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Brain Functional State Analysis of Mindfulness Using Graph Theory and Functional Connectivity

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Abstract

We human beings spend about fifty percent of the time of our waking hours without any awareness what we are doing now. It is said that such a mind wandering affects happiness. To overcome this issue, mindfulness meditation—paying attention to one's experience in an accepting and nonjudgmental way is getting popular. In spite of its popularity, meditation needs a lot of practice until we can experience its benefit. A key to a good practice of the meditation is quality evaluation and feedback of it. In this paper, we proposed a novel feature extraction method to define the meditation state. We measured brain activity during a breath-counting meditation using functional magnetic resonance imaging, and the whole-brain functional connectivity and the amplitude of low-frequency fluctuation were derived and utilized as feature vectors. The experimental results showed that resting and meditation states were classified on the feature space constructed by proposed method.

Introduction

The studies of Killingsworth et al. (Killingsworth and Gilbert 2010) revealed that we human beings spent about fifty percent of the time of our waking hours without any awareness about what we are doing now. This absent mind is referred to as mind wandering, and is associated with our happiness. People tend to feel less happy when their minds wander because in this state they often think about the past event which drives their negative thoughts, or feel anxious about the future. Reducing mind-wandering will lead to improving our concentration on the current activity, and make us more productive. One of the ways to suppress mind-wandering by ourselves is *mindfulness meditation*. It is a practical method to pay attention to one's experience in an accepting and nonjudgmental way. Although its origin is in Buddhist practice (e.g. Zen meditation), nowadays a modernized form of mindfulness meditation such as mindfulness-based stress reduction (MBSR) and mindfulness-based cognitive therapy (MBCT) has also been used as a clinical application. Meditation is increasingly being popularized in our daily life. In the mindfulness meditation practice, practitioners try to observe their current experiences such as emotion, thoughts and sensations inside and around them. It is widely used as means of relaxation and stress reduction. The mindfulness meditation includes at least three components of enhanced attention control, improved emotion regulation and altered self-awareness, and contributes to enhanced self-regulation (Tang, Hölzel, and Posner 2015). These components allow us to stay away from mind-wandering into negative thoughts and feelings, and to focus on what we should do now.

The neural mechanism of mindfulness meditation has also attracted attention in neuroscientific research in recent years (Davidson et al. 2003; Lutz, Dunne, and Davidson 2007; Fox et al. 2014; Khalsa et al. 2015). Many studies have investigated structural and functional brain changes through the meditation practice, and their mechanism has been discussed based on the anatomical aspects of brain functions, as well as the functional brain networks. Marchand et al. (Marchand 2014) revealed that expert meditators differed from novice or non-meditators in activities of a medial cortex, default mode network (DMN), insular cortex, amygdala, lateral frontal regions and basal ganglia. Lazaret et al. (Lazar et al. 2006) indicated that an extensive practice of meditation also caused structural changes such as the increased cortical thickness.

However, in most situations, these variations in the brain activities are observed for the well-practiced meditators who experienced several months or years of meditation practice or retreat. It is not easy for novices to obtain the specific effect of the meditation. We assume that this difficulty comes from unclearness of the meditation quality. If its quality would be characterized and quantified during an early stage of practice, we can improve our practices by ourselves with the help of quality feedback.

Therefore, we aimed to describe the brain activity during meditation. The brain activities of novice practitioners without any meditation experience and the practitioners with a thousand hour of meditation experience were measured by functional magnetic resonance imaging (fMRI). Their brain activities were compared each other regarding the functional connectivity networks. The characteristics of the functional connectivity networks were quantified based on the graph theoretical analysis. Low-frequency fluctuations in the blood oxygen level-dependent (BOLD) signal was also utilized as the metrics of spontaneous brain activity. Since the fMRI data is high-dimensional, the fea-

ture selection is a crucial issue. One of the motivations to use these metrics to characterize the brain activities is low-dimensional feature representation of brain activation patterns. We expected to characterize the meditation state of practitioners using low-dimensional feature vector based on the brain functional information of connectivity and signal intensity of low-frequency fluctuation.

Proposed method

Feature representation by fusion of functional connectivity and signal intensity of brain activity

One of the most effective method to classify the state of brain activity is to define the functional brain network. A number of researches have revealed the existence of several important brain networks including DMN, salience network (SN), and central-executive network (CEN) (Seeley et al. 2007), and besides other task-specific networks may have existed. Differential brain networks have been often analyzed using functional connectivity analysis (FCA). Voxel-wise Pearson's correlation coefficients were calculated from BOLD time courses obtained by 4D-fMRI data. Several nuisance signal regression method have been developed to derive less noisy neural activities. Nowadays the functional connectivity analysis is a very effective tool to grasp overall structures of our brain networks.

However, since the functional connectivity is just an indicator of similarity of relative changes of BOLD signals, they does not deal with the activation of BOLD signals. That is, good correlation does not automatically imply high activation. Therefore, we introduces the feature extraction method using functional connectivity as well as activation level of brain regions. The framework of our proposed method is illustrated in Fig. 1. In the proposed method, at first the voxel-wise BOLD time courses are extracted. There are two processes to extract the functional connectivity measure and the activation level of the brain activity. Detailed description of each process is introduced in the following subsections.

Graph theoretical approach for functional connectivity analysis

The functional connectivity metric was extracted from 4D-MRI data. Voxel-wise BOLD time courses were bandpass-filtered at 0.008–0.09Hz, and then averaged within each region-of-interest (ROI) segmented based on automatic anatomical labeling (AAL). Then Pearson's correlation coefficients were computed among ROI-wise time courses for all 116 regions. Finally, Fisher z-transform was performed to 116×116 matrix of ROI-to-ROI functional connectivity.

The functional connectivity matrix was regarded as the weighted undirected network whose nodes and edges corresponded to brain regions and correlation coefficients respectively, and then it was analyzed using graph-theoretical analysis. Note that we removed the negative connection (functional anticorrelation) and analyzed only positive correlation in the following calculation of graph theoretical metrics because the algorithms to calculate them was established only for positive weights in the network edges (Rubinov and Sporns 2010; Kinnison et al. 2012).

In this research, we used an eigenvector centrality as the graph theoretical metric. The centrality is an indicator of the importance of the node within the network. One of the simplest way to calculate the centrality is degree centrality which is the number of edges connected to a certain node. Eigenvector centrality is an extended form of the degree centrality reflecting the centrality of neighbor nodes. It can be derived by calculating an eigenvector of the adjacency matrix (connectivity matrix). Each element of the eigenvector associated with the maximum eigenvalue corresponds to the centrality of each node. Finally, we obtained the 116-dimensional eigenvector centrality values for each individual subject.

Fractional amplitude of low frequency fluctuation (fALFF)

The amplitude of low frequency fluctuations (ALFF) was originally developed in resting-state fMRI studies. It indicates regional spontaneous neural activity, and can be used as an index reflecting regional intensity of resting-state BOLD signals (Yu-Feng et al. 2007; Zou et al. 2008; Yin et al. 2014). The voxel-wise BOLD time course was transformed to the frequency domain, and then the square root of the amplitude of each frequency was calculated across the entire frequency range. Finally the averaged value of square root was derived for a certain frequency range that is relevant to neural activity. Fractional ALFF (fALFF) is an improved version of ALFF. In fALFF calculation, the sum of square root within a certain frequency band was divided by that of the entire frequency range. fALFF can indicate the relative contribution of specific low-frequency fluctuation within a detectable frequency range (Zuo et al. 2010). Since we needed to compare fALFF values among individual subjects, Z-transform, which was subtracting the mean fALFF derived for the entire brain and dividing by the standard deviation, was performed. The Z-score of fALFF was referred to as **z**fALFF in this paper. The voxel-wise zfALFF map for a single subject is converted into ROI-wise zfALFF values by averaging across the voxels within each ROI. Finally, we obtained the 116-dimensional zfALFF values for each subject.

Dimensionality reduction using linear discriminant analysis

We could obtain the two dataset of $116 \times N$ matrix of zfALFF and eigenvector centrality, where N was the number of subjects. However the feature dimension was still high and hard to analyze. The 116-dimensional feature vector was decomposed into a single axis where two brain states of resting and meditation states were discriminated using linear discriminant analysis (LDA). This process was separately applied for degree and zfALFF metrics. Each decomposed component of zfALFF and eigenvector centrality was newly utilized as one axis of the feature space. Mapping MRI data into this two-dimensional space allowed us to analyze it in terms of both the network structure and the activation intensity.

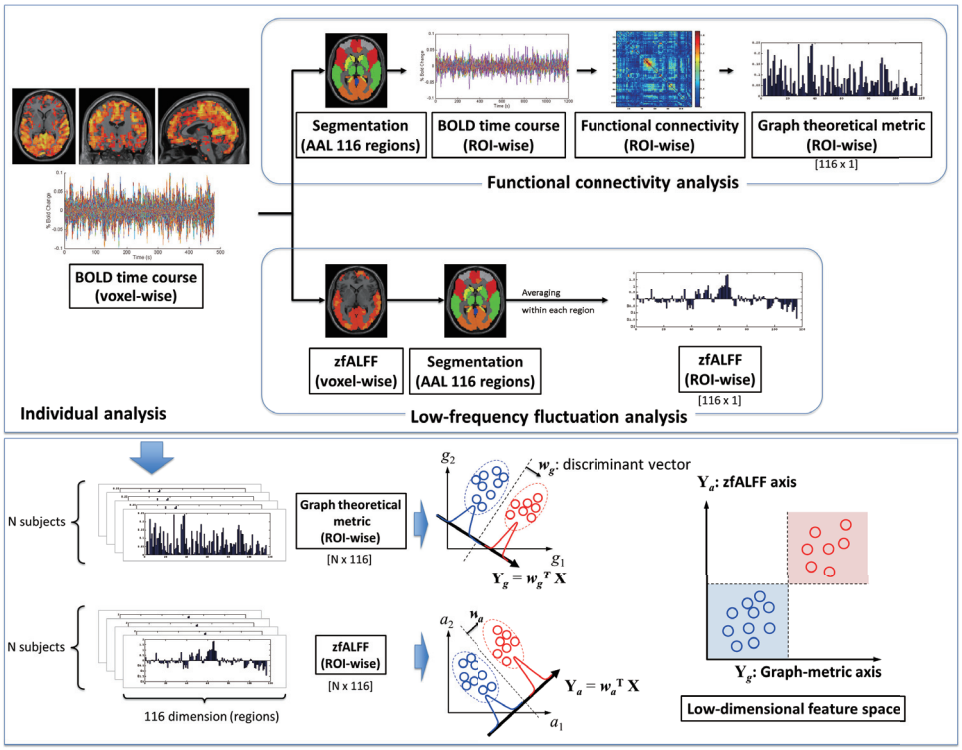


Figure 1: Framework of the proposed method

Experiments

Characterization of brain activity during breath-counting meditation

In order to verify effectiveness of our proposed method, we examined characterization of brain activity during meditation using our method. In this experiment, we expected even the meditation beginners can derive any positive effect by meditation. Thus, we employed one of the easiest meditation method called breath-counting meditation (*Susokukan* in Japanese). Its is originated by Zen Buddhism, and is easy to understand because it requires only focusing own breathing and counting it. Participants were asked to count their breath silently from one to ten, not with voice but just mentally. They were also instructed to restart counting from one if they got to ten, or their mind got distracted. Especially in case of distraction, they were asked to try to bring back their attention to breath. MRI data derived during resting and meditation states were decomposed into two-dimensional (connectivity – zfALFF) space, and their characterization were discussed.

Participants

Four healthy male adults (average age: 25.3 ± 5.2 years, right-handed) with no experience of meditation (**novice** group), one healthy male adult (aged 25 years, right-handed) has practiced breathing meditation cumulatively for 30 hours but with no experience of any retreat (**early**-stage group), and two healthy male adults (average age: 37.0 ± 0 years, right-handed) with about 1000 hours of *Vipassana*

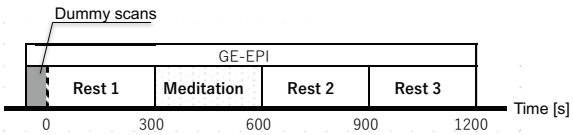
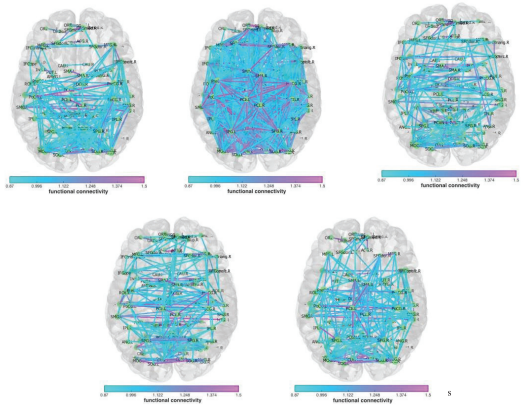


Figure 2: Experimental design

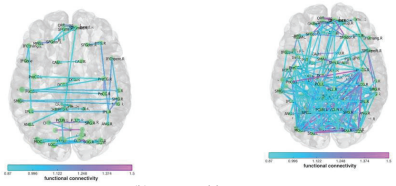
Buddhist meditation experience (**middle**-stage group) were asked to mediate in the functional magnetic resonance imaging (fMRI) scanner, by breath counting meditation. All participants gave written informed consent to participate in this experiment. The study protocol was approved by the Ethics Committee of Doshisha University.

Procedure and design

The experiments consisted of 5-min resting state block, 5-min meditation block, and 10-min resting state block as shown in Fig. 2. Start and stop of meditation was informed by an auditory signal via headphones. The total duration of the experiment was 20 minutes. Participants practiced a simple-guided breath-counting meditation for a few minutes before entering the fMRI scanner. They are asked to close their eyes consistently in the scanner. The dummy 6 volumes were acquired before the start of the first resting block to eliminate non-equilibrium effects of magnetization.



(a) beginner subjects



(b) expert subjects

Figure 3: Functional connectome

MRI data acquisition

MRI data were acquired on a 1.5 T Echelon Vega scanner (Hitachi,Ltd., Tokyo, Japan). Functional volumes were collected using a gradient-echo echo-planer imaging (GE-EPI) sequence (TR=2500ms, TE=40ms, flip angle=90°, FOV=240mm, 5.0-mm thick slices, matrix size=644, number of slices=25). We also employed a Rf-spoiled steady state gradient echo (RSSG) sequence to obtain T1-weighted structural images (TR=9.8ms, TE=4.0ms, flip angle=8°, FOV=256mm, 1.0-mm thick slices, matrix size=256x256, number of slices=192).

MRI data preprocessing

The images were preprocessed using Data Processing Assistant for Resting-State fMRI (DPARSF) (Yan & Zang, 2010, http://www.restfmri.net) (Yan and Zang 2010) which is based on Statistical Parametric Mapping (SPM8) (http://www.fil.ion.ucl.ac.uk/spm), which included slice timing correction, realignment, spatial normalization and resampling to Montreal Neurological Institute (MNI) template (3 mm isotropic voxels), nuisance regression using component based noise reduction method (CompCor) (Behzadi et al. 2007) and Friston-24 motion parameters model (Friston et al. 1996). Then the images were spatially smoothed with a 8-mm full width at half maximum Gaussian kernel. After these processes, finally the linear trend was removed. Preprocessed BOLD time course for each individual subject was divided into four session data, and each session data was analyzed and decomposed into two-dimensional feature space by our proposed method.

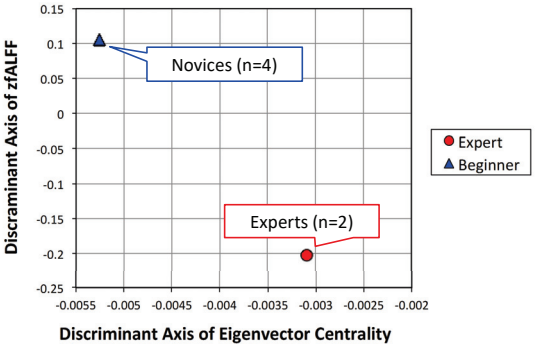


Figure 4: Derivation of a discriminant axis using LDA

Results and Discussions

In Fig.3, the functional connectivity metric is described. Here, only the edge whose correlation value is bigger than 0.8 is expressed. Binding between areas of the experts is less than binding of the novices. The beginners are not used to meditation, so coupling between various regions is tried, whereas the experts may be performing meditation efficiently. Thus, in the meditative state, the states of brain function of experts and beginners are different. This result suggests that if appropriate transformations are used, it is possible to express experts and beginners' brain function states separately.

Fig.4 shows the result of converting zfALFF and Eigenvector centrality into space dimensionally reduced by LDA. In the proposed method, the algorithm was designed so that the condition of experts and beginners differed and each group of subjects concentrated. It is confirmed that its design is working well. Fig. 5 shows the transitions of functional brain states during rest from rest, meditation, meditation, using this process. Fig.5 is fascinating. Because in the two experts, each initial state is different, but the meditation state is consistent. Also, after meditation, various movements are performed, but each brain function state returns to the initial state. Therefore, the brain functional state of the expert varies depending on the individual, but the state transition is robust, and its state is controlled. On the other hand, the beginner's transition is disjointed by individuals. In addition, the state of the brain function in the rest state after meditation is different from the state of the brain function in the state of the first rest. Therefore, the brain functional state can not be controlled. From this result, the proposed method describes the functional brain status during the meditation.

The values of zfALFF and Eigenvector centrality were dimensionally reduced by LDA. The contribution of each region is shown in Fig.6. We will examine the brain regions related to the contribution in the future.

Conclusions

Mindfulness meditation needs a lot of practice until we can experience its benefit. A key to a good practice of the med-

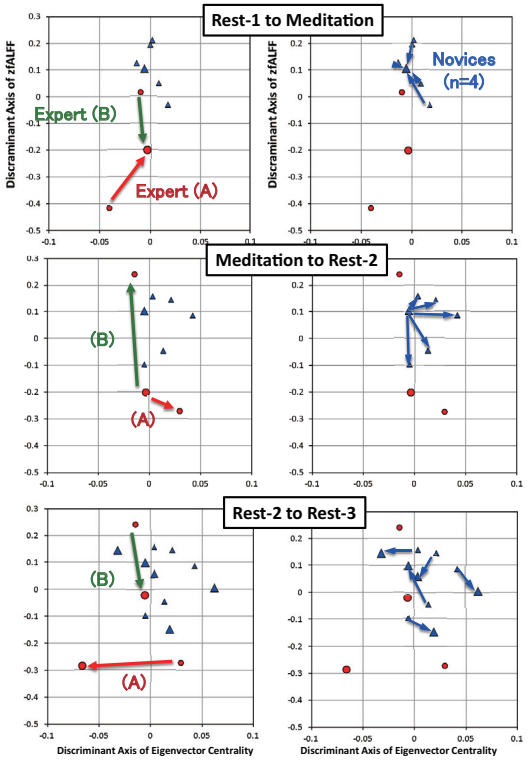


Figure 5: Brain state transitions through the meditation

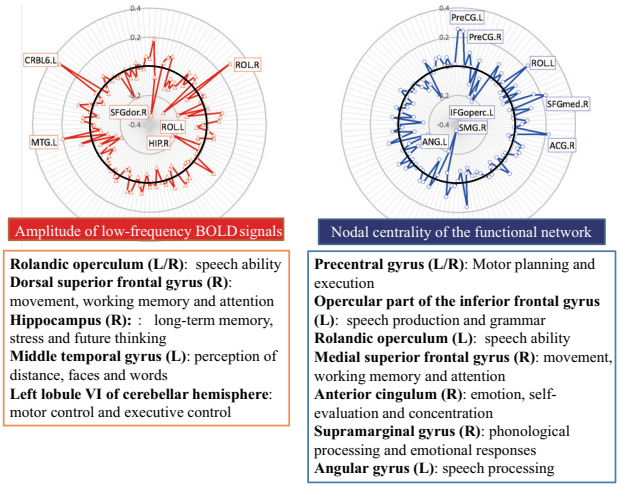


Figure 6: Element values of discriminant vectors

itation is quality evaluation and feedback. In this paper, we proposed a feature extraction method to define the brain activity. Eigenvector centrality derived through the functional connectivity analysis and zfALFF value were utilized as feature vectors, and then dimensionality reduction is conducted on each feature vector using PCA. The experimental results revealed that resting and meditation states were classified on the feature space constructed by proposed method.

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