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Cortical networks of hemianopia stroke patients: A graph theoretical analysis of EEG signals at resting state

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***Abstract*—Visual cortical stroke patients may have hemianopia symptom, which affects a number of visual functions. Most studies on hemianopia stroke have mainly focused on cortical activation during visual stimulation, leaving the pattern of functional connectivity between different brain regions uncovered yet. In the present study, we investigate the resting neural networks of hemianopia stroke patients by graph theoretical analysis of functional brain networks constructed with phase synchronization indexes of multichannel electroencephalography (EEG) signals. Our results showed that although the global network topological metrics, i.e., weighted clustering coefficient and characteristic path length of patients and healthy controls are comparable, the left primary visual cortex of patients tend to be less active than that of age-matched healthy subjects. However, hemianopia patients showed greater activation in the ipsilesional (left) temporopolar and orbit frontal areas and the contralesional (right) associative visual cortex. These results may offer new insight into neural substrates of the hemianopia stroke, and the further study of neural plasticity and brain reorganization after hemianopia.**

I. Introduction

Stroke is a worldwide disease with high mortality and disability. Approximately one third of stroke survivors may suffer homonymous hemianopia according to a study of 682,000 incidents of stroke in the United States in 1995 [1]. Hemianopia is a kind of anopsia that can result in decreased vision or blindness in one or both eyes. Ischemic stroke may damage the visual pathway, resulting in vision loss, blurry vision and visual neglect to some extent. Infarction in one hemisphere can result in vision loss on the opposite side. The hemianopia is commonly attributed to lesions in occipital lobe. Some hemianopia stroke patients may have visual neglect and suffer significant cognitive deficit if not properly treated, resulting in difficulty in their daily life like reading, driving or walking [2, 3].

Currently, the most commonly used therapeutics is to improve the patients' performance of visual function with the guidance of visual stimuli in their seeing and non-seeing visual field. Cortical activations of hemianopia patients under visual stimuli have been studied with functional magnetic resonance imaging (fMRI). Nelles found an increased activation in the left extra striate cortex of ipsilateral hemisphere after blind field had been stimulated several times, and more activations in the right extra striate cortex of contralateral hemisphere after stimulation in a long period [4, 5]. However, brain activity of hemianopia stroke patients at resting state remains unknown.

Functional neural connectivity provides an effective method to analyze the spatiotemporal interactions in brain, which can be examined at different scales, e.g., the connectivity to a single brain region, the organization of connectivity among multiple brain regions in a local cortical area, or the connection across the global cortex. The pattern of connectivity in a local brain region may reflect the specialized function of that local cortex, while the global organization of connectivity among different brain regions could characterize the functional integration of different brain regions [6-11]. Various methods, such as partial directed coherence (PDC) [12], phase synchronization index (PSI) [12, 13], and correlation coefficient, have been applied to the quantification of neural connectivity of different brain regions based on multi-dimensional neural signals including EEG and fMRI data. Among these methods, PSI, which could quantify the interaction between rhythms between neural waves, but neglect the effect of instantaneous amplitude, has been proved effective in inferring functional connectivity between neural oscillations [12].

In this study, we used PS to investigate the resting neural connectivity of the hemianopia stroke patients with multichannel scalp EEG and investigated the underlying neural network correlates of the hemianopia stroke based on graph theoretical analysis.

II. Materials and Methods

A. Subjects

Seven stroke patients with hemianopia (age=65.7±14.2 yrs, from 46 to 83 yrs, male) were recruited from the Neurology Department of The Fifth People's Hospital of Shanghai, Shanghai, China. All patients were diagnosed with hemianopia stroke according to visual threshold test and MRI/CT scanning. The lesion sites were located in the occipital lobe, parietal lobe or temporal lobe in the left hemisphere. In order to compare the results with that of normal subjects, we also recruited 7 healthy control subjects with matched gender and age (age=66.7±10.4 yrs, from 52 to 78 yrs, male). All control subjects had reported no history of

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neurological or psychological diseases. The experimental protocols were approved by the ethic committee of the Fifth People's Hospital of Shanghai.

B. EEG recording

EEG data was recorded with 30 scalp electrodes (Fp1, Fp2, F3, F4, F7, F8, Fz, FC1, FC2, FC5, FC6, C3, C4, T7, T8, CP1, CP2, CP5, CP6, Cz, TP9, TP10, P3, P4, P7, P8, Pz, O1, O2, Oz) placed on an EasyCap^{TM} connected to BrainAmp (Brain Product GmbH, Germany) at 1000Hz. Horizontal and vertical electrooculograms were recorded for rejecting eye movements and blinks off-line. All subjects were seated in relaxation, keeping awake with eye closed throughout the EEG recording for 2 minutes. EEG signals were filtered and then referenced to global average. Alpha band (8-12Hz) was selected for the phase synchronization analysis since alpha power manifesting in surface EEG was confirmed as an index of little or no ongoing functional activity [14].

C. Phase synchronization analysis

Given an EEG signal $s(t)$, its analytic signal is defined as

$$z(t) = s(t) + js_{\mathrm{H}}(t) = A(t)^{if(t)}, \tag{1}$$

where

$$s_{\mathrm{H}}(t) = \frac{1}{\pi}\mathrm{P}.V.\int_{-\infty}^{\infty}\frac{s(\tau)}{t-\tau}d\tau, \tag{2}$$

is the Hilbert transform of $s(t)$. $A(t)$ and $\phi(t) = \arg[z(t)] = \arctan\frac{s_{\mathrm{H}}(t)}{s(t)}$ are the instantaneous amplitude (IA) and instantaneous phase (IP) of signal $s(t)$, respectively, and P.*V*. means that the integral is taken in the sense of Cauchy principal value. Let $\phi_1(t)$ and $\phi_2(t)$ denote the cumulative IPs of two coupled systems respectively. Then the coupled systems are said to be in $l:m$ PS when the inequality $\left|l\phi_1(t) - m\phi_2(t)\right| < const.$ hold, where l and m are positive integers [12, 15].

Mean phase coherence (MPC) of IP difference is commonly used as PSI. With the estimated sequences of IP difference $\{\hat{\varphi}(n)\}_{n=0}^{N-1}$ [i.e., $\hat{\varphi}(n) = \phi_1(n) - \phi_2(n)$], the MPC-based PSI can be estimated via

$$\lambda = \frac{1}{N}\left\{\left[\sum_{n=0}^{N-1}\cos\hat{\varphi}(n)\right]^2 + \left[\sum_{n=0}^{N-1}\sin\hat{\varphi}(n)\right]^2\right\}^{\frac{1}{2}}, \tag{3}$$

where N is the number of samples in $\{s(n)\}_{n=0}^{N-1}$. Note that the value of λ is among [0, 1] with $\lambda = 1$ implying perfect PS and $\lambda = 0$ indicating no PS at all.

D. Network metrics

With PSIs estimated for each pair of EEG signals in alpha band, functional brain network for each subject are constructed by thresholding the PSIs. That is, each EEG channel is defined as one node in brain network, and the pairs of nodes with PSIs greater than a preset threshold are linked by edges, and the values of the PSI are set as the weights of the edges respectively. For a weighted network, the node strength of node n_i is defined as

$$s_i = \sum_j w_{ij}, \tag{4}$$

where w_{ij} is the weight of edge linking node n_i and n_j [16].

The weighted clustering coefficient of node n_i is defined as

$$C_i^w = \frac{1}{s_i(k_i - 1)}\sum_{(j,k)}\frac{w_{ij} + w_{ik}}{2}a_{ij}a_{ik}a_{jk}, \tag{5}$$

where k_i represents the number of nodes connecting to the node n_i, and a_{ij} is the element of adjacency matrix with $a_{ij} = 1$ if edge exists between node n_i and n_j and $a_{ij} = 0$ otherwise. The clustering coefficient of the whole network is defined as the average of the clustering coefficients of all nodes in networks, and can characterize the pattern of connectivity in local sub-networks in general.

The weighted characteristic path length of the whole network is defined as [17]

$$L^w = \frac{N(N-1)}{\sum_{i=1}^{N}\sum_{j\neq i}^{N} 1/I_{ij}^w}, \tag{6}$$

where I_{ij}^w is the weighted characteristic path length between node n_i and n_j. This metric is used to quantify the global brain network.

III. Results

For each subject, we selected a segment of EEG signals (1 sec), and constructed brain network based on PSIs estimated from all pairs of alpha waves of EEG signals. We further examined the network metrics for cases of the brain cortical networks containing 90, 105, 120, 135, 150, 165, and 180 edges. For each case of brain network with different number of edges, the weighted clustering coefficient of network of the hemianopia stroke patients appears to be overall greater than that of normal controls (Fig. 1). The weighted characteristic path length showed an opposite trend (Fig.2), i.e. the hemianopia stroke patients had overall smaller weighted characteristic path length than the controls. Nevertheless, both weighted clustering coefficient and weighted characteristic path length didn't show significant difference between two groups.

The scatter plot of the weighted clustering coefficients with respect to the weighted characteristic path lengths (Fig. 3) was drawn for a typical network with 165 edges for all patients and controls. Fig.3 didn't show hemianopia-specific pattern either.

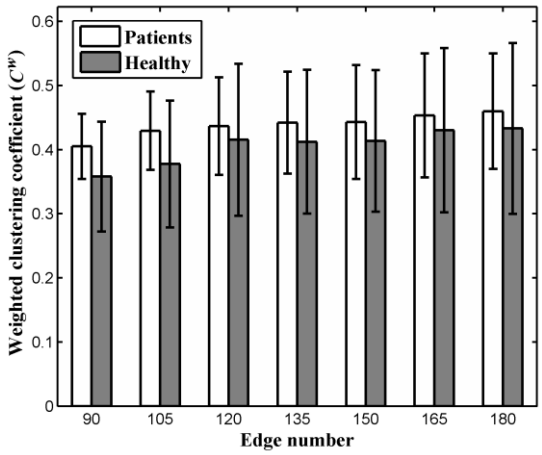

Figure 1. Weighted clustering coefficient (mean±std) of networks for the hemianopia stroke patients and healthy controls. The mean value of this metric of the patients is overall larger than that of the healthy controls, nevertheless, difference between the two groups for each number of edges are under a statistical significance level.

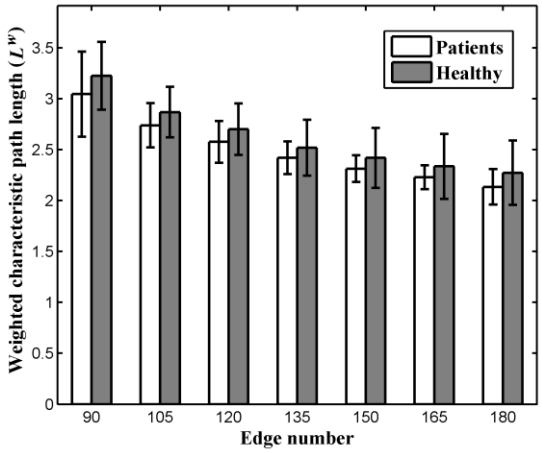

Figure 2. Weighted characteristic path length (mean±std) of the hemianopia stroke patients and healthy controls. The mean value of this metric of the patients is overall smaller than that of the healthy controls, nevertheless, difference between the two groups for each number of edges are under a statistical significance level.

Although there is no difference between the two groups in these two global metrics for the PS network, we further compare the patterns of connectivity in local sub-networks. The result reveals that, at resting state, the hemianopia stroke patients tend to have less connections than the healthy controls with the left primary visual cortex, with significant difference at loci P7 (P=0.021) (Fig. 4, 5). In contrast, the hemianopia stroke patients show significantly greater connectivity at the left temporopolar area, orbit frontal area and the right associative visual cortex at loci T7, Pz, P4, and T8 (all P<0.05) (Fig. 4, 5). These results imply a reorganization of different brain areas after hemianopia stroke, although there is no significant difference between the hemianopia stroke patients and the normal controls globally.

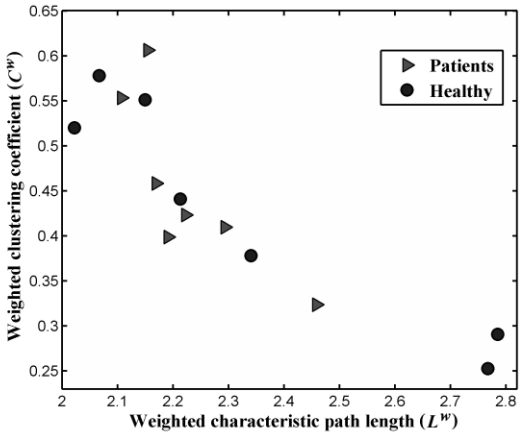

Figure 3. Scatter plot of the weighted clustering coefficient with respect to the weighted characteristic path length for each subject. Each symbol is corresponding to one subject (round: healthy subject;triangle: stroke patient).

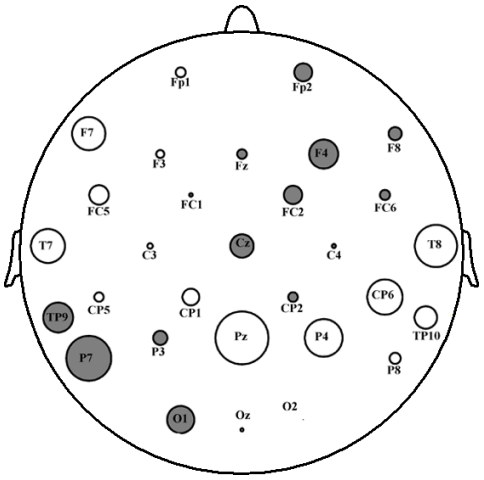

Figure 4. The Difference of the average node strength (across subjects) between the stroke patients and the healthy controls. The radius of each node represents the value of the difference. The blank nodes designate that the node strength of patients is bigger than that of healthy controls, while the grey nodes imply that the node strength of healthy controls is bigger than that of patients.

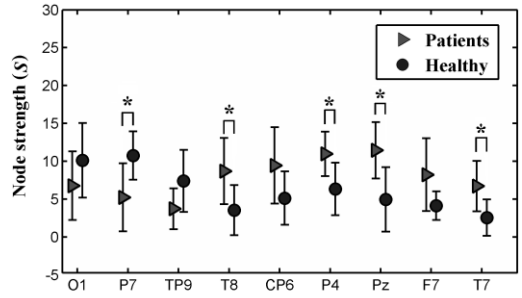

Figure 5. Statistical analysis of the average node strength of the hemianopia stroke patients and healthy controls on 9 selected loci, showing that the stroke injury resulted in significantly lower node strength at the left primary visual cortex, but significantly higher node strength at the right associative visual cortex and the temporopolar area.

IV. DISCUSSION

In this study, we investigated the connectivity of resting cortical network of hemianopia stroke patients with ischemic injury in their left hemisphere. PS analysis was applied to construct the cortical network using alpha band EEG. Our results didn't show that there was difference at weighted clustering coefficient and characteristic path length of global networks between the hemianopia stroke patients and healthy subjects. However, the connectivity at some nodes in local sub-networks showed significant hemianopia specificity. Hypoactivation in the left primary visual cortex was found in the hemianopia stroke patients, indicating that the connectivity in this cortex has been injured by the ischemic stroke. In contrast, significantly enhanced activation in the right visual cortex of the hemianopia patients reflected a contralesional compensation of the local network connectivity in the hemianopia patients after the left hemispheric stroke.

There have been researches regarding the cortical activations under functional stimulation in hemianopia patients. Nelles's study on poststroke hemianopia patients revealed that during the stimulation of hemianopic side, significantly enhanced neural activation could be detected in the unaffected associative visual cortex (Brodmann area 19), while the primary visual cortex was not evidently activated in either hemisphere [5]. Raninen and colleagues found the strongest activation in the posterior superior temporal area of affected hemisphere after 5 months of flicker stimulation [18].

The results at resting state in this study also found accordant activation with weaker neural connectivity in the left primary visual cortex and stronger connectivity in the contralesional associative visual cortex and the left temporopolar area for the hemianopia stroke patients.

These results might imply the damage of the visual information pathway in patients' visual cortex due to the ischemic stroke, and as compensation, more contralesional counterpart were involved. In particular, those adjacent unaffected associative visual cortex are activated for locating visual stimuli and other spatial logic. Meanwhile, the ipsilesional associative visual cortex of hemianopia patients were building more connections with temporal lobe instead of the damage area, indicating a more active ipsilesional temporopolar area. Therefore, the neural networks for visual information processing system in hemianopia patients might involve two subsystems, i.e. (i) the contralesional dorsal network, which projected the visual stimuli to the associative visual cortex, and (ii) the ipsilesional temporal network, which was likely to be related to the cross-modal compensation. A possible neural network substrate for enhanced neural activation in the temporopolar area in hemianopia stroke patients might result from enhanced connections between the occipital lobe and the temporal lobe as the cross-modal plasticity [19].

This preliminary study only included a small number of the hemianopia patients all with left-hemispheric stroke. Further study on the detail neural network needs a larger gender-balanced database to have a more reliable statistical analysis.

The neural network study on hemianopia could help the development of early therapeutic interventions and understand the visual cortical reorganization after the hemianopic stroke.

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