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The Effect of Body-Mind Relaxation Meditation Induction on Major Depressive Disorder: A Resting-State FMRI Study

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Abstract

Background: Meditation has been increasingly evaluated as an important complementary therapeutic tool for the treatment of depression. The present study employed resting-state functional magnetic resonance imaging (rs-fMRI) to examine the effect of body-mind relaxation meditation induction (BMRMI) on the brain activity of depressed patients and to investigate possible mechanisms of action for this complex intervention.

Method: 21 major depressive disorder patients (MDDs) and 24 age and gender-matched healthy controls (HCs) received rs-fMRI scans at baseline and after listening to a selection of audio designed to induce body-mind relaxation.
meditation. The rs-fMRI data were analyzed using Matlab toolbox to obtain the amplitude of low-frequency fluctuations (ALFF) of the BOLD signal for the whole brain. A mixed-design repeated measures analysis of variance (ANOVA) was performed on the whole brain to find which brain regions were affected by the BMRMI. An additional functional connectivity analysis was used to identify any atypical connection patterns after the BMRMI.

**Results:** After the BMRMI experience, both the MDDs and HCs showed decreased ALFF values in the bilateral frontal pole (BA10). Additionally, increased functional connectivity from the right dorsal medial prefrontal cortex (dmPFC) to the left dorsal lateral prefrontal cortex (dlPFC) and the left lateral orbitofrontal cortex (OFC) was identified only in the MDDs after the BMRMI.

**Limitation:** In order to exclude the impact of other events on the participants’ brain activity, the Hamilton Rating Scales for Depression (HDRS) were not measured after the body-mind relaxation induction.

**Conclusion:** Our findings support the hypothesis that body-mind relaxation meditation induction may regulate the activities of the prefrontal cortex and thus may have the potential to help patients construct reappraisal strategies that can modulate the brain activity in multiple emotion-processing systems.

**Keywords:** Major depressive disorder, body-mind relaxation meditation, fMRI, right precuneus, cognitive reappraisal, medial frontal cortex, orbitofrontal cortex.

1 Introduction

Major depressive disorder (MDD) is a serious clinical mood disorder characterized by mood dysregulation and cognitive impairment. According to the World Health Organization, MDD will be the second-leading cause of disability in the world by the year 2020, following heart disease (Sliz and Hayley, 2012). Despite this high prevalence, the pathogenesis of MDD remains unclear and the diagnosis of depression is often delayed or missed, leading to poor outcomes, including high relapse rates, suicide, and diminished psychosocial functioning.

The most frequently used treatment for MDD is antidepressant medication. In spite of the development of new and effective medications for depression, as many as 30% to 50% of patients do not respond to medication treatment (Baghai et al., 2006). Furthermore, medications may induce unwanted side effects that can impair patients’ quality of life (Kupfer et al., 2012). As a result, they may not be suitable for patients with mild to moderate depressive symptoms, which represent the majority of clinical cases.

In contrast, new non-pharmacological treatments strategies, including electroconvulsive therapy (ECT), cognitive behavioral therapy (CBT), repetitive transcranial magnetic stimulation (rTMS), and so on, are currently under
development. Their clinical efficacy has been confirmed at least in subgroups of depression, although more insight into the main mechanisms underlying their antidepressant efficacy is still necessary. Furthermore, depression is a highly recurrent disorder that causes great suffering for patients and their families. Even among patients who show improvement with short-term antidepressant use, there is a significant risk for relapse within one year after treatment termination (Hsu and Lai, 2004).

Meditation, an easy, low cost practice that seems to have the ability to regulate emotion, has been used in the treatment of depression (Goyal et al., 2014; Little et al., 2009). Meditation has been shown to produce benefits for anxiety, depression, and other negative emotional symptoms (Jain et al., 2014; Simkin and Black, 2014). Review studies have pointed out that adding mindfulness meditation to conventional CBT offers a promising, cost-efficient psychological approach for preventing relapse/recurrence in recovered recurrently depressed patients (Beshai et al., 2011; Shelton, 2004). Prior exposure to mindfulness-based cognitive therapy (MBCT) appears to be about as efficacious as keeping patients on medications; in fact, most of the patients exposed to MBCT in one study were able to discontinue medications (Kuyken et al., 2008). A previous review study indicated that alterations in attention, memory specificity, self-discrepancy, activity-pleasantness appraisal, emotional reactivity, and momentary positive and negative affect may play a role in how MBCT exerts clinical effects in MDD treatment (van der Velden et al., 2015).

A version of mindfulness meditation, body–mind relaxation meditation, which originates from ancient Eastern traditions, has been showed to be an important complementary therapy for both the treatment and prevention of many stress-related conditions (Tang, 2011). This type of meditation does not stress controlling thoughts, but instead encourages a state of restful alertness that allows for a high degree of awareness of the body, of breathing, and of external instructions. The inducing passage helps trainees to relax, adjust their breathing, and use mental imagery to achieve a balanced state of relaxation while focusing attention. This approach is suitable for novices and MDD patients, who might have difficulty spontaneously entering into and remaining in a state of mindfulness.

Despite the various benefits of body-mind relaxation meditation induction for depression, its effects on brain activity have not been adequately established. In the current study, we used a brief, guided body-mind relaxation intervention, based on observations that short meditation interventions have significant effects on mood (Zeidan et al., 2010b), cognition (Zeidan et al., 2010a), and self-regulation (Tang et al., 2007). Our hypothesis was that after a single brief session of guided meditation, participants would show functional changes in the brain. We collected rs-fMRI data before and after a body-mind relaxation meditation induction session to identify the affected brain regions.

The amplitude of low-frequency fluctuations (ALFF) of the BOLD signal, an index that measures the total power of a given time course within a specific frequency range (0.01 - 0.08 Hz) (Zang et al., 2007), was employed to compare the
resting-state brain activity before and after body-mind relaxation meditation induction. Due to its high temporal stability
(Kublbock et al., 2014) and test-retest reliability (Zuo and Xing, 2014), ALFF has been suggested as a biologically
meaningful index for assessing the altered neural activity associated with behavioral performance or psychiatric
disorders (Hoptman et al., 2010; Yan et al., 2009; Yang et al., 2007).

Functional connectivity (FC) is another widely-used fMRI data analysis method, which measures the temporal
correlation between different brain regions. Although either standard seed-ROI-based functional connectivity or whole
brain functional connectivity can provide more holistic information about a set of brain regions within a network, they do
not reveal the BOLD signal change of the regional spontaneous activity. Moreover, altered connectivity between brain
regions cannot precisely reveal which brain region has altered spontaneous activity (Jiang et al., 2011). In contrast, ALFF
analyses are only concerned with the activity level of each area of the brain without taking into account the activity in
other brain areas.

The purpose of the present study was to assess whether subsequent rs-fMRI scanning could detect changes in the
brain activity of the participants after experiencing BMRMI. We chose ALFF combined with functional connectivity as
our analysis method. In light of the previous studies mentioned above, we hypothesized that the BMRMI might affect
people with MDD and healthy controls (HC) differently. The general method used in the BMRMI is briefly described in
the next section.

2 Materials and methods

2.1 Participants

The study was approved by the Institute of Medicine Review Board, Guang’anmen Hospital, China Academy of
Chinese Medical Sciences. Patients meeting the following criteria were recruited: SCID-IV diagnostic criteria for
depression; Hamilton Rating Scales for Depression (HDRS) score > 20; age range from 18 to 50 years old; medication
naive or withdrawn for 2 weeks before the rs-fMRI scanning; no other drug therapy; no other psychiatric illnesses or
severe physical illness; disease course longer than 2 weeks; right-handed; no history of qigong practice, yoga practice, or
relaxation training; and no contradiction to undergoing an MRI scan based on an MRI screening questionnaire. The
criteria for the healthy controls were as follows: no psychiatric disorders or severe physical disorders; right-handed; no
history of qigong practice, yoga practice, or relaxation training.

Two patients with MDD were excluded from the analyses due to excessive head motion during the image
acquisition. The patient group and the control group did not differ significantly in age (two tailed two sample \( t \) test: \( p = 0.74 \)) or gender (Pearson chi-square \( t \) test: \( p = 0.81 \)) (Table 1).
The depressed patients and the healthy controls were scanned for rs-fMRI data before and after body-mind relaxation meditation (BMRM) induction. During the BMRM induction, the participants lay still in a bed. The BMRM induction adopted in our experiment contained background music and a human voice reading relaxing-inducing passages, which were read by a woman broadcaster in standard Chinese Mandarin. A type of soft and slow Chinese lute music called Saishangqu was the background music. The induction passage included two sessions: a whole body relaxation induction with words such as “Relax your head, …, relax your neck, …”, and a mind relaxation session with words such as “Now calm your mind, …, remove all your worries, …”. Each subject listened to the BMRM induction for 15 minutes with the goal of becoming completely relaxed.

2.2 rs-fMRI data acquisition

Functional images were acquired on a 1.5 T GE Signal scanner using a standard GE whole-head coil. A custom-built head holder was used to prevent head movement. The echo planar imaging (EPI) sequence was acquired in 41 axial slices with TR = 2500 ms, TE = 30 ms, flip angle = 90°, field of view = 24 cm; 3 mm thickness and 0.5 mm gap; the sequence duration was 370 seconds for each subject, 150 time points were acquired, and the voxel dimensions were 64 x 64 x 20. All the subjects were asked to close their eyes, remain awake, not think about anything specific, and not move while scanning. All the subjects were scanned twice: before and after the BMRM induction session.

2.3 Functional image analysis

We utilized two rs-fMRI metrics: the amplitude of low-frequency fluctuation (ALFF) and functional connectivity (FC), to assess the effects of BMRM experience on brain activity. In contrast to FC, ALFF requires no a priori definition of ROIs and can provide information about the local activity of separate brain regions. We first performed a voxel-based ANOVA analysis on the four groups of mALFF maps, that is, the MDD patients’ mALFF maps before the BMRM (denoted as DP_01), the MDD patients’ mALFF maps after the BMRM (denoted as DP_02), the healthy controls’ mALFF maps before the BMRM (denoted as HC_01), and the healthy controls’ mALFF maps after the BMRM (denoted as HC_02), to identify the ROIs with a main effect of diagnosis, a main effect of BMRM, and an interaction effect of diagnosis × BMRM. For the ROIs showing a significant interaction effect, further functional connectivity analysis was performed to find differences between the effects of the BMRM on the MDD patients and HCs. This process is described in detail below.

2.3.1 Data preprocessing

The image data were preprocessed using SPM8 (http://www.fil.ion.ucl.ac.uk/spm) and MATLAB R2009a (The Mathworks, Natick, MA). The first 10 volumes from each participant were discarded. The functional images underwent slice-timing correction and realignment for head motion correction. Data from participants whose head motion during
scanning exceeded 2 mm or rotation exceeded 2° were excluded. The motion-corrected functional volumes were then spatially normalized to a standard EPI template and resampled to a voxel size of $3\times3\times3$ mm$^3$. Subsequently, the functional images were spatially smoothed with a Gaussian kernel of 6 mm full-width at half maximum. Finally, the linear trend of the time series was removed, and band-pass filtering (0.01–0.08 Hz) was performed to reduce the effects of low-frequency drift and high-frequency noises, such as from respiratory and cardiac rhythms.

2.3.2 Individual ALFF map calculation

After band-pass filtering and linear trend removal, the time series were transformed to the frequency domain using a fast Fourier transform (FFT) and the power spectrum was obtained. Since the power of a given frequency is proportional to the square of the amplitude of this frequency component in the original time series, the square root of the power spectrum obtained by FFT was taken and was then averaged across 0.01–0.08 Hz at each voxel.

For the purpose of standardization, the ALFF for each voxel was divided by the mean ALFF value within the same brain mask. Mean ALFF (mALFF) maps were calculated for each subject and then four groups of data were created: the MDD patients’ mALFF maps before the BMRMI (denoted as DP_01), the MDD patients’ mALFF maps after the BMRMI (denoted as DP_02), the healthy controls’ mALFF maps before the BMRMI (denoted as HC_01) and the healthy controls’ mALFF maps after the BMRMI (denoted as HC_02). All further statistical analyses were performed based on these four groups of data.

2.3.3 Seed-ROI functional connectivity

Regions showing a significant interaction effect were defined as seed-ROIs. After normalization and smoothing, the time series for the whole brain were further preprocessed as follows: First, six head motion parameters, the averaged signals from the CSF and white matter, and the global brain signal were regressed. Second, to reduce the effects of low-frequency drifts and high frequency noise, the time series were band filtered (0.01–0.08 Hz) and linearly detrended. The regional mean time series were obtained by averaging the fMRI time series over all the voxels in the seed region. Then, functional connectivity maps were produced by computing the Pearson correlation coefficients between each averaged seed-ROI signal and the time series from all other voxels within the brain mask. In addition, all correlation coefficients were converted to $z$-scores by applying the Fisher r-to-z transformation.
2.3.4 Statistical analysis

A two way mixed design repeated ANOVA with a between-subjects factor of diagnosis and a within-subjects factor of BMRMI was performed using SPM software to identify the ROIs with a main effect of diagnosis, a main effect of BMRMI, and an interaction effect of diagnosis \( \times \) BMRMI. Significance was first assessed at the whole brain level. The resulting maps were formed using a threshold of \( p < 0.001 \) at the voxel level and \( p < 0.05 \) at the cluster level (minimal cluster volume of 13 contiguous voxels). The significance thresholds were determined by Monte Carlo simulations and corrected for multiple comparisons using the Alphasim tool in AFNI (http://afni.nimh.nih.gov/docpdf/AlphaSim.pdf) within the whole brain mask (size: \( 61 \times 73 \times 61 \) mm\(^3\)). A post hoc analysis was performed to find the average mALFF value for each ROI, the resulting average mALFF values for the four groups of data (DP_01, DP_02, HC_01, HC_02) are displayed in Figs 1, 2, and 3.

To further explore how BMRMI can affect functional connectivity patterns, the brain region showing significant interaction effect was identified as a seed-ROI, and whole brain functional connectivity maps of this seed-ROI were calculated. Further paired \( t \)-tests were performed separately on the MDD and HC groups to compare their connectivity maps before and after the BMRM induction. The significance level was set at \( p < 0.05 \) (corrected for AlphaSim correction, with a combined individual voxel \( p < 0.001 \) and a cluster size \( \geq 13 \) voxels).

3 Results

3.1 Anova Analysis

A whole brain ANOVA analysis on the mALFF revealed a significant main effect of diagnosis \( (F_{1,86} = 11.6096, \ p < .001, \ \text{cluster size} \geq 13) \) in three structures, see Table 2 and Fig. 1. The MDD patients exhibited higher mALFF values in the right insular (BA13) cortex extending to the right inferior frontal cortex as well as lower mALFF values in the right precuneus (BA7) and the right supplementary motor area.

The bilateral frontal polar cortex (BA10) showed a main effect of BMRMI (Table 2, Fig. 1). Both sides showed decreased mALFF values after the BMRM induction in both the MDD and HC groups.

The interaction between diagnosis and BMRMI showed a single cluster in the right dorsal medial frontal cortex (BA8/9). The BMRMI decreased the mALFF value for this structure in the MDD patients while increasing the mALFF value of the same region for the HCs (Table 2, Fig. 3).
3.2 Seed-based resting-state Functional Connectivity

After the BMRM induction, the MDD patients demonstrated significantly increased functional connectivity (FC) between the right dorsal medial prefrontal cortex (dmPFC) and the left dorsal lateral prefrontal cortex (dlPFC). The BMRMI experience also seemed to alter the functional connectivity of MDDs from negative to positive between the right dorsal medial prefrontal cortex (dmPFC) and the left lateral orbitofrontal cortex (OFC). This alteration was detected in both the MDD patients and the HCs, albeit much more significantly in the MDDs (Table 3 and Fig. 4). The two significantly increased FCs observed in the MDDs were interhemispheric and were located in the frontal lobes.

4 Discussion

In this paper, we investigated the effects of BMRMI on brain activity in MDD patients and HCs. We found (1) an effect of BMRMI that was similar between the MDD patients and the HCs, (2) a specific effect of BMRMI on the MDD patients, and (3) group differences in the mALFF maps between the MDD patients and the controls.

Similar effect of BMRMI on MDDs and HCs

After the BMRM induction, the mALFF in the bilateral frontopolar cortex (FPC)(rostrolateral prefrontal cortex) decreased in both the MDD and the HC groups, although this decrease showed a lower level of statistical significance in the HC group. Numerous neuroimaging studies have provided support for the role of the bilateral rostral prefrontal cortex in “evaluation, monitoring, or manipulation of internally generated information” (Burgess et al., 2007). The FPC (BA10) receives no direct input from the sensory cortex leaving it well-positioned to consider events beyond the present moment: self-reflection, long-term goals, past or future events, or hypothetical scenarios (Downar and Daskalakis, 2013). A meta-analysis demonstrated increased resting-state activity in the BA10 as a consistent finding in patients with depression (Fitzgerald et al., 2008). Correcting the excessive activity in the FPC has also been correlated with the success of MDD treatment in therapy modalities such as rTMS, DBS, and CBT (Bewernick et al., 2010; Goldapple et al., 2004; Henry et al., 2001).

The anterior prefrontal cortex (frontopolar cortex) is also a meditation-related region. Anatomical likelihood estimation (ALE) meta-analysis found consistent morphological differences in the frontopolar cortex (BA10) in meditators compared with controls with no meditation experience or short term meditators (Fox et al., 2014). Other research indicated that long-term meditation practice is associated with altered cortical thickness in the frontopolar cortex (Lazar et al., 2005). Based on these previous studies and our findings, we suggest that BMRMI decreases the
activity of the anterior superior prefrontal cortex. This lowered activity may contribute to weakening of the rumination process and short circuiting of complex thought, helping participants stay relaxed.

**Specific effect of BMRMI on MDDs**

We also detected three brain regions, the right dmPFC, left dorsal dlPFC, and left lateral OFC, that showed effects of the BMRMI that were specific to the MDD patients.

The particular regions of the dmPFC, dlPFC, and lateral OFC that we detected are similar to regions commonly activated by cognitive reappraisal, an emotion regulation strategy that involves changing the trajectory of an emotional response by reinterpreting the meaning of the emotional stimulus (Kalisch et al., 2006; Ochsner et al., 2002; Smoski et al., 2013). This reappraisal process is an important mechanism of self-regulation that has consequences for mental and physical well-being, as being exemplified by the central role of reappraisal processes in cognitive behavioral therapy (Willner et al., 2013).

In general, cognitive reappraisal has been shown to depend upon interactions between prefrontal systems that support control processes and posterior cortical and subcortical systems that form representations of the different types of modality specific (e.g. visual, spatial, auditory) information (Ochsner and Gross, 2005). A recent meta-analysis identified the dorsolateral and dorsomedial prefrontal cortex (dlPFC and dmPFC), the orbitofrontal cortex (OFC), and the parietal cortex as the most important nodes of the cognitive reappraisal network (Kalisch, 2009). A study by Golkar et al. confirmed that both the dorsolateral prefrontal cortex (DLPFC) and the lateral orbitofrontal cortex (OFC) contribute to emotion regulation through reappraisal (Golkar et al., 2012). A review study by Ridderinkhof and others concluded that converging evidence points to the presence of functional interactions between the posterior medial frontal cortex (pMFC) and the lateral prefrontal cortex (LPFC), such that monitoring-related pMFC activity serves as a signal that engages regulatory process in the LPFC that implement adjustments in cognitive control performance (Ridderinkhof et al., 2004).

A previous study found decreases in the gamma oscillation in the frontal regions of MDD patients, indicating that the top-down inhibitory control systems involved in emotion regulation are impaired (Lee et al., 2010). The prefrontal cortex (PFC) governs the executive control of information processing and behavioral expression, including the ability to selectively attend to and maintain information, to inhibit irrelevant stimuli and impulses, and to evaluate and select appropriate responses. In the current study, increased functional connectivity between the interhemispheric prefrontal nodes of MDD patients was observed after BMRMI, a finding which may suggest that BMRMI could modulate cognitive reappraisal through regulating functional interactions in the prefrontal cortex. A recent study demonstrated that MDD patients showed lower voxel-mirrored homotopic connectivity (VMHC) in the medial prefrontal cortex (MPFC) than healthy subjects (Guo et al., 2013). Decreased connectivity in the frontal regions has been related to cognitive deficits in
depression, and successful treatments appear to normalize these relationships (Beall et al., 2012). The present findings in our research raise the possibility that BMRMI may improve the cognitive reappraisal ability of MDD patients by regulating the functional interactions in the prefrontal cortex. However, more rigorous designs will be needed to assess greater levels of causal specificity.

**Group differences in mALFF maps between MDDs and HCs**

In addition, an ANOVA analysis found group differences between the MDD patients and the controls. Three regions, the right anterior insula, the right precuneus, and the right supplementary motor area, showed significantly different mALFF values.

The anterior insular cortex (AIC) has been reported to be an important cortical structure involved in awareness, pain, attention, and interoception (Craig, 2009). The AIC is also considered to be a limbic-related cortex. Major depressive disorder is characterized by a dysregulated fronto-limbic network. Hyperactivation of the limbic regions leads to increased attention and processing of emotional information, with a bias toward negative stimuli. In the current study, the right anterior insula showed greater activity in the resting state in the MDD patients than in the HCs, supporting the concept that MDD patients are unable to disengage from externally cued events and negative emotions, a combination which may lead to pathologically self-focused mental ruminative behaviors.

The precuneus, which is centrally located in the default mode network, has consistently been reported to be involved in the pathophysiology of depression. Resting electroencephalography has showed hypoactivity of the precuneus in depressed subjects (Pizzagalli et al., 2002). Patients with MDD have also showed significantly lower signal intensities in the precuneus during a paradigm that focused on judgments about self-relatedness (Grimm et al., 2009). Moreover, decreased grey matter density in the precuneus (BA 7) has been showed to contribute to the diagnosis of depression (Costafreda et al., 2009). A recent study also found decreased regional amplitudes (fALFF and ALFF) in MDD patients in the precuneus (Jing et al., 2013), a finding which is consistent with our findings.

The supplementary motor area (SMA) (including BA6), is a brain area that has been given little attention in emotion processing. However, recent studies have suggested that this region is related to MDD. Indeed, a reduced grey matter volume was found in the right SMA (BA 6) of depressed patients (Cheng et al., 2010; Yuan et al., 2008). Abnormal activity in the SMA (BA6) was observed when MDD patients performed an emotion recognition task (Scheuerecker et al., 2010; Stuhrmann et al., 2011). Our study detected a decrease in the mALFF value for the right SMA of MDD patients using resting-state fMRI.
Limitations

In addition to the relatively small sample size, a few limitations to this study should be noted. In order to exclude the impact of other events on the participants’ brain activity, we opted not to measure the Hamilton Rating Scales for Depression (HDRS) after the body-mind relaxation induction. This made it difficult to estimate the clinical efficacy of the BMRMI. Therefore, although our results suggest that the BMRMI experience may improve MDD patients’ cognitive reappraisal, this hypothesis has to be considered as preliminary. Other analytical techniques such as dynamic causal modeling or network-based analysis might be helpful for identifying a more specific role for BMRM induction in MDD treatment.

5 Conclusions

In this study, we sought to detect how body-mind relaxation meditation induction (BMRMI) influences resting-state brain activity in MDD patients and HCs. Our results revealed altered regional brain activity in both groups after the BMRMI. In summary, the BMRMI decreased the activity of the anterior superior prefrontal cortex in both groups, a finding which implies a role for this region in keeping the mind in a relaxed state. Moreover, the BMRMI enhanced the resting-state functional connectivity in the MDD group between the right dmPFC and the left dlPFC and between the right dmPFC and the left lateral OFC, all regions which play important roles in cognitive reappraisal. This suggests that BMRMI may improve the cognitive reappraisal ability of MDD patients by regulating the functional interactions in their prefrontal cortex. Taken together, our findings provide new insights into possible mechanisms of action for body-mind relaxation meditation induction in MDD therapy.

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References


Author contribution

Conceived and designed the experiments: Tianzi Jiang, Weidong Wang, Xueyu Lv. Performed the experiments: Xueyu Lv, Jiliang Fang, Tao Li, Yang Hong, Xiaoling Wang. Analyzed the data: Fangfang Chen, Lingzhong Fan, Jing Sui. Wrote the manuscript: Fangfang Chen, Xueyu Lv, Tianzi Jiang, Shan Yu, Lingzhong Fan, Jing Sui. All authors contributed to and have approved the final manuscript.

Table 1 – Group demographics and clinical measures

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>MDD patients</th>
<th>Healthy controls</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Year (Mean ± SD)</td>
<td>36.05 ± 9.18</td>
<td>35.21 ± 7.92</td>
<td>0.74 a</td>
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<tr>
<td>HAMD (Mean ± SD)</td>
<td>30.48 ± 5.86</td>
<td>2.00 ± 2.02</td>
<td>&lt;0.001 a</td>
</tr>
<tr>
<td>Gender(Female/Male)</td>
<td>16/5</td>
<td>19/5</td>
<td>0.811 b</td>
</tr>
</tbody>
</table>

Abbreviations: SD: standard deviation; HAMD: Hamilton Depression Rating Scale

a Indicates p values for two-sample t-test

b Indicates p values for Pearson chi² t-test

Table 2 – Brain areas showing significant ALFF differences in 2 groups (MDD/HC) × 2 conditions (before BMRMI/after BMRMI) Repeated Measure Anova

<table>
<thead>
<tr>
<th>Brain region</th>
<th>side</th>
<th>BA</th>
<th>MNI Coordinates</th>
<th>Voxels</th>
<th>F value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>x</td>
<td>y</td>
<td>z</td>
</tr>
<tr>
<td>Main effect of diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dorsal anterior insula</td>
<td>R</td>
<td>13</td>
<td>36</td>
<td>9</td>
<td>15</td>
</tr>
<tr>
<td>Precuneus</td>
<td>R</td>
<td>7</td>
<td>6</td>
<td>-66</td>
<td>45</td>
</tr>
<tr>
<td>Supplementary motor area</td>
<td>R</td>
<td>6</td>
<td>6</td>
<td>-24</td>
<td>45</td>
</tr>
<tr>
<td>Main effect of BMRMI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Frontal Pole</td>
<td>L</td>
<td>10</td>
<td>-6</td>
<td>69</td>
<td>-9</td>
</tr>
<tr>
<td>Frontal Pole</td>
<td>R</td>
<td>10</td>
<td>12</td>
<td>72</td>
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<tr>
<td>Group × BMRMI interaction</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Dorsal medial prefrontal cortex</td>
<td>R</td>
<td>8</td>
<td>9</td>
<td>33</td>
<td>36</td>
</tr>
</tbody>
</table>

Abbreviations: BMRMI: body-mind relaxation meditation induction; ANOVA: analysis of variance; ALFF: amplitude of low-frequency fluctuation; BA: Brodmann area; MNI: Montreal Neurological Institute; L= left; R = right.

Table 3 – Functional connectivity alterations after BMRMI on MDDs and HC

<table>
<thead>
<tr>
<th>Seed region</th>
<th>FC sig. region</th>
<th>BA</th>
<th>MNI Coordinates</th>
<th>voxels</th>
<th>T value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDD group</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Region</td>
<td>Coordinates</td>
<td>z-score</td>
<td>MNI</td>
<td>p-value</td>
<td></td>
</tr>
<tr>
<td>------------------------</td>
<td>-------------</td>
<td>---------</td>
<td>------</td>
<td>---------</td>
<td></td>
</tr>
<tr>
<td>Right dmPFC (BA8/9)</td>
<td>8 -36 15 48 13</td>
<td>4.9025</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left dorsal LPFC</td>
<td>47/12 -39 54 -9 13</td>
<td>5.5586</td>
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</tr>
</tbody>
</table>

**HC group**

<table>
<thead>
<tr>
<th>Region</th>
<th>Coordinates</th>
<th>z-score</th>
<th>MNI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right dmPFC (BA8/9)</td>
<td>No significant region</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Left lateral OFC**

Abbreviations: BMRMI: body-mind relaxation meditation induction; dmPFC: dorsal medial prefrontal cortex; LPFC: lateral prefrontal cortex; OFC: orbitofrontal cortex; BA: Brodmann area; MNI: Montreal Neurological Institute; L = left; R = right.

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**Conflict of interest**

The Authors have declared that there are no conflicts of interest in relation to the subject of this study.
Fig. 1. Main effect of diagnosis: MDD patients exhibited higher mALFF values in the right dorsal anterior insula/BA13 extending to the right inferior frontal gyrus, and lower mALFF values in the right precuneus/BA7 and right supplementary motor area. L = left, R = right. * $0.01 \leq p < 0.05$, ** $0.001 \leq p < 0.01$, *** $p < 0.001$. 
Fig.2. Main effect of BMRMI: BMRMI had the same effect on the healthy controls and MDD patients in the bilateral superior frontal cortex (BA10/BA11). Decreased mALFF values were observed after the BMRMI.

Abbreviations: BMRMI: body-mind relaxation meditation induction; L = left, R = right. * 0.01 ≤ p < 0.05, ** 0.001 ≤ p < 0.01, *** p < 0.001.

Fig.3. Interaction effect of group × BMRMI: BMRMI had a different effect on the healthy controls and the MDD patients in right superior medial frontal cortex: after the body-mind relaxation meditation induction, the MDD patients showed increased mALFF values in the area, whereas the healthy controls showed decreased mALFF values.

Abbreviations: BMRMI: body-mind relaxation meditation induction; L = left, R = right. * 0.01 ≤ p < 0.05, ** 0.001 ≤ p < 0.01.
Fig.4. Functional connectivity alterations after BMRMI on MDDs and HCs:

Abbreviations: BMRMI: body-mind relaxation meditation induction; dmPFC: dorsal medial prefrontal cortex; LPFC: lateral prefrontal cortex; OFC: orbitofrontal cortex.

L= left; R = right; *** p < 0.001.

Highlights

(1) We employed resting-state functional magnetic resonance imaging to examine the effect of body-mind relaxation meditation induction (BMRMI) on the brain activity of depressed patients (MDDs) and healthy controls (HCs).

(2) After the BMRMI experience, both the MDDs and HCs showed decreased ALFF values in the bilateral frontal pole (BA10).

(3) Increased functional connectivity between the interhemispheric prefrontal nodes was identified only in the MDDs after the BMRMI.

(4) BMRMI may have the potential to help patients construct reappraisal strategies.