Promising Subjective and Objective Benefits of Modified Mindfulness-Based Stress Reduction Training for Chinese Adults with Chronic Pain: A Pilot Randomized Control Study

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Image acquisition and processing

High-resolution T1-weighted structural images were acquired using a magnetization-prepared rapid acquisition gradient-echo sequence with the following parameters: TR/TE = 2530 ms/2.98 ms, inversion time = 1100 ms, flip angle = 7◦, FOV = 256×256 mm^2, slices = 192, thickness = 1.00 mm, and voxel size = 0.5×0.5×1.0 mm^3. Resting-state neuroimaging data were obtained via a Siemens Magnetom Prisma 3.0 T. During resting-state fMRI scanning, participants were instructed to lie in a supine position with their heads snugly fixed by foam pads to minimize head movement. They were also instructed not to think about anything in particular, to keep their eyes open and focus on a fixation ("+") presented onscreen. Resting-state fMRI was acquired using an echo-planar image (EPI) pulse sequence with the following parameters: 62 slices; 2 mm slice thickness; voxel size = 2.0 × 2.0 × 2.0 mm; TR = 2000 ms; TE = 30 ms; FOV = 224×224 mm^2; flip angle = 90°. For each participant, 240 EPI functional volumes were collected in 8 minutes. After the scan, all participants reported compliance with the instruction to remain awake during their scan.

Initially, images were converted from Dicom to Nifiti format with the DCM2Nii tool. Next, each MR image was displayed on a screen to detect any artifacts or gross anatomical abnormalities using Statistical Parametric Mapping (SPM) on the Matlab platform. For better registration, the reorientation of images was manually set to the anterior commissure. Anatomical images underwent unified segmentation using light regularization and TPM.nii included in SPM as the reference tissue probability map,

after which probability maps of gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF) segments were obtained by the VBM8 Toolbox. Finally, non-linear normalized GM segments were smoothed with a Gaussian kernel set to 8-mm full width at half maximum (FWHM) to reduce possible errors from between-participant variability in local anatomy and make data more normally distributed. Smoothed GM segments were analyzed using SPM in a general linear modeling (GLM) framework based on voxel-wise comparisons.

Resting-state fMRI data were preprocessed using a Data Processing & Analysis for Brain Imaging toolbox (DPABI 4.0, http:/rfmri.org/dpabi) based on Statistical Parametric Mapping (SPM8) (http://www.fil.ion.ucl.ac.uk/spm), and running on Matlab R2014a (https://in.mathworks.com). Specifically, the first 10 time points were discarded to allow the signal to reach MRI equilibrium. The remaining 230 consecutive volumes were corrected for acquisition time delay by shifting the signal measured in each slice relative to the acquisition of the slice at the mid-point of each TR. The time series of images for each participant were realigned using a six-parameter (rigid body) linear transformation with a two-pass procedure (registered to the first image and then registered to the mean of images after the first realignment). T1-weighted images were co-registered to EPI mean images and segmented into WM, GM, and CSF. Then, a Friston 24-parameter model addressed head motion effects. WM and CSF signals extracted were removed to reduce the potential effects of respiratory and cardiac influences. Functional images were then normalized to Montreal Neurological Institute (MNI) space and resampled to $3 \times 3 \times 3$ mm^3 voxel size with the Diffeomorphic Anatomical Registration Through Exponentiated Lie algebra (DARTEL) tool (Ashburner, 2007).

We first smoothed ALFF and fALFF images with an 8-mm FWHM Gaussian kernel and extracted the power spectrum. The ALFF/fALFF value was then computed from an averaged square root by calculating the square root at each frequency of the power spectrum across the 0.01-0.1 Hz frequency range. Finally, we applied a Fisher's z-transformation and performed temporal band-pass filtering ($0.01 < f < 0.1$ Hz) for each voxel. ReHo is measured by Kendall's coefficient of concordance (KCC) and evaluated by the synchronization of time courses between a given voxel and its nearest neighbors (here, 27 voxels) (Zang et al., 2004). To obtain ReHo, band-pass filtering (0.01–0.1 Hz) was first performed on normalized images. Then, each ReHo map was divided by its own mean ReHo within the mask for standardization. Finally, we executed smoothing on modulated ReHo maps with an 8 mm FWHM Gaussian kernel to obtain the smReHo map.

References

Ashburner, J. (2007). A fast diffeomorphic image registration algorithm. *Neuroimage*, *38*(1), 95-113. https://doi.org/10.1016/j.neuroimage.2007.07.007

Zang, Y., Jiang, T., Lu, Y., He, Y., & Tian, L. (2004). Regional homogeneity approach to fMRI data analysis. *Neuroimage*, *22*(1), 394-400. https://doi.org/10.1016/j.neuroimage.2003.12.030

Table S1. Outline of the modified Mindfulness-Based Stress Reduction (MBSR) course for Chinese adults with chronic pain

Sessions	Themes and topics for discussion	Mindfulness meditation exercises	Homework
1	a) Orientation: Introduce to the programme Explanation conceptual framework and rational of mindfulness meditation Structure of the programme Confidentiality and privacy b) Introductions: Leader introduces self to group Participants introduce themselves to group c) Discussion of the purpose of participation d) Discussion of awareness of body sensation and thoughts	• Standing yoga/tai chi stretching • Raisin-eating exercise • Abdominal breathing • Body scan	Complete the body scan mediation using the prepared recording for at least for 6 days Try to do the 9 dots puzzle exercise. Complete mindful eating at least once a week
2	a）Introductions: Attitudes in mindfulness meditation Breath or pain sensation as the anchor of present moment b）Discussion of body scan exercise c）Discussion of the 9 dots puzzle exercise	• Standing yoga/tai chi stretching • Body scan • Breathing mediation	Complete the body scan and breathing mediation using the prepared recording for at least 6 days Fill out Pleasant Events Calendar

3	a) Introductions: Awareness of pleasantness and body sensations Non-judgment of mind-wandering and inner experiences b) Discussion of sitting mediation and body scan c) Discussion of pleasant events	• Sitting meditation • Mindful lying down yoga • Body scan • Pleasant events mediation • Waking mediation	Practise the body scan and mindful lying down yoga using the prepared recording at least for 6 days Fill out Unpleasant Events Calendar
4	a) Introductions: Automatic habitual stress reactions and behaviors toward pain b) Discussion of the unpleasant events	• Standing yoga/tai chi stretching • Sitting mediation	Practise the body scan, mindful lying down yoga, and sitting meditation using the prepared recording at least for 6 days Mid-term summary of MBSR
5	a) Introductions: Non-judgment of and non-reactivity to inner experience Transition from reaction to respond b）Discussion of their usual coping methods toward stress and/or pain	• Standing yoga/tai chi stretching • Sitting mediation with unpleasant feelings	Practise sitting mediation and one of the following practices: Standing yoga/tai chi stretching, body scan, and mindful lying down yoga) using the prepared recording at least for 6 days. Fill out Difficult Communications Log
6	a) Introductions: Decouple painful body sensations from emotional distress	• Standing yoga/tai chi stretching • Sitting mediation • Self-compassion mediation	Practise sitting mediation and one of the following practices: Standing yoga/tai chi stretching, body scan,

	Acceptance of disappointment Self-compassion and loving kindness b) Discussion of expectations and gains from the course c) Discussion of difficult communications		and mindful lying down yoga) using the prepared recording at least for 6 days.
7	a) Introductions: Pain as a vital sign, gratitude of pain Spicy flavor, the sensation of pain b) Discussion of mindful yoga/tai chi stretching to release pain in daily life c) Ten things in daily life: five good things that others did for me and five good things that I did for others	• Body scan • Waking mediation • Loving kindness mediation	Complete formal mediation practice without recording at least for 6 days. Maintain awareness and clarity in daily life as possible as you can.
8	a) Introductions: A summary of the MBSR Course Informal mindfulness practice in daily life b) Discussion of gains from the MBSR c) Discussion and commitment to practice after this course	• Body scan • Standing yoga/tai chi stretching • Self-compassion meditation	Choose the way you like to practice and commit it in daily life

Table S2. Intention-to-treat analyses of differences between MBSR (n = 40) and TAU (n = 27) groups

	Mean (SD)			Group ×Time			T2-T1			T3-T1		
	T1	T2	T3	*F*	*p*	η_p^2	*t*	*p*	*d*	*t*	*p*	*d*
Pain severity												
MBSR	5.05 (1.60)	4.27 (1.82)	4.48 (1.71)	0.35	.708	0.01	-0.60	.553	-0.15	0.21	.837	0.05
TAU	5.23 (1.91)	4.70 (1.73)	4.58 (1.90)									
Pain interference												
MBSR	4.37 (1.93)	3.46 (1.67)	3.61 (1.80)	2.66	.074	0.04	-2.13	.035	-0.54	-1.84	.068	-0.46
TAU	3.93 (2.13)	3.94 (2.09)	3.96 (2.07)									
Perceived stress												
MBSR	20.23 (2.64)	19.98 (2.66)	19.48 (3.63)	0.86	.424	0.01	-0.18	.857	-0.05	-1.22	.225	-0.31
TAU	19.74 (3.11)	19.63 (3.00)	19.93 (2.66)									
Depression												
MBSR	20.77 (11.49)	18.80 (11.08)	19.10 (12.71)	0.55	.579	0.01	0.64	.523	0.16	1.04	.301	0.26
TAU	20.49 (9.14)	17.26 (8.94)	16.78 (9.60)									
Pain catastrophizing												
MBSR	27.08 (11.21)	21.20 (10.42)	22.42 (12.21)	3.51	.033	0.05	-2.39	.018	-0.60	-0.21	.836	-0.05
TAU	25.56 (12.98)	25.48 (14.13)	21.41 (12.16)									
Describe												

MBSR	13.25 (2.72)	12.82 (2.83)	12.85 (2.64)	2.39	.095	0.04	-0.77	.440	-0.19	-2.16	.033	-0.54
TAU	11.67 (3.16)	11.70 (2.83)	12.56 (3.52)									
Awareness												
MBSR	9.65 (2.94)	9.95 (2.98)	9.90 (2.82)	1.09	.338	0.02	0.83	.409	0.21	-0.65	.519	-0.16
TAU	9.52 (3.24)	9.19 (3.31)	10.19 (3.49)									
Non-judge												
MBSR	8.30 (2.59)	8.40 (2.84)	8.28 (3.27)	0.45	.641	0.01	0.32	.749	0.08	0.93	.354	0.23
TAU	8.48 (3.34)	8.30 (2.07)	7.63 (3.32)									
Pain resilience												
MBSR	32.08 (7.99)	34.12 (7.24)	33.90 (7.61)	1.76	.176	0.03	1.70	.092	0.43	0.15	.880	0.04
TAU	32.26 (7.43)	30.89 (7.16)	33.78 (7.56)									
General resilience												
MBSR	2.83 (0.67)	2.90 (0.79)	3.00 (0.76)	0.32	.728	0.01	0.80	.427	0.20	0.37	.710	0.09
TAU	2.99 (0.52)	2.94 (0.53)	3.10 (0.63)									

Note. MBSR = mindfulness-based stress reduction; TAU = treatment-as-usual. T1 = baseline; T2 = post-treatment; T3 = 3-month follow-up. η_p^2 = partial η^2. T2-T1 = MBSR (T2-T1) vs. TAU (T2-T1); T3-T1 = MBSR (T3-T1) vs. TAU (T3-T1).

Table S3. Completer analyses of differences between MBSR (n = 19) and TAU (n = 27) groups

	Mean (SD)			Group ×Time			T2-T1			T3-T1		
	T1	T2	T3	*F*	*p*	η_p^2	*t*	*p*	*d*	*t*	*p*	*d*
Pain severity												
MBSR	4.91 (1.70)	3.95 (1.73)	4.63 (1.79)	1.16	.317	0.03	-0.82	.415	-0.25	0.71	.483	0.21
TAU	5.23 (1.91)	4.70 (1.73)	4.58 (1.90)									
Pain interference												
MBSR	4.86 (1.81)	3.26 (1.46)	3.88 (1.81)	4.40	.015	0.09	-2.93	.004	-0.91	-1.86	.066	-0.56
TAU	3.93 (2.13)	3.94 (2.09)	3.96 (2.07)									
Perceived stress												
MBSR	20.26 (2.98)	19.58 (2.81)	18.42 (3.31)	3.14	.048	0.07	-0.69	.484	-0.21	-2.43	.017	-0.74
TAU	19.74 (3.11)	19.63 (3.00)	19.93 (2.66)									
Depression												
MBSR	20.95 (12.57)	20.11 (10.95)	19.11 (15.44)	0.51	.601	0.01	0.96	.339	0.29	0.75	.453	0.23
TAU	20.49 (9.14)	17.26 (8.94)	16.78 (9.60)									
Pain catastrophizing												
MBSR	27.95 (11.89)	22.53 (11.62)	23.84 (13.36)	2.23	.114	0.05	-1.82	.072	-0.55	0.02	.998	0.01
TAU	25.56 (12.98)	25.48 (14.13)	21.41 (12.16)									
Describe												

MBSR	13.05 (3.01)	12.84 (2.87)	12.53 (2.82)	2.20	.116	0.05	-0.34	.732	-0.10	-1.97	.053	-0.60
TAU	11.67 (3.16)	11.70 (2.83)	12.56 (3.52)									
Awareness												
MBSR	9.32 (3.33)	9.95 (2.93)	10.21 (2.82)	0.82	.442	0.02	1.23	.222	0.37	0.29	.772	0.09
TAU	9.52 (3.24)	9.19 (3.31)	10.19 (3.49)									
Non-judge												
MBSR	8.95 (2.61)	8.63 (3.11)	8.79 (3.81)	0.31	.737	0.01	-0.12	.908	-0.03	0.61	.542	0.18
TAU	8.48 (3.34)	8.30 (2.07)	7.63 (3.32)									
Pain resilience												
MBSR	30.21 (7.00)	32.37 (5.89)	33.16 (8.44)	1.22	.302	0.03	1.55	.125	0.47	0.63	.532	0.19
TAU	32.26 (7.43)	30.89 (7.16)	33.78 (7.56)									
General resilience												
MBSR	2.75 (0.72)	2.90 (0.79)	2.93 (0.75)	0.34	.715	0.01	0.82	.414	0.25	0.40	.688	0.12
TAU	2.99 (0.52)	2.84 (0.71)	3.10 (0.63)									

Note. MBSR = mindfulness-based stress reduction; TAU = treatment-as-usual. T1 = baseline; T2 = post-treatment; T3 = 3-month follow-up. η_p^2 = partial η^2.T2-T1 = MBSR (T2-T1) vs. TAU (T2-T1); T3-T1 = MBSR (T3-T1) vs. TAU (T3-T1).