Adaptation of Dynamics in Default Mode Network Dependent on Mental States

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Abstract

We suggest a novel analysis method called one-to-many dynamic functional connectivity (DFC) analysis to detect adaptations in dynamics of a brain network dependent on mental states with a single case study. The analysis method assesses the major direction of the variance in the partial correlations of a center that are time-windowed functional correlations of a brain region (a center) to the rest of the regions in a brain network. This analysis method uses principal component analysis (PCA) to define an orthonormal basis of the variance in the partial correlations of a center. We assume that the weights of each correlation in the partial correlations to a chosen major principal component define a configuration of the brain network corresponding to its functional state. We compare how similar the major principal components in the same mental states or distinct mental states are by taking the configurations. In the current study, we collected fMRI BOLD signals from a blind subject whom with advanced ability in mental imagery while the subject was resting and then retrieving a morning routine three times. The default mode network (DMN), which is known for its high correlation to episodic memory retrieval and resting-state tasks, was analyzed with one-to-many DFC analysis. We compare the configurations of the DMN in the two mental states. The results imply that the dynamic adaption in the DMN in the two mental states could be well depicted when the posterior cingulate cortex (PCC) is the center of the analysis in this single case study.

Keywords

One-to-many dynamic functional connectivity, Default mode network, episodic memory retrieval, resting state, fMRI

1 Introduction

For the last few decades, research on human brains has found that some brain regions are highly active when they are at rest without performing external tasks [24, 29]. These brain regions include roughly the posterior medial and the inferior lateral part of the parietal lobe and the medial prefrontal cortex. Also, resting-state functional connectivity analysis

found that their activities are distinctly correlated [10, 24, 55]. Because of these reasons, the set of brain regions was named the default mode network (DMN). The 1 function of the DMN is an ongoing research topic. Meta-analysis revealed that the DMN is highly active not only in a resting state but also in task-related mental states like episodic memory retrieval tasks, episodic future thinking tasks, theory of mind tasks, or navigation tasks [65, 64]. All these task-related mental states construct internal mental imagery and focus on the imagery.

One of the suggested functions of the DMN regarding the commonalities between different brain states is "self-projection" [7, 12, 21]. Self-projection explains that the DMN processes the frame of reference of cognition formed with subjective experiences. Hence, these cognitive activities happen internally regardless of sensory inputs from outside. For example, one can listen to a bird song without subjective experiences by self-projection. However, retrieving memory related to the bird song requires self-projection. Another interesting suggestion for the possible function of the DMN is "scene construction" [32]. The previously mentioned mental states in meta-analysis commonly require mental imagery of scenes. Sensory imageries from memory are ingredients to form and maintain such scenes. The DMN might be the spatial domain to process such mental imagery. The two suggestions, self-projection and scene construction, stress two pivotal aspects of the mental states mentioned by meta-analysis. One is the differentiation from perceptions generated with spontaneous sensory inputs, and the other is the creation of a coherent form of mental imagery.

The autobiographical episodic memory retrieval (AEMR) state is a mental state realizing these two suggested functions of the DMN [19, 70]. Autobiographical episodic memory has an order between episodes (scenes) abstracted from subjective experiences in past [69, 75]. The AEMR state asks subjects to retrieve successive scenes of their experiences in the past. Both self-projection and scene construction are keys for retrieving autobiographical episodic memory. In contrast to the AEMR state, a resting state is a mental state allowing the subject to drift in subjective perspective without the order of mental imagery or the need of picturing specific contents from past experiences. As the result, the resting state means often spontaneous mind wandering [34]. When the DMN is the spatial domain processing the two mental states, could it be possible to observe the differences between the mental states from the dynamics of the DMN? To test this idea, we compared the dynamics of the DMN in the two mental states.

1.1 Dynamic Functional Connectivity

Functional connectivity analysis measures the correlation between the activities of two brain regions for the total measurement duration [25]. Research on functional connectivity has defined a few brain networks with and without tasks by functional connectivity analysis [3, 62, 72]. At the same time, correlations in and between brain networks might change over time as cognitive activities do. Dynamic functional connectivity (DFC) is an analysis method to measure the changes in correlations between

two brain regions over time [3, 18, 35]. Consequently, DFC research often focuses on the links between spontaneous alternations in cognitive activities and changes in functional connectivity [9, 40, 60]. In this paper, we explore how two different mental states executed in the DMN could be differentiated in dynamics of its functional connectivity.

To analyze dynamics of a network and understand its implication, one should solve technical problems. There are two main concerns about analysis of BOLD signals from the perspective of network analysis. One of the concerns is the high dimension of data. It implies that we should consider many variables and their dependency on each other. Thus, it is hard to catch the causality of such multivariate time series signals. Further, when the connection between the observational method (fMRI BOLD) and the system under observation (neuronal substrates) is complex, it should be considered carefully to interpret observations on our hands. Previous studies on this issue have shown that the BOLD signals represent the neuronal activities of the brain reliably. [22, 44].

The concern over the complexity of the data due to its high dimension could be resolved by selecting well-defined features of brain networks. DFC studies in general analyze values of Pearson correlation coefficients of every pair in brain networks simultaneously (all-to-all). For n brain regions, therefore one considers $n(n-1)/2$ correlations. To find regularity in the DFC of brain networks, many researchers have hired various multivariate time series analyses using pattern recognition algorithms mainly [16, 35, 43, 54]. Instead of using all-to-all DFC analysis, we inspect the variances in correlations of a brain region to the rest of the brain region in the DMN simultaneously. We call it one-to-many DFC in this paper. This analysis method measures the changes in DFC for a selected brain region called a center in a local network at once. It includes not only a smaller number of relevant variables but also conveys different aspects of the local network compared to all-to-all analysis. Further, we analyze DFC of a local brain network, the DMN. When the DMN is the spatial domain processing the two mental states we are interested in, then it might be enough to focus only on the local network instead of inspecting the whole brain connectivity. As mentioned previously, what we consider is the variances of the correlations between a brain region and the rest of brain regions, which we call the partial correlations of the brain region, in the DMN. Whereas the value of the correlation coefficients measures the similarity between BOLD signals, their variance measures the stability of the similarity. Correlations of some brain regions to a selected center might be steady in a mental state and highly fluctuated in other mental states within a local brain network. It means that the brain region could be a reference region of dynamic adaptation within the local network.

If a brain network is a dynamic system, it might have certain configurations defining its functional states. First, we assumed that there is a reference brain region of a brain network and its partial correlations are the main dynamic feature defining its functional state. Therefore, the $n-1$ partial correlations of a center are the interest of our analysis for the case of a brain network with n brain regions. Second, we consider the simultaneous variance of the partial correlations in an $n-1$ dimensional space. We apply principal

component analysis (PCA) to find a direction explaining the major variance of the partial correlations [76]. The weight of each correlation of the partial correlations to the major variance might be preserved in a mental state. It means that we hypothesized that the weights are the configuration of the brain network defining its functional states.

The steps of one-to-many DFC analysis are as follows: we chose a brain region, a center, from the DMN and then compute windowed Pearson correlation coefficients between the center and the other brain regions in the DMN, which we call the partial correlations of the center in the DMN. After that, the principal component analysis was applied to the partial correlations of the center. Given the variance of the partial correlations of the center in the DMN, the principal component analysis defines an orthonormal basis of the variances called the principal components. The weights from each correlation in the partial correlations represent the principal components on an orthonormal basis. The first few principal components are the direction explaining the most variance of the partial correlations. We compare the first or the second principal component of the partial correlations of a center in the same and distinct mental states by measuring angles between them. If we observe differences or similarities in principal components in the distinct or the same mental states respectively, we could say that the DMN adjusts itself to a chosen center dependent on mental states. We tested this hypothesis with an fMRI BOLD signal collected from a late-blind subject.

1.2 Mental Imagery of the Blind

Because of the advanced visual system of humans, it is reckoned that visual stimuli dominate sensory inputs and are closely related to mental imagery [36, 52]. Consequently, researchers have widely investigated the relationship between mental imagery and visual impairment to learn the mechanism of mental imagery [17]. The visual sensory input is spontaneous, and its sensory field is wide, so humans mainly rely on it to navigate spaces [42, 61, 66]. Some research on blind people shows that congenitally and late blind people can perform spatial navigation tasks as much as blindfolded sighted people can, although they are visually impaired [61, 67]. At the same time, it found differences between the blind and the sighted people also. The size of sensory fields for auditory and tactile perception is smaller than those of the visual field. Hence, auditory and tactile perceptions contain local information and are naturally serial [2, 45, 58]. Contrastingly, the visual field offers global and local information simultaneously [49]. Such a difference in sensory inputs leads blind people who prefer to employ auditory and tactile perceptions to process mental imagery through relative locations of objects in series [38, 50, 51, 71]. Accordingly, research on serial memory of blind people shows that they could perform serial memory tasks better than sighted people do [4, 53, 57, 58]. It might reflect their familiarity with the serial process. In addition to that, in the case of late blind people, activities of the visual cortex, including the primary visual cortex and the medial temporal lobe, were observed from mental imagery tasks [4, 11, 28, 56]. It implies that late blind people can transfer the local and serial sensory inputs into global visual imagery. In short, the late blind people

have advanced auditory and tactile perceptions contributing to local information and visual memory capturing a global structure of scenes by transferring local information into global visual imagery.

Concerning these facts, we assume that the late blind people have the advantage of having vivid mental imagery. In our study, we compared dynamics of neuronal activities at the network level with a single case of a late blind subject in two mental states, an autobiographical episodic memory retrieval state and a resting state. Following the ample studies on the late blind people summarized above, they have an advanced ability to retrieve serial memory fluently using vivid mental imagery that is closely related to episodic memory retrieval ability. Therefore, studying a late blind subject might facilitate catching the differences in dynamics of neuronal activities of the two mental states: the episodic memory retrieval state and the resting state. Furthermore, a late blind female subject aged 78 (called B.L.) who participated in this experiment previously attended a study showed that she could visualize vividly her episodic memory [74]. We collected the fMRI BOLD signals during two mental states and analyzed dynamic functional connectivity in the DMN using one-to-many DFC analysis.

2 Material and Method

2.1 Experiment

The subject B.L. had enucleation of both eyes in her adolescence due to infections. She had used the Braille system since her twenties. She had neither known brain damages nor neuronal diseases at the time she attended the experiment. In a previous experiment that she attended, her primary visual cortex activated highly when she was touching familiar geometric objects like a cylinder [74]. It might imply that she had an advantage of retrieving episodic memory as summarized above. We asked the subject to retrieve her morning routine which is a type of autobiographical episodic memory. First, the subject described her morning routine verbally, then she repeated it three times in silence. After the behavioral experiment, the fMRI BOLD signals of the subject were collected while she was retrieving her morning routine and resting. The study was approved by the local ethics committee of the university's medical faculty.

2.1.1 Behavior

Before an fMRI session, the subject verbally described her morning routine and the description was recorded as an audio file. After the verbal statement, she retrieved the same morning routine three times in silence. The subject cued the beginning and the end of task performance verbally. An experimenter recorded the duration of each trial based on the cue.

2.1.2 fMRI

We scanned the T1-weighted structural image with high resolution then the EPI sequences functional images. A foam cushion was used to minimize the effect of head movement. In the first fMRI run, B.L. was asked to rest without focusing on any specific thoughts or mental imagery. After the resting state run, she repeated the retrieval of her morning routine three times, and a short pause (less than a minute) was given in between fMRI runs. An experimenter cued the beginning and end of each run. The subject listened to the cue through a speaker in the MRI room. All four runs were 7 minutes 40 seconds following the result of the behavioral experiment. Imaging was performed with a 3T MRI clinical scanner (Phillips Healthcare, Ingenia). A T1-weighted 3D structural image was acquired in sagittal orientation. Its arrangements are as follows: repetition time (TR) = 8.2 ms, echo time (TE) = 3.76 ms, flip angle (FA) = 8°, number of slices = 220, matrix = 256 x 256, 1mm isotropic voxel size. Functional images were acquired after the T1-weighted anatomical reference scan using an echo-planar image (EPI) sequence. Its arrangements are as follows: repetition time (TR) = 2500 ms, echo time (TE) = 30 ms, flip angle (FA) = 90°, number of slices = 48, number of volumes = 180, matrix = 144 x 144, 3 mm isotropic voxel size, ascending sequential acquisition in axial orientation.

2.2 Analysis

2.2.1 Data Preprocessing

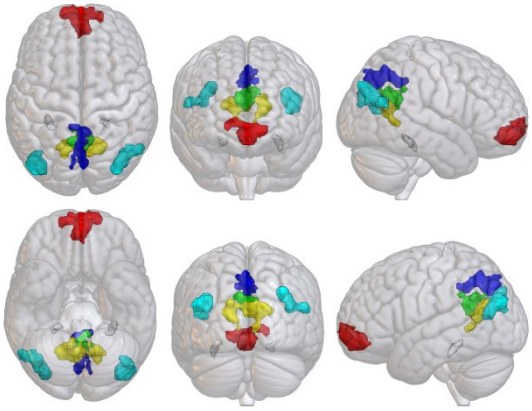
Acquired T1-weighted anatomical images and EPI sequences were preprocessed by the default pre-processing pipeline of the CONN toolbox (www.nitrc.org/projects/conn, RRID: SCR 009550), which is a toolbox for SPM 12 (https://www.fil.ion.ucl.ac.uk/spm/software/spm12/). The first six functional images were discarded, and 174 functional images (7 minutes 15 seconds) were used for further analysis. The preprocessing pipeline includes the realignment and unwrap, slice timing correction, outlier detection using ART (http://web.mit.edu/swg/software.htm), direct segmentation, normalization to MNI space, and functional smoothing. Realignment and unwrap were done to the first scan using b-spline interpolation. Slice timing correction was done to match the slice at each TR/2. Images showing their frame-wise displacement above 0.9mm due to head motion or the deviation of the global BOLD signal above five standard deviations were marked as outliers and scrubbed. Segmented functional and structural data were normalized to MNI space with 2 mm and 1 mm isotropic voxels respectively using 4th order spline interpolation. Functional smoothing was done with a Gaussian kernel of 6mm full width half maximum. To remove the slow physiological noises, the high pass filter with a 0.008 Hz threshold was applied.

2.2.2 Regions of Interest

We employed group ICA of CONN toolbox and defined the DMN of the subject from images of the four fMRI runs. First, fast ICA with G1 contrast function abstracted the 40 spatial

independent components after dimensionality reduction (dimension=64) [15, 37]. We picked one of the components as the DMN by comparing spatial correlation and spatial overlap to the predefined DMN offered in CONN toolbox. The predefined DMN is defined with ICA of the resting-state data (n=497) of the Human Connectome Project [41]. The chosen independent spatial component contained the left and right angular gyrus (AG), the left and right parahippocampal cortex (PHC), the retrosplenial cortex (RSC), the precuneus (PRC), and a minor part of the posterior cingulate cortex (PCC) representing the posterior subsystem of the DMN. Additionally, we selected one more independent spatial component that could be regarded as the anterior subsystem or the midline core subsystem of the DMN mainly consisting of the PCC and the mPFC. Research on the DMN found that the DMN consists of a few subnetworks that may alter in number or appearance dependent on the study design and analysis methods [6, 20, 21, 47]. For that reason, we chose eight brain regions from two independent components in our study (Table 1). We extracted ROI marks of the PCC and the mPFC from an independent component with a threshold z-score ≥ 3, and the rest in another independent component with a threshold z-score ≥ 4 except for the L/R PHC using CONN toolbox. We chose a threshold of the z-score for the L PHC and R PHC as 2.5 to include a nontrivial number of voxels.

Figure 1: Regions of Interest (ROIs)



L/R AG: Cyan, L/R PHC: white, PCC: green, mPFC: red, PRC: blue, RSC: yellow, The image was created by MRIcroGL.

Table 1: MNI Coordinates of ROIs

	x,y,z	Number of Voxels
L AG	-40, -75, 22	517
R AG	40, -71, 26	510
L PHC	-29, -38, -17	86
R PHC	22, -38, -16	41
PCC	0, -53, 25	420
mPFC	0, 57, -7	847
PRC	0, -60, 42	539
RSC	2, -60, 16	765

Coordinates of the center for regions of interest in the MNI space

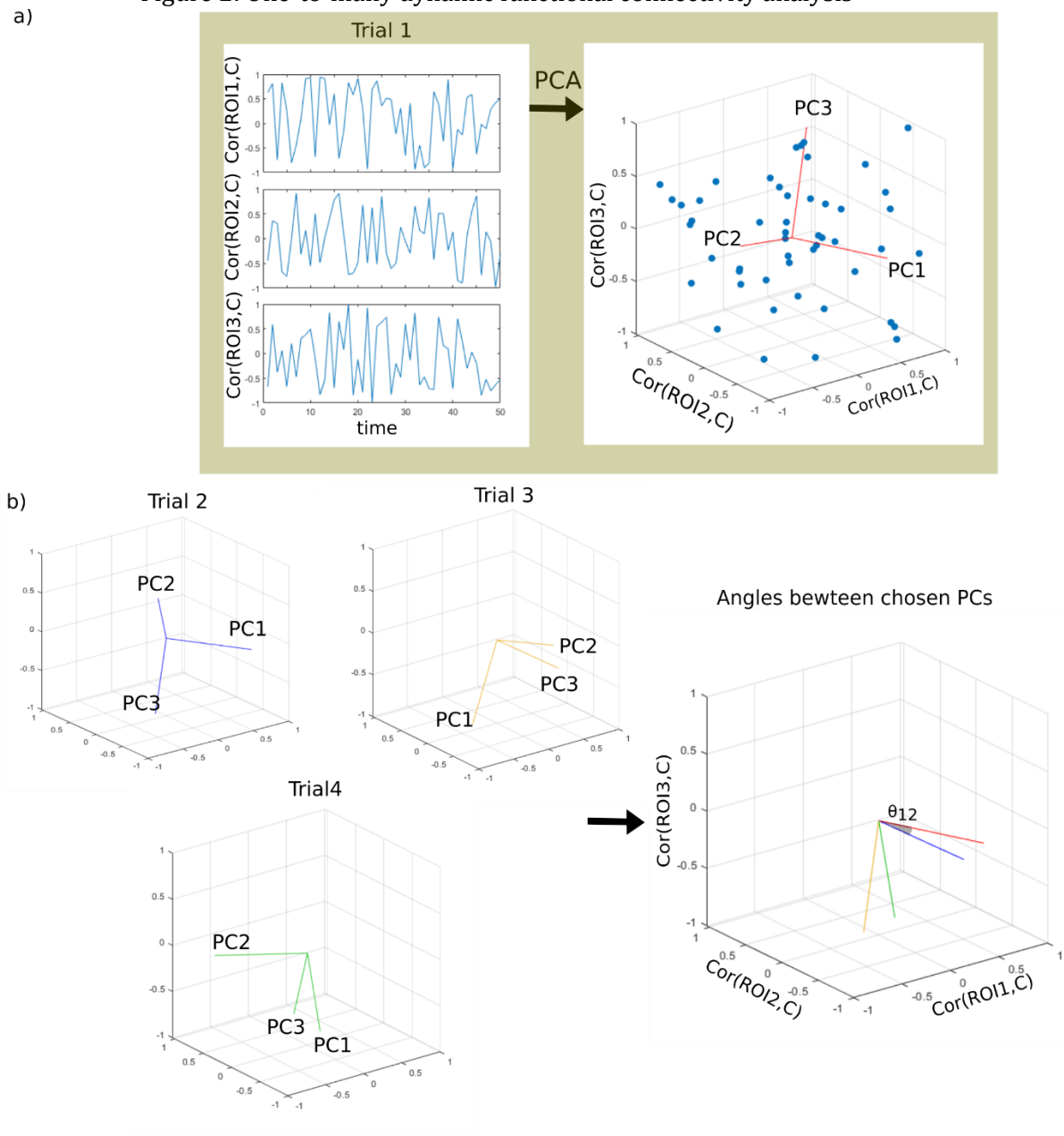
2.2.3 One-to-All Dynamic Functional Connectivity

One-to-many DFC analysis considers only correlations between a chosen brain region, a center, and its connection to other brain regions in the same brain network at once. After calculating Pearson correlation coefficients of the partial correlations of the center, we recentered them to have the zero mean to consider only the variance. When we apply PCA to the time series of the seven partial correlations of the center in the DMN, we have an orthogonal basis of the variance called principal components. The first principal component is the direction explaining the most variance in the partial correlations. The second most variance lies in the direction of the second principal component that is orthogonal to the first principal component and so on. The biggest advantage of using PCA is the first few principal components explain the most variance of the multivariable system. If the first or the second principal component from the three trials of the AEMR state are similar to each other, then one can say that the partial correlations of a chosen center have high similarity in direction encoding their major variance. On the contrary, one expects that the first or the second principal components from the three AEMR trials and a resting state trial are distinct when it is indeed a configuration of the DMN defining its functional state. We choose mainly the first principal components for most of our analysis. In the case of the second principal component of a trial explaining equivalently large variances in the partial correlations compared to the first principal component, we choose the one having a smaller angle to the chosen principal components of the other trials (Table 2).

The similarity of the chosen principal components from the four fMRI trials (three AEMR trials and a resting state trial) can be depicted as angles between them [27, 39]. Loadings of a principal component, L, indicate the weights of each correlation of the partial correlations to the principal component. Let us call the first principal component of a center C from a trial A is A_1. Then $A_1 = A_1(L_{11},...,L_{17})$ means that the L_{1i} amount of contribution, or weight from the correlation between C and the brain region i to the A_1. When B_1 is a first principal component of a trial B to the center C, the angle $\theta_{A,B}(0 \leq \theta_{A,B} \leq \frac{\pi}{2})$ between two principal components is calculated, such that $\theta_{A,B} = \cos^{-1}(A_1 \cdot B_1)$ when $A_1 \cdot B_1$ is the inner product of A_1 and B_1 (the norm of A_1 and B_1 is 1). The angle $\theta_{A,B}$ tells how parallel, or in other words, how similar the directions of the first principal components of trial A and trial B. Similar methods to define the similarity of principal components between groups were suggested previously [39, 78]. When one of the first two principal components of trial A is aligned parallel to that of trial B (i.e., $\leq \theta_{A,B}$) is close to zero degree, the chosen principal components are highly similar to each other. If the angle between chosen principal components is close to 90 degrees, then the principal components are highly dissimilar. If a chosen center C is a reference region to adapt DFC of the DMN, we expect to see the small angles (close to 0 degree) between chosen principal components of the partial correlations of the center C for three AEMR trials. Contrastingly, we expect big angles (close to 90 degrees) between these principal components and the chosen principal component of the resting-state trial.

In this study, we employed the Pearson correlation coefficient to calculate the bidirectional and linear correlation between two brain regions and the sliding window method with the window width of 10 consecutive images (=25 sec with TR=2.5 sec). The weight of the window is constant so that the window has a rectangular shape. The window slides an image per step; therefore, 165-time points for 174 preprocessed images described the variance in partial correlations. Given distributions of partial correlations of a center, we applied PCA to the partial correlations of the center for four trials each. Before the application of PCA, we aligned the data to have the zero mean. We calculated angles between the first and the second principal components of each trial, then picked only one principal component from each of them having a smaller angle to principal components from the other trials. We repeated the same analysis by choosing every brain region in the DMN as a center of the analysis at a time.

Figure 2: One-to-many dynamic functional connectivity analysis



a) An example with a brain network of 4 ROIs. When C is the center, the correlations between C and the other three ROIs are computed using the sliding window method. The principal components (PC) of the partial correlations of C show its distribution on an orthonormal basis. The first and second principal component explain the most variance in the partial correlations of C. b) Therefore, we chose one of two principal components from each trial to compare their similarity. The angle between chosen principal components, for example, θ_{12}, measures the similarity of the chosen principal components from trial 1 and trial 2.

3 Results

3.1 Behavior

B.L. reported that she could retrieve the same morning routine for the retrieval trials outside and inside the MRI machine. The subject described her morning routine as a sequence of episodes. The term 'episode' is used here to refer to events that happened in a specific location. Between episodes, navigational descriptions to move to the next location appeared. As an example, a scene in her bedroom is as follows:

> I imagined lying in bed having just woken up. I then put my feet to the left, as usual. Out of the bed, got the shoes, that were right there. Get up. Making my way around the bed, then there is the door. Through the door into the corridor. To the right and immediately to the left again, there is the toilet, something one needs in the morning. [translation from German]

In the verbal statement, retrieval in silence, and trials in the MRI machine, she reported that the last scene of her morning routine was when she is waiting for her husband sitting at the breakfast table in the living room. 7 minutes 40 seconds was the mean of measured time for the three retrieval trials in silence (SD < 10 sec).

3.2 fMRI

The first three principal components of four trials explain over 80% of the entire variance in the partial correlations for each chosen center in the DMN. Criteria for selecting a principal component from a trial were as follows: we computed angles between the first three principal components of the partial correlation of a center from the three AEMR trials one by one, i.e. $\theta_{AB}(i,j)$ for A,B = 1,2,3 and i,j = 1,2,3 is the angle between the ith and jth principal components of a trial A and a trial B respectively $\theta_{AB}(i,j) = (PC_A(i),PC_B(j))$. Then we chose $PC_A(i)$ having the smallest angle to $PC_B(j)$ for $A \neq B$. For the resting state trial, we chose the principal component having the smallest angle to the chosen principal components of three AEMR trials. When a $PC_A(i)$ has the smallest angle to a chosen principal component of a trial B and $PC_A(j)(i \neq j)$ has the smallest angle to the chosen principal components of another trial, then we chose the principal components having the smaller mean angle between them. The same holds for the choice of a principal component of the resting-state trial. As shown in Table 2, we chose the first principal components of the partial correlations of each center except for the left and right AG and the RSC center cases. Table 3 showed the angles between the chosen principal components. The ratio of the mean angles between the chosen principal components of only the three AEMR trials to that of all four trials including the resting state trial of each center was calculated to assess the similarity between the chosen principal components of a center from the three AEMR trials and that of from a resting state trial (Table 4). The implication of the ratio is as follows: when the mean angle of three principal components from the AEMR trials does

not change after including the angles between them and the chosen principal component of the resting-state trial, the ratio is 1. The chosen principal components of three AEMR trials have higher similarity between them compared to that of the resting-state trial when the ratio is smaller than 1. The smaller the more differences in the chosen principal components of the AEMR trials and the resting-state trail. The chosen principal components of the three AEMR trials have higher similarity to that of the resting-state trial than they do between themselves when the ratio is bigger than 1.

The result, as shown in Table 4, principal components from the partial correlations of the PCC center had the smallest mean angle (13.05 degrees) between the three AEMR trials. In addition, its ratio to the mean angle of four trials (AEMR/+Rest = 0.67) was the smallest compared to the ratios of the cases choosing other centers in the DMN (Table 4). The small angles between the first principal components of three AMER trials indicate that the DMN relatively well preserved the weights of the partial correlations of the PCC to the major principal components for the AMER trials. Furthermore, the ratio between the mean angle from the AEMR trials and the mean angle together with a resting state trial showed the weights have relatively large dissimilarity in the two different mental states. In Figure 3, differences between the mean weights of the partial correlations of the PCC to the chosen principal components of the AEMR trials and that of the resting-state trial are presented. The largest difference in the weights was observed in the weights of the R PHC to the PCC correlations.

The chosen principal components of three AEMR trials with the mPFC center also had a relatively small mean angle (13.91 degrees). However, in contrast to the case of the PCC center, its ratio to the mean angle together with the chosen principal component of the resting-state trial was relatively large (0.88). This result implies that the weights of the chosen principal components were rather similar in both mental states compared to the PCC center case. For the case of the right PHC center, the ratio of the two mean angles is relatively small (0.71). Nevertheless, the mean angle between the chosen principal components of the AEMR trials (23.15 degrees) is almost twice larger as that of the PCC center case. Except for the PCC, the mPFC, and the right PHC center, we could not find other brain regions either having a high similarity between the chosen principal components of the three AEMR trials or having clear dissimilarity between them and that of the resting-state trial.

Figure3: Loadings of the partial correlations of the PCC center

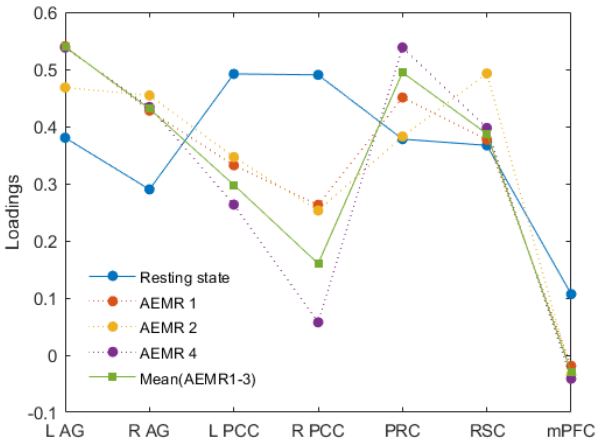


Figure4: Differences in Loadings of the partial correlations of the PCC center

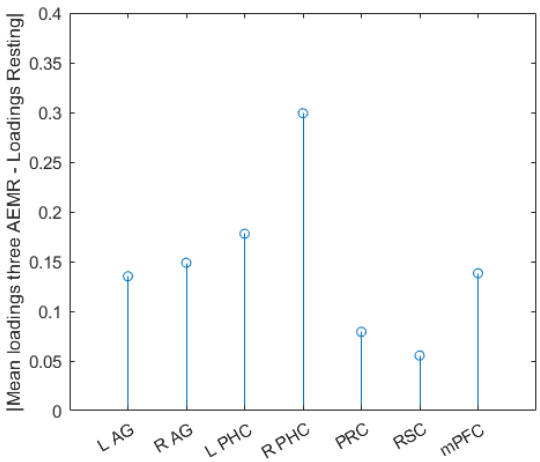


Table 2: Chosen principal components (PC) and the amount of explained variance it explains

PC(%)	PCC	mPFC	L AG	R AG	L PHC	R PHC	PRC	RSC
AEMR1	1(66)	1(61)	1(54)	2(31)	1(43)	1(46)	1(49)	1(39)
AEMR2	1(65)	1(60)	1(50)	1(55)	2(32)	1(59)	2(24)	2(21)
AEMR3	1(51)	1(53)	1(49)	1(50)	1(37)	1(46)	2(25)	1(37)
Resting	1(62)	1(61)	2(28)	1(49)	1(65)	1(64)	1(52)	1(42)

Table 3: Angles between chosen principal components of each fMRI run

(°)	PCC	mPFC	L AG	R AG	L PHC	R PHC	PRC	RSC
AEMR1-AEMR2	8.98	12.88	49.37	33.09	25.00	20.64	35.84	48.50
AEMR2-AEMR3	16.64	15.42	10.71	18.17	49.64	30.75	29.40	52.64
AEMR3-AEMR1	13.54	13.44	44.43	48.14	34.96	18.05	31.09	10.06
Resting-AEMR1	21.80	13.25	58.80	14.39	6.53	25.58	24.83	35.41
Resting-AEMR2	22.17	19.28	13.22	45.06	22.07	44.62	34.42	52.41
Resting-AEMR3	33.58	20.26	16.83	60.55	34.01	55.70	17.73	29.97

Table 4: Mean angles between chosen principal components and the ratio between them

Center	PCC	mPFC	L AG	R AG	L PHC	R PHC	PRC	RSC
AEMR(°)	13.05	13.91	34.84	33.14	36.53	23.15	32.11	37.07
+ Rest(°)	19.45	15.75	32.23	36.57	28.7	32.56	28.88	38.17
Ratio	0.67	0.88	1.08	0.91	1.27	0.71	1.11	0.97

Center: the center region of the DMN, AEMR: the mean angle between principal components of three AEMR trials (Sample size = 3), +Rest: the mean angle between principal components of three AEMR and a resting state trial (Sample size = 6), Ratio: AEMR/+Rest

4 Discussion

In this exploratory study, we aimed to investigate adaptations of the DMN in two mental states, an AEMR state and a resting state, with a new analysis method called one-to-many DFC. For this purpose, we conducted behavioral and fMRI experiments with a blind subject who has an advanced ability to envisage mental imagery. Given the verbal description of the morning routine from the AEMR tasks, we could see that the spatial navigation guided the streaming of episodes mainly. In the behavioral experiment in silence, the subject could retrieve the morning routine with a constant retrieval duration for each trial. These results from behavioral experiments imply that there is regularity in dynamics of the DMN to retrieve the morning routine, which is a distinctive feature of the AEMR state compared to a resting state. In the further fMRI experiment, dynamics of the DMN in the AEMR state and a resting-state were analyzed by one-to-many DFC analysis. The new analysis method measured only the partial correlations of a center in the DMN at once, then computed an orthonormal basis of the variance in the partial correlations using principal component analysis (PCA). The most parallelly aligned principal component among the first three principal components of each trial was chosen to compare their similarity by measuring the angle between them. In summary, we suggested probing the configuration of the DMN in the two mental states by comparing the directions of the major variance in the partial correlations of a center regardless of the intensity of the correlations. In the case of the three AEMR trials, we could show that the major variance of the principal components of the PCC center aligns with each other most closely (13.05 degrees) by comparing it to the results of the other centers (Table 4). It implies that the configuration of the DMN measured at the PCC center was most consistent for the three AEMR trials. At the same time, we computed changes in the mean angle when the chosen principal component of the resting-state trial was included. The result suggested that the principal components of the three AEMR trials align with that of the resting-state trial in the most distinct direction when the PCC is the center of the partial correlations (AEMR/+Rest = 0.67) (Table 4). Previous fMRI studies on the DMN showed that the PCC is the most reliable marker in the adaptation of the DMN with general linear models using self-referential stimuli [21, 77]. In our study, we could prove consistent results by hiring a subject-driven experimental paradigm with a data-driven analysis method [62]. Furthermore, we could demonstrate the relatively consistent configurations of the DMN in the AEMR states and their distinction from that of in a resting state by one-to-many DFC analysis. To sum up the results of our study, we could observe such adaptations of the configuration in the DMN via the partial correlations of the PCC using one-to-many DFC analysis.

Interestingly, the PCC is a well-known functional and structural hub of the brain networks [1, 13, 31, 33, 68]. To date, several studies on brain networks have speculated that hubs in human brains boost efficient communication between brain regions [8, 14, 59, 72]. Following the idea of hubs of brain networks, it is reasonable to expect to see that connections between brain regions in a local brain network adapt themselves via its hubs.

Correspondingly, the results of one-to-many DFC analysis on the DMN demonstrated that the DMN adjusts its configuration via the PCC dependent on the mental states. By contrast, the analysis results of the mPFC center, which is also one of the known functional and structural hubs of the brain, did not demonstrate the distinctive configurations in the two mental states (AEMR/+Rest = 0.88) compared to the PCC center case. We could therefore speculate that the local hub of the DMN mediating adjustment within the network is the PCC, but not the mPFC. Consistent with the implication, the anatomical and structural connections between the PCC and the other brain regions in the DMN are confirmed by cytoarchitecture and diffusion tensor imaging [30, 73].

Besides the results of the PCC center case, the R PHC demonstrated that the configurations of the DMN in the two mental states were relatively discriminated, which were represented by the small ratio between the two mean angles (AEMR/+Rest = 0.71). Unlike the PCC and the mPFC, the R PHC is not one of the known hubs in brain networks. As one would expect, the chosen principal components of three AEMR trials of the R PHC center aligned in less coherent directions (23.15 degrees) compared to that of the PCC (13.05 degrees) and the mPFC (13.91 degrees). The results could be explained by the fact that the weights of the correlation between the PCC and the R PHC varied considerably in the two mental states. As we suggested in Figure 4, the loading of the R PHC to the PCC center varied around twice bigger as that of the other regions. A possible implication of this result is that the functional connectivity between the PCC and the R PHC takes a pivotal role in explaining the difference between the two mental states for the current study. One of the known functions of the PHC is the recognition of local scenes and contextual association [5, 23, 46]. Accordingly, the activity of the PHC might be the key to retrieving coherent mental imagery of scenes, in contrast to a resting state which does not require such a function. Moreover, studies on the lateralization of the medial temporal lobe (MTL) have suggested that the major function of the right MTL is related to spatial navigation [26, 48, 63]. The result from one-to-many DFC analysis together with the verbal statement of our subject, therefore, could be interpreted as follows: spatial navigation in the mental imagery of the subject might drive the substantial adaptation of the functional connectivity between the R PHC and the PCC in the DMN in our study.

In this paper, we aimed to explore the new analysis method thoroughly. We took a single subject having an advanced ability to perform mental imagery tasks, thereby facilitating the validity of the analysis method. However, being limited to a single subject, this study lacks generality. In order to achieve meaningful statistics, we conducted the same experiment with several subjects, which will be reported separately. We would like to close this section by pointing out an interesting possible extension of the present study. The configuration of a local brain network defined by one-to-many DFC analysis focuses only on linear properties of DFC of partial correlations. The nonlinear properties of partial correlations may reveal further instructive information on functional states of a local brain network.

5 Conclusion

It is believed that dynamic adaptation in brain networks reflects the streaming of mental states, which is the nature of humans. One-to-many DFC analysis may offer us an interesting dynamic feature of a local brain network that is preserved in specific mental states. In terms of methodology, it is a simple data-driven analysis method hiring subject-driven mental states. This research has thrown up many questions in need of further investigation, like its application to other known brain networks in various mental states including psychological disorders.

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Disclosure of conflict of interest

None

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