Changes in Functional Connectivity of Resting-state after Motor Imagery Training Detected by Eigenvector Centrality Mapping

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Abstract: - Motor imagery training has been indicated to be effective in motor function rehabilitation and motor skill learning. The neural mechanism underlying motor training has attracted increased neuroimaging explorations. Related neuroimaging studies demonstrated that resting-state can offer the possibility to examine the neural mechanism of motor execution training. However, motor imagery training, as another part of motor training, has been few investigated. To address this issue, eigenvector centrality mapping (ECM) method was applied to explore functional connectivity of resting-state in motor imagery training. As a data-driven analysis method, although ECM can assess the computational measurement of eigenvector centrality for capturing intrinsic neural architecture on a voxel-wise level without any prior assumptions, it is still limited in application for making pseudo enhancement in some nodes or zero centrality in all nodes. In this study, we proposed an improved ECM by adding threshold, dispersion coefficient, weighted coefficient and the initial parameters referring to Google Webpage search ranking algorithm, and applied the proposed ECM to functional connectivity measure of resting-state before and after motor imagery training. The proposed ECM showed the advantage of automatic discharge weak links and the enhancement in node ordering resolution comparing with the original ECM. The results from voxel-based comparison of the centrality between the resting-state after and before motor imagery training revealed that the significantly increased eigenvector centrality was detected in the precuneus and medial frontal gyrus for the experimental group while no significant alterations were found for the control group after training. These alterations may be related to the spatial information integration and inner state modulation of motor imagery training, and further provided new insights into the understanding of the neural mechanism underlying motor imagery training.

Key-Words: - motor imagery; motor training; resting-state; eigenvector centrality mapping; PageRank algorithm.

1 Introduction

Motor training, including motor execution and motor imagery training, has been indicated to be effective in mental disorders rehabilitation and motor skill learning [1,2]. Motor imagery training, in particular, brought about new prospect for rehabilitation of those who had completely lost their motor functions. Although many research confirmed that cortical activities and even the interactions between brain areas can be altered by motor training [3,4], most of them were based on motor execution. The neural imaging research on motor imagery training is still limited and the neural mechanism of motor training is open to further exploration.

Recently, many researchers have put forward that resting-state may contain rich information on the neural mechanism of motor execution training and may enable a more complete detection of a specific neural system [5,6]. Many analytical measures were suggested by research on resting-state to estimate functional connectivity, such as correlation, graph theory and so on. These metrics usually require certain priori knowledge to localize regions of interest and choose an appropriate analytical model. Eigenvector Centrality Mapping (ECM) is a data-driven measure, which can assess the significance of a specific brain area in functional connectivity without any priori assumption [7]. Using this method, Taubert et al. studied the impact of motor execution training on resting-state functional networks [8].

Although the data-driven ECM can capture intrinsic neural architecture on a voxel-wise level through the computation of eigenvector centrality, its application is still confined to fMRI data. Firstly, ECM takes every voxel as a network node and generates a fully connected network with a tremendous topological structure. Then, the noise in fMRI images may interfere the similarity between nodes and affect the network topology, thus leading to the emergence of weak connections. Secondly, while calculating the centrality of a given node, ECM takes into account all weighted centrality of its neighbor nodes, which may result in the pseudo enhancement of this node [9]. Moreover, the weighted centrality may also lead to zero centrality in all nodes after iterations [10].

In this study, inspired by Google's Page Rank algorithm, we proposed an improved ECM by introducing a threshold, a dispersion coefficient, a weighted coefficient and initial parameters and applied the proposed ECM to functional connectivity measure of resting-state before and after motor imagery training. Compared with standard ECM, the proposed ECM has distinct advantages in automatically discharging weak connections and promoting the discrimination in centrality of different nodes. We got some meaningful results that may provide new insights into the neural mechanism underlying motor imagery training.

2 Methods and materials

2.1 Standard Eigenvector Centrality Mapping

Eigenvector centrality mapping (ECM) specifies an eigenvector centrality value to each voxel in the brain. As a result, a voxel has a higher value if it is more strongly correlated with other voxels. The ECM analysis includes four steps. First, a whole brain mask is defined according to a prior anatomical automatic labeling (AAL) atlas which contains 90 areas (40,743 voxels in total). Second, time series are extracted from each voxel in the defined mask. Linear correlation, which acts as a metric of functional connectivity, is calculated between any pair of nodes as follows:

$$r_{ij} = \frac{\sum_{t=1}^{T}\left[x_i(t)-\overline{x_i}\right]\left[x_j(t)-\overline{x_j}\right]}{\sqrt{\sum_{t=1}^{T}\left[x_i(t)-\overline{x_i}\right]^2}\sqrt{\sum_{t=1}^{T}\left[x_j(t)-\overline{x_j}\right]^2}} \quad (1)$$

Where $x_i(t)$, $x_j(t)$ (t = 1,..., T = 200) represent the time series of voxel i and j respectively. Then we can get a similarity matrix A and we replace r_{ij} in A with r_{ij} + 1 to make sure that all values in A are positive [7]. After that, using the following formula, the eigenvector centrality value of voxel i is defined as the i-th entry in the normalized eigenvector x that belongs to the largest eigenvalue λ of the similarity matrix A.

$$Ax=\lambda x \iff x=\frac{1}{\lambda}Ax, x_i=\mu\sum_{j=1}^{n}a_{ij}x_j \quad (2)$$

Where $\mu = 1/\lambda$, and a_{ij} represents the element in row i and column j of matrix A.

2.2 The choice of network threshold

In order to remove weak connections，which indicate random noise or indirect connections, we introduced a threshold to A so as to filter connections [11]. First of all, we sorted the z-scores of correlation coefficients in a descending order and set the threshold z_T to a significance level of 5% of the sorted z-scores as follows:

$$z_T = \max\left\{ i : P_i \le \frac{i\times 0.05}{n} / \left(\sum_{j=1}^{n} 1/j\right)\right\} \quad (3)$$

Then z_T was transformed to its corresponding correlation coefficient threshold r_T:

$$r_T = \frac{e^{2z_T}-1}{e^{2z_T}+1} \quad (4)$$

All connections with an absolute correlation coefficient lower than r_T were taken as weak connections and were removed from further analysis.

2.3 The optimization of algorithm parameters

Inspired by Google's PageRank algorithm, we introduced the initial parameter β, dispersion coefficient k, and weighted coefficient α [12-14] based on formula (2):

$$x_i = \alpha\sum_{j=1}^{n}a_{ij}\frac{x_j}{k_j}+\beta \quad (5)$$

Where n is the number of nodes in the network and α denotes the dependence of neighbor nodes on a given node ranging from 0 to 1. β denotes the initial value of each node before iteration. The ratio between α and β reflects how much a node's significance is influenced by its neighbor nodes. If α=0, the node's significance is completely independent from its neighbors, and if β=0，the node's significance is largely influenced by its neighbors. k denotes the dispersion value of all the neighbors' importance to the given node and is often chosen according to the number of connections of each node [12].

Similar to Google's PageRank algorithm, we set α=0.85 and β=1-α=0.15. Given the value following "+", 0.15 is supposed to be a large value, which determines to a large extent the centrality values of independent nodes in the network. However, these independent nodes usually turn out to be the least important nodes in the network, so we set $\beta=(1-\alpha)/n$.

To alleviate the excessive impact of the neighbor nodes on a given node, we assigned the centrality value of the given node to all its connected neighbor nodes evenly according to the following formula:

$$k = \sum_{(j,k)\in E} a_{jk} \tag{6}$$

Where E denotes the set of all the nodes in the network.

2.3 Motor Imagery Training Experiment and Data Preprocessing

Fourteen right hand-dominant subjects (seven males, mean age: 22±2 years) participated in the training, and another twelve right hand-dominant subjects (five males, mean age: 24±2 years) were recruited as a control group. Participants with histories of neurological disorders, psychiatric disorders, experience with typewriters, or any experience learning to play musical instruments were excluded. All participants provided written consent according to the guidelines set by the MRI Center of Beijing Normal University.

The experiment procedure included a pre-resting-state session, two pre-task sessions, a motor imagery training period, a post- resting-state session and two post-task sessions. Here, only the resting-state data was examined. In each 10-min resting-state session, subjects were instructed to keep their eyes closed, relax their mind, and remain motionless as much as possible. In the training period, all participants were instructed that from their index to little finger, each of the four fingers of their right hand represented a single digit number: one, two, three, and four. Fourteen motor imagery practice sessions were employed over 14 consecutive days to make sure the sufficient training. Each training session consisted of two 15-min sections, metronome-pacing and self-pacing respectively. In each section, participants were instructed to imagine tapping sequence 4–2–3–1–3–4–2 with their right hand fingers repeatedly as fast as the pace of the metronome or the pace controlled by themselves for 30 seconds with an interval of 30-s rest. The training period were only performed in the experimental group while participants did not attend any training during the 14 days in the control group.

Brain scans were performed at the MRI Center of Beijing Normal University using a 3.0-T Siemens whole-body MRI scanner. A single-shot T2*-weighted gradient-echo, EPI sequence was used for the functional imaging acquisition, with the parameters: TR/TE/flip angle=3000ms/40ms/90°, the acquisition matrix was 64×64, the field of view (FOV) was 240 mm and slice thickness=5 mm with no inter-slice gap. 32 axial slices parallel to the AC-PC line were obtained in an interleaved order to cover the whole cerebrum and cerebellum.

The functional images of both groups were first realigned, spatially normalization, re-sliced to 3×3×4 mm voxels and smoothed with a 8×8×8 full-width at half maximum (FWHM) Gaussian kernel by SPM8 (http://www.fil.ion.ucl.ac.uk/spm).

3 Results

3.1 Simulations

To verify the effectiveness of the proposed ECM, we used several simulated network topological graphs with different structures (Fig. 1) comparing with the standard ECM. The centrality values of each node are shown in Table 1 and Table 2.

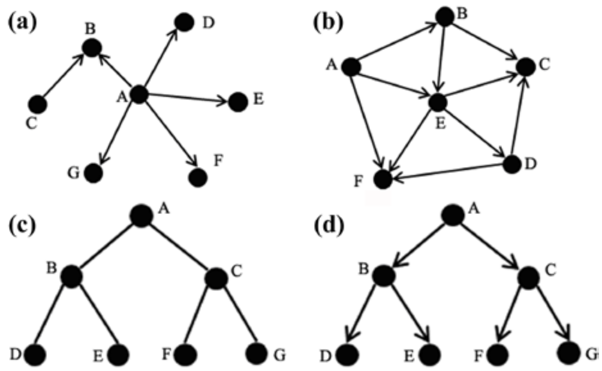

Fig. 1 The simulated network topological graph.

As shown in Table 1, the centrality value of node B in network (a) is higher than that of node A due to the fact that the standard algorithm takes into account all the neighbor nodes' influence while calculating the centrality value of a given node. Apparently, node A controls other nodes and should be the center of network (a). The proposed ECM confirmed this result. In network (b), suppose the centrality value of node A is zero， then its contribution to its three neighbors should also be zero. Since the node at the top is only influenced by node A, its centrality value also should be zero. We can conclude that after several iterations, the centrality values of all the nodes in the network should be zero. Distinctly, this can be avoided by the proposed ECM due to the introduction of initial parameters.

Table 2 shows that the discrimination of centrality values is different between the standard and proposed ECM. The centrality values of the proposed ECM present a much more prominent hierarchical structure to distinguish the significance of different nodes by increasing the difference between centrality values of nodes belonging to different level. Nodes of less significance are marked with lower centrality values and nodes of more significance are marked with higher centrality values. This reveals that the proposed ECM can highlight the significance of each node in the network in a much more clear way without changing the original significance rank.

3.2 ECM of Resting-state during Motor Imagery Training

After preprocessing, the data was analyzed using the proposed ECM. For each subject in the two resting scans, an ECM containing the eigenvector centrality value of each voxel in the mask was obtained. At last, a paired t-test was performed between the ECMs of pre- and post- resting scan. At the statistical analysis level, a voxel-cluster threshold correction was used to control the Type I error rate in the whole-brain statistics, yielding an overall corrected alpha rate of $p<0.05$. The cluster-level inference was performed within SPM8.

Fig. 2 shows the group averages of eigenvector centrality maps. After motor imagery training, the significantly increased eigenvector centrality was detected in the precuneus and medial frontal gyrus (MFG) for the experimental group while no significant alterations were found for the control group (Fig. 3 and Table 3).

Table 1. Centrality values of nodes in network (a) and network (b) of Fig. 1 calculated by the standard and improved ECM.

order	**(a)**				**(b)**		
	standard	**node**	**improved**	**node**	**standard**	**improved**	**node**
1	0.513612	B	0.696271	A	0	0.798813	A
2	0.296226	A	0.683440	B	0	0.402367	E
3	0.038032	C	0.098099	C	0	0.375417	B
4	0.038032	D	0.098099	D	0	0.189100	D
5	0.038032	E	0.098099	E	0	0.107941	C
6	0.038032	F	0.098099	F	0	0.107941	F
7	0.038032	G	0.098099	G	-	-	-

Table 2. Centrality values of nodes in network (c) and network (d) of Fig. 1 calculated by the standard and improved ECM.

(c)				**(d)**			
order	**standard**	**improved**	**node**	**order**	**standard**	**improved**	**node**
1	0.4238	0.5837	B	**1**	0.4428	0.8623	A
1	0.4238	0.5837	C	**2**	0.4209	0.3294	B
2	0.3960	0.3851	A	**2**	0.4209	0.3294	C
3	0.3478	0.2063	D	**3**	0.3353	0.0993	D
3	0.3478	0.2063	E	**3**	0.3353	0.0993	E
3	0.3478	0.2063	F	**3**	0.3353	0.0993	F
3	0.3478	0.2063	G	**3**	0.3353	0.0993	G

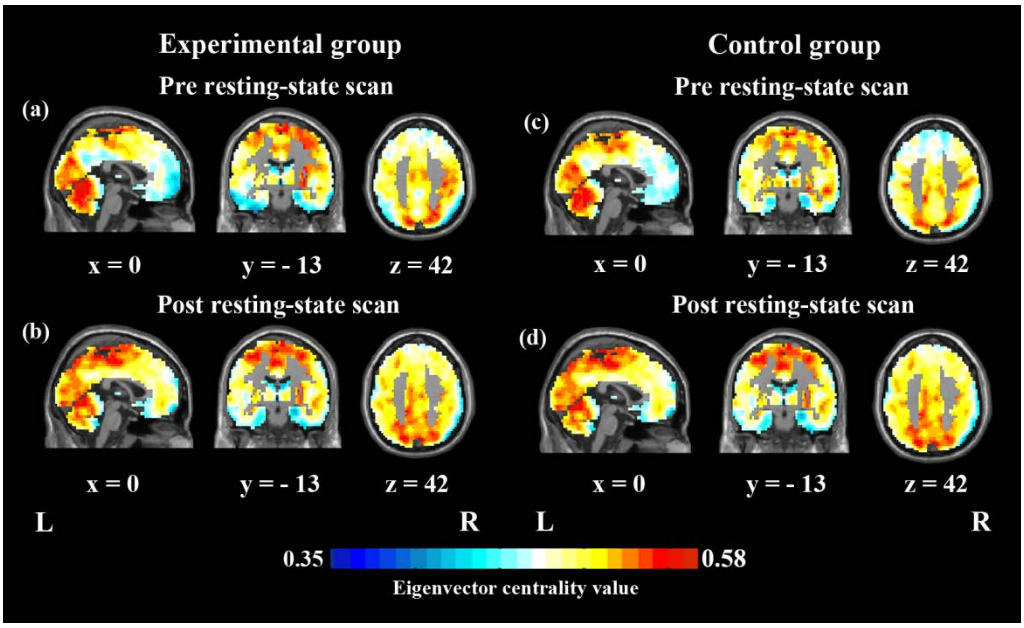

Fig. 2 Group averages of eigenvector centrality maps. (a) pre-resting scan, experimental group; (b) post-resting scan, experimental group; (c) pre-resting scan, control group; (d) post-resting scan, control group.

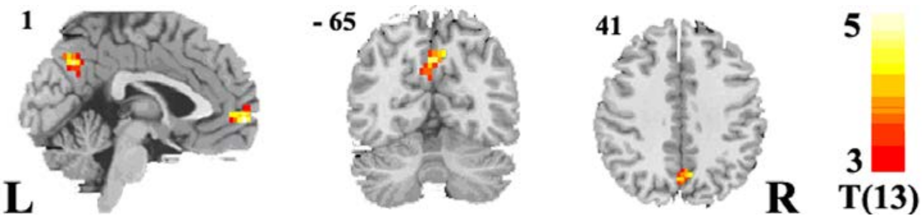

Fig. 3 Statistical parametric map of eigenvector centrality enhancement in experimental group induced by motor imagery learning ($p<0.05$, cluster size>41, FDR (false discovery rate) correction).

Table 3. Brain regions where eigenvector centrality significantly increased in the resting-state after motor imagery training in the experimental group.

Region	Brodmann's Area	MNI coordinates x	y	z	t_{max}
Left precuneus	BA 7	-3	-64	42	4.12
Left medial frontal gyrus	BA 10	0	59	-2	4.38

4 Discussion and Conclusion

Aiming at solving the pseudo enhancement and the zero centrality in ECM, we referred to Google's PageRank algorithm and improved ECM through introducing a threshold, a dispersion coefficient, a weighted coefficient and initial parameters. The proposed algorithm has prominent advantages in removing weak connections automatically and improving the discrimination in centrality of different nodes. We applied the proposed ECM to the resting-state in motor imagery training and the results revealed that the eigenvector centrality of two brain regions, including the precuneus and medial frontal gyrus (MFG), were significantly increased by the motor imagery training.

Previous studies have suggested that the MFG may be involved in inner state modulation and motor planning, as well as complex non-motor tasks such as decision making, discrimination, computation, and reasoning [15,16]. The MFG was implied to be associated with the ability to reflect on one's own mental states and self referential processing such as mediate less-deliberate, emotion-driven influences on action selection [17, 18]. It was also suggested to be important in allowing subject to guide actions by internal or overarching plans so as to achieve an optimal behavior performance [15]. Thus, we proposed that the changes in MFG may be the result of the modulation of subjects' inner state to get an optimal behavior and decisions about motor plans.

The role of precunues in motor imagery has been suggested that it could be activated when subjects learned sequences of finger movements, indicating that precuneus may be related to spatial motor sequence information integration and retrieval [19]. A Magnetoencephalography (MEG) study confirmed that the precuneus may involve in retrieval of spatial information and/or setting up spatial attributes for motor imagery [20]. Therefore, the alteration of precuneus in the current study may due to spatial information processing and retrieval.

In summary, the results observed in this study confirmed the effectiveness of improved ECM and the alterations in the resting-state induced by motor imagery training, extending the understanding of the neural mechanism underlying motor imagery training.

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References:
[1] N. Sharma, V. M. Pomeroy, and J. Baron, Motor Imagery A Backdoor to the Motor System After Stroke, *Stroke*, Vol. 37, 2006, pp. 1941-1952.
[2] C. J. Olsson, B. Jonsson and L. Nyberg, Learning by doing and learning by thinking: an fMRI study of combining motor and mental training, *Frontiers in Human Neuroscience*, Vol.2, 2008, pp. 1-7.
[3] M. G. Lacourse, E. L. R. Orr, S. C. Cramer and M. J. Cohen, Brain activation during execution and motor imagery of novel and skilled sequential hand movements, *Neuroimage*, Vol.27, 2005, pp. 505-519.
[4] L. Ma, B. Wang, S. Narayana, E. Hazeltine, X. Chen, D. A. Robin, P. T. Fox and J. Xiong, Changes in regional activity are accompanied with changes in inter-regional connectivity during 4-weeks motor learning, *Brain research*, Vol.1318, 2010, pp. 64-76.
[5] J. Xiong, L. Ma, B. Wang, S. Narayana, E. P. Duff, G. F. Egan and P.T. Fox, Long-term motor training induced changes in regional cerebral blood flow in both task and resting states, *Neuroimage*, Vol.45, 2009, pp. 75-82.
[6] L. Ma, S. Narayana, D. A. Robin, P. T. Fox and J. Xiong, Changes occur in resting state network of motor system during 4weeks of motor skill learning, *NeuroImage*, Vol.58, 2011, pp. 226-233.
[7] G. Lohmann, D. S. Margulies, A. Horstmann, B. Pleger, J. Lepsien, D. Goldhahn, H. Schloegl, M. Stumvoll, A. Villringer and R. Turner, Eigenvector centrality mapping for analyzing connectivity patterns in fMRI data of the human brain, *PLoS One*, Vol.5, 2010, e10232.
[8] M. Taubert, G. Lohmann, D. S. Margulies, A. Villringer and P. Ragert, Long-term effects of motor training on resting-state networks and underlying brain structure, *Neuroimage*, Vol.57, 2011, pp. 1492-1498.
[9] P. Bonacich, Some unique properties of eigenvector centrality, *Social Networks*, Vol.29, 2007, pp. 555-564.
[10] B. Ruhnau, Eigenvector-centrality: a node-centrality, *Social networks*, Vol.22, 2000, pp. 357-365.
[11] Q. K. Telesford, S. L. Simpson, J. H. Burdette, S. Hayasaka, P. J. Laurienti, The brain as a complex system: using network science as a tool for understanding the brain, *Brain connectivity*, Vol.1, 2011, pp. 295-308.
[12] T. H. Haveliwala, Efficient computation of PageRank, Stanford Univ, *Technical Report*, 1999.
[13] R. S. Sinha and R. Mihalcea, Unsupervised graph-based word sense disambiguation using measures of word semantic similarity, *Proceeding of International Conference on Semantic Computing*, 2007, pp. 363-369.
[14] R. Mihalcea, Graph-based ranking algorithms for sentence extraction applied to text summarization, *Proceedings of Association for Computational Linguistics*, 2004, 20.
[15] M. A. Roca, T. Torralva, E. Gleichgerrcht, A. Woolgar, R. Thompson, J. Duncan and F. Manes, The role of area 10 (BA10) in human multitasking and in social cognition: a lesion study, *Neuropsychologia*, Vol.49, 2011, pp.3525-3531.
[16] A. Talati, J. Hirsch, Functional specialization within the medial frontal gyrus for perceptual go/no-go decisions based on? "what", "when", and "where" related information: an fMRI study, *Journal of Cognitive Neuroscience* 17, 2005, pp. 981-993.
[17] K. R. Ridderinkhof, W. P. van den Wildenberg, S. J. Segalowitz and C. S. Carter, Neurocognitive mechanisms of cognitive control: the role of prefrontal cortex in action

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selection, response inhibition, performance monitoring, and reward-based learning, *Brain and Cognition*, Vol.56, 2004, pp. 129-140.

[18] M. K. Johnson, C. L. Raye, K. J. Mitchell, S. R. Touryan, E. J. Greene and Nolen-Hoeksema, Dissociating medial frontal and posterior cingulate activity during self-reflection, *Social Cognitive and Affective Neuroscience*, Vol.1, 2006, pp. 56-64.

[19] K. Sakai, O. Hikosaka, S. Miyauchi, R. Takino, Y. Sasaki and B. Pütz, Transition of brain activation from frontal to parietal areas in visuomotor sequence learning, *The Journal of Neuroscience*, Vol.18, 1998, pp. 1827-1840.

[20] T. Ogiso, K. Kobayashi and M. Sugishita, The precuneus in motor imagery: a magneto-encephalographic study, *Neuroreport*, Vol.11, 2000, pp. 1345-1349.