



# Preliminary Evidence for Changes in Functional Connectivity Associated with Emotional Awareness after Mobile-Based Mindfulness Meditation

Minjung Kim<sup>1</sup>, Jungeun You<sup>2</sup>, Goeun Seong<sup>1</sup>, Heeyeon Kim<sup>1,3</sup>,  
Imhong Jeon<sup>4</sup>, Young-Chul Jung<sup>1,5,6</sup>, and Deokjong Lee<sup>1,4</sup>

<sup>1</sup>Institute of Behavioral Science in Medicine, Yonsei University College of Medicine, Seoul;

<sup>2</sup>Mabo Inc., Seoul;

<sup>3</sup>Department of Psychiatry, Yongin Severance Hospital, Yonsei University College of Medicine, Yongin;

<sup>4</sup>Yonsei Empathy Psychiatry Clinic, Seoul;

<sup>5</sup>Department of Psychiatry, Severance Hospital, Yonsei University College of Medicine, Seoul;

<sup>6</sup>Institute for Innovation in Digital Healthcare, Yonsei University, Seoul, Korea.

**Purpose:** Recently, mental health interventions through mobile applications have been increasing. This study sought to explore what changes occurred in psychometric properties and brain functional connectivity (FC) among people who practiced mindfulness meditation through a mobile application.

**Materials and Methods:** Subjects underwent mindfulness-based intervention (MBI) for about 24 minutes every day for 8 weeks through a mobile application. Before and after MBI, a total of 21 adult men and women completed self-report questionnaires and functional magnetic resonance imaging (fMRI) tests. The fMRI data were acquired during an attention network test and during the resting state.

**Results:** In self-report questionnaires, participants reported increased levels of mindfulness and decreased emotion regulation difficulties after MBI. In task-based fMRI, the time-by-intervention effect was not significant. In resting-state fMRI, FC between the right posterior insula and the left ventromedial prefrontal cortex (VMPFC) increased after MBI. FC between the default mode network-related regions and the occipital regions decreased after MBI. The decrease in FC between the VMPFC and the cuneus showed a significant correlation with the improvement in emotional awareness after MBI.

**Conclusion:** In a pre- and post-MBI comparison of a single group, subjects who underwent mobile-based MBI showed FC changes including the VMPFC. In particular, some of these FC changes were correlated with changes in emotional awareness. The results of this study suggest that further research is needed to verify whether mobile-based MBI affects improvement in emotion regulation through neural changes in functional brain networks.

**Key Words:** Awareness, emotional regulation, functional connectivity, functional MRI, meditation, mindfulness

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**Co-corresponding authors:** Deokjong Lee, MD, PhD, Yonsei Empathy Psychiatry Clinic, 109 Dongjak-daero, Dongjak-gu, Seoul 07008, Korea.

E-mail: pangelt20@gmail.com and

Young-Chul Jung, MD, PhD, Department of Psychiatry, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea.

E-mail: eugenejung@yuhs.ac

• Jungeun You, one of the authors, declares a potential competing interest as the chief executive officer (CEO) of Mabo Inc., which develops mobile applications for mindfulness meditation. The other authors declare that they have no conflicts of interest.

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## INTRODUCTION

Since the 2000s, research on mindfulness-based intervention (MBI) has been actively conducted, and quantitative growth has been achieved.<sup>1</sup> Mindfulness means “the awareness that emerges through paying attention on purpose, in the present moment, and nonjudgmentally to the unfolding of experience moment by moment,”<sup>2</sup> and MBI has been shown to be effective for mental problems such as depression, anxiety, stress, insomnia, and addiction, as well as physical problems such as pain, high blood pressure, and weight control.<sup>1</sup> Traditional face-to-face MBI appeared to not only reduce negative emotion and increase positive emotion but also increase cognitive control such as attentional ability and emotion regulation.<sup>3</sup> The following mechanisms have been proposed for the effects of MBI: 1) more access to sensory representations; 2) less activation of networks associated with habitual ruminative thinking about the self; and 3) altered cognitive processes such as emotion regulation and attention by increasing attention stability and reducing reactivity to emotional stimuli.<sup>4</sup> For instance, a previous study explored the effects of mindfulness-based cognitive therapy (MBCT), one of the MBIs, on executive function and emotional interference using task-based functional magnetic resonance imaging (fMRI) that employed the numerical Stroop test in bereaved people.<sup>5</sup> The results of the study showed that reaction time (RT) of incongruent trials and overall activation of the dorsal attention network decreased after MBCT. This finding suggested that executive function was enhanced, and emotional interference caused by excessive internal thinking was alleviated after MBI.

Thanks to the development of digital technology, the limitations of face-to-face interventions have been highlighted, such as cost, insurance limitations, and stigma. To overcome those limitations, interventions using various digital technologies (e.g. apps, text messaging, video chat, and artificial intelligence) were developed and explored. In previous studies, digital-based interventions delivered via websites, text messages, and emails aimed at improving depression were found to be effective in reducing depressive symptoms in non-clinical populations.<sup>6</sup> The same tendency appears in MBI. A meta-analysis of the effectiveness of digital-based MBI, including commercial mindfulness training applications, found that digital-based MBI can promote mindfulness.<sup>7</sup> Previous studies have also reported that digital-based MBI can be of great help in terms of emotional regulation and mental health. Mental health applications based on mindfulness training showed effects in reducing negative emotions and increasing well-being and emotional regulation for stress, anxiety, and depression.<sup>8</sup> In addition to academically developed applications, various commercial mindfulness apps have also proved their effectiveness. For example, Headspace, a mindfulness application developed in the United Kingdom, has been shown to reduce stress and enhance emotional regulation.<sup>9</sup> Calm, another meditation application developed in the United States, also appeared to be effective for psychologi-

cal stress.<sup>10</sup> A previous study also reported that attention and working memory improved after using a meditation-based app for 6 weeks.<sup>11</sup>

Previous studies, including fMRI research, have suggested that changes in the activity of brain regions responsible for emotion and cognition underlie the positive effects of MBI on mental health. Mindfulness meditation has been found to increase the activity of the insula and enhance awareness of one's emotions and physical sensations.<sup>12</sup> On the other hand, it has been reported that mindfulness meditation may contribute to increasing resilience by reducing the reactivity of the amygdala to stressful stimuli.<sup>13</sup> Neuroimaging studies have also been conducted on whether mindfulness meditation can induce changes in the activation patterns of major brain functional networks during rest.<sup>14</sup> Previous studies have suggested that changes in functional connectivity (FC) centered on the insular cortex occur after mindfulness meditation, and this has been associated with improvements in attentional control and interoceptive awareness.<sup>15</sup> Previous studies have also suggested that mindfulness meditation can reduce the tendency to mind wander and strengthen a non-judgmental attitude by alleviating hyperactivation of the default mode network (DMN).<sup>16</sup> These results commonly suggest that the positive effects of mindfulness meditation on mental health are accompanied by changes in brain activation patterns. However, what must be taken into consideration when interpreting prior evidence is that the context in which mindfulness meditation is practiced can vary greatly, and elements of this context can influence differences in results. Additionally, no clear conclusion has yet been drawn about how often and for how long meditation should be practiced to induce changes in brain activation patterns. Previous studies on mindfulness have suggested that the pattern of brain response to external stimuli and the FC between major brain regions appear different depending on whether the person is a beginner or an expert in meditation training.<sup>13</sup> Additionally, the impact of mobile-based interventions such as mindfulness meditation through mobile apps on functional brain changes has not been sufficiently investigated.

This study aimed to explore whether the MBI application could affect users' attention and emotion regulation abilities. We also sought to explore neurobiological features underlying these clinical changes through a fMRI study. Before and after participants enrolled in the 8-week MBI program delivered through the mobile application, we measured levels of mindfulness, psychological features, and emotion regulation ability through self-report. We also compared the attentional control under emotional interference through a task fMRI, using an attention network test (ANT) with emotional face stimuli. We performed not only task fMRI but also resting-state fMRI and explored functional brain changes before and after MBI through seed-based FC analysis. Based on previous neuroimaging studies on mindfulness, we set subregions of the insular cortex and major components of the DMN as seed regions. Afterwards, we

explored the correlation between psychometric variables and FC findings that changed after mobile-based MBI. Through this, we sought to identify the neural changes underlying the improvement in emotion regulation or attention control caused by mobile-based MBI.

## MATERIALS AND METHODS

### Participants

In this study, beginners in mindfulness meditation among adults older than 19 years were recruited through the online bulletin board. Previous experience with mindfulness meditation was assessed through two questions: “Do you consider yourself a beginner in mindfulness meditation?” and “Have you ever used mindfulness-based therapy, meditation practice, meditation-related mobile apps, or yoga regularly or consistently?” Only participants who agreed with the first question and disagreed with the second question were enrolled in the study. Exclusion criteria other than significant prior meditation experience were as follows: 1) being left-handed; 2) wearing braces or having claustrophobia; 3) having being diagnosed with or received medication for major psychiatric disorders such as major depressive disorder, bipolar disorder, or schizophrenia in the past year; and 4) a full-scale intelligence quotient (FSIQ) score lower than 85. The subjects’ FSIQ was assessed using the Korean Wechsler Adult Intelligence Scale-IV. Twenty-four subjects (7 men, 17 women, mean age  $35.0 \pm 7.9$ ) were enrolled in this study. This study received approval from the Institutional Review Board at Yongin Severance Hospital (9-2022-0188). Participants provided written informed consent after being fully informed about the study.

### Intervention

In this study, the Mabo app (MABO Inc., Seoul, Korea)—a mindfulness-based application developed in Korea—was used for research. The Mabo app was launched in 2016 and aims to enable the general population to practice mindfulness meditation daily to achieve a healthier and happier life. Currently, the Mabo app is one of the most popular mindfulness-meditation mobile apps in Korea, with over 850000 cumulative downloads. It boasts over 450000 cumulative subscribers and offers a wide range of mindfulness-related content, including over 910 meditation audio tracks. The Mabo app provides a variety of meditation programs via a mobile platform to enhance usability for beginners in meditation. Users can find the meditations that suit them according to their targets (e.g., anxiety, depression, loneliness, or insomnia) and conditions (e.g., at work, coming home, when walking, or during a panic attack). A study of college students found that Mabo users reported reduced depression, anxiety, and stress, as well as increased positive emotions and life satisfaction compared to controls.<sup>17</sup>

In this study, participants were provided with a voucher for

the use of the Mabo app and were then encouraged to practice mindfulness meditation independently according to the program that the Mabo app suggested. The program has a duration of 8 weeks and consists of listening to mindfulness-related content every day without a face-to-face session. Participants were asked to perform one main meditation and one supplementary meditation each day that matched the theme of the week. The mindfulness contents included various formal and informal meditations, including breathing meditation, sound meditation, body scan, walking meditation, and loving-kindness meditation. Specific week-by-week topics, goals, and meditation arrangements are presented in Table 1. The specific daily meditation arrangements and meditation practice times are presented in Supplementary Table 1 (only online). The length of each audio content ranged from 2 to 41 minutes, and the total length of content per day ranged from 10 to 73 minutes. The total length of the meditation session for the 8-week program was 1329 minutes. This corresponded to, on average,  $23.7 \pm 7.6$  minutes of meditation time per day.

After each meditation audio content was played, a pop-up window appeared in which the subject could write a comment about the meditation. Therefore, the presence or absence of a comment indicated whether the meditation audio content had been played. Subjects were also instructed to send their daily comments to the research assistant. App usage compliance was calculated as the percentage of meditation audio contents played out of a total of 112. Based on previous research showing that at least 15 minutes of meditation practice can yield significant benefits,<sup>18,19</sup> we included in our study analysis only subjects who listened to meditation audio content for more than 15 minutes per day on average in our analysis. This corresponds to a compliance rate of over 63.2% for the current MBI program.

### Clinical measurements

Self-report questionnaires to assess psychological variables were administered equally before and after MBI. First, to explore the level of mindfulness, the Five Facet Mindfulness Questionnaire-Short Form (FFMQ-SF)<sup>20</sup> and the Mindful Attention Awareness Scale (MAAS)<sup>21</sup> were administered. The MAAS evaluates the level of mindful awareness, and the FFMQ evaluates the following subfactors of mindfulness-related traits: observing, describing, acting with awareness, non-judging, and non-reactivity. Subsequently, to measure negative emotions and psychological stress, the following scales were completed: the Beck Anxiety Inventory (BAI), Beck Depression Inventory (BDI), and Perceived Stress Scale (PSS). Subjects were also administered the Barratt Impulsiveness Scale (BIS) to evaluate impulsivity and the Pittsburgh Sleep Quality Index (PSQI) to evaluate sleep quality. In addition, the Difficulties in Emotion Regulation Scale (DERS)<sup>22</sup> and the Cognitive Emotion Regulation Questionnaire (CERQ)<sup>23</sup> were administered to evaluate the subjects’ emotion regulation ability. The DERS consists of the following

**Table 1.** Weekly Themes, Goals, and Mindfulness Meditation Structure of the Mindfulness-Based Intervention Program

Week	Themes and goals	Main meditation	Supplementary meditation	Time (minutes)
1	Mindfulness basics training: learn the principles of mindfulness meditation	<ul style="list-style-type: none"> <li>• Feeling the sensation of breathing</li> <li>• Bring attention to the here and now</li> <li>• Becoming aware of thoughts and emotions</li> <li>• Breath-counting meditation</li> </ul>	Breathing meditation	105
2	Focused attention meditation: bringing attention to the present in everyday life	<ul style="list-style-type: none"> <li>• Training to bring attention to the present moment</li> <li>• Focusing on sounds</li> <li>• Focusing on repeated words</li> <li>• Being aware of thoughts that arise</li> <li>• Mindful eating</li> </ul>	Breathing meditation	134
3	Focusing on body sensations	<ul style="list-style-type: none"> <li>• Meditation for waking and sleeping</li> <li>• Body scan</li> <li>• Body relaxation meditation</li> <li>• Walking meditation</li> </ul>	Awareness meditation	192
4	Open monitoring meditation: becoming aware of thoughts that arise	<ul style="list-style-type: none"> <li>• Naming emotions that come to mind</li> <li>• Meditation to observe all passing thoughts</li> <li>• Cloud meditation: gazing at the sky</li> <li>• Tree of thoughts meditation</li> </ul>	Breath-focused meditation	194
5	Deepening breathing meditation practice	<ul style="list-style-type: none"> <li>• Breath-focused meditation</li> <li>• Expanding awareness through breathing</li> <li>• Breath-counting meditation</li> <li>• Breathing while clearing the mind</li> </ul>	Becoming aware of the space between breaths	194
6	Becoming aware of reactions to external stimuli and managing negative emotions	<ul style="list-style-type: none"> <li>• Acknowledging inner courage and practicing self-compassion</li> <li>• Letting go of negative thoughts</li> <li>• Meditation on anxiety before important events</li> <li>• Healing meditation: Transforming suffering into joy</li> <li>• Observing-my-funeral meditation</li> </ul>	Becoming aware of the space between thoughts	186
7	Practicing meditation in everyday life	<ul style="list-style-type: none"> <li>• Meditation in spring sunshine</li> <li>• Meditation when leaving and returning home</li> <li>• Meditation to savor present happiness</li> <li>• Loving-kindness meditation</li> <li>• Meditation to find meaning in life</li> </ul>	Acceptance meditation	201
8	Gratitude meditation and creating a positive mindset	<ul style="list-style-type: none"> <li>• Loving-kindness meditation</li> <li>• Gratitude meditation</li> <li>• Self-care meditation: finding a chair where the mind can rest</li> <li>• Awakening inner goodness</li> <li>• Meditation to wish oneself happiness, anytime and anywhere</li> </ul>	Breathing meditation	123

subscales: impulse control difficulties, lack of emotional awareness, nonacceptance of emotional responses, lack of emotional clarity, limited access to emotion regulation strategies, and difficulty engaging in goal-directed behavior. The CERQ consists of the following subscales: acceptance, refocus on planning, putting into perspective, positive refocusing, positive reappraisal, self-blame, other-blame, rumination, and catastrophizing.

### MRI data acquisition

Subjects underwent the same MRI data acquisition protocol before and after MBI. MRI data acquisition was performed in the following order: T1-weighted structural MRI, T2-weighted resting-state fMRI, and T2-weighted task fMRI. MRI data were acquired using a 3T Siemens MAGNETOM Vida MRI scanner (Siemens Healthcare, Erlangen, Germany) equipped with a

64-channel head coil. The T2-weighted gradient echo-planar pulse sequence was as follows: echo time (TE)=30 ms, repetition time (TR)=2000 ms, flip angle 90°, field of view 240 mm, matrix 64×64, slice thickness 4 mm. The T1-weighted spoiled gradient echo sequence was as follows: TE=2.47 ms, TR=1900 ms, flip angle 9°, field of view 250 mm, matrix 256×256, slice thickness 1 mm. Task fMRI data were acquired while the subject was performing the ANT. Resting-state fMRI data were recorded for 6 minutes and 20 seconds.

### Task fMRI analysis

Subjects underwent the same task fMRI procedure before and after MBI. In the current task fMRI, we used ANT to assess attentional ability. ANT is an attention measurement task developed by Fan, et al.<sup>24</sup> by combining the spatial cueing paradigm

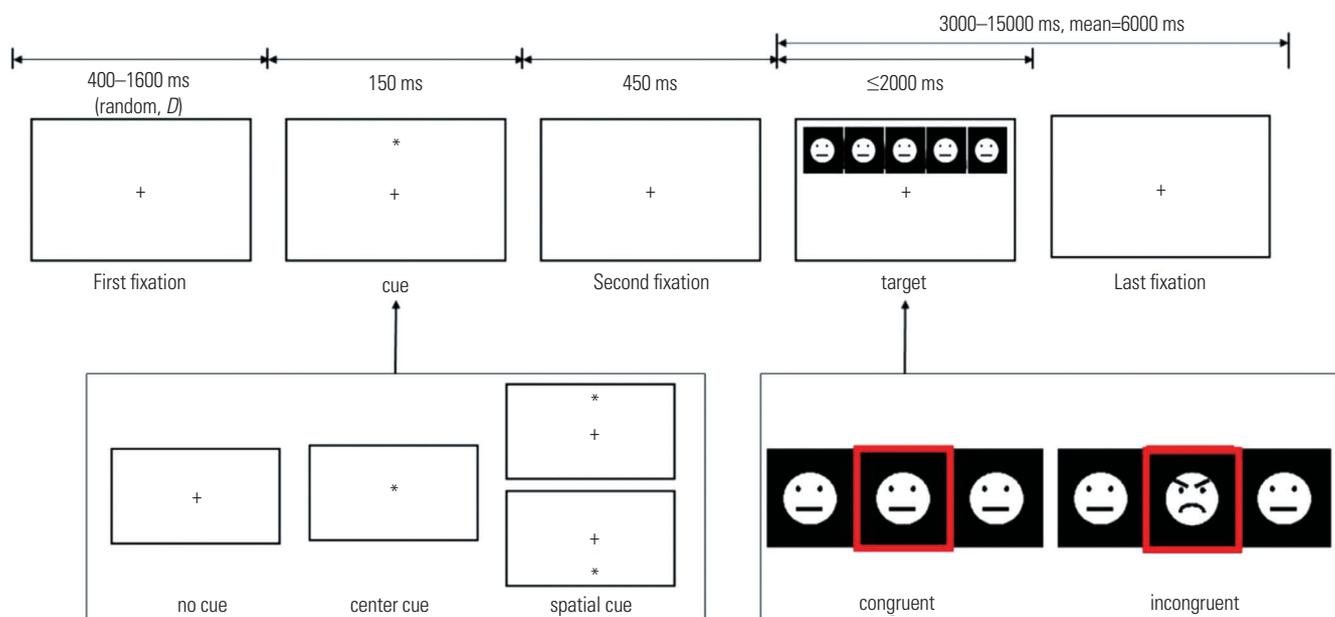
and the flanker test. We modified the fMRI version of ANT developed by Fan, et al.<sup>25</sup> to measure brain activity related to the attention network. As emotional interference stimuli, we used pictures of emotional faces instead of arrows in the original ANT. Two types of emotional face photos were used: angry and neutral faces.<sup>26</sup> Based on previous findings that mindfulness meditation enhances anger regulation and is associated with neural processing of angry faces,<sup>27,28</sup> the modified version of ANT used in this study employed photographs of angry faces as emotional interference stimuli. There were two blocks, each with three runs with 36 test trials. Each run was 236160 ms, and each block was 721600 ms including buffer trials. The total time of ANT in this study was 24 minutes and 3.2 seconds. The sequence and duration of cues and targets were presented in Fig. 1. The specific design for ANT used in this study is presented in the Supplementary Material (only online).

The accuracy and RT of subjects' responses were recorded for total trials, angry facial trials, and neutral facial trials, respectively. Additionally, alerting, orienting, and executive function were indexed for attention ability using RT values. fMRI data were acquired during ANT to measure brain activity for ANT performance. For task fMRI analysis, a two-way analysis of variance (ANOVA) was conducted for brain voxels with the time (pre- and post-MBI) as the between-group factor and the emotion (angry and neutral facial trials) as the within-group factor. The imaging thresholds were set to a combination of voxel-level thresholds ( $p < 0.001$ ) and cluster extent threshold false discovery rate correction ( $p < 0.05$ ). A detailed description of preprocessing and analysis of task fMRI data is presented in the Supplementary Material (only online).

### Resting-state fMRI FC analysis

The CONN-fMRI Functional Connectivity toolbox, version 19.c (Cognitive and Affective Neuroscience Laboratory, Massachusetts Institute of Technology, Cambridge, MA, USA) was used to perform resting-state FC analysis. The default CONN preprocessing pipeline was applied. The denoising process to reduce noise caused by muscle movement and breathing included the following steps: temporal de-spiking, regressing out confounders (including rigid body realignment parameters), anatomical component-based noise correction (aCompCor), linear detrending to remove linear signal drift, band-pass filtering with a range of frequencies of interest (0.008–0.09 Hz), and outlier detection and scrubbing. Outlier detection and scrubbing were performed using the Artifact Detection Tools built into the CONN-fMRI toolbox. Frames were classified as outliers if the signal intensity was more than 5 standard deviations from the mean or if the displacement relative to the previous volume was greater than 0.9 mm. In this study, it was confirmed that for all subjects, less than 15% of the total frames were detected as outliers and removed during scrubbing. Functional images were aligned through a least-squares minimization and a six-parameter rigid body spatial transformation. Afterwards, unwarping, slice-timing correction and segmentation were conducted. Functional images were spatially normalized in parallel through non-linear transformations to the montreal neurological institute (MNI) coordinate system. Data were then re-sampled to a 2-mm isotropic resolution and smoothed using an 8-mm full-width at half-maximum (FWHM) Gaussian kernel.

In this study, resting-state fMRI data were analyzed through a seed-to-voxel analysis. Seed-to-voxel FC maps for each subject were created through the CONN-fMRI toolbox. All seeds were spheres with a radius of 6 mm and were created using the



**Fig. 1.** Diagram illustrating the protocol of the attention network test in this study. In the diagram, face photo stimuli were replaced with emotional face icons. The photo stimuli actually used in this study were selected from the Korean Facial Expressions of Emotion (KOFEE) developed by Park JY, et al.<sup>26</sup>

MarsBar toolbox program in SPM (<https://marsbar.sourceforge.net>). Based on a previous study,<sup>29</sup> the seeds of the insula were set as follows: right dorsal anterior insula (35, 7, 3), left dorsal anterior insula (-38, 6, 2), right ventral anterior insula (32, 10, -6), left ventral anterior insula (-33, 13, -7), right posterior insula (35, -11, 6) and left posterior insula (-38, -6, 5). Based on a previous study,<sup>30</sup> the seeds of the DMN-related regions were set as follows: posterior cingulate cortex (-2, -36, 37), right ventromedial prefrontal cortex (VMPFC) (1, 54, 21), and left VMPFC (-3, 39, -2). Correlation coefficients were estimated and converted to z-values using Fisher's r-to-z transformation for the calculation of FC strengths. FC strengths were then compared between pre- and post-MBI using an ANOVA on each voxel. The imaging thresholds were set to a combination of voxel-level thresholds ( $p < 0.001$ ) and cluster extent threshold false discovery rate correction ( $p < 0.05$ ).

### Statistical analysis

We used SPSS version 25.0 (IBM Corp., Armonk, NY, USA) for statistical analyses. The threshold of significance used for statistical analysis was set to  $p < 0.05$  (two-tailed). Descriptive statistics were employed to determine the demographic characteristics of the participants. A paired t-test was used to compare the changes in self-reported psychological measurements. When comparing the subscales of FFMQ-SF, DERS, and CERQ between pre- and post-MBI, a Bonferroni correction was applied for multiple comparisons. For ANT, changes in RT and accuracy between pre- and post-MBI were compared using a paired t-test. To assess attentional ability, a 2 (pre- and post-MBI) × 2 (angry and neutral facial trials) repeated-measures ANOVA was performed to identify differences in alerting, orienting, and executive functions according to time and emotion. For brain-behavior relationships, we explored the relationship between 1) scales that showed significant differences between pre- and post-MBI and 2) FC strengths for regions identified as significant clusters in the FC analysis. The Pearson correlation analysis was performed between scale scores and FC strengths.

## RESULTS

### Demographic and psychometric characteristics of participants

Three participants dropped out of the study due to poor app usage compliance. The following factors were investigated as hindrances that lowered app usage compliance: 1) time constraints: "I had a hard time finding time to meditate during the day, and when I did meditate before bed, I found it hard to concentrate because of drowsiness."; 2) failure to generate sustained interest in the app: "Since meditation audio content is provided in a uniform manner, I lost interest because I couldn't collect and listen only to the content I wanted."; and 3) distur-

bances due to one-way meditation practice via the app: "The voice of the meditation expert guiding the meditation actually distracted me from focusing on my inner self."

Finally, the subjects included in this study analysis comprised five men and 16 women, and their average age was  $34.4 \pm 8.1$  years. The average app usage compliance among subjects included in the analysis was  $92.7 \pm 12.4\%$ . The average FSIQ was  $111.7 \pm 8.6$ . None of the participants smoked; however, except for three individuals, all reported to be social drinkers. In terms of religion, the participants answered that they had a religion in the following order: no religion (66.7%), Catholicism (19.0%), Protestantism (9.5%), and Buddhism (4.8%).

We compared the level of mindfulness and psychometric properties between pre- and post-MBI by the paired t-test (Table 2). As a result, the total scores of participants' FFMQ-SF and MAAS were higher at post-MBI than at pre-MBI (FFMQ-SF:  $t = 2.802$ ,  $p = 0.011$ ; MAAS:  $t = 3.096$ ,  $p = 0.006$ ). For subscales of the FFMQ-SF, statistical significance was set at  $< 0.05/5 = 0.01$ . There were significant differences between pre- and post-MBI in subscales, including describing ( $t = 2.911$ ,  $p = 0.009$ ) and acting with awareness ( $t = 3.328$ ,  $p = 0.003$ ). In terms of other psychological factors, there were no changes between pre- and post-MBI in BAI, PSS, BIS, and PSQI, except for BDI. The post-MBI BDI score was significantly lower than the pre-MBI score ( $t = -2.458$ ,  $p = 0.023$ ).

In Table 3, the results of paired t-tests of emotional regulation-related variables are presented. The total score of the DERS showed a significant decrease after MBI compared with pre-MBI ( $t = -3.063$ ,  $p = 0.006$ ). For the DERS subscales, statistical significance was set at  $< 0.05/6 = 0.0083$ . Subjects showed significantly lower scores in lack of emotional awareness ( $t = -3.065$ ,  $p = 0.006$ ) at post-MBI than at pre-MBI. For the CERQ subscales,

**Table 2.** Results of Paired t-test of Psychological Variables (n=21)

	Pre-MBI	Post-MBI	t	p	Cohen's d
FFMQ-SF	84.0±15.6	91.1±11.0	2.802	0.011	0.611
Observing	14.6±3.7	15.7±2.2	1.638	0.117	0.357
Describing	17.6±3.6	19.3±3.2	2.911	0.009	0.635
Acting with awareness	18.0±3.4	20.0±2.8	3.328	0.003	0.726
Non-judging	17.7±4.3	18.4±4.4	0.830	0.416	0.181
Non-reactivity	16.1±4.1	17.7±2.5	1.782	0.090	0.389
MAAS	67.7±9.1	72.6±8.2	3.096	0.006	0.676
BDI	10.1±7.3	6.8±5.8	-2.458	0.023	-0.536
BAI	6.2±5.9	4.1±5.4	-1.802	0.087	-0.393
PSS	15.5±6.0	14.1±6.3	-1.245	0.228	-0.272
BIS	63.0±9.5	61.5±8.5	-1.084	0.291	-0.237
PSQI	5.9±2.9	5.1±3.3	-1.078	0.294	-0.235

MBI, mindfulness-based intervention; FFMQ-SF, Five Facet Mindfulness Questionnaire-Short Form; MAAS, Mindful Attention Awareness Scale; BDI, Beck Depression Inventory; BAI, Beck Anxiety Inventory; BIS, Barratt Impulsiveness Scale; PSS, Perceived Stress Scale; PSQI, Pittsburgh Sleep Quality Index. Values are presented as mean ± standard deviation. Statistics were analyzed using a paired t-test.

**Table 3.** Results of Paired t-test of Emotion Regulation (n=21)

	Pre-MBI	Post-MBI	t	p	Cohen's d
DERS	82.1±21.7	69.6±17.1	-3.063	0.006	-0.668
Impulse control difficulties	9.6±4.2	8.6±3.3	-1.307	0.206	-0.285
Lack of emotional awareness	16.9±6.1	13.4±4.0	-3.065	0.006	-0.669
Nonacceptance of emotional responses	14.7±5.9	12.1±4.4	-2.257	0.035	-0.492
Lack of emotional clarity	5.9±2.2	4.9±1.9	-2.038	0.055	-0.445
Limited access to emotion regulation strategies	10.1±4.0	8.2±2.7	-2.772	0.012	-0.605
Difficulty engaging in goal-directed behavior	9.0±3.1	8.0±2.6	-1.578	0.130	-0.344
CERQ					
Acceptance	11.8±2.1	13.3±1.9	4.146	<0.001	0.904
Putting into perspective	12.5±3.3	14.1±2.6	3.109	0.006	0.679
Positive refocusing	9.5±3.3	11.4±4.3	2.622	0.016	0.572
Refocus on planning	15.5±3.5	16.6±2.7	2.317	0.031	0.506
Positive reappraisal	15.5±3.3	17.1±2.5	2.943	0.008	0.642
Self-blame	12.7±2.5	12.5±2.8	-0.521	0.608	0.114
Catastrophizing	7.8±3.3	7.1±2.3	-0.881	0.389	0.192
Other-blame	8.6±3.1	8.1±3.1	-0.885	0.387	0.193
Rumination	13.1±3.1	13.5±2.3	0.632	0.535	0.138

MBI, mindfulness-based intervention; DERS, Difficulties in Emotion Regulation Scale; CERQ, Cognitive Emotion Regulation Questionnaire. Values are presented as mean±standard deviation. Statistics were analyzed using a paired t-test.

**Table 4.** Results of Paired t-test of Reaction Time and Accuracy in Attention Network Test (n=18)

	Pre-MBI	Post-MBI	t	p	Cohen's d
Reaction time (ms)					
Total trials	744.6±77.9	745.7±53.2	0.067	0.947	0.022
Trials with angry facial stimuli	743.5±88.1	741.8±50.8	-0.093	0.927	-0.079
Trials with neutral facial stimuli	745.5±72.8	751.4±62.7	0.337	0.740	0.016
Accuracy (%)					
Total trials	98.4±1.2	98.5±2.1	0.201	0.843	0.047
Trials with angry facial stimuli	98.6±1.3	97.7±2.7	-1.501	0.152	-0.354
Trials with neutral facial stimuli	98.2±1.8	99.2±1.8	2.881	0.010	0.679

MBI, mindfulness-based intervention. Values are presented as mean±standard deviation. Statistics were analyzed using a paired t-test.

statistical significance was set at  $<0.05/9=0.0056$ . Subjects appeared to use more positive emotion regulation strategies, such as acceptance ( $t=4.146, p<0.001$ ), at post-MBI.

**Task fMRI results**

In this study, we excluded three participants from the ANT analysis. Two of them showed an accuracy of less than 80%, raising concerns about the validity of their performance, while the third participant's performance was interrupted due to a transient MRI machine error. Regarding the subjects' ANT performance, the results of the paired t-test on the RT and accuracy of ANT before and after MBI are presented in Table 4. Overall, there was no difference in RT and accuracy between pre- and post-MBI. However, the accuracy of trials with neutral facial stimuli was higher at post-MBI than at pre-MBI ( $t=2.881, p=0.010$ ). For the attention ability scores of the ANT, the results of a 2 (pre- and post-MBI)×2 (angry and neutral facial trials) repeated-measures ANOVA are presented in Supplementary Table 2 (only online). There was no significant time×emotion interaction effect for alerting, orienting, and executive function.

There was no significant time×emotion interaction effect for alerting, orienting, and executive function.

In the task-based fMRI analyses, there was no brain cluster that showed a significant time×emotion interaction effect. The interaction effects for the time×emotion condition were significant in the left insula (peak MNI coordinates: -42, 16, 4; cluster size  $k=66$ ; peak T value=3.42), but this significance disappeared when corrected for multiple comparisons. There was also no brain cluster that showed a significant main effect of time (pre- and post-MBI). The main effects of emotion (angry facial trials and neutral facial trials) were significant in the right postcentral gyrus (peak MNI coordinates: 14, -40, 74; cluster size  $k=64$ ; peak T value=5.15). Post hoc analyses revealed that the angry facial trials had weaker BOLD activity in the postcentral gyrus than the neutral facial trials.

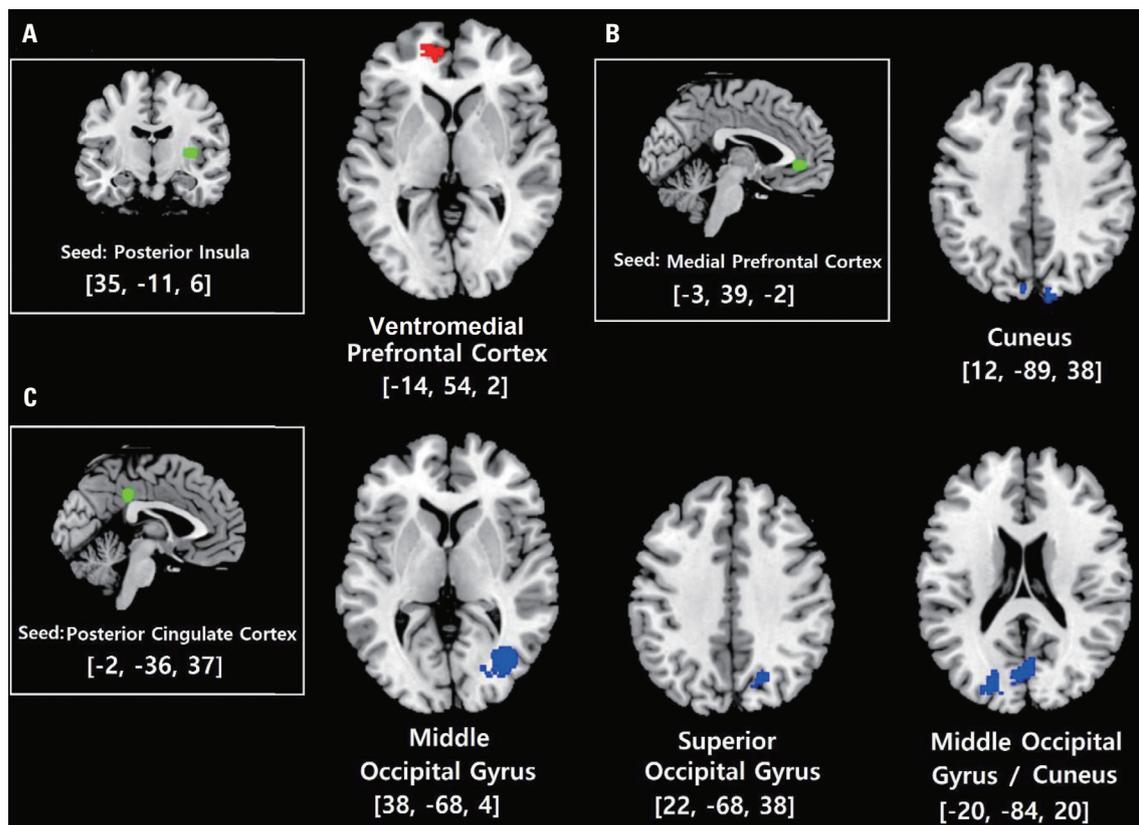
### Resting state FC analysis results

The comparative analysis results of resting state FC before and after MBI are presented in Fig. 2 and Table 5. Seed-to-voxel analysis using the insular seeds suggested that FC between the right posterior insula and the left VMPFC was stronger after MBI compared to before MBI. Seed-based FC analyses that set DMN-related regions as seeds revealed that FC between the left VMPFC and the right cuneus was weaker after MBI compared to before MBI. Also, FC of the posterior cingulate cortex with the cuneus, the bilateral middle occipital gyrus, and the right superior occipital gyrus was weakened after MBI compared to before MBI. In other seed-based FC analyses, no significant brain clusters were identified.

The results of the correlation analysis between the identified FC strengths and psychometric variables are presented in Table 6. The difference before and after MBI in the left VMPFC-right cuneus FC strengths showed a significant positive correlation with the difference before and after MBI in the lack of emotional awareness (a subscale of the DERS). Other correlation analyses showed no significant findings.

### DISCUSSION

In this study, we explored whether the level of mindfulness, attention abilities, emotional regulation, and neurobiological features changed after the mobile-based MBI. Participants in this study significantly increased their FFMQ-SF and MAAS scores, which reflect the traits of mindfulness, after 8 weeks of mobile-based MBI. These findings are consistent with previous evidence suggesting that the usage of mobile-based MBI is effective in improving mindfulness.<sup>10</sup> Brown and Ryan,<sup>21</sup> who developed MAAS, defined mindfulness as “an enhanced attention to and awareness of current experience or present reality” and excluded other mindfulness constructs such as attitudes, including patience and acceptance. On the other hand, the research of Baer, et al.,<sup>31</sup> which developed the FFMQ, suggested that other constructs of mindfulness are also important. They identified the five factors of mindfulness (observing, describing, acting with awareness, non-judgmental, non-reactivity) through analysis of existing mindfulness measurements, and developed the FFMQ based on those factors. In this study, among the FFMQ-SF subscales, acting with awareness and describing showed a significant increase, but no changes were



**Fig. 2.** Seed-based resting-state functional magnetic resonance imaging FC analysis. The statistical inference was set as an uncorrected  $p$ -value height threshold of 0.001 in conjunction with an extent threshold correction using the false discovery rate of  $p < 0.05$ . (A) FC between the left posterior insula and the left VMPFC was stronger after MBI compared to before MBI. (B) FC between the left VMPFC and the right cuneus was weaker after MBI compared to before MBI. (C) FC between the posterior cingulate cortex and occipital regions was weaker after MBI compared to before MBI. FC, functional connectivity; MBI, mindfulness-based intervention; VMPFC, ventromedial prefrontal cortex.

**Table 5.** Whole-Brain Seed-Based FC Analysis Results (n=21)

Seed	Region	Side	$k_E$	$T_{max}$	x	y	z	Comparison
Right posterior insula	Ventromedial prefrontal cortex	Left	407	4.67	-14	54	2	Pre-MBI<Post-MBI
Left ventromedial prefrontal cortex	Cuneus	Right	2341	5.71	12	-89	38	Pre-MBI>Post-MBI
Posterior cingulate cortex	Middle occipital gyrus	Right	558	5.24	38	-68	4	Pre-MBI>Post-MBI
Posterior cingulate cortex	Superior occipital gyrus	Right	115	4.83	22	-68	38	Pre-MBI>Post-MBI
Posterior cingulate cortex	Middle occipital gyrus/cuneus	Left	634	4.38	-20	-84	20	Pre-MBI>Post-MBI

FC, functional connectivity; MBI, mindfulness-based intervention;  $k_E$ , extent threshold (i.e., number of significant voxels). Brain regions showing significant differences in FC before and after MBI.

**Table 6.** Correlation Matrix between FC Strengths and Psychometric Scale Scores in All Subjects (n=21)

Variables	PI-VMPFC FC		VMPFC-cuneus FC		PCC-MOG (right) FC		PCC-SOG FC		PCC-MOG (left) FC	
	R	p	r	p	r	p	r	p	r	p
BDI	0.361	0.108	-0.048	0.838	0.197	0.391	-0.032	0.889	-0.013	0.955
FFMQ-SF – Describing	-0.222	0.334	-0.294	0.196	0.146	0.529	-0.148	0.523	-0.178	0.439
FFMQ-SF – Acting with awareness	-0.293	0.197	-0.325	0.151	0.186	0.420	-0.200	0.384	-0.251	0.273
MAAS	-0.282	0.215	-0.260	0.256	-0.051	0.826	-0.247	0.280	-0.069	0.766
DERS – Lack of emotional awareness	0.246	0.283	0.466	0.033	0.311	0.170	0.345	0.125	-0.107	0.645
CERQ – Acceptance	0.016	0.945	0.271	0.235	-0.279	0.221	0.018	0.939	0.335	0.138

FC, functional connectivity; PI, posterior insula; VMPFC, ventromedial prefrontal cortex; PCC, posterior cingulate cortex; MOG, middle occipital gyrus; SOG, superior occipital gyrus; BDI, Beck Depression Inventory; FFMQ-SF, Five Facet Mindfulness Questionnaire-Short Form; MAAS, Mindful Attention Awareness Scale; DERS, Difficulties in Emotion Regulation Scale; CERQ, Cognitive Emotion Regulation Questionnaire.

For each variable, the difference before and after meditation training (post-training minus pre-training) was calculated and used for the correlation analysis. Statistics were calculated using Pearson’s correlation test.

observed in other subscales. When considered together with the significant increase in the MAAS, these results suggest that the intervention in this study may be specifically related to the awareness aspect of mindfulness traits. These results partially conflict with previous studies reporting that mobile-based MBI has shown significant improvement not only in awareness but also in all facets of the FFMQ. We suggest that the context of providing mindfulness meditation in the mobile MBI program applied in this study is likely to be the reason why it works more effectively in improving the awareness facet of mindfulness. In this study’s mobile-based MBI program, more than half of the total was devoted to exercises that promote awareness of body sensations, thoughts, and emotions (e.g., breathing meditation or open monitoring meditation). In future research on the mobile-based MBI, more in-depth design studies are needed to determine which type of meditation, over what period of time, and with what program composition can effectively promote the improvement of individual facets of mindfulness.

After the subjects of this study received 8 weeks of mobile-based MBI, depressive symptoms were significantly reduced, and emotional regulation was also improved. Previous studies have suggested that improving the ability to differentiate and recognize emotions plays an important role in the high correlation between mindfulness and emotional regulation.<sup>32</sup> Among the facets of mindfulness, the subjects in this study showed particularly significant improvement in describing and awareness after mobile-based MBI. We suggest that enhancement of these facets would be related to the subjects’ ability to differentiate and recognize emotions. The subjects in this study showed a

more noticeable increase in adaptive emotional regulation strategies than a decrease in maladaptive emotional regulation strategies. This is consistent with prior evidence showing that the improvement of adaptive top-down emotional regulation appears more prominently in novice mindfulness practitioners.<sup>33</sup> Previous studies have suggested that increasing the level of emotional awareness can help people respond more acceptably to negative emotions.<sup>34</sup> Previous studies have also indicated that applying successful emotional regulation strategies can help control depressive symptoms.<sup>35</sup> Taken together, our current results are consistent with previous studies that suggested the effectiveness of MBI on depression and emotional regulation.<sup>36</sup>

In the ANT indices calculated based on RT, the interaction effect between time (pre- and post-MBI) and emotion (angry and neutral facial trials) was not significant in alerting, orienting, and executive function. The main effect of time (pre- and post-MBI) for the ANT indices was also not significant. However, in terms of ANT accuracy, the accuracy of the neutral-face trials increased after using the mobile-based MBI program. Although accuracy is often overlooked in studies of ANT, accuracy has also been known to partially reflect the efficiency of attentional control in ANT.<sup>37</sup> Therefore, our findings partially correspond to previous studies showing that mindfulness meditation improves attention ability.<sup>38</sup>

Previous studies on mindfulness meditation have reported meditation-related changes in brain activity in brain regions such as the prefrontal cortex, insular cortex, and anterior cingulate cortex, which are associated with attention and emotion regulation.<sup>39,40</sup> However, the effect of time by training was not

significant for brain activity in the current task fMRI study. Changes in brain activity in response to emotional interference were also not identified in the task fMRI of this study. Changes in insular activity were identified as uncorrected findings, which were consistent with the hypothesis of this study that the insula plays an important role in emotion-cognition integration.<sup>41</sup> However, this finding lost statistical significance after correction for multiple comparisons. We speculate that future task fMRI studies with larger numbers of subjects are warranted to increase statistical power. Furthermore, in the present study, we used a newly created behavioral task by modifying the ANT using emotional face stimuli. Therefore, sufficient verification was not conducted as to whether it appropriately induced the interference effect of emotional stimuli on attentional control. The original version of ANT used simple, clearly directional arrow figures, so the contrast between arrow stimuli with different directions was clear. However, the modified ANT used in this study utilized facial photo stimuli, and the contrast between facial photo stimuli with different emotions may have been insufficient. To investigate the effects of emotional interference on attentional control, it might have been more effective to present the emotional interference in a more implicit manner while assessing attentional control using the original ANT task. Another limitation of ANT used in this study is that only angry and neutral facial photographs were used as emotional stimuli, without using various types of emotions. Although the design of the ANT was simplified by reducing the types of emotional stimuli in order to elicit clear contrasts, this task design narrowed the range of emotional processes that could be explored in this study. For instance, previous studies have reported that mindfulness meditation can also affect fear extinction neurocircuitry and positive emotional responses such as happiness.<sup>42,43</sup> In addition, previous research has shown that neutral facial photographs are sometimes interpreted by subjects as having emotional meaning in psychological experimental settings.<sup>44</sup> Therefore, it is possible that the emotional contrast between neutral and angry photo stimuli was insufficient to derive a significant interaction between emotion and time in task fMRI analysis in this study.

This study observed several changes in resting-state FC analysis centered on insular subregions and DMN-related seeds after mobile-based MBI. First, subjects showed an increase in FC between the right posterior insula and the left VMPFC after MBI. The posterior insula has been linked to somatosensory processing and interoceptive awareness.<sup>45</sup> Mindfulness includes training in bodily sensations, and previous studies have reported an increase in FC centered on the posterior insula after mindfulness meditation.<sup>15</sup> Regarding the role of the VMPFC, prior evidence has suggested that it plays several roles related to cognitive control, including attentional modulation.<sup>46</sup> Therefore, we interpret the increase in FC between the posterior insula and the VMPFC observed in this study as suggesting that mindfulness meditation would be related to attentional mod-

ulation of interoception. Additionally, from the perspective of emotional processing, the VMPFC has been found to be involved in emotional regulation by encoding emotional value.<sup>47</sup> The posterior insula has been involved in mediating negative emotions such as fear by engaging in aversive state processing.<sup>48</sup> A previous study showed that MBI can modulate value signals by altering interoceptive input from the posterior insular cortex to the VMPFC.<sup>49</sup> Therefore, the increased FC between the posterior insula and the VMPFC in this study may be related to the enhanced ability to regulate negative emotions after MBI.

Another result of the FC analysis in this study is the decrease in FC between DMN-related seeds and occipital regions after MBI. The results of this study are consistent with previous studies on mindfulness showing that MBI attenuates FC of the DMN.<sup>50</sup> The occipital regions are known to be mainly involved in visual processing, and anticorrelation with the DMN has been identified in FC analysis.<sup>51</sup> Therefore, we interpret the FC results of this study as being associated with the restoration of the anticorrelation between the DMN and the visual network. In particular, the visual network including the occipital cortex is closely related to the formation of visual mental imagery.<sup>52</sup> Therefore, the weakening of the FC of the occipital cortex in this study can be interpreted in relation to the reduction of attentional distraction due to visual representation in meditators.<sup>53</sup> In addition, the decrease in FC between the VMPFC and the cuneus showed a significant correlation with the decrease in the "lack of emotional awareness" subscale of the DERS. Many previous studies have suggested that the activation pattern of the DMN and its interaction with other brain networks play an important role in the discrimination and awareness of emotions.<sup>54</sup> The results of this study suggest that FC changes of the DMN may play a role in the relationship between the effects of mindfulness and improved emotional awareness.

This study has several limitations. First, this study did not set up a control group and only compared before and after MBI in a single group. Therefore, the results of this study should be considered preliminary evidence of the effectiveness of mobile-based MBI. Setting up a control group, such as a wait-list control group or a group receiving a psychological intervention other than MBI, is necessary to clearly identify the effects of mobile-based MBI. Second, as discussed above, the ANT used in this study was limited in sufficiently elucidating the effects of emotional interference on attentional control. Unlike the original version of ANT, the modified version of ANT used in this study did not undergo a validation process prior to the fMRI study. In follow-up studies, it will be necessary to explore changes in brain activity associated with mindfulness meditation through more validated behavioral tasks. Third, due to the small number of subjects, deriving meaningful results from fMRI data was difficult. Previous studies performing power analyses on fMRI have reported that sample sizes should be close to 30 per group to increase statistical power and ensure reliability of results.<sup>55,56</sup> Although this study was a paired con-

trast test in a single group, the small sample size may have had a significant impact on the risk of false findings. In particular, in the case of task fMRI, differences in task performance may additionally affect the results of fMRI. The analysis of task fMRI in this study was performed on a smaller sample size ( $n=18$ ) than resting fMRI ( $n=21$ ) due to this problem. This small sample size may be closely related to the negative findings of task fMRI in this study. Fourth, a relatively large number of correlative analyses were performed compared to the small number of subjects. We were able to provide clinical interpretation of this study through correlative analyses, but were unable to apply corrections for multiple comparisons. As a result, there is a risk of false positives in the results of correlation analyses, so the interpretation of the brain-behavior relationship in this study should not be considered definitive. The results of the correlation analysis in this study need to be verified by applying a higher statistical threshold and targeting a larger number of subjects. Fifth, in this study, mindfulness meditation was applied only as a mobile application and no face-to-face training was conducted. Therefore, it was not possible to verify how intensively they actually practiced mindfulness meditation. Based on existing research on mindfulness meditation,<sup>18,19</sup> we assumed a time threshold for meaningful meditation practice and analyzed data only from subjects who exceeded this threshold. However, since this threshold was set based on face-to-face MBI, there were limitations in using it as an established standard in this study that implemented a mobile-based MBI. Because there is no established evidence of sufficient adherence criteria for mobile-based MBIs, further research is needed to define them. In addition, the overall compliance rate with app use in this study was high because subjects were asked to report to the researchers whether they used the app daily and were required to use the app as part of their participation in the clinical study. Therefore, future studies utilizing real-world data should also focus on identifying ways to increase compliance with mobile-based MBI. Sixth, in the 8-week MBI protocol of this study, the length of meditation practice time varied each day. This inconsistency in meditation practice time may act as a hindrance to the participants' continuous and stable pattern of meditation practice. Seventh, the proportion of women was much higher than that of men in this study. We did not artificially adjust the gender ratio in this study because of evidence reporting that gender distribution did not affect the outcome of mobile-based MBI.<sup>57</sup> However, on the other hand, there may be controversy about the influence of gender on mobile-based MBI, as there are existing studies that show that the effectiveness of MBI differs depending on gender.<sup>58,59</sup> Moreover, it has been established that gender may influence resting-state FC analysis.<sup>60</sup> Therefore, the lack of consideration of gender distribution may be a significant limitation in generalizing the results of the current study. Lastly, the study's investigation of prior experience with mindfulness meditation, consisting only of simple questions, may not have been sufficient. Given the differences in

brain activation patterns between beginners and experienced meditators, it is important to examine prior meditation experience in MBI-related fMRI studies.<sup>13</sup> Future research would benefit from an assessment tool that more structurally explores prior meditation experiences. There is also a need to identify broader prior experiences that may be related to mindfulness meditation and consider them as confounding factors in MBI studies.

Despite the limitations described above, this study provides several important implications regarding the impact that mobile-based MBI can have on the public's mental health. Subjects completed an 8-week mobile-based MBI incorporating a variety of mindfulness meditation practices, with relatively high compliance. After the mobile-based MBI, subjects reported improvements in mindfulness and emotion regulation. Although there have been many previous studies on the neurobiological mechanisms of mindfulness meditation, there has been a relative lack of brain imaging studies on the effects of mindfulness meditation when performed on mobile devices. In this study, several FC changes were observed in resting-state fMRI analysis after 8 weeks of mobile-based MBI. These include changes in brain regions associated with attention and emotions, such as the VMPFC and the insular cortex. In particular, the weakening of FC between the VMPFC and the cuneus was correlated with the enhancement of emotional awareness after MBI. Because this study explored changes within a single group without a control group, it was limited in establishing a causal relationship between the clinical and neurobiological findings of this study and the effects of mobile-based MBI. Our current study suggests that further studies are warranted to elucidate the clinical and neurobiological effects of mobile-based MBI.

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## AUTHOR CONTRIBUTIONS

**Conceptualization:** Jungeun You, Young-Chul Jung, and Deokjong Lee. **Data curation:** Minjung Kim and Goeun Seong. **Formal analysis:** Minjung Kim and Heeyeon Kim. **Funding acquisition:** Young-Chul Jung and Deokjong Lee. **Investigation:** Minjung Kim, Goeun Seong, and Deokjong Lee. **Methodology:** Jungeun You, Heeyeon Kim, and Imhong Jeon. **Project administration:** Young-Chul Jung and Deokjong Lee. **Resources:** Jungeun You, Heeyeon Kim, and Imhong Jeon. **Software:** Jungeun You. **Supervision:** Jungeun You and Young-Chul Jung. **Validation:** Young-Chul Jung and Deokjong Lee. **Visualization:** Minjung Kim and Deokjong Lee. **Writing—original draft:** Minjung Kim and Deokjong Lee. **Writing—review & editing:** Deokjong Lee. **Approval of**

final manuscript: all authors.

## ORCID iDs

Minjung Kim <https://orcid.org/0000-0002-6586-4374>  
 Jungeun You <https://orcid.org/0009-0002-4200-3122>  
 Goeun Seong <https://orcid.org/0000-0002-1853-2887>  
 Heeyeon Kim <https://orcid.org/0000-0003-0104-8041>  
 Imhong Jeon <https://orcid.org/0009-0004-3125-3139>  
 Young-Chul Jung <https://orcid.org/0000-0002-0578-2510>  
 Deokjong Lee <https://orcid.org/0000-0002-5425-4677>

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