2021 43rd Annual International Conference of the
IEEE Engineering in Medicine & Biology Society (EMBC)
Oct 31 - Nov 4, 2021. Virtual Conference

Phase Synchronization of EEG in Bilateral, Cyclical Ankle Alternating Movements of Stroke

Xianle Shi[#], Jun Liang[#], Hengyu Zhang, Chunxiao Wan, Rui Xu*, *Member, IEEE* and Dong Ming, *Senior Member, IEEE*

***Abstract*— Electroencephalogram (EEG) is a basic physiological signal of human body, which can effectively record the nervous system activities of the brain and contains rich information. The synchronization of EEG signals is not only the key to the exchange of information between different brain regions, but also reflects the neural activity of the brain, which in turn can infer people's cognitive activities. Therefore, studying the phase synchronization of EEG signals after stroke is of great significance for understanding the communication and neuroplasticity of neurons after brain injury. In this paper, the changes of EEG phase synchronization in bilateral, cyclical ankle movements alternately after stroke were studied by Hilbert transform. Ten stroke patients and six healthy adults participated in the test. The results showed that the inter-hemisphere phase synchronization index (inter-PSI) and the global PSI of patients were significantly lower than that of the healthy subjects during the task. The PSI between Cz and the affected sensory cortex associated with lower limb movements was also significantly lower than that in the control group. There was a significant negative correlation between National Institutes of Health Stroke Scale (NIHSS) and cortical synchronization. The above results indicated that PSI under ankle alternating movements may be used as a new biomarker to evaluate the recovery of patients' brain neurons.**

Key words — phase synchronization; stroke; ankle movements; Electroencephalography

I. INTRODUCTION

Stroke is an accidental vascular disease in the brain causing local dysfunction. For stroke patients, the fundamental cause of movement disorders is precisely the cerebral cortex control problems. Therefore, many studies have focused on the changes of cerebral cortex function after stroke, in order to provide theoretical basis for patients' rehabilitation. Brain function is based on the interaction between neurons in different regions or cross-regions of the brain [1]. Electroencephalography (EEG) is one of the most commonly-used method to monitor the real-time dynamic activity of the brain. Different sources of EEG signals will produce different rhythms, among which β oscillation is mainly generated in the motor cortex [2]. Experiments in both monkeys [3] and humans [4] demonstrated that synchronous β oscillating activity between various regions of the sensorimotor cortex correlated with motor performance. Synchronized brain activity plays an important role in evaluating neural networks and their interactions with various clinical states [5]. Therefore, studying the multi-regional interaction of cerebral cortex within the β range during motor executive phase in stroke patients is valuable for understanding the pathophysiological mechanisms and neurological dysfunction following stroke [6,7].

The phase synchronization index (PSI) based on EEG represents synchronous brain activity. PSI not only excludes the influence of signal amplitude and can detect the weak interdependence between signals, but also quantify the neural oscillations and evaluate the synchronization of neurons between different cortical regions. Therefore, it becomes a new parameter of neural network analysis.

At present, most of the research on phase synchronization has focused on mental diseases such as epilepsy and schizophrenia, and more valuable research results have been achieved [8,9]. The studies on the neurosynchrony of stroke patients are mainly based on the resting state EEG in the acute phase. By collecting resting EEG, Wu et al. compared PSI between healthy elderly and patients with acute ischemic stroke in alpha band, and found that stroke interrupted the cortical synchronization networks and affected large-scale neural communication. The PSI between the hemispheres was significantly related to the National Institutes of Health Stroke Scale (NIHSS) score two months later, that is, inter-hemispheric synchrony was related to long-term functional recovery [10]. This study illustrated that the PSI could reflect the severity of stroke. Kawano et al. analyzed the correlation between the inter-hemispheric PSI and some clinical scales, including Functional Independence Measure (FIM), NIHSS and Fugl-Meyer Motor Assessment (FMA), in the α band (8-12Hz) and low β band (13-18Hz) by collecting EEG in the resting state of acute ischemic stroke patients. The result showed that large-scale phase synchronization represented by PSI was significantly relevant to clinical evaluation [11]. Therefore, the PSI based on resting EEG is a promising index to estimate motor recovery of stroke.

For stroke patients, walking is the basis for other social activities of human beings. The neural synchronization between different cortical regions of stroke patients during walking reflects neural activities for walking control and remains to be explored. However, walking of stroke patients during the early stage is mostly impossible. Previous studies have proved that walking is consistent with the activation of brain neurons during simple periodic movements of the feet[12]. Therefore, this paper designed an experimental task

The work was supported by National Key Research and Development Program of China (2020YFC2004302), National Natural Science Foundation of China (No.81901860, 81630051 and 81925020), China Postdoctoral Science Foundation Grant (2019M651043), and Tianjin Key Technology R&D Program (No. 17ZXRGGX00010).

[#]Xianle Shi and Jun Liang contributed equally to this work.

*Corresponding author: Rui Xu, email: xrblue@tju.edu.cn

Xianle Shi, Jun Liang, Rui Xu and Dong Ming are with Department of Biomedical Engineering, College of Precision Instruments and Optoelectronics Engineering, Tianjin University, Tianjin, 300072, China.

Hengyu Zhang and Dong Ming are with Academy of Medical Engineering and Translational Medicine, Tianjin University, Tianjin, 300072, China.

Jun Liang and Chunxiao Wan are with Department of Rehabilitation, Tianjin Medical University General Hospital, Tianjin, 301700, China.

978-1-7281-1178-0/21/$31.00 ©2021 IEEE

that simulated the movements of the lower limbs when walking, that is, the cyclical alternating movements of the bilateral ankle. On one hand, the simplification of exercise eliminates many requirements for bipedal exercise and reduces the risk of patients during exercise; on the other hand, it also avoids the generation of motion artifacts during walking, and better reflects the activation of brain neurons in the state of exercise [12]. The purpose of this study is to explore the changes of PSI under bilateral ankle movements between stroke patients and healthy subjects, and validate the correlation between PSI and clinical scales, so as to verify the feasibility of this index.

II. MATERIALS AND METHODS

A. *Participants*

In this study, ten stroke patients (age: 55±13.55, male/female = 8/2, ischemia/hemorrhage=7/3)) from the Rehabilitation Department of Tianjin Medical University General Hospital were recruited. The location of the stroke was determined by CT or MRI scanning. The selection criteria are as follows: (1) the first stroke (2) unilateral hemiplegia after unilateral stroke (3) MMSE>24 points (4) ability to perform ankle movements autonomously. The control group came from 9 healthy college students (age: 23.67±1.0328) from Tianjin University. Exclusion criteria included a history of epilepsy and severe cognitive deficits and other neurological diseases. All subjects were informed of the experimental protocol and signed an informed consent form before the experiment. According to the Declaration of Helsinki, the Ethics Committee of Tianjin Medical University General Hospital approved the experimental protocol.

B. *Experiment*

As shown in Fig. 1, each subject sat on a chair with a back, staring at the computer monitor in front of them, and their feet were naturally placed on the ground. The task would begin as soon as the subject was ready. When the word "start" appeared on the screen, the subject began to perform cyclical ankle movements. During the movements, the screen display turned into a blue circle, which was designed to improve the subjects' attention. When the blue circle disappeared, the subject should stop moving. Participants were asked to relax their upper body, keep their upper body and head as still as possible, and avoid moving their head, talking, swallowing, and blinking excessively throughout the movements. The stimulation interface of the experiment was completed based on E-Prime 3.0 software ((Psychology Software Tools, Pittsburgh, PA, USA)). Each subject did two sets of movements, each of which lasted three minutes.

Fig. 1 Experimental scene diagram

C. *EEG recording and processing*

A 32-channel wireless EEG acquisition system (Neuroscan Greal EEG, Australia) was used to record EEG data. The electrode arrangement configuration was based on the international 10-20 system (Fig. 2). EEG data were sampled at 1024 Hz. The ground electrode was placed on the GND of the forehead, and the reference electrode was placed between FCz and Cz.

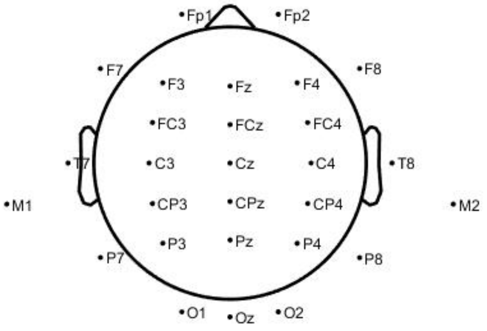

Fig. 2 10-20 electrode arrangement system

All the signals were filtered to 0.5-45Hz, and the EEG were downsampled to 512Hz. Then, components of eye-movements and excessive muscle activity were identified by visual inspection and removed after independent component analysis (ICA). According to the EEG anatomical and physiological structure, the cortical functional area involved in lower limb movements is the sensorimotor functional area located in the center. Therefore, we analyzed the phase synchronization index of β-band (13-30Hz). Data processing was carried out using MATLAB R2017b and EEGLAB toolbox for analysis.

The phase synchronization index can be regarded as a normalized parameter, which can measure the relationship between a pair of variables, and can be effectively used to describe the integration between neurons. First, the preprocessed signal is filtered to the band of interest, and then the instantaneous phase of the filtered EEG signal is extracted by using the Hilbert transform. The specific steps are as follows:

The Hilbert transform of the filtered continuous-time EEG signal is

$$\tilde{x}(t) = H[x(t)] = \frac{1}{\pi} P \cdot V \int_{-\infty}^{+\infty} \frac{x(\tau)}{t-\tau} d\tau \qquad (1)$$

$P \cdot V$ refers to the integral taken in the sense of the Cauchy principal value. $H[\cdot]$ is the Hilbert transform, which decomposes the signal into independent amplitude and phase parts. Given an EEG signal $x(t)$, its analytical signal is defined as:

$$Z_x(t) = x(t) + j\tilde{x}(t) = A_x^H(t) e^{j\phi_x^H(t)} \qquad (2)$$

where $A_x^H(t)$ and $\phi_x^H(t)$ are the instantaneous amplitude and the instantaneous phase of signal $x(t)$, respectively. Similarly, the instantaneous phase of signal $y(t)$, denoted as ϕ_y^H, can be obtained. If ϕ_x^H and ϕ_y^H satisfy

$$\phi_{xy}^H(t) = \left| n\phi_x^H(t) - m\phi_y^H(t) \right| \leq const \qquad (3)$$

where n and m are positive integers, called signals $x(t)$ and $y(t)$ are phase synchronization of $n{:}m$. $\phi_{xy}^{H}(t)$ is the instantaneous phase difference between signals $x(t)$ and $y(t)$, and $const$ represents a constant boundary of the instantaneous phase difference. The most commonly used is 1:1 phase synchronization for neurobiological signals[13]. This article will use 1:1 phase synchronization.

To quantify the phase synchronization level of the signal, the phase synchronization index is calculated as follows:

$$PSI = \sqrt{\langle \cos \phi_{xy}^{H}(t) \rangle_t^2 + \langle \sin \phi_{xy}^{H}(t) \rangle_t^2} \qquad (4)$$

In the formula, $\phi_{xy}^{H}(t)$ is the instantaneous phase difference between the signals $x(t)$ and $y(t)$, and $\langle\cdot\rangle$ represents the averaging operation over a period of time. PSI is a real number between 0 and 1. When PSI=1, the two signals are completely synchronized, and when PSI=0, it means completely out of sync.

According to the distribution of the electrodes, the interaction can be divided into four types. (1) The synchronization between Cz and the affected hemisphere, that is, the average value of the PSIs between EEG at Cz and each channel of the affected hemisphere. (2) The synchronization between Cz and the unaffected hemisphere, which is the average value of the PSIs between EEG at Cz and each channel of the unaffected hemisphere. (3) The global synchronization (global-PSI), which is the average value of PSIs between EEG at any two of the channels. (4) The inter-hemisphere synchronization (inter-PSI), which is the average value of PSIs between EEG at any two channels from the unaffected and the affected sides separately.

D. *Statistics*

Statistical differences between the control group and the patient group were examined by one-way analysis of variance. All data were expressed as mean ± standard deviation. $p<0.05$ was considered statistically significant.

III. RESULTS

A. *Comparison of PSI between patients and control subjects*

To explore the differences in cortical synchronization between patients and healthy subjects during the lower limb task, we calculated the PSI of Cz and affected hemisphere, Cz and unaffected hemisphere. The PSI of Cz and the left hemisphere, Cz and the right hemisphere in the control group were averaged to be used as the PSI of Cz and the hemisphere in the healthy control group. As shown in Fig. 3 (a), the synchrony of Cz and neurons on the affected side was significantly lower in patients than in healthy controls (p=0.0048). Meanwhile, the PSI of Cz and unaffected hemisphere also showed significant differences. (p=0.001, *:p<0.05, **:p<0.01, ***:p<0.001)

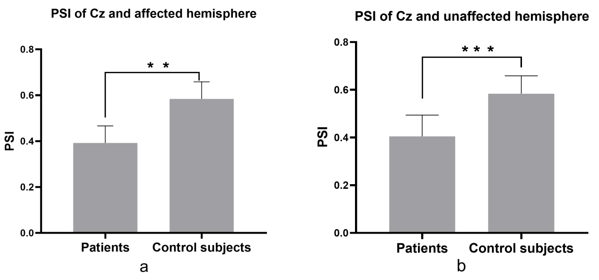

Fig. 3 PSI between (a) Cz and affected hemisphere and (b) Cz and unaffected hemisphere forpatients and control subjects

To understand the synchrony of the whole brain better, we also compared inter-hemisphere phase synchronization index (inter-PSI) and globe PSI between patients and healthy controls. As shown in Figure 4 (a) and (b), both hemispheric and globe PSI were lower in patients than in healthy controls. (p =0.0037, p=0.0486).

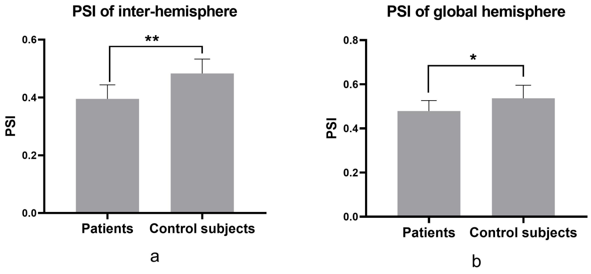

Fig. 4 (a) PSI of inter-hemisphere (b) PSI of global hemisphere

B. *Correlation between PSI and clinical scales*

NIHSS represents the severity of stroke. We divided the patients in this study into three grades: I, II, and III: 2 of them were nearly normal (0~1 points), 7 had mild strokes (2~4 points), and moderate 1 person with a degree of stroke (5-15 points). The higher the grade, the greater the severity of the stroke. We calculated the inter-PSI of the patients in each grade and compared them with the control group. The results were shown in Fig. 5. The inter-PSI of the patients showed a step-like distribution according to the severity of stroke, even the inter-PSI of the patients with the lowest degree of disease was lower than that of the healthy control group. Because of the limited number of subjects, statistical analysis could not be done. However, the above results indicated a trend, that is, the higher the severity of stroke, the lower the inter-PSI.

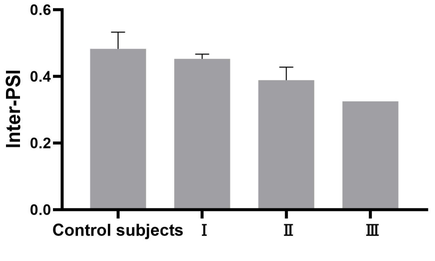

Fig. 5 Inter-PSI under different NIHSS grades

Different clinical scales assess different motor functions. In order to compare the relationship between NIHSS and cortical synchronization in patients more clearly, we calculated the correlation between NIHSS and inter-PSI in the state of motion, and the results were shown in Fig.5. Inter=PSI and NIHSS showed a significant negative correlation. (R^2=0.4318, p =0.0390).

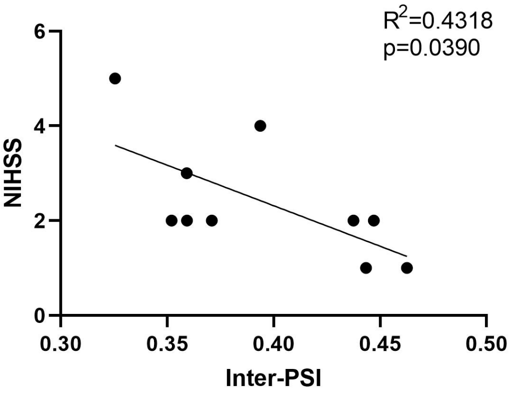

Fig.5 Correlation plots of NIHSS with respect to inter-PSI

IV. Discussion And Conclusion

Different from the previous studies on the PSI with resting EEG of stroke patients, this work studied the PSI of the EEG under periodic movements of the bilateral ankle. The PSI between Cz and the affected side of the patients showed significant differences from the healthy control group. This indicates that the cortical interaction between the sensorimotor region and the affected hemisphere is weakened after stroke [6]. Meanwhile, the PSI of Cz and unaffected hemisphere also showed significant differences. It may be speculated that (1) the effect was confounded by the age difference, and (2) stroke can also lead to a breakdown in communication in the unaffected hemisphere. The decrease in global brain synchrony in patients compared to the control suggested that stroke inactivated part of the cortical network [14]. The difference in PSI between hemispheres also indicated that the dynamic mode of synchronous activation between the two hemispheres is weakened in functional communication caused by brain injury [15]. Although there were a small number of young people in the patient group, the healthy control group was mostly young, which may be a reason for the difference in PSI between the patients and the control group. Therefore, future studies will conduct further analysis in a larger database to reveal more details about the impact of stroke on cortical synchronization.

It is the first study to explore the changes of EEG phase synchronization index in stroke patients during movements. There was a significant negative correlation between inter-PSI and NIHSS during ankle alternating movements. Compared with the resting state of previous studies, the alternating movements are more representative of a state of movement of the lower limbs. Therefore, inter-PSI in the movement state may be used as a new biomarker to evaluate the recovery of patients.

Acknowledgment

The author thanks Motor Rehabilitation Laboratory of Tianjin University and Rehabilitation Department, Tianjin Medical University General Hospital for their help.

References

[1] B. J. He, A. Z. Snyder, J. L. Vincent, A. Epstein, G. L. Shulman, and M. Corbetta, “Breakdown of functional connectivity in frontoparietal networks underlies behavioral deficits in spatial neglect,” *Neuron,* vol. 53, no. 6, pp. 905-918, Mar 15, 2007.

[2] R. Hari, and R. Salmelin, “Human cortical oscillations: a neuromagnetic view through the skull,” *Trends in neurosciences,* vol. 20, no. 1, pp. 44-9, 1997-Jan, 1997.

[3] V. N. Murthy, and E. E. Fetz, “Coherent 25- to 35-Hz oscillations in the sensorimotor cortex of awake behaving monkeys,” *Proceedings of the National Academy of Sciences of the United States of America,* vol. 89, no. 12, pp. 5670-4, 1992-Jun-15, 1992.

[4] B. A. Conway, D. M. Halliday, S. F. Farmer, U. Shahani, P. Maas, A. I. Weir, and J. R. Rosenberg, “Synchronization between motor cortex and spinal motoneuronal pool during the performance of a maintained motor task in man,” *The Journal of physiology,* vol. 489 (Pt 3), pp. 917-24, 1995-Dec-15, 1995.

[5] A. K. Engel, C. Gerloff, C. C. Hilgetag, and G. Nolte, “Intrinsic Coupling Modes: Multiscale Interactions in Ongoing Brain Activity,” *Neuron,* vol. 80, no. 4, pp. 867-886, Nov 20, 2013.

[6] J. Du, J. Hu, J. Hu, Q. Xu, Q. Zhang, L. Liu, M. Ma, G. Xu, Y. Zhang, X. Liu, G. Lu, Z. Zhang, and F. Yang, “Aberrances of Cortex Excitability and Connectivity Underlying Motor Deficit in Acute Stroke,” *Neural Plasticity,* vol. 2018, 2018, 2018.

[7] J. A. Palmer, L. A. Wheaton, W. A. Gray, M. A. S. da Silva, S. L. Wolf, and M. R. Borich, “Role of Interhemispheric Cortical Interactions in Poststroke Motor Function,” *Neurorehabilitation and Neural Repair,* vol. 33, no. 9, pp. 762-774, Sep, 2019.

[8] Y. Miron-Shahar, J. W. Kantelhardt, A. Grinberg, S. Hassin-Baer, I. Blatt, R. Inzelberg, and M. Plotnik, “Excessive phase synchronization in cortical activation during locomotion in persons with Parkinson's disease,” *Parkinsonism & Related Disorders,* vol. 65, pp. 210-216, Aug, 2019.

[9] H. T. Yu, L. H. Cai, X. Y. Wu, Z. X. Song, J. Wang, Z. J. Xia, J. Liu, and Y. B. Cao, “Investigation of phase synchronization of interictal EEG in right temporal lobe epilepsy,” *Physica a-Statistical Mechanics and Its Applications,* vol. 492, pp. 931-940, Feb, 2018.

[10] W. Wu, J. Sun, Z. Jin, X. Guo, Y. Qiu, Y. Zhu, and S. Tong, “Impaired neuronal synchrony after focal ischemic stroke in elderly patients,” *Clinical Neurophysiology,* vol. 122, no. 1, pp. 21-26, Jan, 2011.

[11] T. Kawano, N. Hattori, Y. Uno, K. Kitajo, M. Hatakenaka, H. Yagura, H. Fujimoto, T. Yoshioka, M. Nagasako, H. Otomune, and I. Miyai, “Large-Scale Phase Synchrony Reflects Clinical Status After Stroke: An EEG Study,” *Neurorehabilitation and Neural Repair,* vol. 31, no. 6, pp. 561-570, Jun, 2017.

[12] T. Yoshida, K. Masani, K. Zabjek, R. Chen, and M. R. Popovic, “Dynamic Increase in Corticomuscular Coherence during Bilateral, Cyclical Ankle Movements,” *Frontiers in Human Neuroscience,* vol. 11, Apr 4, 2017.

[13] L. Angelini, M. D. Tommaso, M. Guido, K. Hu, P. C. Ivanov, D. Marinazzo, G. Nardulli, L. Nitti, M. Pellicoro, C. Pierro, and S. Stramaglia, “Steady-state visual evoked potentials and phase synchronization in migraine patients,” *Physical Review Letters,* vol. 93, no. 3, Jul 16, 2004.

[14] F. Vecchio, C. Tomino, F. Miraglia, F. Iodice, C. Erra, R. Di Iorio, E. Judica, F. Alu, M. Fini, and P. M. Rossini, “Cortical connectivity from EEG data in acute stroke: A study via graph theory as a potential biomarker for functional recovery,” *International Journal of Psychophysiology,* vol. 146, pp. 133-138, Dec, 2019.

[15] M. Saes, C. G. M. Meskers, A. Daffertshofer, J. C. de Munck, G. Kwakkel, E. E. H. van Wegen, C. Winters, A. Andringa, D. Hoevenaars, L. Haring, E. van Duijnhoven, S. Zandvliet, J. Yao, J. Dewald, M. Vlaar, T. Solis-Escalante, A. Schouten, F. van der Helm, Y. Yang, M. van de Ruit, K. Kalogianni, J. van Kordelaar, L. Filatova, and D. E. Consortium, “How does upper extremity Fugl-Meyer motor score relate to resting-state EEG in chronic stroke? A power spectral density analysis,” *Clinical Neurophysiology,* vol. 130, no. 5, pp. 856-862, May, 2019.