
Occipital fusiform gyrus*	R	2	43,784	36	−72	−16	3.88	
Cerebellum	R	2	43,784	22	−60	−38	3.87	
Lingual gyrus	R	2	43,784	14	−78	−10	3.07	
Cerebellum	L	2	43,784	−28	−68	−22	3.01	
Lingual gyrus	L	2	43,784	−12	−68	8	2.60	
Thalamus*	L	3	6475	−12	−6	8	3.75	
Thalamus	R	3	6475	18	−28	10	3.41	
Pallidum	L	3	6475	−18	−4	2	2.79	
Paracingulate*	L	4	28,784	−8	44	26	3.55	
mPFC	L	4	28,784	−1	60	10	3.24	
dACC	M	4	28,784	0	22	44	2.41	
Precuneus*	R	5	11,512	12	−60	30	3.49	
Precuneus	L	5	11,512	−10	−74	32	3.34	
vPCC	L	5	11,512	−4	−44	26	2.99	
Angular gyrus	L	5	11,512	−46	−60	32	2.93	
Hippocampus	L	5	11,512	−34	−26	−10	2.85	
dlPFC*	L	6	928	−44	20	44	3.41	
rACC*	R	7	7656	6	32	12	2.88	
B. Self-Criticism < Neutral								
Precentral gyrus*	L	1	15,672	−14	−24	70	5.39	
Parahippocampal gyrus*	L	2	14,376	−18	2	−24	4.99	
Subcallosal cortex*	L	3	12,784	−8	22	−10	4.54	
C. Self-Reassurance > Neutral								
Cerebellum*	L	1	44,864	−40	−56	−32	4.32	
Cerebellum	L	1	44,864	34	−60	32	4.02	
Frontal Pole*	L	2	125,384	−28	58	4	4.30	
dlPFC	L	2	125,384	−48	20	44	3.83	
Paracingulate	L	2	125,384	−4	36	36	3.72	
mPFC	R	2	125,384	2	62	2	2.47	
vlPFC	L	2	125,384	−56	16	8	3.46	
Caudate	L	2	125,384	10	8	6	3.35	
Caudate	R	2	125,384	−10	8	6	3.32	
Insula	L	2	125,384	−36	24	−2	3.10	
MTG*	L	3	5256	−66	−38	−16	3.77	
Precuneus*	L	4	10,600	−6	−70	38	3.54	
vPCC	L	4	10,600	−2	−44	20	3.00	
Angular gyrus*	R	5	7872	38	−52	34	3.49	
Thalamus*	R	6	4024	8	−2	10	3.25	
Thalamus	L	6	4024	−10	−8	10	3.23	
Pallidum	L	6	4024	−18	−2	2	2.86	
D. Self-Reassurance < Neutral								
Superior parietal lobule*	R	1	19,344	22	−56	60	4.27	
Subcallosal cortex*	L	2	16,848	−10	26	−14	4.23	
Precentral gyrus*	L	3	6472	47	54	64	3.90	
Central operculum*	R	4	5424	58	6	2	3.51	
Insula	R	4	5424	38	−10	6	3.40	
Temporal pole*	R	5	1216	48	14	−10	3.02	
E. Self-Criticism > Self-Reassurance								
Occipital cortex*	L	1	10,368	−18	−86	22	3.40	
Precuneus*	R	2	4104	22	−58	22	3.21	
F. Self-Reassurance < Self-Criticism								
Frontal Pole	R	1	21,336	30	62	2	3.45	
dlPFC	R	1	21,336	46	22	44	3.01	
dmPFC	R	1	21,336	14	24	64	2.43	
Temporal pole*	R	2	4416	42	20	−28	3.36	

neural responses involved in self-criticism and self-reassurance both pre- and post-training assessment visits (Fig. 2). While undergoing fMRI scanning, patients were visually presented with a list of 120 statements: 60 describing negative personal situations (e.g. "You are typing up an important document and accidentally delete it") and 60 describing non-emotive, neutral scenarios ("You are typing on your laptop on the train and can see others doing the same"). Each statement was presented for a total of 12 s. For the negative scenarios, patients were instructed to be either self-reassuring or self-critical while imagining themselves in that scenario. Patients were asked to simply imagine being in the situation during the neutral scenarios.

Scenarios were presented in blocks of five, with all trials in each block corresponding to one of the three experimental conditions. Each condition was presented three times over the course of a single scan session, yielding nine total blocks per session. All blocks were preceded by a 1700 ms instruction presented on the screen (e.g., "Self-Criticism") and followed by an 18 second rest period during which the word "relax" was displayed. The block order was pseudo-random (with no blocks

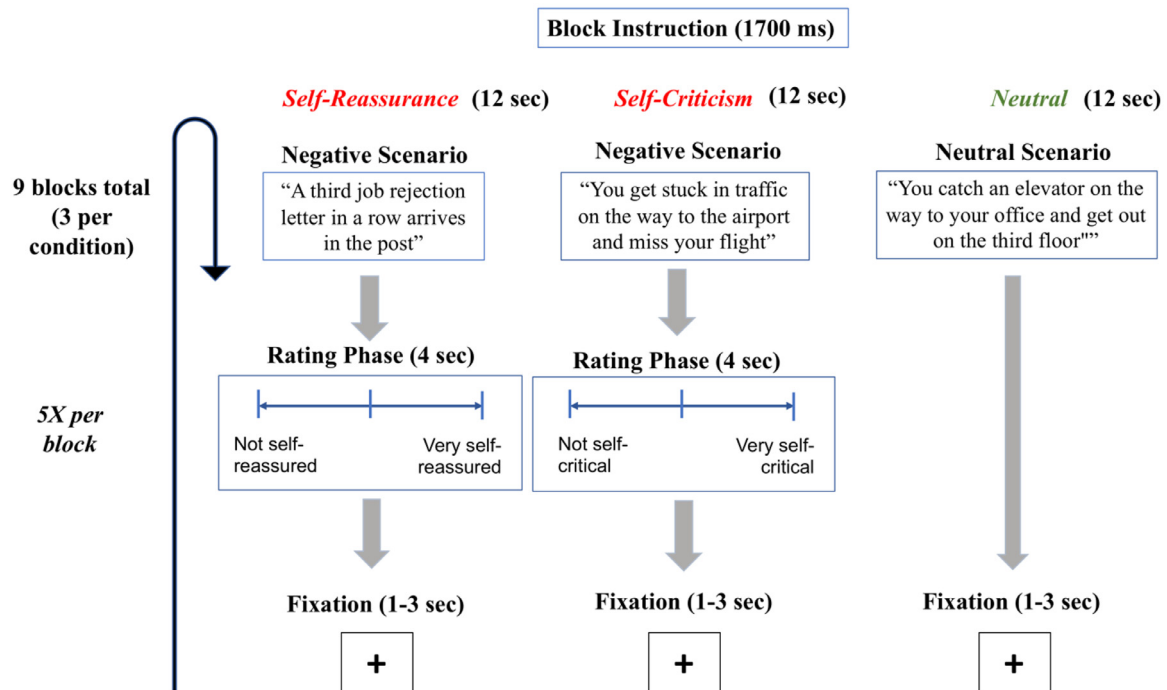*Self-compassion alters self-criticism*

Fig. 2. fMRI tasks - Overview of the self-appraisal fMRI task. Patients were presented with a block instruction for 1700 ms (self-reassurance, self-criticism or neutral), following which they viewed five different negative (self-reassurance, self-criticism) or neutral scenarios. Patients viewed each scenario for 12 s and imagined themselves in that scenario through the perspective provided in the block instruction. After viewing negative scenarios, patients used a keypad to rate the extent to which they felt either self-critical or self-reassuring while reading the scenario, and then viewed a fixation cross for another 1–3 s. No ratings were provided following the neutral scenarios.

presented twice in a row) across subjects and assessment points (pre-training and post-training). Further, within subjects, assessment points were balanced regarding whether they started with a self-criticism or a self-reassurance block, with 50% of the sample receiving self-criticism as the first block at the pre-training scan.

Patients were also instructed to use two buttons on a keypad to rate the extent to which they felt feelings of self-reassurance or self-criticism after each negative personal situation, using a visual analog scale with the extreme points labeled as follows: "not at all self-reassuring/self-critical" and "extremely self-reassuring/self-critical." Numerical values for ratings were recorded on a scale of −250 (not at all self-reassuring/self-critical) to 250 (extremely self-reassuring/self-critical), with each keypad press increasing or decreasing the rating by an increment of 25. However, the numerical values were not displayed on the visual ana-logue scale (patients only viewed the labels at the extreme endpoints), and patients were instructed that they could choose any point on the scale that reflected their feelings. The rating period lasted for 5 s and was followed by a jittered fixation period varying between 1 and 3 s and averaging 2 s in duration, throughout which a black fixation cross was presented on the screen. No ratings were collected following the neutral scenarios; therefore, 30 ratings in total were provided per scan session (corresponding to fifteen self-criticism and fifteen self-reassurance trials). Prior to scanning, participants were trained to use the visual analog scale (VAS) within the given timeframe of 5 s. The task lasted for approximately 16 min in total.

A linear mixed-effects model was used to investigate changes to task ratings of self-reassuring and self-critical feelings from pre- to post-training. This approach was selected for its ability to model variability in ratings between patients and for its robustness to missing observations (Goldstein, 2011). Moreover, the mixed-effects approach is well-suited to the analysis of ratings from this particular task, which asked patients to quantify a complex emotional state and therefore likely yielded highly variable response patterns between individuals. Trial type (self-reassurance vs. self-criticism) and assessment point (pre- vs. post-training) were modeled as fixed predictors of task rating, along with the interaction term between trial type and assessment point (pre- vs. post-training). The model included subject as a random effect, in addition to random effects for cue and time within each subject. All random effects were modeled as both a random intercept and a random slope. The model used an unstructured covariance matrix and restricted maximum likelihood estimation (REML) and allowed for covariances between random slopes and intercepts. All mixed-effects modeling analysis was carried out in R (R Foundation for Statistical Computing, Vienna, Austria) using the packages *lme4* (Bates, Maechler, Bolker & Walker, 2015) and lmerTest to estimate degrees of freedom and obtain two-tailed p-values for each predictor (Kuznetsova et al., 2017).

2.5. MRI data acquisition

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). Functional data (732 vol / run) were obtained using a gradient echo T2*-weighted pulse sequence with simultaneous multi-slice (SMS) acquisition for improved spatio-temporal 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).

2.6. MRI data processing and analysis

FMRI data processing was carried out using FSL (FMRIB's Software Library, fsl.fmrib.ox.ac.uk), and FreeSurfer (https://surfer.nmr.mgh.

harvard.edu/fswiki). 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 signal drift noise. We excluded all runs exhibiting TR-to-TR displacement greater than 2 mm. For co-registration of structural and functional data to standard MNI space (FSL-FNIRT), structural images were aligned to fMRI data (BBREGISTER).

A first-level, within-subject general linear model (GLM) analysis was performed including the self-reassurance, self-criticism and neutral reflection periods as explanatory variables. In addition to these variables, the following contrasts were modeled as regressors of interest: the difference between self-criticism and neutral (SC > NEU), the difference between self-reassurance and neutral (SR > NEU) and the difference between self-reassurance and self-criticism (SR > SC). The rating period was included as a regressor of no interest. All regressors were convolved with the canonical double-gamma hemodynamic response function (FSL-FEAT). In addition, head motion and rotation parameters (FSL-MCFLIRT) were modeled for each scan as regressors of no interest, as were temporal derivatives for each explanatory variable. The first-level parameter estimates and corresponding variance maps from each fMRI run were registered to standard space (MNI152) using the FMRIB's Nonlinear Image Registration Tool (FNIRT). Group analysis was performed using FMRIB's Local Analysis of Mixed Effects (FLAME1 + 2). Cluster-level thresholding was performed using Gaussian random-field theory (RFT) to control the family-wise error rate (FWE), and thresholds were set for all statistical parametric maps using clusters determined by a voxelwise threshold ($z > 2.3$) and a corrected cluster significance threshold of $p < 0.05$. One-sample group means were calculated for all regressors of interest at pre-training ($n = 17$) and at post-training ($n = 13$), and results were compared between pre- and post-training using a paired two-sample t-test. Unthresholded group maps at pre, and pre-post changes can be accessed on NeuroVault, a public repository of unthresholded statistical maps (Gorgolewski et al., 2015, https://identifiers.org/neurovault.collection:7763).

Based on the results of the group analysis, the difference map between pre- and post-training for SC > NEU was used to identify regions of interest (ROI), defined as 4-mm diameter, non-overlapping spheres centered at the peak voxel of each significant cluster (vlPFC, Frontal pole, dlPFC, Insula/Central Operculum, Fig. 5/Table 4). 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 pre-training) for each subject. These difference values were then used to investigate associations with changes in independent variables: the total self-compassion score (SCS) and total minutes of home practice during the training. Relationships between changes to brain response and clinical/psychometric measures were assessed using Spearman rank-order correlations to account for the small sample size. No correction for multiple ROI comparison was applied due to the exploratory nature of our pilot study.

3. Results

3.1. Clinical/psychometric measures

At post-training, patients showed significantly increased trait self-

compassion (SCS). No significant change was observed for total score on the five-facet mindfulness questionnaire (FFMQ), verifying that the training targeted self-compassion primarily and only affected general trait mindfulness to a small, non-significant degree (Table 2). Sample size (N) indicates all subjects who completed a given questionnaire or subscale of a questionnaire.

3.2. Meditation practice

Mean at-home meditation practice over the course of the 2 weeks from the first group training day was 254 min ($SD = 114$, range: 110–520 min). Daily means were 18.2 min ($SD = 8.11$, range: 0 to 60 min), which is consistent with the study instruction to practice for at least 15 min per day.

3.3. Self-appraisal task ratings

Mean self-reassurance and self-criticism ratings at both pre- and post-training assessment visits are calculated from 19 subjects at pre-training (due to technical difficulties, one subject was not able to provide any ratings during the task), and 16 subjects at post-training. Subjects that were excluded from the fMRI analysis for excessive head motion but still had usable task rating data were included in the pre- vs. post-training comparison of task ratings. Overall, 33 of 1050 trials (3.2%) were missed by subjects, and none of the subjects missed more than 7 out of 30 trial ratings in a given scan session. The majority of scan sessions had no missing data (20 out of 35). Overall, ratings of self-reassurance and self-criticism were high at both time-points (overall mean = 82.8, $SD = 108$ at pre-training and overall mean = 68.5, $SD = 114$ at post-training) indicating that at both assessment points, the task reliably elicited feelings of self-criticism and self-reassurance as intended.

Results of the linear mixed-effects model revealed a significant interaction between trial type and assessment point (pre- vs. post-training) in predicting task ratings ($b = 28.36$, 95% CI [3.81, 50.62]). Pairwise Tukey-corrected post-hoc comparisons revealed that ratings of self-criticism decreased significantly from pre- to post-training by a mean value of 29.9 ($SE = 12.5$, $df = 24.0$, $t = 2.40$, $p = 0.025$) representing a decrease of 28.9% relative to the mean pre-training rating of 103.3 (Fig. 3), while self-reassurance ratings did not decrease significantly (change 1.55, $SE = 12.5$, $df = 24.4$, $t = 0.123$, $p = 0.902$).

3.4. fMRI results (Table 3)

Out of twenty CLBP patients who enrolled in the study, seventeen were included in pre-training fMRI analysis. Three patients were excluded from pre-training analysis due to excessive head motion; two of these patients were excluded from post-training analysis for the same reason, and the other did not complete the self-appraisal task at their post-training scan due to visual difficulties which impeded viewing the task stimuli. Two additional patients were excluded from post-training due to excessive head motion, and another two discontinued their study participation prior to the post-training scan. Thus, thirteen subjects were included in pre-post fMRI comparisons.

Group averages at pre-training controlled for reading and imagining neutral scenarios, indicated that self-criticism (SC > NEU) and self-

Table 4

Brain areas exhibiting increased response to Self-Criticism at post-training (POST) relative to baseline (PRE), controlling for response changes to neutral scenarios.

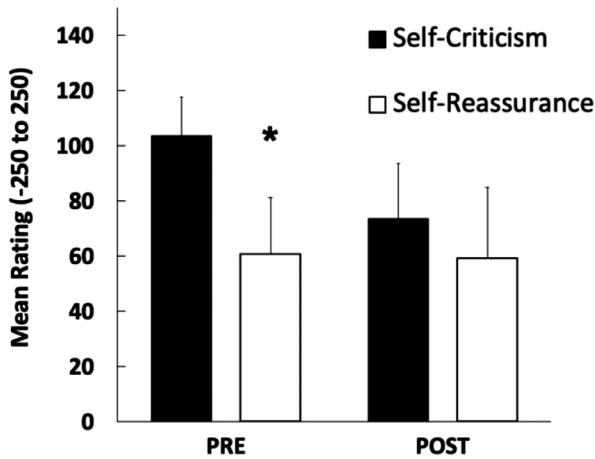|	Side	Size (mm³)	Location (MNI, mm)			Z-score (POST-PRE)		
			X	Y	Z	SC−NEU	SC	NEU
vlPFC	R	1672	54	20	26	3.26	0.89	− 0.81
Frontal Pole	R	4704	20	60	24	3.22	0.93	− 0.66
dlPFC	R	1336	48	10	46	3.13	1.27	− 0.28
Insula	R	5344	44	12	− 2	2.91	1.12	− 0.83

Fig. 3. Change to within-task self-criticism and self-reassurance ratings over the course of self-compassion training. Error bars represent standard error of the mean (SEM). Ratings were provided on a scale from −250 (no self-reassuring or self-critical feelings) to 250 (very strong self-reassuring or self-critical feelings).
.

reassurance (SR > NEU) elicited activity in a similar network of brain regions including lateral prefrontal areas (dlPFC, vlPFC) and cortical midline areas (mPFC, precuneus, vPCC, frontal pole), paracingulate cortex, cerebellum, basal ganglia (caudate, pallidum), thalamus, insula and middle temporal gyrus. Relative to self-criticism, increased activity was observed during self-reassurance in frontal pole, dlPFC, dmPFC and

right temporal pole and decreased activity in occipital pole and pre-cuneus (Figure 4).

Comparison of pre- and post-training responses to self-reassurance (SR > NEU) did not yield any significant differences following cluster correction. In contrast, comparison of pre- and post-training responses to self-criticism (SC > NEU) revealed increased activity at post-training in four left hemisphere brain regions: frontal pole, dlPFC, insula and vlPFC. The cluster of increased insula activation to self-criticism at post-training appeared to be located in dorsal anterior insula (Deen et al., 2011). No brain regions showed decreased responses to self-criticism from pre- to post-training (Fig. 5, Table 4).

Associations between brain responses to self-criticism and clinical/psychometric measures

A significant positive association was observed between pre-post activation increases in the right dlPFC and increased self-compassion (SCS) from pre- to post-training ($r = 0.79$, $p = 0.001$, Fig. 5B). No significant relationships were observed between changes to self-compassion and increases to brain response to self-criticism in frontal pole, insula or vlPFC. In addition, no relationships were observed between total practice amount (minutes) and changes to brain response in any of these regions.

4. Discussion

The current study presents first insights into brain activations and behavioral ratings during states of self-criticism and self-reassurance in a population with chronic pain and the effects of a brief self-compassion training, which increased self-compassion skills, as measured with the self-compassion scale (SCS)on these variables .
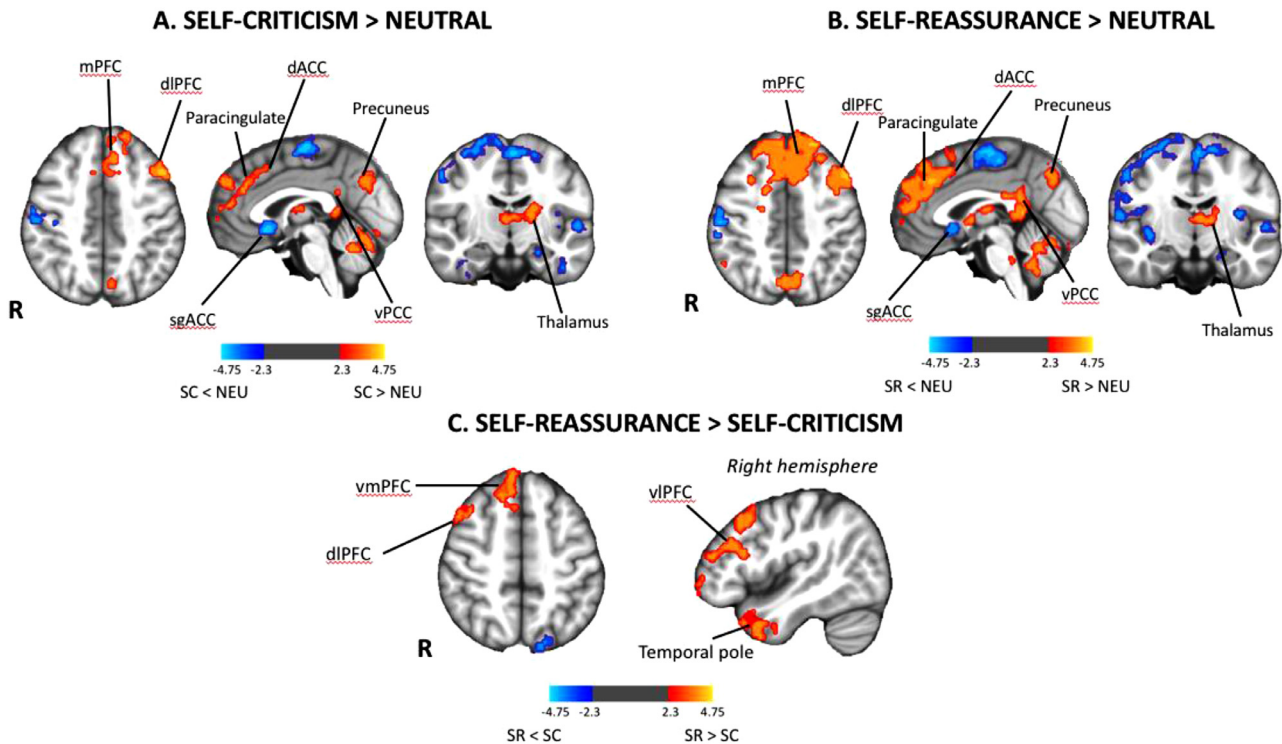

Fig. 4. Brain responses before training (n = 17) during self-criticism (top left), self-reassurance (top right) and in the contrast of self-compassion with self-criticism (bottom). Contrasts of both self-criticism and self-reassurance with the neutral reflection period revealed significant activation clusters in midline prefrontal areas, including medial prefrontal cortex (mPFC) and dorsolateral prefrontal cortex (dlPFC), in addition to cerebellum, thalamus, precuneus, dorsal anterior cingulate cortex (dACC) and ventral posterior cingulate cortex (vPCC). Relative to self-criticism, self-reassurance was found to elicit greater activity in right dlPFC, frontal pole, temporal pole and mPFC. Brain responses before training (n = 17) during self-criticism (top left), self-reassurance (top right) and in the contrast of self-compassion with self-criticism (bottom). Contrasts of both self-criticism and self-reassurance with the neutral reflection period revealed significant activation clusters in midline prefrontal areas, including medial prefrontal cortex (mPFC) and dorsolateral prefrontal cortex (dlPFC), in addition to cerebellum, thalamus, precuneus, dorsal anterior cingulate cortex (dACC) and ventral posterior cingulate cortex (vPCC). Relative to self-criticism, self-reassurance was found to elicit greater activity in right dlPFC, frontal pole, temporal pole and mPFC.
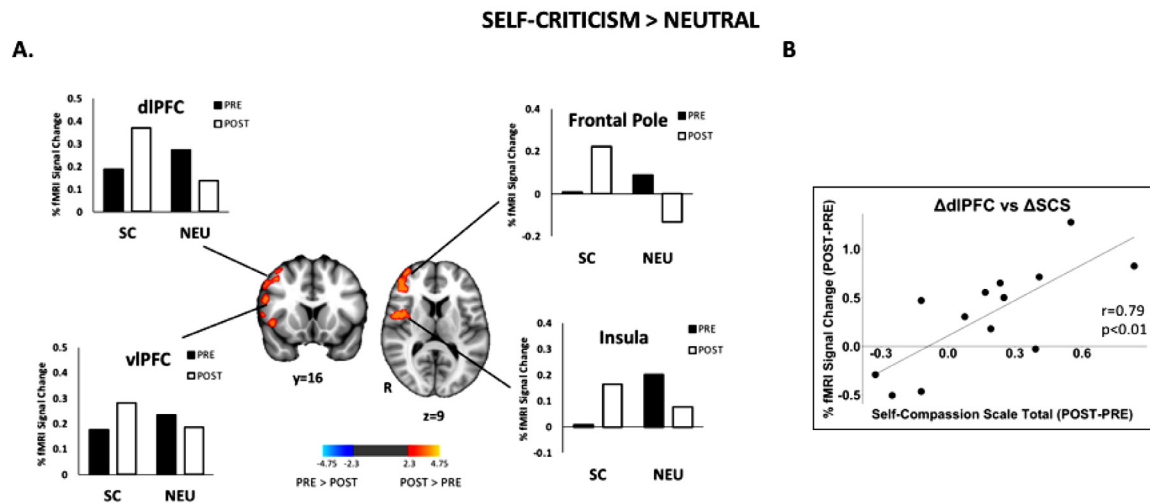
Fig. 5. Changes to brain activation to self-criticism following self-compassion training. A. Increases to activation (POST > PRE, *n* = 13) for the Self-Criticism > Neutral contrast were observed in multiple right hemisphere regions, including dlPFC, frontal pole, insula/operculum and vlPFC. B. Increases to activation for the Self-Criticism > Neutral contrast were also associated with increases to total score on the self-compassion scale. .

4.1. Brain correlates of self-criticism and self-reassurance in chronic pain patients at pre-training

We observed similar brain activations during states of self-criticism and self-reassurance, consistent with previous reports on the brain correlates of positive and negative self-evaluations (Brühl et al., 2014; Doerig et al., 2014; Longe et al., 2010). Specifically, both conditions activated prefrontal and emotion-related areas such as insula, dACC and dlPFC, in addition to cortical midline regions involved in self-referential processing (Northoff and Bermpohl, 2004), and default-mode network (DMN) regions (Raichle, 2015) such as posterior cingulate, precuneus and medial prefrontal cortex. Indeed, the strong resemblance of the activation patterns elicited by our self-appraisal task to the DMN is consistent with self-referential tasks used by other studies, including those that have required subjects to reappraise negative images related to the self (Sheline et al., 2009) and make judgments about whether a particular trait describes oneself (Davey et al., 2016). Thus, the baseline neuroimaging results observed in the current study suggest that our task successfully engaged self-referential cognitive processes. Furthermore, the general patterns of activations we observed are in line with previous reports on the effects of both positive and negative self-evaluations on brain activations (Brühl et al., 2014; Qin and Northoff, 2011), which suggests that the current task elicited states of self-reassurance and self-criticism reliably and that our patient sample showed similar patterns to previous reports in healthy populations.

In the current study, self-reassurance resulted in more widespread and stronger activations relative to negative self-evaluations, mainly in prefrontal areas, which has also been observed previously (Brühl et al., 2014; Lutz et al., 2016a). Increased prefrontal activation during self-reassurance could relate to negative evaluations being more 'habitual' and thus requiring fewer mental resources to instantiate, or it may highlight a positive self-related bias modulated by prefrontal areas (Brühl et al., 2014; Sharot et al., 2007). However, Longe et al. (2010) reported reduced prefrontal activation during self-reassurance, contrasting the results of the present study. Finally, Parrish et al. (2018) reported stronger connectivity between prefrontal cortex (vmPFC) and amygdala during social criticism associated with lower trait self-compassion, further suggesting prefrontal areas play a role in self-compassionately dealing with criticism. Self-criticism elicited stronger occipital and precuneus activations compared to self-reassurance, which might be related to stronger visual attentional processing (Brühl et al., 2014), potentiated autobiographical memory retrieval (Cavanna and Trimble, 2006; Northoff et al., 2006) or more vivid mental imagery

(Servaas et al., 2014) during self-criticism relative to self-reassurance/self-compassion. Levels of self-reported self-criticism during self-criticism trials were greater than reported self-reassuring feelings during self-reassurance trials at pre-training, consistent with the interpretation that on average, self-criticism may have elicited greater attentional resources and/or stronger visual imagery relative to self-reassurance.

4.2. Brain correlates of self-criticism and self-reassurance after a brief self-compassion training

Following self-compassion training, we found increased activation during self-criticism (compared to neutral situations) in right frontal brain areas (frontal pole, dlPFC, vlPFC) and the dorsal anterior insula. Prefrontal activation has been linked to cognitive reappraisal of evoked negative affect (Ochsner et al., 2012; Phan et al., 2002). Similarly, the vlPFC has been associated with emotion regulation, particularly the evaluation of emotional salience and subsequent regulation of negative affect (Kohn et al., 2014). In fact, dlPFC and vlPFC activation have been reported in previous studies on self-criticism, and have been hypothesized to reflect emotion regulation during self-criticism (Doerig et al., 2014).

Increased insula activation at post-training may suggest stronger arousal and/or emotional response to self-criticism, as this region has been linked to experiencing internal stressful cognitions and emotions (Craig, 2003; Phan et al., 2002). Greater emotional arousal at post-training might result from increased openness, awareness and compassion towards the self while viewing self-critical stimuli, consistent with the focus of the training. Accordingly, increased prefrontal (dlPFC) activation to self-criticism during the same period could indicate a form of automatic 'compassionate' cognitive reappraisal of self-critical stimuli (e.g. Banks et al., 2007; Doerig et al., 2014; Ochsner et al., 2002), such that these 'negative' stimuli are now attended to with compassion. This interpretation that participants may have engaged in a form of automatic 'self-compassionate' reappraisal during self-criticism at post-training is consistent with our finding that pre- to post-training increases in dlPFC activation were correlated with participants' increases in self-compassion skills (SCS). Alternatively, increased prefrontal activation might partly reflect increased effort needed to instantiate self-criticism after the training. However, the positive correlation observed between increased SCS and increases in dlPFC activation during self-criticism suggests that altered neural responses to self-criticism were to some extent driven by the acquisition of self-compassion skills following training, and not merely by difficulty instantiating a state of self-

criticism.

We note that contrary to our hypotheses, we did not observe any relation between the brain changes we observed and total time spent on home meditation practice. Thus, it is not clear from the data whether the observed changes following training were driven more strongly by regular formal self-compassion practice or by the effects of being introduced to the concept of self-compassion through the group training sessions. Future investigations on relations between amount of formal meditation practice and changes to brain activity during negative self-evaluation will be crucial for optimizing self-compassion training in the clinical setting. Also contrary to our hypotheses, we did not observe significant changes to brain response during self-reassurance after self-compassion training. While we can only speculate about this interesting null result, it is possible that we were underpowered to find this effect, though training duration may have played an important role considering that improved ability to regulate self-criticism may represent an early effect of self-compassion training. Indeed, self-compassion has been previously cited as a potential antidote to self-criticism (Leary et al., 2007; Luoma and Platt, 2015; Neff, 2003), particularly in patients with chronic medical conditions (Friis et al., 2015; Pinto-Gouveia et al., 2014).

Self-reassurance, particularly while imagining the personal negative situations in our task, might require more training. While a speculative interpretation, decreased self-criticism preceding increased self-compassion might also represent a usual trajectory in self-compassion skill acquisition, and achieving a low level of self-criticism has been proposed as an important factor for cultivating compassion towards the self (Neff, 2003) but note that other authors suggest self-compassion and self-criticism to constitute more distinct factors (López et al., 2015). Alternately, this progression may be specific to patient populations experiencing increased negative self-evaluations. Future studies should verify how these two skills evolve over time.

The current study had several limitations, most importantly the small sample size for our self-compassion pre-post comparisons. Thus, the study was not sufficiently powered to detect significant effects of self-compassion training on changes in self-reassurance related to self-compassion training. Further, the reliability of the results, particularly correlations between self-report measures and fMRI data (Schönbrodt et al., 2013) and accompanying interpretation should remain tentative until replication is conducted in larger samples. For example, it is known that small sample sizes can substantially impact reliability and reproducibility of fMRI results, and in some cases may result in spurious findings (Button et al., 2013; Cremers et al., 2017; Turner et al., 2018). In addition, without a control condition, the specificity of the current results is unclear. For example, it is not possible to determine whether the effects observed are specific to *self*-compassion or could be more broadly attributable to compassion training in general. Thus, future studies are warranted to examine the unique mechanisms of self-compassion as compared to other compassion and mindfulness-based interventions.

Finally, current pilot study only allows insights into a very short self-compassion training. Such short training studies or even shorter meditation inductions have been conducted previously (e.g., Dickenson et al., 2013; Eddy et al., 2015; Herwig et al., 2010; Lutz et al., 2014; Zeidan et al., 2011) and we believe that there is value in studying short self-compassion trainings. Firstly, self-compassion has been proposed to constitute a mechanism underlying the positive effects of mindfulness-based therapies (Kuyken et al., 2010; Van Dam et al., 2014). Secondly, the amount of self-compassion content and practice provided in most mindfulness-based therapies is relatively modest (Santorelli et al., 2007) certainly less than the quantity provided in the current study. Thus, if self-compassion indeed represents a mechanism underlying the effects of mindfulness-based trainings, then at least some benefits should be observed after a short training entirely focused on self-compassion. Finally, some mindfulness studies and reviews suggest that a shorter duration of meditation practice may not

necessarily lead to fundamentally different brain activations compared to long-term practice (Gotink et al., 2016; Lutz et al., 2016b). Thus, while there might be a change in the relative strength of brain activations following training dependent on training duration, the qualitative patterns observed in early training might already inform our understanding of the neural changes that accompany longer-term self-compassion practice. Nevertheless, future studies on the effect of self-compassion for patients with chronic conditions should complement our preliminary results using controlled designs, and by using longer self-compassion trainings, such as the full 8-week Mindful Self-compassion course.

4.3. Conclusions

Our study is the first to describe both neural and self-reported states of both self-criticism and self-reassurance in patients with chronic pain before and after a brief training designed to increase self-compassion. Feelings of self-criticism were reduced after the training, while brain activations to self-criticism increased in insular and prefrontal brain regions. Increased dlPFC response at post-training was associated with increased trait self-compassion, suggesting that patients successfully applied self-compassionate emotion regulation skills learned during training while undergoing negative self-evaluation. No changes to either brain activation or task ratings were found during self-reassurance. Future studies on self-compassion in this population seem warranted and should verify results from this pilot training in a controlled longitudinal study.

Declaration of Competing Interest

Jacqueline Lutz: Dr. Lutz was a postdoctoral fellow at CHA Center for Mindfulness and Compassion (CMC) within the last 3 years. CHA CMC is an academic mindfulness center, affiliated with the Harvard Medical School Department of Psychiatry, administratively within the Cambridge Health Alliance (CHA) academic community healthcare system, which is a public entity within the Cambridge Public Health Commission. Dr. Lutz's salary was not tied to the quantity or content of programs offered through CMC. Dr. Lutz has no financial conflict of interest.

Michael Berry: Author has no conflicts of interest to report.

Chris Germer: Dr. Christopher Germer is a lecturer in psychiatry (part-time) at Harvard Medical School/Cambridge Health Alliance (CHA). He is also on the teaching faculty of the CHA Center for Mindfulness and Compassion (CMC). Dr. Germer is a co-developer of the Mindful Self-Compassion (MSC) training program from which this brief self-compassion intervention derived, and he is on the Board of the Center for Mindful Self-Compassion (CMSC). He does not receive a salary from CHA, CMC or CMSC, but he receives financial compensation when he teaches MSC workshops and he receives royalties from two books he co-authored about MSC. Due to his expertise, Dr. Germer was primarily responsible for designing and delivering the intervention in this study, but he did not participate in data collection, analysis, or interpretation.

Susan Pollak: Dr. Susan Pollak is a teaching associate in psychiatry (part-time) at Harvard Medical School/Cambridge Health Alliance (CHA). She is on the teaching faculty of the CHA Center for Mindfulness and Compassion (CMC) and she receives financial compensation when she teaches MSC programs. Due to her expertise, Dr. Pollak collaborated with Dr. Germer co-developing and co-delivering the intervention in this study, but she did not participate in data collection, analysis, or interpretation.

Paula Gardiner: Dr. Paula Gardiner is affiliated with the University of Massachusetts Medical School and Boston University Medical School. She has no financial conflict of interest.

Robert Edwards: Dr. Robert Edwards is a pain psychologist and

Associate Professor of Anesthesiology at Brigham & Women's Hospital, a non-profit teaching hospital affiliated with Harvard Medical School. Dr. Edwards' salary derives from BWH and he is not compensated by CHA or its affiliates, including CMC. Author has no conflicts of interest to report.

Gaelle Desbordes: Author has no conflicts of interest to report.

Zev Schuman-Olivier: Dr. Schuman-Olivier is the Director of the CHA Center for Mindfulness and Compassion, which is an academic mindfulness center, affiliated with the Harvard Medical School Department of Psychiatry, administratively within the Cambridge Health Alliance (CHA) academic community healthcare system, which is a public entity within the Cambridge Public Health Commission. CMC has an educational unit that offers educational and community programs that provides mindfulness- and compassion-based program delivery to the general public for registration fees that cover the costs of the programs. Dr. Schuman-Olivier's salary is through CHA and is not tied to the quantity or content of programs offered through CMC. Dr. Schuman-Olivier has no financial conflict of interest.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.pscychresns.2020.111155.

References

Abenhaim, L., Rossignol, M., Valat, J., Nordin, M., Avouac, B., Blotman, B., Charlot, J., Dreiser, R.L., Legrand, E., Rozenberg, S., Vautravers, P., 2003. The Role of Activity in the Therapeutic Management of Back Pain. Spine (Phila. Pa. 1976) 25, 1S–33S https://doi.org/10.1097/00007632-200002151-00001.

Baer, R.A., Smith, G.T., Lykins, E., Button, D., Krietemeyer, J., Sauer, S., Walsh, E., Duggan, D., Williams, J.M.G., 2008. Construct validity of the five facet mindfulness questionnaire in meditating and nonmeditating samples. Assessment 15 329–342 https://doi.org/10.1177/1073191107313003.

Banks, S.J., Eddy, K.T., Angstadt, M., Nathan, P.J., Phan, K.L., 2007. Amygdala-frontal connectivity during emotion regulation. Soc. Cogn. Affect. Neurosci. 2, 303–312. https://doi.org/10.1093/scan/nsm029.

Bates, D., Maechler, M., Bolker, B., Walker, S., Phan, K.L., 2015. Fitting linear mixed-effects models using lme4. J. Stat. Softw. 67, 1–48 https://doi.org/10.18637/jss.v067.i01.

Brühl, A.B., Rufer, M., Kaffenberger, T., Baur, V., Herwig, U., 2014. Neural circuits associated with positive and negative self-appraisal. Neuroscience 265, 48–59. https://doi.org/10.1016/j.neuroscience.2014.01.053.

Button, K.S., Ioannidis, J.P.A., Mokrysz, C., Nosek, B.A., Flint, J., Robinson, E.S.J., Munafò, M.R., 2013. Power failure: why small sample size undermines the reliability of neuroscience. Nat. Rev. Neurosci. 14, 365–376. https://doi.org/10.1038/nrn3475.

Carson, J.W., 2005. Loving-kindness meditation for chronic low back pain: results from a pilot trial. J. Holist. Nurs. 23, 287–304. https://doi.org/10.1177/0898010105277651.

Cavanna, A.E., Trimble, M.R., 2006. The precuneus: a review of its functional anatomy and behavioural correlates. Brain 129, 564–583. https://doi.org/10.1093/brain/awl004.

Chapin, H.L., Darnall, B.D., Seppala, E.M., Doty, J.R., Hah, J.M., Mackey, S.C., 2014. Pilot study of a compassion meditation intervention in chronic pain. J. Compassionate Heal. Care 1, 4. https://doi.org/10.1186/s40639-014-0004-x.

Craig, A.D., 2003. Interoception: the sense of the physiological condition of the body. Curr. Opin. Neurobiol. 13, 500–505. https://doi.org/10.1016/S0959-4388(03)00090-4.

Cremers, H.R., Wager, T.D., Yarkoni, T., 2017. The relation between statistical power and inference in fMRI. 10.1371/journal.pone.0184923.

Craig, B.M., Reeve, B.B., Brown, P.M., Cella, D., Hays, R.D., Lipscomb, J., Simon Pickard, A., Revicki, D.A., 2014. US Valuation of Health Outcomes Measured Using the PROMIS-29. Value Heal. 17, 846–853 https://doi.org/10.1016/J.JVAL.2014.09.005.

Davey, C.G., Pujol, J., Harrison, B.J., 2016. Mapping the self in the brain's default mode network. Neuroimage 132, 390–397. https://doi.org/10.1016/j.neuroimage.2016.02.022.

Deen, B., Pitskel, N.B., Pelphrey, K.A., 2011. Three systems of insular functional connectivity identified with cluster analysis. Cereb. Cortex 21, 1498–1506. https://doi.org/10.1093/cercor/bhq186.

Dickenson, J., Berkman, E.T., Arch, J., Lieberman, M.D., 2013. Neural correlates of focused attention during a brief mindfulness induction. Soc. Cogn. Affect. Neurosci. 8, 40–47. https://doi.org/10.1093/scan/nss030.

Doerig, N., Schlumpf, Y., Spinelli, S., Späti, J., Brakowski, J., Quednow, B.B., Seifritz, E., Grosse Holtforth, M., Holtforth, M.G., 2014. Neural representation and clinically relevant moderators of individualised self-criticism in healthy subjects. Soc. Cogn. Affect. Neurosci. 9, 1333–1340. https://doi.org/10.1093/scan/nst123.

Eddy, M.D., Brunyé, T.T., Tower-Richardi, S., Mahoney, C.R., Taylor, H.A., 2015. The effect of a brief mindfulness induction on processing of emotional images: an ERP study. Front. Psychol. 6, 1391. https://doi.org/10.3389/fpsyg.2015.01391.

Friis, A.M., Consedine, N.S., Johnson, M.H., 2015. Does kindness matter? Diabetes, depression, and self-compassion: a selective review and research agenda. Diabetes Spectr 28, 252–257. https://doi.org/10.2337/diaspect.28.4.252.

Gorgolewski, K.J., Varoquaux, G., Rivera, G., Schwarz, Y., Ghosh, S.S., Maumet, C., Sochat, V.V., Nichols, T.E., Poldrack, R.A., Poline, J.-B., Yarkoni, T., Margulies, D.S., 2015. NeuroVault.org: a web-based repository for collecting and sharing unthresholded statistical maps of the human brain. Front. Neuroinform. 9, 8. https://doi.org/10.3389/fninf.2015.00008.

Gotink, R.A., Meijboom, R., Vernooij, M.W., Smits, M., Hunink, M.G.M., 2016. Brain and Cognition 8-week Mindfulness Based Stress Reduction induces brain changes similar to traditional long-term meditation practice – A systematic review. Brain Cogn 108, 32–41. https://doi.org/10.1016/j.bandc.2016.07.001.

Herwig, U., Kaffenberger, T., Jäncke, L., Brühl, A.B., 2010. Self-related awareness and emotion regulation. Neuroimage 50, 734–741. https://doi.org/10.1016/j.neuroimage.2009.12.089.

Hofmann, S.G., Grossman, P., Hinton, D.E., 2011. Loving-kindness and compassion meditation: potential for psychological interventions. Clin. Psychol. Rev. 31, 1126–1132. https://doi.org/10.1016/j.cpr.2011.07.003.

Hooley, J.M., Siegle, G., Gruber, S.A., 2012. Affective and neural reactivity to criticism in individuals high and low on perceived criticism. PLoS ONE 7, e44412. https://doi.org/10.1371/journal.pone.0044412.

Kohn, N., Eickhoff, S.B., Scheller, M., Laird, A.R., Fox, P.T., Habel, U., 2014. Neural network of cognitive emotion regulation - An ALE meta-analysis and MACM analysis. Neuroimage 87, 345–355. https://doi.org/10.1016/j.neuroimage.2013.11.001.

Kuyken, W., Watkins, E., Holden, E., White, K., Taylor, R.S., Byford, S., Evans, A., Radford, S., Teasdale, J.D., Dalgleish, T., 2010. How does mindfulness-based cognitive therapy work. Behav. Res. Ther 48, 1105–1112. https://doi.org/10.1016/j.brat.2010.08.003.

Kuznetsova, A., Brockhoff, P.B., Christensen, R.H.B., 2017. lmerTest Package: Tests in Linear Mixed Effects Models. J. Stat. Softw. 82, 1-26. https://doi.org/10.18637/jss.v082.i13.

Leary, M.R., Tate, E.B., Adams, C.E., Allen, A.B., Hancock, J., 2007. Self-compassion and reactions to unpleasant self-relevant events: the implications of treating oneself kindly. J. Pers. Soc. Psychol. 92, 887–904. https://doi.org/10.1037/0022-3514.92.5.887.

Longe, O., Maratos, F.A., Gilbert, P., Evans, G., Volker, F., Rockliff, H., Rippon, G., 2010. Having a word with yourself: neural correlates of self-criticism and self-reassurance. Neuroimage 49, 1849–1856. https://doi.org/10.1016/j.neuroimage.2009.09.019.

López, A., Sanderman, R., Smink, A., Zhang, Y., van Sonderen, E., Ranchor, A., Schroevers, M.J., 2015. A reconsideration of the self-compassion scale's total score: self-Compassion versus self-criticism. PLoS ONE 10, e0132940. https://doi.org/10.1371/journal.pone.0132940.

Loisel, P., Vachon, B., Lemaire, J., Durand, M.-J., Poitras, S., Stock, S., Tremblay, C., 2002. Discriminative and Predictive Validity Assessment of the Quebec Task Force Classification. Spine (Phila. Pa. 1976) 27, 851–857 https://doi.org/10.1097/00007632-200204150-00013.

Luoma, J.B., Platt, M.G., 2015. Shame, self-criticism, self-stigma, and compassion in Acceptance and Commitment Therapy. Curr. Opin. Psychol. 2, 97–101. https://doi.org/10.1016/j.copsyc.2014.12.016.

Lutz, J., Brühl, A.B., Doerig, N., Scheerer, H., Achermann, R., Weibel, A., Jäncke, L., Herwig, U., Dörig, N., Scheerer, H., Achermann, R., Weibel, A., Jäncke, L., Herwig, U., 2016a. Altered processing of self-related emotional stimuli in mindfulness meditators. Neuroimage 124, 958–967. https://doi.org/10.1016/j.neuroimage.2015.09.057.

Lutz, J., Brühl, A.B., Scheerer, J., Jäncke, L., Herwig, U., 2016b. Neural correlates of mindful self-awareness in mindfulness meditators and meditation-naive subjects revisited. Biol. Psychol. 119, 21–30. https://doi.org/10.1016/j.biopsycho.2016.06.010.

Lutz, J., Herwig, U., Opialla, S., Hittmeyer, A., Jäncke, L., Rufer, M., Holtforth, M.G., Brühl, A.B., Grosse Holtforth, M., Brühl, A.B., 2014. Mindfulness and emotion regulation-an fMRI study. Soc. Cogn. Affect. Neurosci. 9, 776–785. https://doi.org/10.1093/scan/nst043.

Meucci, R.D., Fassa, A.G., Faria, N.M.X., 2015. Prevalence of chronic low back pain: systematic review. Rev. Saude Publica 49. https://doi.org/10.1590/S0034-8910.

2015049005874.

Neff, K.D., 2003. Self-compassion: an alternative conceptualization of a healthy attitude toward oneself. Self Identity 2, 85–101. https://doi.org/10.1080/15298860309032.

Neff, K.D., Germer, C.K., 2013. A pilot study and randomized controlled trial of the mindful self-compassion program. J. Clin. Psychol. 69, 28–44 https://doi.org/10.1002/jclp.21923.

Neff, K.D., Rude, S.S., Kirkpatrick, K.L., 2007. An examination of self-compassion in relation to positive psychological functioning and personality traits. J. Res. Pers. 41, 908–916. https://doi.org/10.1016/j.jrp.2006.08.002.

Northoff, G., Bermpohl, F., 2004. Cortical midline structures and the self. Trends Cogn. Sci. 8, 102–107. https://doi.org/10.1016/j.tics.2004.01.004.

Northoff, G., Heinzel, 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. 10.1016/j.neuroimage.2005.12.002.

Ochsner, K.N., Bunge, S.A., Gross, J.J., Gabrieli, J.D.E., 2002. Rethinking feelings: an FMRI study of the cognitive regulation of emotion. J. Cogn. Neurosci. 14, 1215–1229. https://doi.org/10.1162/089892902760807212.

Ochsner, K.N., Silvers, J.A., Buhle, J.T., 2012. Functional imaging studies of emotion regulation: a synthetic review and evolving model of the cognitive control of emotion. Ann. N. Y. Acad. Sci. 1251, E1–24. https://doi.org/10.1111/j.1749-6632.2012.06751.x.

Osborn, M., Smith, J.A., 1998. The personal experience of chronic benign lower back pain: an interpretative phenomenological analysis. Br. J. Health Psychol. 3, 65–83. https://doi.org/10.1111/j.2044-8287.1998.tb00556.x.

Parrish, M.H., Inagaki, T.K., Muscatell, K.A., Haltom, K.E.B., Leary, M.R., Eisenberger, N.I., 2018. Self and Identity Self-compassion and responses to negative social feedback: the role of fronto-amygdala circuit connectivity. 10.1080/15298868.2018.1490344.

Phan, K.L., Wager, T., Taylor, S.F., Liberzon, I., 2002. Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. Neuroimage 16, 331–348. https://doi.org/10.1006/nimg.2002.1087.

Pinto-Gouveia, J., Duarte, C., Matos, M., Fráguas, S., 2014. The protective role of self-compassion in relation to psychopathology symptoms and quality of life in chronic and in cancer patients. Clin. Psychol. Psychother. 21, 311–323. https://doi.org/10.1002/cpp.1838.

Purdie, F., Morley, S., 2015. Self-compassion, pain and breaking a social contract. Pain 156, 2354–2363. https://doi.org/10.1097/j.pain.000000.

Qin, P., Northoff, G., 2011. How is our self related to midline regions and the default-mode network?. Neuroimage 57, 1221-1233. https://doi.org/10.1016/j.neuroimage.2011.05.028.

Raichle, M.E., 2015. The brain's default mode network. Annu. Rev. Neurosci. 38, 433–447 https://doi.org/10.1146/annurev-neuro-071013-014030.

Sharot, T., Riccardi, A.M., Raio, C.M., Phelps, E.A., 2007. Neural mechanisms mediating optimism bias. Nature 450, 102–105. https://doi.org/10.1038/nature06280.

Santorelli, S.F., Meleo-Meyer, F., Koerbel, L., Kabat-Zinn, J., 2007. Mindfulness-Based Stress Reduction (MBSR) Authorized Curriculum Guide. Center for Mindfulness in Medicine. Health Care, and Society (CFM) University of Massachusetts Medical School.

Schönbrodt, F.D., Perugini, M., Marco Perugini, S., 2013. At what sample size do correlations stabilize? J. Res. Pers. https://doi.org/10.1016/j.jrp.2013.05.009.

Servaas, M.N., Riese, H., Ormel, J., Aleman, A., 2014. The neural correlates of worry in association with individual differences in neuroticism. Hum. Brain Mapp. 35, 4303–4315. https://doi.org/10.1002/hbm.22476.

Simons, L.E., Elman, I., Borsook, D., 2014. Psychological processing in chronic pain: a neural systems approach. Neurosci. Biobehav. Rev. 39, 61–78. https://doi.org/10.1016/j.neubiorev.2013.12.006.

Sirois, F.M., Molnar, D.S., Hirsch, J.K., 2015. Self-compassion, stress, and coping in the context of chronic illness. Self Identity 14, 334–347. https://doi.org/10.1080/15298868.2014.996249.

Sutherland, R., Morley, S., 2008. Self-pain enmeshment: future possible selves, sociotropy, autonomy and adjustment to chronic pain. PAIN® 137, 366–377. https://doi.org/10.1016/j.pain.2007.09.023.

Turner, B.O., Paul, E.J., Miller, M.B., Barbey, A.K., 2018. Small sample sizes reduce the replicability of task-based fMRI studies. Commun. Biol. 1, 1–10. https://doi.org/10.1038/s42003-018-0073-z.

Van Dam, N.T., Hobkirk, A.L., Sheppard, S.C., Aviles-Andrews, R., Earleywine, M., 2014. How does mindfulness reduce anxiety, depression, and stress? An exploratory examination of change processes in wait-list controlled mindfulness meditation training. Mindfulness (N. Y) 5, 574–588. https://doi.org/10.1007/s12671-013-0229-3.

Wren, A.A., Somers, T.J., Wright, M.A., Goetz, M.C., Leary, M.R., Fras, A.M., Huh, B.K., Rogers, L.L., Keefe, F.J., 2012. Self-compassion in patients with persistent musculoskeletal pain: relationship of self-compassion to adjustment to persistent pain. J. Pain Symptom Manage. 43, 759–770. https://doi.org/10.1016/j.jpainsymman.2011.04.014.

Yu, L., Norton, S., Harrison, A., McCracken, L.M., 2015. In search of the person in pain: a systematic review of conceptualization, assessment methods, and evidence for self and identity in chronic pain. J. Context. Behav. Sci. 4, 246–262. https://doi.org/10.1016/j.jcbs.2015.10.003.

Zeidan, F., Martucci, K.T., Kraft, R.A., Gordon, N.S., McHaffie, J.G., Coghill, R.C., 2011. Brain mechanisms supporting the modulation of pain by mindfulness meditation. J. Neurosci. 31, 5540–5548. https://doi.org/10.1523/JNEUROSCI.5791-10.2011.