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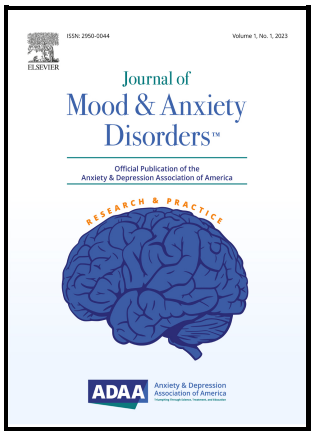

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Neural correlates of reduction in self-judgment after mindful self-compassion training: a pilot study with resting state fMRI

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Conflict of Interest
The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Ethics Statement
The study was approved by the Institutional Review Board of Georgetown University, study number: STUDY00005683, PI: Dr. Elizabeth Hoge. All study procedures were conducted according to IRB-approved study protocol.

Abstract

Self-judgment is a trans-diagnostic symptom among various psychological disorders, therefore can be a therapeutic target for many common psychiatric conditions. Self-judgment often arises among those who experienced childhood maltreatment, which increases the risk for developing comorbid psychiatric disorders that are resistant to traditional pharmacological and psychological interventions. Understanding the neural correlates of the therapeutic effect of behavioral interventions for reducing self-judgment is key for developing and refining evidence-based intervention programs. This single arm pilot study (N=24) explored the neural correlates of reduction in self-judgment after an eight-week mindful self-compassion (MSC) intervention program for a sample of adult patients with either anxiety or depressive disorders, with 83% having more than one diagnoses. The results demonstrated significant reduction of self-judgment after the intervention ($p < 0.001$, $d = -1.04$) along with increased self-compassion ($p < 0.001$, $d = 1.20$); in particular, participants with above median score on the Childhood Trauma Questionnaire had significantly more improvement than those with below median scores

(p<0.05). Resting state fMRI was used to study neural correlates and showed that reduced self-judgment was associated with increased posterior cingulate cortex functional connectivity with dorsal lateral prefrontal cortex, inferior frontal gyrus, and dorsal medial prefrontal cortex, accompanied by reduced posterior cingulate cortex functional connectivity with the amygdala-hippocampal complex. These findings suggest reduced self-judgment after MSC training was substantiated by reduced fear circuitry influences on self-referential processes along with enhanced frontal regulation from the executive network and language network.

Keywords: childhood trauma, neuroimaging, neural plasticity, contemplative, compassion, mindfulness

Introduction

Self-judgment is a common psychological symptom across various mental health conditions such as depressive disorders [1, 2] and anxiety disorders [3, 4]. Self-judgment is not only a transdiagnostic risk factor for various psychological disorders, it is also associated with pervasive psychosocial impairments with occupational [5] and social functioning [6]. Self-judgment as a mental activity is the process of casting negative evaluation for oneself and things related to oneself [7]. Self-judgment as a personality trait is the tendency for consistently and readily judging oneself in a negative light [8] with feelings of inferiority, guilt, and worthlessness [4, 9]. The trait for self-judgment has been found to be a major factor in multiple psychosocial dysfunctions, such as depressive disorders, generalized anxiety disorder, social anxiety disorder [10], and many other transdiagnostic symptoms such as body dissatisfaction [11], self-injury [12], and attachment dysfunction [6]. Self-judgment not only perpetuates the symptoms across psychological disorders, but also hinders psychological healing and compromises the effectiveness of psychotherapy [13, 14] as well as adherence to pharmacological interventions [15]. Individuals with high trait levels of self-judgment tend to perceive more criticism and stigma, which compromises their willingness to initiate or adhere to psychiatric treatments, which has been reported in prior research on mood disorders [15] and substance use disorders [16]. Therefore, understanding and addressing this transdiagnostic trait is critical in psychological research.

In the Research Domain Criteria (RDoC) framework of the National Institute of Mental Health (NIMH) [17, 18], " self-judgment" is at the intersection of the "negative valence systems" domain and the "self-knowledge" subconstruct of the "perception and understanding of self" construct in the "social processes" domain. "Self-knowledge" is the ability to make judgments about one's internal states and traits. Self-judgment reflects negatively distorted self-knowledge. One's sense of self and relatedness to others represent core lifespan developmental tasks [4, 9]. While there are complex biosocial causes for developing the trait for critical self-judgment, it has been known to often arise among those who experienced childhood maltreatment [10, 13, 19], and can be a form of internalized negative social cognition towards oneself. Interpersonal trauma and insecure attachment during childhood have been found to affect personality development especially related to self-worth and self-criticism [20], thereby creating developmental vulnerability for depression and other psychological disorders. Because of its fundamental role in social processes, self-judgment also impacts psychosocial functioning commonly seen in depression [21], especially during [22] and after the Covid-19 global pandemic.

The goal of the present study is to investigate the neural mechanism of self-judgment through a mechanistic clinical trial in which self-judgment can be effectively reduced thus enabling investigation on the corresponding neural changes associated with reduction of self-judgment. The Mindful Self-Compassion (MSC) [23] program was used as a mechanistic probe to reduce self-judgment in a patient sample with either anxiety or depressive disorders. Self-compassion is the opposite of self-judgment, and self-compassion entails being warm and kind towards one's shortcomings and taking a balanced non-judgmental view of one's emotions [24]. The MSC program was developed specifically for cultivating self-compassion [23], therefore MSC was used in this study to target self-judgment. The choice of patient population was based on prior evidence of MSC effectively reducing symptoms of depression and anxiety [25, 26], prior knowledge on the relationship between self-judgment [10, 13, 19] and psychiatric disorder comorbidities [27, 28], as well as shared neural characteristics of depression and

anxiety [29, 30]. Therefore, focusing on a patient sample with either anxiety or depressive disorders is an ideal initial step for a pilot study to have sufficient generalizability for neural mechanistic findings. Because childhood maltreatment plays an important role in the etiology of self-judgment as well as the development of anxiety and depressive disorders, and prior research has demonstrated that patients with childhood maltreatment histories might benefit more from mindfulness-based interventions [31-33], we also collected measurements on childhood maltreatment and lifetime trauma to further evaluate whether childhood maltreatment affects the effects of MSC on reducing self-judgment, and whether similar effects also exist for lifetime trauma experiences not specifically captured by childhood maltreatment measures.

There have not been prior studies on the specific neural correlates of reduction of trait self-judgment resulting from the 8-week standard MSC program. Previous studies have demonstrated effects of meditation practices or mindfulness training on the default mode network [34, 35], executive network [36] and attention networks [35]. Therefore, this study focuses on the following Regions of Interest (ROIs): posterior cingulate cortex (PCC), which is the core hub of the default mode network [37-39] and was used as the seed for functional connectivity analysis in this study; dorsal medial frontal cortex (DMFC), which is critical for self-referential processes [40] and also a core region of the default mode network [37, 41, 42]; dorsal lateral prefrontal cortex (DLPFC) as the core region of the executive network [43]; and the amygdala-hippocampal complex which are core regions of the fear circuitry [44] and have been shown to have abnormalities associated with childhood trauma [45-49]; as well as the left inferior frontal gyrus-pars triangularis ($LIFG_{PT}$) which is a key region in the language network and plays a critical role in inner speech production [50], involuntary recall of traumatic memories [51], and self-reflection [52-54], and likely plays a critical regulatory role in the process of reducing the trait for self-judgment and increasing the trait for self-compassion. Previous research also showed that $LIFG_{PT}$ hyperconnectivity with the limbic system was a key neural characteristic of childhood trauma survivors' susceptibility to psychopathology [55, 56], therefore $LIFG_{PT}$ was included as an ROI to study the neural mechanism of how self-compassion training affects inner speech and self-criticism [57]. We hypothesized MSC-induced reduction in trait self-judgment was associated with enhanced PCC functional connectivity with DLPFC, $LIFG_{PT,}$ DMFC, and reduced PCC functional connectivity with the amygdala-hippocampal complex.

Methods

Study procedures

All study procedures were approved by the Institutional Review Board (IRB). Patients were recruited through multiple IRB-approved approaches such as referrals, flyers, social media, and local media advertisements. Patients were instructed to fill out an online pre-enrollment form, then complete preliminary phone screening with a research assistant, then participants completed informed consent and structured clinical interviews with a study clinician to determine final eligibility. Consented eligible patients were randomized to either receiving the 8-week MSC program or being placed on a waitlist to participate in a future cohort of MSC program after the waiting period. Online questionnaires and MRI data were collected before and after participating in the 8-week MSC program.

Enrollment and eligibility

Patients included in this MRI study met the following eligibility criteria. Inclusion criteria include: (1) between age 18 and 65 years old; (2) having a current primary anxiety disorder (social anxiety disorder (SAD), generalized anxiety disorder (GAD), panic disorder, or agoraphobia) or major depressive disorder; (3) having baseline total score on the Self-Compassion Scale below 3; (4) able to understand study procedures and provide informed consent; and (5) meeting MRI eligibility criteria. Exclusion Criteria include: (1) Comorbid psychiatric disorder other than anxiety or depression, such as psychotic disorder, obsessive compulsive disorder, eating disorders (i.e., anorexia and bulimia), bipolar disorder; developmental or organic mental disorders; and current (past 6 months) substance use disorders and current post-traumatic stress disorder as assessed by a clinician at screening visit; (2) Having a serious medical condition that may result in surgery or hospitalization; (3) A history of head trauma causing prolonged loss of consciousness, or ongoing cognitive impairment; (4) Inability to understand study

procedures or informed consent process; (5) Inability to reliably participate in study procedures and prescribed intervention sessions; (6) Routinely taking barbiturates, or antipsychotics. Sleep medications (other than anti-depressants) were allowed, if they had been taken at stable dose 4 weeks prior to baseline and the patient planned to continue at the same dose throughout the period of participation in this study. SSRIs and anti-depressants were allowed if the subject had been on a stable dose for at least 8 weeks and stays at the same dose during the trial; (7) Concurrent psychotherapy initiated within one month of screening interview, or ongoing psychotherapy of any duration directed specifically toward the treatment of anxiety (such as Cognitive Behavioral Therapy). (8) Prior participation in MSC or other systematic meditation training in the last year, or having an ongoing daily meditation practice. (9) Reporting significant active suicidal ideation or suicidal behaviors within the past year. (10) Individuals with medical conditions (e.g., upcoming surgery) that could interfere the ability to participate in the intervention. (11) Being left-handed; (12) self-reported current or imminently planned pregnancy.

Questionnaires

The following questionnaires were administered with the REDCap electronic data capture tools [58].

The Self-Compassion Scale [59] is a 26-item self-report questionnaire for measuring self-compassion with 3 pairs of subscales: Self-Kindness vs. Self-Judgment, Mindfulness vs. Over-identification, Common-Humanity vs. Isolation. This scale has been shown to have good internal reliability with Cronbach's α =0.92 for the total score and α =0.77 for the self-judgment subscale.

Childhood Trauma Questionnaire-short form (CTQ) is a 28-item questionnaire for retrospective measurement of abuse and neglect during the first 18 years of one's life [60], including five subscales with five items each: emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect, and 3 additional validity items. The CTQ has been shown with good internal validity in previous studies [61, 62] with Cronbach's α =0.85 [63].

Life Event Checklist (LEC) for DSM-5 (LEC-5) assesses lifetime exposure to 17 kinds traumatic events [64, 65] such as natural disaster, combat, captivity, motor vehicle accident, physical or sexual assault, and life threatening injuries or illnesses. These events could have taken place at any point of one's lifetime and is not confined to the period of childhood. LEC has been demonstrated to have good internal validity with Cronbach's α = 0.87 [66].

Patient-Reported Outcomes Measurement Information System (PROMIS®) Adult Short Form v1.0 with anxiety and depression modules [67] were used to measure depression and anxiety symptoms. Each module includes 8 items to be responded to on a 5-point Likert scale, with example items include (in the last 7 days) "I felt fearful/uneasy/nervous" for the anxiety module and "I felt worthless/helpless/hopeless/unhappy" for the depression module. Both modules have high validity and reliability, with the anxiety and depression module having Cronbach alpha of 0.97 [68] and 0.92 [67] respectively. Standardized T scores were used in this study.

Curriculum of the MSC program

The MSC program was co-developed by Kristin Neff and Christopher Germer [23]. The 8-week program included weekly 2.5-hour in-person group meetings with group sizes ranging 10-15. The program was led by a certified MSC teacher. The curriculum included teaching the concepts and meditation practices of mindfulness and self-compassion, as well as coping skills for difficult emotions and interpersonal relationships. Interpersonal exercises were frequently used during the program to practice self-compassion with fellow participants. Weekly topics of the 8-week program are summarized in Table 1. Several meditation practices were taught including the following: loving-kindness meditation [69] based an ancient Buddhism practice for cultivating good will for oneself and others; affectionate breathing which integrate feelings affection and warmth into the mindfulness practice of breath awareness meditation; self-soothing touch [70] such as hands-over-heart during which participants practiced placing one's hands over the heart area of the chest at times of stress to practice compassion towards oneself; repeating self-compassion phrases throughout daily lives; self-compassion break which is a brief meditation to acknowledge moments of suffering in daily lives and apply kindness to oneself. Participants were

instructed to maintain 20 minutes of formal and informal self-compassion practices per day and submitted weekly home practice record cards throughout the 8-week program for a total duration of 7 weeks.

Table 1 about here

MRI acquisition

MRI data was acquired at Georgetown University Medical Center on a Siemens 3T Prisma scanner. Anatomical MRI was acquired with T1-weighted multi-echo MPRAGE (MEMPRAGE) sequence [71], with GRAPPA factor of 2, voxel size of 1.0×1.0×1.0 mm, Field of View (FOV) of 256mm, base resolution of 256, with 176 slices in the R>>L direction, TR=1900ms, TI=900ms, TE=2.52ms, flip angle=9.0 degrees. Resting state fMRI was acquired using EPI sequence with multiband acceleration factor of 5, base resolution of 98, with 75 slices in the I>>S direction, voxel size of TR=1250ms, TE=33ms, flip angle =65, a total of 330 time points were acquired during a total of 6.88 minutes.

Resting state fMRI data analysis

Analyses of resting state fMRI data were performed using CONN [72](RRID:SCR_009550) release 22.v2407[73] and SPM [74] (RRID:SCR_007037) release 12.7771. The first minute of resting state fMRI data was discarded to obtain stable signal, with the remaining 282 timepoints (5.88 minutes) went through further processing and analyses.

Preprocessing: Functional and anatomical data were preprocessed using a modular preprocessing pipeline [75] including realignment with correction of susceptibility distortion interactions, slice timing correction, outlier detection, direct segmentation and MNI-space normalization, and smoothing. Functional data were realigned using SPM realign & unwarp procedure [76], where all scans were coregistered to a reference image (first scan of the first session) using a least squares approach and a 6 parameter (rigid body) transformation [77], and resampled using b-spline interpolation to correct for motion and magnetic susceptibility interactions. Temporal misalignment between different slices of the functional data (acquired in interleaved Siemens order) was corrected following SPM slice-timing correction (STC) procedure [78] [79], using sinc temporal interpolation to resample each slice BOLD timeseries to a common mid-acquisition time. Potential outlier scans were identified using ART[80]as acquisitions with framewise displacement above 0.9 mm or global BOLD signal changes above 5 standard deviations [81, 82], and a reference BOLD image was computed for each subject by averaging all scans excluding outliers. Functional and anatomical data were normalized into standard MNI space, segmented into grey matter, white matter, and CSF tissue classes, and resampled to 2 mm isotropic voxels following a direct normalization procedure [82, 83] using SPM unified segmentation and normalization algorithm [84] [85] with the default IXI-549 tissue probability map template. Last, functional data were smoothed using spatial convolution with a Gaussian kernel of 6 mm full width half maximum (FWHM).

Denoising: In addition, functional data were denoised using a standard denoising pipeline [75] including the regression of potential confounding effects characterized by white matter timeseries (5 CompCor noise components), CSF timeseries (5 CompCor noise components), motion parameters and their first order derivatives (12 factors) [86], outlier scans (below 21 factors) [81], session effects and their first order derivatives (2 factors), and linear trends (2 factors) within each functional run, followed by bandpass frequency filtering of the BOLD timeseries [87] between 0.008 Hz and 0.09 Hz. CompCor [88, 89] noise components within white matter and CSF were estimated by computing the average BOLD signal as well as the largest principal components orthogonal to the BOLD average, motion parameters, and outlier scans within each subject's eroded segmentation masks.

Functional connectivity and statistical analysis: Functional connectivity analysis was conducted using bilateral PCC as the seed Region of Interest (ROI) based on the AAL3 atlas [90]. For each individual subject fMRI data, the average pre-processed BOLD signal from the seed ROI was extracted and correlated with the pre-processed BOLD signals in each voxel, and then underwent r to z transformation to convert into Z scores for further

statistical analyses. The Z maps of PCC functional connectivity at pre-intervention were subtracted from the Z maps at post-intervention, obtaining a difference Z map for each subject. General linear model regression analyses were then conducted with the post- vs. pre- intervention Z maps as dependent variable, and SCS-SJ score changes as independent variable, with covariates including age, gender, race, and educational level. A concatenated ROI map, including the following ROIs: bilateral PCC, bilateral DLFPC, bilateral DMFC, left IFG_{PT}, bilateral amygdala, and bilateral hippocampi were imposed on the final statistical map to identify significant clusters with the *t* statistic of SCS-SJ score changes, at a minimum |t|=2.12, cluster size>15 continuous voxels to reach a false discovery rate (FDR) corrected $p < 0.05$. The average Z score changes of PCC functional connectivity from the combined clusters of each ROI were extracted, Shapiro-Wilk Test of Normality tests were conducted before calculating Pearson correlation coefficients with SCS-SJ score changes for illustration purposes.

Results

Research participants characteristics and questionnaire scores

The sample (N=24, Table 2) consisted mostly white (79%) college-educated (92%) females (67%). The primary diagnosis for the majority (88%) was anxiety disorder, with major depressive disorder as the most common (48%) secondary diagnosis. The majority of the sample (n=20, 83%) had more than one diagnoses. The sample had an average CTQ score of 45.25±14.20 which is in the range of moderate severity of childhood trauma [91], with 37.5% patients having experienced emotional abuse, 16.7% experienced physical abuse, 12.5% experienced sexual abuse, 41.7% experienced emotional neglect and 8.3% experienced physical neglect (Table 2). The sample had an average LEC score of 14.92±11.44, the 3 most frequently reported types of lifetime trauma events were: transportation accidents (54.17%), Unwanted or Uncomfortable Sexual Experience (45.83%) and Physical Assault (25.00%) (Table 2). Most patients (75%) were on a stable dose of at least one kind of psychotropic medication, with SSRIs being the most common type of medication (41.67%). On average patients attended 7.92±0.65 out of the total of 9 sessions and reported an average of 623.67±390.70 minutes of homework practice throughout the program, which breaks down to an average of 12.73 minutes of daily home practice. The average group sizes for the intervention were 10.14 participants with a range of 6-12.

Table 2 about here

Paired t-test showed significant changes (Figure 1.A) with SCS total score ($t(23)=5.85$, $p<0.001$, $d=1.20$) and score of the self-judgment subscale ($t(23)=-5.11$, $p<0.001$, $d=-1.04$), as well as scores of PROMIS-D ($t(23)=3.35$, $p<0.01$) and PROMIS-A ($t(23)=4.55$, $p<0.001$, Table 3). Most importantly, patients with CTQ scores at median level or above, compared to patients with CTQ scores below median level, showed significantly more improvement in total SCS scores ($t(22)=2.27$, $p=0.033$, $d=0.93$) and the self-judgment sub scores ($t(22)=-2.16$, $p=0.042$, $d=-0.89$) (Figure 1). Similar analysis with LEC did not find significant differences on score changes of SCS and SCS-SJ between those above and below median LEC scores.

Figure 1 about here

Table 3 about here

Neural correlates of score changes of self-judgment

Significant clusters were identified within each ROI with regard to the correlations between post vs. pre-intervention difference Z maps of PCC functional connectivity and SCS-SJ score changes (Figure 2, Table 4) to capture the brain-behavior associations between post-intervention neural and behavioral changes. Shapiro-Wilk Test of Normality tests confirmed normality of post- vs. pre- intervention SCS-SJ score changes and difference Z scores from each ROI, with no outliers detected. Correlation coefficients between the average post- vs. pre-intervention difference Z scores of PCC functional connectivity maps and post- vs. pre- intervention SCS-SJ score

changes are plotted in Figure 3 for illustration purposes. Overall, reduced SCS-SJ scores were associated with increased PCC functional connectivity with frontal regions and decreased PCC functional connectivity with the amygdala-hippocampal complex.

Table 4 about here

Figure 2 about here

Discussion

This pilot study found that the MSC program significantly reduced self-judgment, which was associated with enhanced PCC-frontal resting state functional connectivity and reduced PCC connectivity with the amygdala-hippocampal complex.

During the past three decades, mindfulness meditation have rapidly grown in popularity in the United States and worldwide [92]. Several standardized manualized Mindfulness-Based Intervention (MBI) programs have been developed, widely distributed, and well-researched, such as Mindfulness-Based Stress Reduction (MBSR) [93] and Mindfulness-Based Cognitive Therapy (MBCT) [94]. MSC [23] was developed as a versatile program to be beneficial for a wide range of psychological symptoms through cultivating self-compassion. The MSC program was designed to improve mindfulness and self-compassion through meditation practices for cultivating inner-warmth and self-kindness, increasing present-moment awareness, reducing self-judgment and sense of isolation, and promoting a sense of common humanity [23]. The MSC program has been widely disseminated worldwide with research evidences on various clinical benefits such as reducing depression, anxiety [25, 26], stress [23], burnout [95] or chronic pain [96], in addition to reliably increasing self-compassion [23, 97, 98]. A recent meta-analysis of 20 randomized controlled trials (RCTs) showed that various kinds of self-compassion-related trainings produced significant reduction in self-criticism [57]. This meta-analysis [57] also showed that self-judgment was a commonly used measure for self-criticism [99, 100], and that elements from the MSC program were often utilized in self-compassion trainings in previous studies [101-104]. Therefore, this study used the MSC intervention as a mechanistic probe to investigate the neural correlates of an anticipated reduction in self-judgment after the MSC training. As expected, in this study, the program effectively increased self-compassion and reduced self-judgment (Figure 1), and also effectively reduced depression and anxiety symptoms (Table 3). Such findings provide preliminary evidence that the MSC program can be an effective intervention for reducing critical self-judgment as a transdiagnostic therapeutic target [1, 2, 105-108].

Furthermore, this study also found that patients with above-median level of CTQ score had significantly more improvement with self-judgment and self-compassion (Figure 1.B), which indicates patients with high levels of childhood maltreatment benefited more from the MSC program. Similar analysis did not find any significant effects with lifetime trauma as measured by LEC-5, suggesting this finding may be unique to childhood maltreatment. The tendency for childhood maltreatment survivors to benefit more from a mindfulness-based intervention was previously reported in a large clinical trial (N=274) that showed MBCT was only more effective than control conditions among patients with above median levels of CTQ scores for relapse prevention of recurrent depression [31]. Accumulating population health research has demonstrated that childhood trauma increases the risk for developing various mental health disorders [109] and also hinders treatment responses to pharmacological interventions or traditional behavioral interventions[110, 111]. Emerging evidence from this and prior studies [31, 112] suggests mindfulness-based interventions might be particularly advantageous for childhood maltreatment survivors. Our prior study with an MBSR intervention for childhood maltreatment survivors demonstrated that self-compassion was a significant mediator between improvements in mindfulness and psychological symptoms [113]. Therefore, the MSC program used in this study, which cultivates both mindfulness and self-compassion, might be an ideal intervention for childhood maltreatment survivors.

As the first study on the neural correlates of MSC-induced reduction in self-judgment, we found that reduction of self-judgment was associated with increased PCC functional connectivity with three ROIs in the frontal cortex including DLPFC, IFG, and DMFC, which are respectively critical regions of the executive network, the language network [50] and default mode network [37, 41, 42]. This is consistent with prior findings from other mindfulness-based interventions. For example, one prior study with brief body-mind relaxation meditation training found increased resting state functional connectivity between the left and right dorsal lateral prefrontal cortices [114], another study with 3 days of intensive mindfulness meditation training found increased resting state functional connectivity between DLPFC and PCC [115]. Recent review articles suggest mindfulness-based interventions were generally associated with increased frontal connectivity with the default mode network [116] or fear circuitry [117], reflecting enhanced attention control [116] or emotion regulation [117]. Therefore, the strengthened frontal-PCC connectivity found in the present study may indicate enhanced frontal regulation of self-referential processes as a result of the MSC training.

Enhanced frontal regulation is a well-known neural effect of meditation trainings [118, 119]. The increased PCC functional connectivity with DLPFC likely reflects the general effects of mindfulness meditation training for enhancing attention control [120], alertness [121] and awareness [122]. The DMFC has been known to play an important role in self-referential processes [123], although it's also part of the default mode network, it serves a different function than the PCC. While the PCC is a hub region of the default mode network [42] and plays critical roles in internally directed cognition, autobiographic memories, planning for the future, and attention regulation [124], the DMFC is critical for perspective taking [125] and self-reflection [126]. The enhanced PCC functional connectivity with DMFC might suggest improved perspective taking and self-reflection as a result of the MSC training.

Involvement of the language network such as IFG is commonly reported with compassion meditation [127] or other mantra-based meditation practices [128] that utilize language during the meditation, as well as in silent meditation practices [129]. Because the MSC program actively works on inner speech and utilizes mantra-based meditation, e.g., using phrases during loving-kindness meditation such as "may I be safe and protected, may I be happy and contented", the language neural network played an important role during self-compassion meditation practices, leading to an accumulated change in psychological trait and resting state functional connectivity that was reflected from data collected at the post-intervention timepoint. Future studies should also investigate potential structural changes in the language network. At the same time, the neural changes in the language network are also likely critically important for childhood maltreatment survivors, which are susceptible to critical inner speech with self-judgment due to internalized criticism from others, feelings of inferiority, guilt, sense of failure or inadequacy, as well as perceived disapproval or rejection [10, 13, 19]. Therefore, MSC is likely a beneficial intervention program for childhood maltreatment survivors to overcome the impact of childhood maltreatment on self-judgment. The finding of increased PCC-IFG functional connectivity associated with reduced self-judgment after MSC likely reflects enhanced tendencies for frontal regulation of self-referential processes through compassionate inner speech.

Meditation trainings and practices have also been shown to promote structural and functional changes in the fear circuitry [130-133]. For example, mindful attention training was found to reduce amygdala activity to negative images [130] or face pictures [134]. The hippocampus is both part of the fear circuitry [135, 136] and the default mode network [42], and it has been frequently reported to demonstrate structural and functional changes in response to mindfulness meditation training [137-140], including among childhood maltreatment survivors [113, 141]. Our finding of reduced self-judgment being associated with reduced PCC functional connectivity with the amygdala-hippocampal complex likely reflects reduced influence of the fear circuitry on the default mode network, thereby reducing the negative valence in self-referential processes, with behavioral implications such as changing the negative tone and overly critical content of inner speech as a result of the MSC training.

In summary, this pilot study confirmed that MSC was effective for reducing self-judgment in addition to increasing self-compassion, and the effects were significantly better for patients with high level of childhood maltreatment. Reduced self-judgment was associated with reduced influence of fear circuitry on self-referential processes and enhanced frontal regulations from the executive network and language network. These findings may have the following implications for the research field: (1) Mindfulness based interventions may be particularly beneficial for individuals with high levels of childhood maltreatment [31-33], therefore could be considered in treatment recommendations for this population, as well as future intervention development for the subtype of psychiatric patients with high levels of childhood maltreatment which is increasingly recognized as an ecophenotype [142] in various psychiatric disorders [142-147]. (2) Self-compassion training can be beneficial for reducing self-judgment, therefore the MSC program is worth consideration for treating various psychiatric disorders associated with self-judgment [10-12, 148, 149]. (3) Findings on the neural correlates suggest the neural mechanism of MSC heavily relies on enhancing frontal regulation especially through the language network, which highlights the unique advantage of self-compassion training for overcoming trait self-judgment through cultivating positive compassionate self-talk. Such mechanistic findings can inform further research on the neural mechanism of MSC and possibly inspire development of new therapy approaches based on the novel language-network based neurobiological model.

There are several major limitations with this study, such as being a single arm study with a small sample, although similar pilot studies have still yielded meaningful knowledge to the literature. For example, our previous single arm study (N=20) on the effect of a two-day concentrated self-compassion training has found significant changes in frontal activity during a self-appraisal task [7], and another single arm study (N=28) found significant changes with insular activity associated with interoception after an 8-week mindfulness intervention [150]. The N=24 in this study is comparable with the sample size of 20-30 in many previous studies in the meditation literature [131, 151, 152]. With the intrinsic challenge of a longitudinal MRI study with an 8-week long intervention, a N=24 is a reasonable sample size. Furthermore, while resting state functional connectivity is a commonly utilized research approach [39, 42], additional insights could be gained from other MRI methodologies, such as analyzing the anatomical and structural changes, or identifying changes in neural activity in response to fMRI tasks, which will be explored in our future research. This study focused on a patient sample with either anxiety or depressive disorders, while self-judgment is also common in several other psychological phenotypes such as eating disorder [148] and body dissatisfaction [11], self-injury [12], personality disorders [149] and attachment disorders [6], which likely involve additional neural mechanisms and will be explored in future research. The patient sample, which consisted of mixed anxiety and/or major depressive disorder, despite the common comorbidity between the two types of disorders [153, 154], might have also introduced variances and heterogeneity in the data as compared to focusing on a single disorder, which should also be considered in future research. Despite major limitations with this single arm pilot study, it provided useful data for future research with a more rigorous randomized controlled trial with more comprehensive psychological and MRI measures.

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Table 1: Weekly theme of the mindful self-compassion program

	Theme
Week 1	Introduction to Self-Compassion
Week 2	Fundamentals of mindfulness
Week 3	Application of self-compassion in everyday life
Week 4	Developing a compassionate inner voice
Retreat	Four-hour silent retreat with guided meditations, restorative yoga, and mindful eating
Week 5	Living with core values
Week 6	Coping skills for difficult emotions
Week 7	Navigating challenging interpersonal relationships
Week 8	Relating to positive aspects of oneself and living life with appreciation

Table 2: Patient demographic and baseline clinical information.

Characteristics	Frequency
Gender	
Female	16 (67%)
Male	8 (33%)
Race	
American Indian or Alaska Native	0
Asian	1 (4%)
Black or African American	4 (17%)
Native Hawaiian or Other Pacific Islander	0
White	19 (79%)
More than one race	0
Unknown or unreported	0
Ethnicity	
Hispanic or Latino	2 (8%)
Not Hispanic or Latino	22 (92%)
Age (Mean (SD)) = 41.4 (12.4)	
Over 40 years old	11 (46%)
Under 40 years old	13 (54%)
Education level	
College graduate and above	22 (92%)
Partial college	2 (8%)
CTQ (Mean (SD)) = 45.25 (14.20)	
Emotional Abuse	9 (37.5%)
Physical Abuse	4 (16.7%)
Sexual Abuse	3 (12.5%)
Emotional Neglect	10 (41.7%)
Physical Neglect	2 (8.3%)
LEC (Mean (SD)) = 14.92 (11.44)	
Transportation Accident	13 (54.17%)
Unwanted or Uncomfortable Sexual Experience	11 (45.83%)
Physical Assault	6 (25.00%)
Primary Diagnoses	
Depressive Disorders	3 (12%)
Anxiety Disorders	21 (88%)
Secondary Diagnoses	
Major Depressive Disorder	14 (48.3%)
Panic Disorder	1 (3.4%)
Social Anxiety Disorder	4 (13.8%)
Agoraphobia	2 (6.9%)
Generalized Anxiety Disorder	8 (27.6%)
Medications	
SSRIs	10 (41.67%)

Anxiolytics	5 (20.83%)
Stimulants (ADHD medications)	3 (12.50%)
Atypical Antidepressants	3 (12.50%)
Bupropion	3 (12.50%)
Melatonin	2 (8.33%)
Benzodiazepines	2 (8.33%)
Hydroxyzine	1 (4.17%)

Table 3: Pre- and post-intervention scores for Self-Compassion Scale (SCS) total score and the self-judgment subscale score, Patient-Reported Outcomes Measurement Information System – Depression (PROMIS-D), and Patient-Reported Outcomes Measurement Information System – Anxiety (PROMIS-A).

	Baseline (Mean (SD))	**Week 8 (Mean (SD))**	**Paired t-test**
SCS - total	2.11 (0.36)	2.78 (0.63)	$t(23)= -5.85$, $p < 0.001$, $d = -1.32$
SCS - Self-Judgment	1.94 (0.51)	2.61 (0.66)	$t(23)= -5.11$, $p < 0.001$, $d = -1.13$
PROMIS-D	59.77 (5.55)	54.73 (7.37)	$t(23)= 3.35$, $p <0.01$, $d = 0.77$
PROMIS-A	65.11 (5.49)	59.35 (5.97)	$t(23)= 4.55$, $p = 0.0001$, $d = 1.00$

Table 4: Significant clusters of post-intervention changes in PCC functional connectivity predicted by score changes of self-judgment.

Location		Cluster Size (voxels)	Peak Coordinates	Peak t-values
Dorsal Lateral Prefrontal Cortex	L	108	-38.4 46.8 13.4	-2.90
	R	89	-4.0 41.2 45.7	-3.77
	L	27	-28.3 7.6 57.0	-2.75
	R	25	40.4 55.0 16.0	-2.66
Dorsal Medial Prefrontal Cortex	L	88	42.4 45.7 -6.9	-2.91
	R	15	6.1 28.2 58.1	-2.84
Inferior Frontal Gyrus	L	40	30.3 24.5 49.2	-3.25
	L	23	-52.5 16.3 5.2	-3.17
Posterior Cingulate Cortex	L	21	-4.0 -52.9 27.7	3.12
	R	17	10.1 -48.5 21.4	3.25
Amygdala and Hippocampal Complex	R	58	36.4 3.3 -28.4	3.96

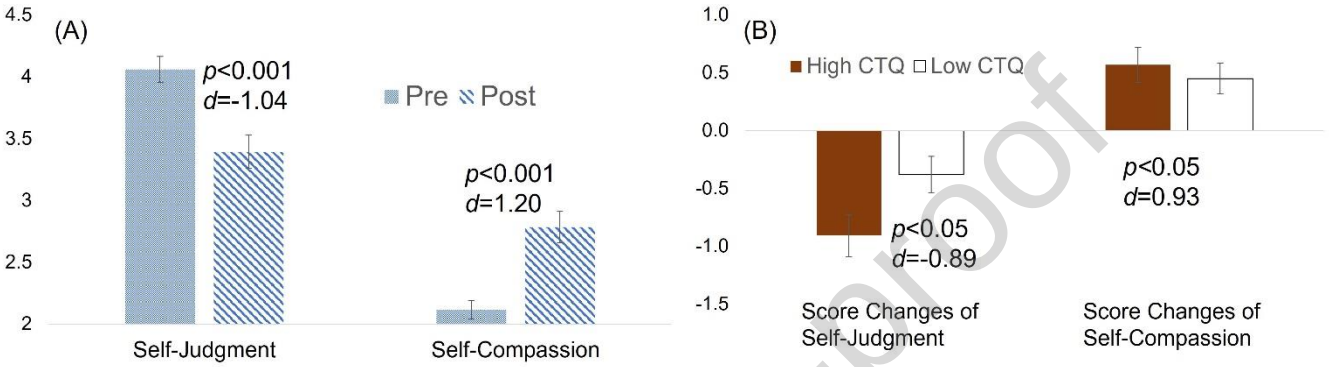

Figure 1: (A) Pre- and post-intervention scores of Self-Judgment subscale of the Self-Compassion Scale along with the total score of self-compassion scale, with each showing significant difference in paired t-test (p<0.001). (B) Patients with median score or above on the (n=13) Childhood Trauma Questionnaire (CTQ) showed significantly more improvement (p<0.05) compared to patients with below median scores (n=11) in self-judgment and self-compassion after the Mindful Self-Compassion (MSC) program. Error bars represent standard error.

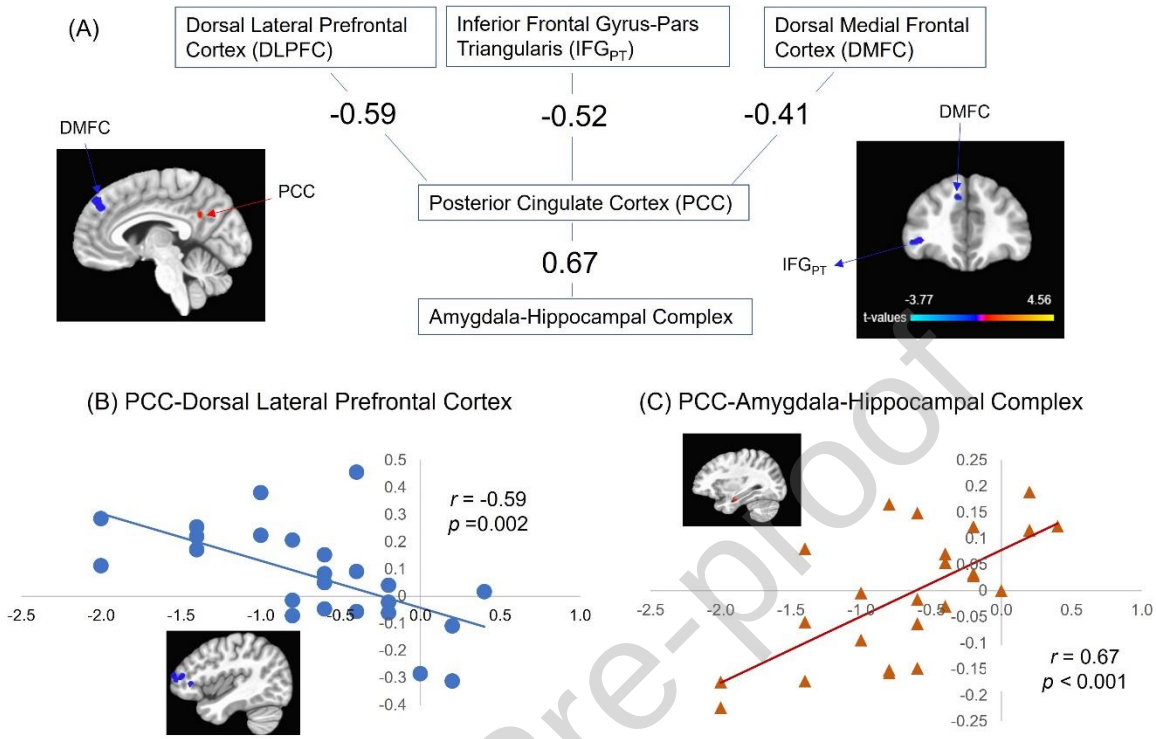

Figure 2: Illustration of associations between post-intervention score changes in self-judgment and post-intervention changes in PCC resting state functional connectivity (RSFC). (A) Correlation coefficients between score changes of self-judgment and post-intervention changes of PCC RSFC from the significant clusters. Overall, reduced self-judgment scores were associated with increased PCC RSFC with frontal regions but decreased PCC RSFC with the amygdala-hippocampal complex (AHC). (B) Scatter plot of the negative correlation between self-judgment score changes (x-axis) and post-intervention changes of PCC RSFC with dorsal lateral prefrontal cortex (DLPFC) (y-axis); post-intervention changes of PCC RSFC with the other two frontal regions have similar scatter plots. (C) Scatter plot of the positive correlation between Self-Judgement score changes (x-axis) and post-intervention changes of PCC RSFC with AHC (y-axis).

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: