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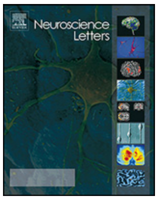

Increased default mode network connectivity associated with meditation

Joon Hwan Jang[a], Wi Hoon Jung[b], Do-Hyung Kang[a], Min Soo Byun[a],
Soo Jin Kwon[c], Chi-Hoon Choi[d], Jun Soo Kwon[a,b,c,e,*]

[a] *Department of Psychiatry, Seoul National University College of Medicine, Seoul, Republic of Korea*
[b] *Interdisciplinary Program in Brain Science, Seoul National University, Seoul, Republic of Korea*
[c] *Clinical Cognitive Neuroscience Center, Neuroscience Institute, SNU-MRC, Seoul, Republic of Korea*
[d] *Department of Diagnostic Radiology, National Medical Center, Seoul, Republic of Korea*
[e] *Department of Brain and Cognitive Sciences – World Class University Program, College of Natural Sciences, Seoul National University, Seoul, Republic of Korea*

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ABSTRACT

Areas associated with the default mode network (DMN) are substantially similar to those associated with meditation practice. However, no studies on DMN connectivity during resting states have been conducted on meditation practitioners. It was hypothesized that meditators would show heightened functional connectivity in areas of cortical midline activity. Thirty-five meditation practitioners and 33 healthy controls without meditation experience were included in this study. All subjects received 4.68-min resting state functional scanning runs. The posterior cingulate cortex and medial prefrontal cortex were chosen as seed regions for the DMN map. Meditation practitioners demonstrated greater functional connectivity within the DMN in the medial prefrontal cortex area ($x\,y\,z = 3\ 39\ -21$) than did controls. These results suggest that the long-term practice of meditation may be associated with functional changes in regions related to internalized attention even when meditation is not being practiced.

Meditation, which had been used as an approach to developing discipline, has been applied to various domains in recent years, including the medical management of stress and a broad spectrum of psychiatric disorders [16]. Most types of meditation include focusing attention on internal events and inhibiting interference from irrelevant external events. Previous studies have reported that meditators demonstrate better attentional functioning and lower levels of stress than do controls [22,39]. Increased cortical thickness and gray matter density, which suggests structural plasticity associated with meditation practice, has also been reported [24,40].

Recent studies have used functional magnetic resonance imaging (fMRI) to demonstrate differences in the brain activations of meditation practitioners [7,19]. Hölzel et al. [19] reported more activation in the anterior cingulate and medial prefrontal cortex (MPFC) of 15 experienced meditators than those of control subjects with no experience of meditation. Another study also found that long-term meditation practitioners showed more activation in the prefrontal cortex during meditation than did novice meditators [7]. However, these studies investigated brain activity using executive task paradigms in relatively small samples. No studies on changes in functional connectivity during resting state have been conducted with meditation practitioners.

Resting-state functional connectivity is a relatively novel fMRI approach that analyzes the temporal correlations of spontaneous low-frequency blood oxygen level-dependent (BOLD) signal fluctuations that are not attributable to specific inputs and outputs in different brain areas. It has been believed that this phenomenon represents neuronal activity intrinsically generated by the brain [13,15]. Among these networks of functional connectivity, the default mode network (DMN), which consistently includes the MPFC, anterior and posterior cingulate cortices, inferior parietal cortex, and lateral temporal cortex, has been associated with stimulus-independent thoughts [13,35]. These stimulation-independent thought-related neural activations, including the engagement in self-referential and reflective thoughts, have also been shown to reflect an automatic tendency that emerges in the absence of a strong requirement to respond to external stimuli [8,29]. Furthermore, areas associated with the DMN have considerable similarities with those associated with meditation practice, which show cortical midline activity, including in the MPFC and the posterior cingulate cortex (PCC) [17,19,26,35]. Among the cortical midline structures, the MPFC has been shown to support an array of self-related capacities, including memory for self-traits [23,28], traits of similar others [30], reflected self-knowledge [25], and aspirations for the future [20]. Thus, cortical midline processes may be characterized as the core of what is called the self that main-

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* Corresponding author at: Department of Psychiatry, Seoul National University College of Medicine, 101 Daehak-no, Chongno-gu, Seoul 110-744, Republic of Korea. Tel.: +82 2 2072 2972; fax: +82 2 747 9063.
E-mail addresses: kwonjs@snu.ac.kr, kwonjs@plaza.snu.ac.kr (J.S. Kwon).

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tains continuity of identity across time [11,31]. According to this prospective, it would be meaningful to investigate the DMN activation of meditators during resting states.

The purpose of the current study was to determine whether meditation practice is associated with changes in the activation of the DMN. Based on previous findings, we predicted that meditators would show heightened functional connectivity in areas of cortical midline activity, such as the MPFC.

Voluntary participants included 35 meditation practitioners and 33 healthy controls. Meditation practitioners were recruited from participants in the "Brain-wave vibration meditation" mind-body training, which combines ancient Eastern philosophy with modern scientific methods to elevate human awareness. Brain-wave vibration meditation is a kind of moving meditation that is designed to help quiet the thinking mind and to release negative emotions through performing natural rhythmic movements and focusing on bodily sensations. For this, the method places importance on focusing attention on their bodily sensations and emotions, and heightening awareness of the movement of energy within the body. Detailed methods are described in our previous report [22].

Meditation practitioners had been engaging in regular meditation practice for a mean of 39.88 months (*SD*: 25.58 months) and practiced a mean of 44.29 min per day (*SD*: 18.11 min) and 4.30 days per week (*SD*: 1.89 days). Control subjects had no previous experience with meditation or similar practices. The Structured Clinical Interview for DSM-IV Non-patient Version was used for assessing psychiatric disorders. All subjects were right-handed. Exclusion criteria included history of psychosis, bipolar disorder, major depressive disorder, substance abuse or dependence, significant head injury, seizure disorder, or mental retardation.

The Beck Depression Inventory (BDI) [6] and the Beck Anxiety Inventory (BAI) [5] were administered to measure the severity of depression and anxiety, respectively. This study was approved by the Institutional Review Board at Seoul National University Hospital, and informed consent was obtained from all the participants.

All data were acquired using a 1.5 T Avanto scanner (Siemens, Erlangen, Germany). Resting-state fMRI data were acquired for 4.68 min (120 volumes) using an echo-planar imaging sequence with the following parameters: 25 axial slices, TR/TE = 2340/52 ms, field of view = 22 cm, flip angle = 90°, voxel size = 3.44 × 3.44 × 5 mm, slice thickness = 5 mm, no interslice gap and interleaved slice acquisition. Before scanning, subjects were instructed to maintain fixation on a foveal crosshair for the duration of the scan. The fMRI scanning was carried out in darkness, and participants were explicitly instructed to relax and to move as little as possible. In addition, T1-weighted axial high resolution structural images covering the whole brain using a 3D magnetization-prepared rapid acquisition gradient echo (MPRAGE) sequence were acquired in 176 contiguous axial slices: TR/TE = 1160/4.76 ms, field of view = 23 cm, flip angle = 15°, voxel size = 0.45 × 0.45 × 0.90 mm, and slice thickness = 0.9 mm. On the basis of visual inspection, all scans were judged to be excellent and without obvious artifacts, signal loss, or gross pathology when evaluated by a neuroradiologist (C.H.C.).

Functional data were preprocessed and analyzed using SPM5 (http://www.fil.ion.ucl.ac.uk/spm). The first four volumes of the functional images were removed to eliminate the non-equilibrium effects of magnetization. Preprocessing steps included slice-timing correction for interleaved acquisition, head motion correction, spatial normalization into standard stereotactic MNI space with resampling to 3-mm cubic voxels, and spatial smoothing using a Gaussian kernel of 4 mm full width at half maximum. Resting-state fMRI Data Analysis Toolkit (REST version 1.3, by SONG Xiaowei, YAN Chaogan et al.; http://resting-fmri.sourceforge.net) was then used for removing the linear trend of time courses and for temporally band-pass filtering ($0.01\,\text{Hz} < f < 0.08\,\text{Hz}$). To examine the functional connectivity of the PCC and MPFC in each subject, linear correlation analysis was performed using the REST package. Two spherical seed regions were first defined on 10-mm radius spheres centered on the coordinates of the PCC (−5, −49, 40) and the MPFC (−1, 47, −4) published in a previous study [14]. Before the correlation analysis, a linear regression was performed using nine nuisance covariates to remove the possibility of spurious correlations: the global mean signal, the white matter signal, the cerebrospinal fluid signal, and six head motion parameters. The averaged time course was obtained from each seed region and the correlation map for each seed was produced by computing the correlation coefficients in a voxel-wise way. That is, the functional connectivity maps of the PCC and MPFC of each subject were generated; these were referred to as the PCC-FC map and the MPFC-FC map, respectively. Finally, the maps of correlation coefficients were converted into *z* maps by Fisher's *z* transform to improve normality.

To reveal within-group functional connectivity patterns, *z* maps of the PCC-FC and MPFC-FC of each individual were entered into second-level one-sample *t*-tests. The average maps for the PCC-FC and MPFC-FC were also computed for each group. Significance values for these maps consisted of false discovery rate-corrected (FDR, $P < 0.001$) and cluster size > 100 voxels. With respect to the average maps, a mean image was constructed from the PCC-FC and MPFC-FC images of each subject, and these mean images were then used to compute the average group maps with one-sample *t*-tests. The average map was defined as the DMN map. For direct between-group comparisons, two-sample *t*-tests were performed using a masking procedure to avoid detection of clusters that did not appear in the DMN of the control group. A binary mask was created by summing the within-group *t*-maps of the PCC-FC and MPFC-FC of the control group, and the search for clusters that differed between the two groups was limited by the binary mask. The resulting statistical maps were thresholded at $P < 0.05$ FDR, corrected for multiple comparisons.

The demographic and clinical characteristics of subjects in each group are presented in Table 1. We found no differences between meditation practitioners and healthy controls in age, sex, and years of education. We also observed no significant differences in levels of anxiety and depression.

The one-sample *t*-tests for each group revealed that the pattern of functional connectivity—including the MPFC, PCC, and inferior parietal and lateral temporal cortices—were similar across seed regions (i.e., the PCC and the MPFC). In addition, we confirmed the DMN maps using mean images derived from the PCC-FC and MPFC-FC maps (Fig. 1).

Between-group differences were found in MPFC areas ($x\,y\,z = 3\;39\;{-21}$; $P < 0.05$ FDR-corrected, cluster size: 37 voxels), and meditation practitioners showed greater DMN connectivity in the MPFC region than did healthy controls (Fig. 2). In addition, between-group comparison of PCC-FC and MPFC-FC maps also revealed significant differences in MPFC areas.

No significant correlations were found between DMN activities in the MPFC and clinical measures (duration of meditation practice and scores on the BDI and BAI).

To our knowledge, this is the first resting-state fMRI study demonstrating altered functional connectivity in the DMN among meditation practitioners. In the current study, meditators showed heightened activation of the DMN in the MPFC. This finding is consistent with previous studies that have reported that structural and functional changes in the medial prefrontal areas are associated with meditations [7,18,19,24].

One unique characteristic of the DMN is that its greatest activity occurs when attention is directed away from external stimuli. On this basis, it has been suggested that the DMN support internal mentation or attention that is detached from the external world [1,8]. On the other hand, self-reflective thoughts robustly

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Table 1
Demographic characteristics and clinical rating scales of meditation practitioners and healthy controls.[a]

	Healthy controls	Meditation subjects	Analysis	
	($N = 33$)	($N = 35$)	T or χ^2 score	P value
Demographic characteristics				
Age (year)	23.67 (3.56)	24.97 (3.48)	−1.529	0.131
Sex (M/F)	22/11	16/19	0.082	0.094
Education (year)	14.39 (1.32)	14.71 (1.90)	−0.802	0.426
Duration of meditation practice (month)		39.88 (25.58)		
BDI score	3.03 (4.75)[b]	2.71 (6.28)[c]	0.231	0.818
BAI score	3.55 (4.17)[b]	4.44 (7.89)[c]	−0.545	0.588

Abbreviations: BDI, Beck Depression Inventory; BAI, Beck Anxiety Inventory.

[a] Data are given as mean (SD).

[b] Assessed in 29 subjects.

[c] Assessed in 34 subjects.

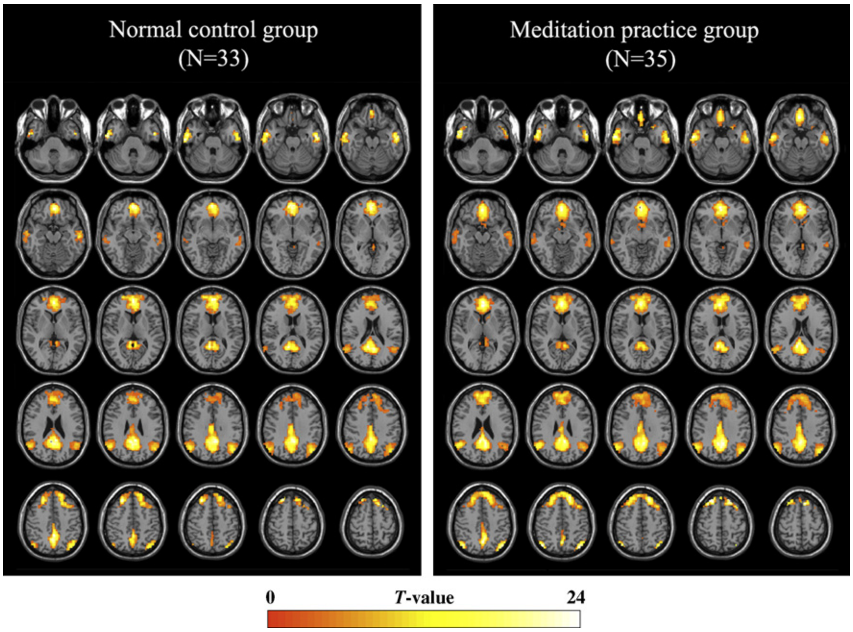

Fig. 1. Default mode network map for healthy controls ($N = 33$) and meditation practitioners ($N = 35$).

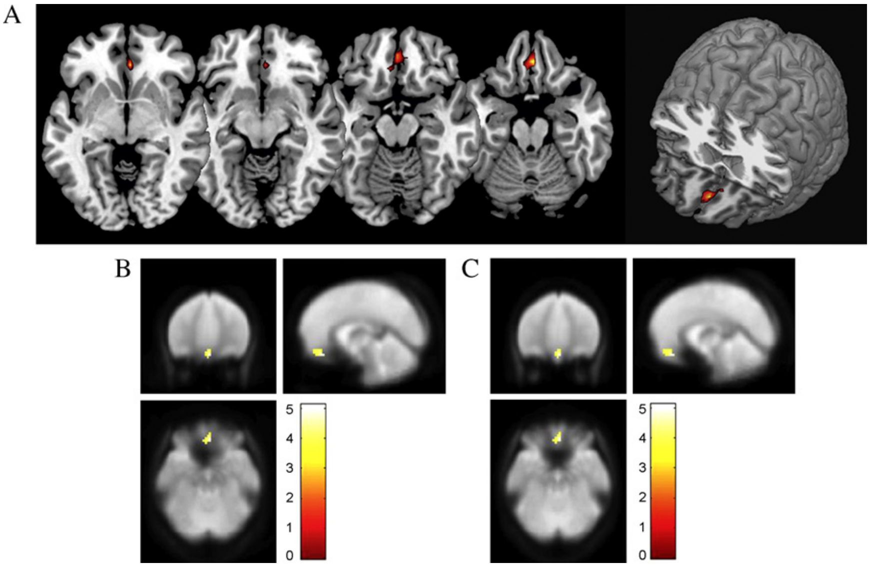

Fig. 2. (A) Areas in which meditation practitioners showed significantly greater default mode network connectivity than healthy controls, and MNI-transformed EPI images for (B) healthy controls and (C) meditation practitioners. *Abbreviations*: MNI, Montreal Neurological Institute; EPI, echo planar imaging.

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activate the MPFC regions within the DMN [17,23,30]. Because this region receives connections from all exteroceptive and interoceptive modalities [4,10], it has been viewed as a polymodal convergence zone that support the integration of stimuli with judgments about their affective relevance to the self [32]. The MPFC is strongly activated by self-relevant mental simulations but not by considerations of a personally unfamiliar public figure in a future setting [38]. These findings suggest that the reduced mental activity during meditation is mediated by the increased activation of networks underpinning internalized attention. It is also plausible that this increased activation persists even in the absence of meditating. This possibility is supported by the structural changes accompanying meditation practice. A study examining the long-term plastic effects of meditation on brain structure found that the cortical thickness of the right middle and superior frontal cortices and the insula of meditators was significantly increased compared to that of controls [24]. This increased thickness probably reflects the impact of meditation-induced neuronal plasticity attributable to years of regularly practicing concentration. A recent study with voxel-based morphometry also reported that meditation training was positively correlated with gray matter concentration in the MPFC [18].

The anterior MPFC region has been associated with susceptibility gradients near air-tissue interfaces, causing signal loss or spatial distortion in functional neuroimaging [12,34]. However, although it was localized, position of the clusters was relevant to previous studies. It has been suggested that the medial frontal cortex can be divided functionally [3,37]. The more posterior region of the medial frontal cortex is activated by cognitive tasks. By contrast, emotion inductions would result in activation in the more anterior region. Activation of the anterior MPFC has also been associated with evaluating self-related traits and monitoring one's own emotional state [21,33]. Increased functional connectivity of the anterior MPFC area might result from the meditation training including focusing attention on their bodily sensations, releasing emotions, and awareness of the movement of energy through natural rhythmic physical movements.

It has been hypothesized that meditators are more aware of sensory stimuli, that this awareness has become automatic through practice, and that such self-awareness is used to manage stress in daily life [36]. During the meditation practice, subjects were instructed to direct attention towards relevant sensory stimuli in a relaxing setting. The results of the current study, which demonstrated increased functional connectivity in the anterior MPFC region, may be attributable to increased neuronal connectivity deriving from neuronal plasticity, which, in turn, may be attributable to repetitive meditation practice. In addition, meditation may strengthen the ability to inhibit mental rumination that can exacerbate stress. Improved self-monitoring and increased ability to inhibit irrelevant interfering external and internal activity has been reported as long-term trait effects of engagement in meditation practices after years of training [9,27]. Electroencephalographic studies reported changes in alpha and theta band power in long-term meditators, compared to control subjects who had no previous experience with meditation practice [9]. A recent study has suggested selective associations of theta and alpha activity with states of internalized attention and positive emotional experience in meditation group [2]. We have recently found that the meditation group showed higher scores on positive affect and lower scores on stress compared to control subjects [22].

This study has limitations. First, as a result of the cross-sectional nature of this study, the longitudinal causal direction of influence cannot be determined. This introduces the important confound that people who decide to practice meditation may differ from others at baseline with respect to their psychological and cultural backgrounds. However, the area that showed increased functional connectivity, the MPFC, corresponds to those associated with concentrating on internal focus and sensations during meditation [19]. Second, it is questionable whether this study, which included meditators who have practiced the Brain-wave vibration meditation method, can be generalized to other kinds of meditation practices. Different kinds of meditation would be expected to have slightly different patterns of functional connectivity that vary according to their approach. Future studies are needed to compare differences among the diverse techniques of meditation.

This study indicates that the long-term practice of meditation may be associated with functional changes in regions related to internalized attention even when meditation is not being practiced. The functional effects of meditation on the DMN may constitute the neurophysiological underpinnings of brain plasticity.

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