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Influences of Bilateral Ischemic Stroke on the Cortical Synchronization

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***Abstract*— Stroke has been one of the leading causes of mortality and long-term morbidity around the world. Describing the cortical synchrony has been useful in understanding of central nervous system disorders after brain injury. In this paper, we investigated the large scale cortical phase synchronization derived from multichannel electroencephalogram (EEG) recordings of bilateral ischemic stroke patients($n = 9$). Compared with the results from the age- and gender-matched control subjects ($n = 8$), stroke patients showed 1) there were not significant changes of the intra-hemispheric synchronization after the bilateral stroke; and however, 2) both global and inter-hemispheric synchronization are vulnerable to the ischemic injury. Our preliminary results indicated that synchrony analysis of the spontaneous scalp EEG during at resting state provided new insight into cortical functional disorder following stroke.**

I. INTRODUCTION

Stroke has been one of the leading causes of mortality and long-term morbidity worldwide [1]. The consequences of stroke have significant influences on the quality of the life of the patients with huge medical cost. In the past decades, both experimental and clinical researches have tried to understand the stroke from the microscopic, mesoscopic to macroscopic levels. Electro-neurophysiology study, especially cortical electroencephalogram (EEG) analysis, has greatly expanded our understanding of pathophysiology and neurological dysfunction of stroke, which would be potentially helpful in improving the treatment and rehabilitation of stroke[2], [3].

In past years, various quantitative electroencephalography (qEEG) methods have been proposed to study the physiological and functional activities of the brain non-invasively [4]. Compared with other methods, the synchronization analysis of multichannel EEG in neurophysiology [5], [6] has been attracting more attention due to its success in quantifying the large scale cortical interactions [7]. The large scale organization of the distributed brain networks has been important for understanding the central nervous system disorders after brain injury [8], [9]. Since synchrony in the brain is a dynamical phenomenon of distributed neuronal oscillators of precise phase locking over a limited period of time [10], the multichannel EEG synchrony analysis for explanation of cortical large scale information processing has showed potential applications in neurophysiology [7]. Synchrony analysis, especially the phase synchronization based on the analytic signal, has clear advantages over the conventional analysis by coherence, because the power spectra-based coherence is highly dependent on the stationarity of analyzed signals, while phase synchronization analysis could separate phase and amplitude information [11].

Although there already have been valuable results of the cortical synchronization network under schizophrenia, epilepsy, Parkinson' disease, etc. [12]–[14]; few comprehensive studies have been undertaken on the neural synchrony following ischemic brain injury. The dynamic patterns of neural synchronization in large scale remains are poorly understood. In this study, we investigated the spatiotemporal pattern of large-scale cortical synchrony derived from multichannel scalp EEG recordings of bilateral stroke patients. Our main hypothesis is that brain synchrony patterns are altered following ischemic brain injury, in particular, the inter-hemispheric connections should be accordingly influenced after the bilateral brain injury.

II. SUBJECTS AND METHODS

A. Subjects

Nine patients (age=68.4 ± 10.5 ys from 53 to 82 ys, male/female=5/4) with mild or moderate bilateral deep cerebral ischemic infarction were recruited from the Fifth People's Hospital of Shanghai (FPHS). Fig.1 is a typical MRI of a patient with mild bilateral corona radiata stroke. Head CT or MRI scanning was performed for confirming the lesion sites of stroke. Details of the subjects are listed in Table 1. Eight control subjects with matched age and gender (age=62.29.5 years from 49 to 77 years, male/female=5/3) were also included in the experiments. All control subjects were reported without history of seizures, neurological diseases or psychiatric disorders. Head CT scanning was also performed on these control subjects to exclude the possible tiny stroke. All subjects had given their written informed consent before the experiments and were told of the experimental protocols approved by the Ethics Committee of FPHS in compliance with the Helsinki Declaration.

B. EEG recording and preprocessing

The EEG data were collected while each participant was seated in a comfortable chair in resting state with eyes closed (30 min). And the experiments were performed in

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TABLE I

SUMMARY OF PATIENT AGE, GENDER, COMPUTERIZED TOMOGRAPHY SCAN FINDINGS AND HOSPITAL STAY.

Stroke Patients	Age	Gender	Computerized tomography scan results	Hospital stay (days)
1	78	F	bilateral ventricle multi-lacunar cerebral infarction	21
2	70	M	bilateral ventricle lacunar cerebral infarction	50
3	64	F	bilateral ventricle lacunar cerebral infarction	33
4	53	M	bilateral corona radiata micro local ischemia	30
5	82	M	bilateral ventricle lacunar cerebral infarction	42
6	74	F	bilateral ventricle multi-lacunar cerebral infarction	15
7	65	F	bilateral corona radiata lacunar cerebral infarction	46
8	53	M	bilateral ventricle lacunar cerebral infarction	25
9	77	M	bilateral corona radiata micro local ischemia	28

an acoustically and electrically shielded room using a 16-channel EEG system (Sunray LQWY-N, Guangzhou, China). The EEGs were recorded at 16 scalp loci (Fp1, Fp2, F3, F4, F7, F8, C3, C4, T3, T4,P3, P4, O1, O2, T5, and T6) complying with the international 10-20 system with reference to linked earlobes. EEG recordings of each subject were acquired using a 12-bit A/D converter at 100 Hz. Data containing artifacts due to eye blinks, significant muscle activities and movements of the electrodes were removed in an offline visual screening by an experienced physician. All signals were band-pass filtered into 0.5-30 Hz range, which accounted for approximately 98% of the power in the EEG [15]. Finally, in order to reduce various noises and artifacts effects, fifteen reliable EEG segments, each consisting non-overlapping 2000 sample points were selected for each subject for a more convincible phase synchronization analysis.

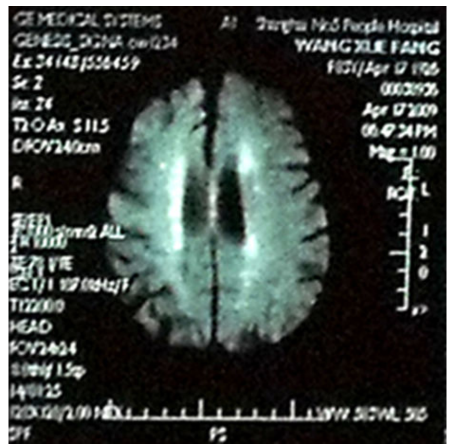

Fig. 1. A typical MRI of stroke patients with bilateral corona radiata micro local ischemia.

C. Phase synchronization analysis of data

Phase synchronization (PS) described the relationship between the phases of two signals and it separated effects of phase and amplitude, which is not dependent on the stationarity of the signals. PS is a normalized index showing the degree of interdependence between pairs of variables and has been useful in characterizing the synchronization structure of neuronal networks and large scale integration of neural activity [9], [16]. The mathematical details of PS index can be briefly described as follows: given a univariate measurement $x(t)$, we first obtain its analytic signal [17]

$$\zeta(t) = x(t) + ix_H(t) = A_x^H(t)e^{i\phi_x^H(t)} \quad (1)$$

where $x_H(t)$ is the Hilbert transform (HT) of signal $x(t)$, defined as:

$$x_H(t) = \frac{1}{\pi} P.V. \int_{-\infty}^{\infty} \frac{x(t')}{t-t'} dt' \quad (2)$$

with P.V. denoting the Cauchy principal value. Analogously, we define A_y^H and ϕ_y^H for signal $y(t)$. If $\phi_x^H(t)$ and $\phi_y^H(t)$ satisfying:

$$\phi_{xy}^H(t) \equiv n\phi_x^H(t) - m\phi_y^H(t) \leq const \quad (3)$$

the two variables $x(t)$ and $y(t)$ are $n:m$ synchronized (n and m are integers). As already mentioned in [18]–[20], 1:1 synchronization is the case for the most neurophysiological signals, then we can define a phase synchronization index (γ_H) as:

$$\gamma_H \equiv |\langle e^{i\phi_{xy}^H(t)} \rangle_t| = \sqrt{\langle \cos\phi_{xy}^H(t) \rangle_t^2 + \langle \sin\phi_{xy}^H(t) \rangle_t^2} \quad (4)$$

where $< \cdot >$ denotes the average over time. The PS index γ_H will be zero if the two signals $x(t)$ and $y(t)$ are not synchronized at all, and $\gamma_H = 1$ when the phase difference is a constant (perfect synchronization). For each subject, we then obtained a matrix of the synchronization for all 16 electrodes in pair. The mean value of the synchronization matrix is defined as the global phase synchronization (GPS) index which evaluates the level of the whole interdependence of the brain. Also, we can get the sub-matrix for the synchronization within the left or the right hemispheres, and accordingly their averages are defined as the left hemispheric phase synchronization (LHPS) index and the right hemispheric phase synchronization (RHPS) index respectively. In addition, the inter-hemispheric phase synchronization (IHPS) index can also be defined from the sub matrix of inter-hemispheric synchronization.

D. Statistical analysis

All data are presented as mean ± standard deviation. Statistical analysis of the difference between two groups

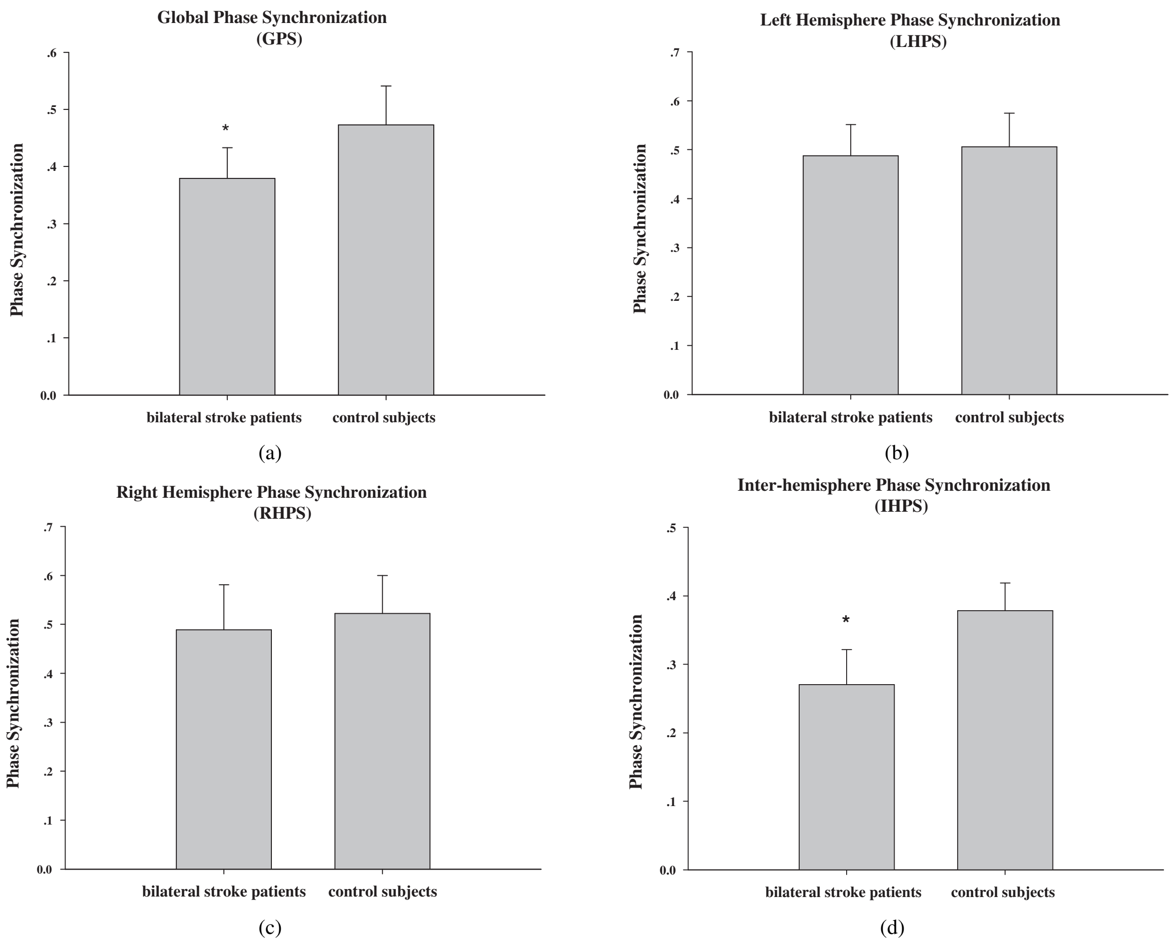

Fig. 2. Phase synchronization index in (a) global brain network (b) left intra-hemispheric area (c) right intra-hemispheric area (d) interhemispheric area. *p<0.01, significant difference compared between two groups

was tested with student *t*-test. Statistical significance was accepted at two-tailed p<0.05.

III. Results

The global interdependence across the cortex were calculated for all electrodes in pair for each subject. The GPS index, which includes the information of both focal and long-distance synchronization across the scalp, showed significant difference between the patients and the control groups ($p < 0.01$, Fig.2(a)). To look into the possible differences of synchronization between the two hemispheres, we further analyzed the intra- and inter- hemispheric synchronization. No significant differences of the mean LHPS index or RHPS index were found between the control subjects and stroke patients (Fig.2(b)(c)). However, Fig. 2(d) showed that the inter-hemispheric synchronization was significantly suppressed in the stroke group.

IV. Discussions and conclusions

It was considered that the synchrony patterns could be established in early development of brain injury which is necessary for the establishment of neuronal circuitry [21], [22]. Thus, the absence or alteration of these cortical synchrony was supposed to be related to the functional disorder of the central neural systems [23]. Many studies have tried to link the cortical information processing and the phase synchronization of scalp EEG signals, and compare the synchronization under functional stimuli [16]. Nevertheless, cortical synchronization in the resting state is also of importance and a study of brain spontaneous activity would be useful as a reference condition, as it reflects the ground state activity of the awake brain [8], [9].

In this paper, we studied the PS of spontaneous EEG activity during the resting state. As the results showed, although statistically significant lower global synchronization was observed in stroke patients, the intra-hemispheric synchronization had no differences between the two groups, while inter-hemispheric synchronization in stroke group is much weaker than that of control subjects. The possible reasons for the insignificant statistical difference for intra-hemispheric synchronization are: 1)since all the patients in in study are deep cerebral infarction, the deep focal stroke might not significantly affect the EEG recordings which usually records the activities in the cortex; 2) many studies have suggested that the brain had plasticity and reorganization after ischemic brain injury [24], we speculate that there might be a compensation with enhanced interdependence in the intact cortex for the focal infarction. While the weakened inter-hemispheric synchronization in the patient group could be due to the bilateral brain injury in corona radiata which connects the two hemispheres. A further study on the synchronization between the lesion area and the intact cortex would help understand the possible plasticity of the cortical intra-dependence. In addition, a comparison with the synchronization under unilateral stroke will also help understand the influence of focal stroke on the cortical synchronization.

In conclusion, the phase synchronization of the spontaneous EEG in a resting state could provide a new insight into cortical interdependence after bilateral stroke. Our preliminary results indicated that focal brain injury following bilateral ischemic stroke could essentially change the cortical functional connections. However, further analysis in larger groups as well as the unilateral stroke subjects would help to uncover more details of the influences of stroke on cortical synchronization. Nevertheless, our preliminary results offered a new aspect of using EEG synchronization to understand the large-scale cortical interaction after ischemic brain injury. Potentially, multichannel EEG synchrony analysis could be complementary to the current neurological scoring (such as NIHSS), CT scan and MRI for further evaluation of stroke and the following neurophysiological recovery.

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