

# Brain function changes induced by intermittent sequential pneumatic compression in patients with stroke as assessed by functional near-infrared spectroscopy

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## Research

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# Abstract

*Background.* Intermittent sequential pneumatic compression (ISPC) can effectively promote blood flow and improve microcirculation. The increase in pressure gradient and blood flow velocity by ISPC has been suggested to be a possible mechanism to improve the microcirculation of patients. However, the effects of ISPC on cerebral oscillations are still unclear.

*Methods.* The tissue concentration of oxyhemoglobin and deoxyhemoglobin oscillations were measured by functional near-infrared spectroscopy under resting and ISPC conditions in 27 right-handed adult patients with stroke. Five characteristic frequency signals (I, 0.6–2 Hz; II, 0.145–0.6 Hz; III, 0.052–0.145 Hz; IV, 0.021–0.052 Hz; and V, 0.0095–0.021 Hz) were identified using the wavelet method. The wavelet amplitude (WA) and laterality index (LI) were calculated to describe the frequency-specific cortical activities.

*Results.* The WA values of the ipsilesional motor cortex (MC) in the frequency intervals III ( $F = 4.378$ ,  $p = 0.041$ ), IV ( $F = 4.281$ ,  $p = 0.044$ ), and V ( $F = 5.33$ ,  $p = 0.025$ ) and those of the contralesional MC in III ( $F = 10.122$ ,  $p = 0.002$ ), IV ( $F = 9.275$ ,  $p = 0.004$ ), and V ( $F = 8.373$ ,  $p = 0.006$ ) were significantly higher when the patients were under the ISPC state than when they were under the resting state. Also, the LI value of the prefrontal cortex (PFC) and MC of the patients decreased more obviously in the ISPC state compared with the resting state despite there was no significant difference.

*Conclusions.* ISPC could induce the activation of bilateral MCs in myogenic and neurogenic innervations and endothelial cell metabolic activities. The decreased LI values in the PFC and MC indicated that the ISPC had a positive effect on these regions' functional rehabilitation. The ISPC of 0.03 Hz is not suitable for all patients with stroke, and personalized treatment options should be considered in subsequent ISPC intervention. This study provides a method for assessing the effects of ISPC on cerebral oscillations, and the results benefit the optimization of ISPC parameters in the personalized treatment for the functional recovery of patients with stroke.

## Background

Stroke is one of the most common neurological diseases. This ailment is characterized by high morbidity, mortality, and disability rates and not only reduces the quality of life of patients but also creates heavy social and economic burden [1]. Stroke survivors generally manifest behavioral deficiencies, such as hemiplegia or cognitive dysfunction, and they have extremely high rehabilitation needs. Effective rehabilitation after stroke is of great significance in the related functional recovery of patients.

Intermittent sequential pneumatic compression (ISPC), as an effective physical therapy, can produce a type of circulating pressure that acts on the extremities and tissues of the hemiplegic side through the repeated inflation and deflation of an air bag in an ordered and regular manner. This process can promote the flow of blood and lymph and improve microcirculation [2]. ISPC has been commonly attributed to antithrombotic, fibrinolytic and vasodilation effects [3]. The increase in the pressure gradient and flow

velocity of blood and the subsequent increase in arterial flow induced by ISPC has been suggested as a possible mechanism to improve the condition of patients with hemiplegia [3–5]. Changes in the pressure gradient and flow of blood can affect the variations in cerebral oscillations [6]. However, the effect of ISPC on the changes in cerebral oscillations remains unclear. Given the popularity of ISPC and its importance in stroke rehabilitation, understanding its effects on brain function is crucial.

With the development of functional near-infrared spectroscopy (fNIRS), its use in the assessment of brain function and brain behavioral interactions has attracted increasing interest. fNIRS is a well-developed optical imaging method based on hemodynamic responses. Specifically, fNIRS can effectively detect changes in oxygenated hemoglobin ( $\Delta [O_2Hb]$ ) and deoxygenated hemoglobin ( $\Delta [HHb]$ ) concentration levels in the microcirculation of brain tissues with a good spatial and temporal resolution [7, 8]. Relative to other noninvasive conventional functional imaging tools, such as functional magnetic resonance imaging (fMRI) and positron emission tomography, fNIRS is a safe, convenient, and inexpensive method with few physical or environmental constraints and contraindications [9, 10]. Thus, fNIRS is readily applicable to clinical settings for the detection of hemodynamic fluctuations in patients with stroke of different states.

Recent neuroscience research shows that the focal damage after stroke exerts a profound effect on the network connectivity structure of the entire cortical region and causes differences in the cerebral hemispheres. Wavelet amplitude (WA) and laterality index (LI) are two important indicators for evaluating the degree of brain activation and hemispheric differences [11, 12]. WA is the magnitude of the fluctuation of the original signal measured by multichannel fNIRS at a certain frequency. This parameter can reflect the activation of the cerebral cortex. The activation of the cerebral hemisphere can be effectively evaluated by the degree of regional damage; that is, a small activation indicates great damage [13]. LI is extensively used to assess the activation balance between hemispheres. The lateralization of ipsilesional and contralesional hemispheres reveals the greatest asymmetry at one month in patients with stroke, and lasted until six months after onset [14]. During recovery, the balance between the hemispheres may be associated with physiologic recovery.

In the present study, changes in  $\Delta [O_2Hb]$  and  $\Delta [HHb]$  were measured in the prefrontal cortex (PFC), motor cortex (MC), and temporal lobe cortex (TLC). We hypothesized that ISPC could induce cortical activation in patients with stroke. This study aimed to investigate the effects of ISPC on cerebral oscillations. The results may help broaden the understanding of the contribution of ISPC to stroke recovery.

## Materials And Methods

### *Subjects*

A total of 30 right-handed adult patients with stroke, which was confirmed with either computed tomography scan or fMRI, were recruited to participate in this study as inpatients of the Department of

Rehabilitation Hospital of the National Research Center for Rehabilitation Technical Aids, China. All patients were stable after a first or recurrent stroke. These patients had unilateral hemiplegia and with moderate to severe motor dysfunction in the upper limbs and hemiplegic lower extremities. Among the selected subjects, 3 patients were excluded because of loose detectors. Thus, 27 subjects (11 left and 16 right hemiplegia) were finally included in the study. The clinical details of the patients are shown in Table 1.

In this ISPC study, the exclusion criteria were as follows: (1) left-handed, (2) extremity dermatitis, (3) postoperative vein ligation, (4) gangrene and recent extremity skin graft, (5) severe varicose veins or arteriosclerosis, (6) severe extremity or pulmonary conditions, (7) extreme leg deformity or open wounds, and (8) brain trauma or previous brain surgery.

The basic information (including experimental purposes, procedures, schedules, announcements, and contributions) of the experiment was explained to the participants. All participants were required to have adequate sleep and were not allowed to participate in ISPC therapy within 24 h before the experiment.

### ***Procedures***

Before the experiment, the subjects were required to sit for 5–10 min in a noiseless environment to eliminate existing hemodynamic reactions induced by their activity. Then, the professional therapist fitted the ISPC equipment to the subjects. One day before the experiment, the staff recorded the subjects' basic information, including sex, age, height and weight, blood pressure, and disease history.

The ISPC experiment was divided into two states, namely, the resting and ISPC states. Each state lasted for 10 min. During the resting state, the subjects were instructed to stay awake with their eyes closed and remain quiet. Then, all participants received ISPC intervention with a cycle of 30 s (15 s of inflation and 15 s of deflation, 0.03 Hz) and a peak of 100 mmHg for their hemiplegic limb. All measurements were performed with the subjects resting in the supine position. In any symptomatic or suspicious event (such as pain and tenderness, swelling, warmth, hypoxia, respiratory events, chest pain, redness or discoloration, or distention of surface veins of the lower limbs), the study was terminated immediately. The fNIRS was implemented continuously throughout the experiment.

### ***Functional near-infrared spectroscopy***

The fNIRS measurement used NirSmart, a technology 24-channel tissue oxygenation monitor with continuous-wave, which produced by Danyang Huichuang Medical Equipment Co., Ltd. Each sensor of the instrument consisted of a two-wavelength light emitting diode, which served as the source optode and emitted light at wavelengths of 760 and 850 nm, and a detector optode. The inter-optode distance was 30 mm. The instrument measured the raw light intensity signals. Based on different absorption spectra, concentration changes of  $\Delta [O_2Hb]$  and  $[HHb]$  were calculated from the changes in detected light intensity using the modified Lambert Beer law, assuming constant scattering. The calibration function of the instrument and the corresponding template were used to ascertain the channels to fill

exactly in correspondence of the 10/10 electrode positions according to different head sizes. The elastic band was completely fixed between the template and the head. The hair of the subject must be fully poked to ensure that the probe was in direct contact with the scalp of the subject when the near-infrared light source and detector probes were placed in the template. The templates and probes were symmetrically positioned over the regions of the left and right PFCs (LPFC/RPFC), MCs (LMC/RMC) and TLCs (LTLC/RTLC) as shown in Fig. 1. Signals with a low signal-to-noise ratio were removed, and the sampling rate was 10 Hz.

### ***Data pre-processing***

The pre-processing method of fNIRS data had been elaborated in our previous studies [15-20]. In brief, a moving average filter with a time window of 3s was used to eliminate the obvious abnormal points in the signal. The artifact portion was determined by identifying the sliding window standard deviation above a certain threshold and was removed by cubic spline interpolation. Then independent component analysis (ICA) analysis was then performed on delta [O<sub>2</sub>Hb] and [HHb] signals of each channel. All the ICA-derived components were visually inspected to determine the components that might be related to noise and artifacts, thereby reducing interference in fNIRS measurements. Finally, we improved signal-to-noise ratio and retained the 0.0095–2 Hz portion of the filtering signal obtained using the six-order Butterworth band-pass filter.

The spontaneous cerebral oxygenation signals have different physiological sources, and each physiological source correspond to specific frequency interval. In our previous studies, five frequency intervals corresponding to different physiological sources have been identified [12, 21, 22]. The frequency intervals of 0.6–2 Hz and 0.145–0.6 Hz reflected the synchronization of cardiac (I) and respiratory (II) activities in the cerebral regions; 0.052–0.145 Hz, 0.021–0.052 Hz, and 0.0095–0.021 Hz were regarded as myogenic (III), neurogenic (IV) and endothelial cell metabolic (V) activities respectively. These provide new ideas and methods for understanding the brain reorganization of the brain. In addition, to facilitate the presentation of the results, the data of the left and right sides of the brain of patients with left hemiplegia were replaced at the channel level. Thus, the left hemisphere of the brain represents the ipsilesional region in subsequent sections of this paper.

### ***Wavelet amplitude***

Continuous wavelet transform, as a transformation method of time series from time domain to frequency domain, was used in this study to obtain the main component of time series in frequency domain. Tunable filter band lengths were used to provide the appropriate time and frequency resolution [23], which projected the time series onto the time–frequency plane, thereby obtaining the time-frequency-amplitude 3D map. The results of wavelet transform were averaged over the time domain to obtain the wavelet amplitude (WA) of each delta [O<sub>2</sub>Hb] and [HHb] signal at each time and frequency, which reflects the magnitude of the fluctuation of the original signal at a certain frequency. WA of the delta [O<sub>2</sub>Hb] and [HHb] signal represents the changes of regional cerebral blood flow with the activity of cerebral cortex

during different conditions. Functional hyperaemia or neurovascular coupling could increase regional cerebral blood flow by activating local neurons to match the needs of local brain cells and the supply of blood and nutrients in the task state [24]. Thus, WA is characterized by the intensity or activation of the cerebral cortex.

### ***Laterality index***

One extensively used method for assessing hemispheric activation balance in brain function studies is the laterality index (LI) [11]. In this study, LI is calculated according to the classical formula [25] and the LI for a given contralesional (*C*) and ipsilesional (*I*) hemispheric is calculated by the sum of WA values. Thus, the LI is defined as:

**See formula 1 in the supplementary files.**

In this case, the value of LI ranges from 1 (contralesional activation only) to -1 (ipsilesional activation only).

### ***Statistical analysis***

Data were analyzed using the normal test (Kolmogorov–Smirnov test) and variance uniformity test (Levene test) to ensure that the assumptions required to analyze the parameters were satisfied. One-way ANOVA was performed according to the region to determine the interregional WA and LI. Bonferroni correction was used for multiple comparisons. The corrected  $p$ -value threshold was set to  $p < 0.05$ .

## **Results**

### **Cerebral activation**

After the application of ISPC, changes in cerebral oscillations mainly occurred in intervals III to V, and the activation of the MC and TLC under the ISPC state was higher than that under the resting state as shown in Fig. 2. The activation of the MC and TLC under the ISPC state was higher than that under the resting state.

Specifically, the ISPC state showed significantly high WA values in the ipsilesional MC in the frequency intervals III ( $F = 4.378$ ,  $p = 0.041$ ), IV ( $F = 4.281$ ,  $p = 0.044$ ), and V ( $F = 5.33$ ,  $p = 0.025$ ) and in the contralesional MC in the frequency intervals III ( $F = 10.122$ ,  $p = 0.002$ ), IV ( $F = 9.275$ ,  $p = 0.004$ ), and V ( $F = 8.373$ ,  $p = 0.006$ ). In addition, the ISPC state was significantly higher in the III frequency interval in the ipsilesional TLC ( $F = 4.969$ ,  $p = 0.03$ ) and contralesional TLC ( $F = 4.1$ ,  $p = 0.048$ ) than in the resting state as shown in Fig. 3.

### **Lateralization**

During the resting state, the WAs of the ipsilesional and contralesional PFC, MC, and TLC were close to equilibrium, and the LIs of the MC and TLC were negative showed in Fig. 4. No significant difference in LI was found between the two states. Relative to the results in the resting state, the LIs of the PFC and MC of the patients decreased in the ISPC state in the frequency intervals III–V, whereas that of the TLC showed minimal change.

Changes in the individual LI values of the 27 patients with stroke under the ISPC state compared with those under the resting state are displayed in Fig. 5. After ISPC administration, most subjects showed greater activation in the ipsilesional hemisphere than in the contralesional hemisphere. However, several patients did not show a change in hemispheric activation balance.

## Discussion

This study mainly investigated the effects of ISPC on the cerebral oscillations in patients with stroke as measured by fNIRS. The fNIRS signals are mainly composed of systemic activity components, evoked neurovascular couplings, and nonevoked neurovascular couplings [26]. Five characteristic frequency intervals possibly reflect systemic regulation activities and neurovascular couplings. Frequency intervals I and II reflect systemic regulation activities, whereas frequency intervals III–V indicate neurovascular coupling. In this work, the WAs were significantly higher in the bilateral MCs in the frequency intervals III – V and in the TLCs in the frequency interval III under the ISPC state than under the resting state. In addition, the LIs showed a downward trend in the PFC and MC with the application of ISPC. Personalized studies showed that the LIs of a number of subjects did not change or only slightly increased after the application of 0.03 Hz ISPC.

In this study, the WAs of the bilateral MCs in the interval III–V and those of the bilateral TLCs in the interval III increased more obviously under the ISPC state than under the resting state. This result indicated that ISPC could facilitate the activation of bilateral MCs and TLCs in various spontaneous oscillations. A seminal observation was that the changes of WA in bilateral MCs and TLCs by ISPC mainly occurred in interval III. This interval is associated with myogenic activity, which might originate locally from the intrinsic myogenic activity of the smooth muscle cells of the vessels [27, 28] that are partly under autonomic control [29]. The remarkable activation in the frequency interval III may be related to the intervention of patients using 0.03 Hz ISPC. The frequency of 0.03 Hz is within the range of the frequency interval III (0.052–0.145 Hz), hence the positive effect of ISPC on the myogenic activity in the bilateral MCs and TLCs of the patients with stroke. Within the 0.1 Hz frequency, arterial pressure oscillations occurred spontaneously with Mayer waves in the conscious subjects [30, 31]. As the Mayer wave is closely related to the arterial baroreceptor reflex and is usually enhanced during states of sympathetic activation, the mechanical pressure and stimulation of the sympathetic nerve caused by ISPC exert an effect on the amplitude of the Mayer wave. Both factors may explain the markedly higher ISPC state in interval III than in the resting state.

The WAs of the bilateral MCs in intervals IV and V showed a greater increase in the ISPC state than in the resting state. The cerebral oscillations in frequency interval IV are vascular reactions of neurogenic origin [32]. The autonomous nervous system participates in vasoconstriction by regulating the release of substances that affect the activities of smooth muscles. This process can regulate the overall blood flow in response to local conditions. Frequency interval V is associated with endothelial cell metabolic activities, which can produce and release potent vasodilatory and vasoconstrictive factors, such as nitric oxide and endothelin [32]. Given that neuronal cells, glial cells, vascular endothelial cells, and other cells jointly comprise the basic unit of the neurovascular coupling effect, the endothelial cell activities are closely related to nervous activities [24]. The substance that affects smooth muscle activity released by the sustained activity of the autonomic nervous system and endothelial cells maintains the basal level of vasoconstriction, thus causing the vascular smooth muscle to contract or relax as the intravascular pressure changes. In summary, ISPC may not be limited to the intervention of limbs and may affect cerebral oscillations. The increased WAs in this work indicated that ISPC could enhance the myogenic, neurological, and endothelial cell metabolic activities of bilateral MCs in patients with stroke.

One of the primary interests in this study was to assess the hemispheric activation balance. Previous studies have shown that enhanced contralesional activation after stroke translates into a reduced or even negative LI; accordingly, the LI of patients with stroke is lower than normal values on average [25]. This result is consistent with our findings, in which the patients' LI of the MC and TLC was lateralized to the ipsilesional hemispheric region. The ipsilesional MC and PFC exhibited great laterality when ISPC was applied; this result reflected an increased WA in the ipsilesional hemispheric region or a decreased WA in the contralateral hemispheric region. On the one hand, the correlation between the activation of ipsilesional MC and the recovery of motor function has been demonstrated in early stroke rehabilitation [14, 33, 34]. Although PFC is not considered as a primary motor region, the activation of the ipsilesional PFC may benefit the reinforcement of the management of the cognitive load required for motor performance [35–37]. On the other hand, the decreased contralesional cortical activation after stroke is common regardless of the lesion location, and this phenomenon may be related to physiologic recovery [38, 39]. Studies have demonstrated that the noninjured MC may aid ipsilesional MC via ipsilateral projections or by acting on the ipsilateral MC by the connection [40]. In fact, motor deficits associated with stroke may be worsened by increased inhibition from activated contralesional MC back onto ipsilesional MC [39, 41]. Hence, the ipsilesional activation caused by ISPC may have a positive effect on regional function rehabilitation.

However, according to a personalized analysis of patients, the LIs of several patients did not change or only slightly increased after the application of ISPC. This result indicates that the 0.03 Hz ISPC therapy is inappropriate for certain subjects. Cerebral autoregulation, which is a blood flow regulating mechanism, protects the brain tissue from hyperperfusion or hypoperfusion within a wide range of blood pressure fluctuations [42]. This mechanism is closely related to spontaneous oscillation and is controlled and affected by myogenic, neurogenic, and metabolic mechanisms [43]. After the onset of stroke, the effectiveness of cerebral autoregulation has been demonstrated to decrease and change with the progression of the disease's time course [44–47]. Therefore, the cerebral autoregulation in different

rehabilitation nodes is affected distinctly by myogenicity. This phenomenon may explain the nonsensitivity of several subjects to 0.03 Hz ISPC. Our study shows that the ISPC of 0.03 Hz is not suitable for all patients with stroke and more personalized treatment options should be considered in subsequent ISPC intervention.

Our study has several limitations. The severity of patients was not classified. Different effects of ISPC on patients with mild and severe stroke were not analyzed in detail. Given the preliminary nature of this work, clinical trials on other key parameters of ISPC were not conducted. According to the existing research results, the ISPC parameters adopted by stroke patients with different degrees of disease and different stages of rehabilitation should be different. Therefore, a personalized ISPC intervention plan should be the focus of future research.

## **Conclusion**

As an effective physiotherapy, ISPC exerted an important effect on cerebral oscillation. The application of ISPC significantly increased the WAs in the bilateral MCs in the intervals III, IV, and V. This result indicated the ISPC-induced activations of the bilateral MCs in the myogenic and neurogenic innervations and endothelial cell metabolic activities. The LIs in the PFC and MC decreased more obviously in the ISPC state than in the resting state, thereby reflecting the increase in WA in the ipsilesional hemispheric region. This phenomenon may have a positive effect on regions' functional rehabilitation. In addition, personalized analysis showed that the ipsilateral hemisphere of several patients was not responsive to 0.03 Hz ISPC. This result suggests that patients should not be treated with ISPC at the same parameters and that more personalized options should be considered in future ISPC intervention. This study provides evidence for the changes in cerebral oscillation associated with ISPC. The results should benefit the optimization of the key parameters of ISPC in personalized treatment and promote functional recovery in patients with stroke.

## **Declarations**

### **Ethics approval and consent to participate**

The experimental procedures were approved by the Human Ethics Committee of the National Research Center for Rehabilitation Technical Aids and were in accordance with the ethical standards specified by the Helsinki Declaration of 1975 (revised in 2008). All participants provided written informed consent prior to participation.

### **Consent for publication**

All authors have approved the manuscript for publication.

### **Availability of data and materials**

The dataset used and/or analyzed during the current study available from the corresponding author on reasonable request.

### **Competing interests**

The authors declare no any competing financial and/or non–financial interests.

### **Authors' contributions**

H.X. and Z.Y.L. contributed to the conception of the study. G.C.X., C.C.H. and W.H.L contributed significantly to analysis and manuscript preparation; H.X. and G.C.X. performed the data analyses and wrote the manuscript; Z.Y.L., H.H.Z. and Z.P.L helped perform the analysis with constructive discussions. All authors have read and approved the final manuscript.

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## **Abbreviations**

ISPC: Intermittent sequential pneumatic compression

fNIRS: functional Near-infrared spectroscopy

WA: Wavelet amplitude

LI: Laterality index

O<sub>2</sub>Hb: Oxygenated hemoglobin

HHb: Deoxygenated hemoglobin

fMRI: functional Magnetic resonance imaging

PFC: Prefrontal cortex

MC: Motor cortex

TLC: Temporal lobe cortex

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## Table

**Table 1. Clinical details of patients with stroke**

Patients	Age	Gender	Type of stroke	Hemiplegia side	Site of lesion	Time post stroke (Month)	Other diseases
Pt 1	69	M	Hemorrhagic	R	Thalamus	4	CAD, EH
Pt 2	53	M	Ischemic	R	Basal ganglia, Thalamus	3	EH
Pt 3	71	M	Ischemic	L	Thalamus	2	EH
Pt 4	69	M	Hemorrhagic	R	Thalamus	6	CAD, EH
Pt 5	80	F	Ischemic	R	Basal ganglia	3	CAD
Pt 6	75	M	Hemorrhagic	L	Thalamus	2	DM, EH
Pt 7	66	F	Ischemic	L	Basal ganglia	2	HLP
Pt 8	74	M	Ischemic	R	Basal ganglia	3	EH, HLP
Pt 9	76	M	Ischemic	R	Basal ganglia, Thalamus	2	DM, CAD, EH
Pt 10	61	M	Ischemic	R	Basal ganglia	2	DM, EH
Pt 11	75	M	Hemorrhagic	L	Thalamus	5	DM, EH
Pt 12	66	F	Ischemic	L	Basal ganglia	3	HLP
Pt 13	74	M	Ischemic	R	Basal ganglia	4	EH, HLP
Pt 14	61	M	Ischemic	L	Basal ganglia, Corona radiata	5	EH, HLP
Pt 15	50	M	Ischemic	R	Basal ganglia	5	EH
Pt 16	57	M	Ischemic	L	Basal ganglia	1	CAD, EH
Pt 17	67	M	Hemorrhagic	R	Basal ganglia	5	EH, HLP
Pt 18	76	M	Ischemic	R	Basal ganglia, Thalamus	5	DM, CAD, EH
Pt 19	61	M	Ischemic	R	Basal ganglia	5	EH, HLP
Pt 20	74	M	Ischemic	R	Basal ganglia	5	EH, HLP
Pt 21	54	M	Hemorrhagic	L	Basal ganglia	3	EH, HLP
Pt 22	75	M	Hemorrhagic	L	Thalamus	3	DM, EH
Pt 23	61	M	Ischemic	R	Basal ganglia	6	EH, HLP
Pt 24	45	M	Hemorrhagic	R	Basal ganglia	2	EH, HLP
Pt 25	54	M	Hemorrhagic	L	Basal ganglia	4	EH, HLP
Pt 26	50	M	Ischemic	R	Basal ganglia	6	EH
Pt 27	54	M	Hemorrhagic	L	Basal ganglia	5	EH, HLP

Abbreviations: Pt, Patient; M, Male; F, Female; L, Left; R, Right; DM, Diabetes mellitus; CAD, Coronary artery disease; EH, Essential hypertension; HLP, Hyperlipidaemia

## Figures

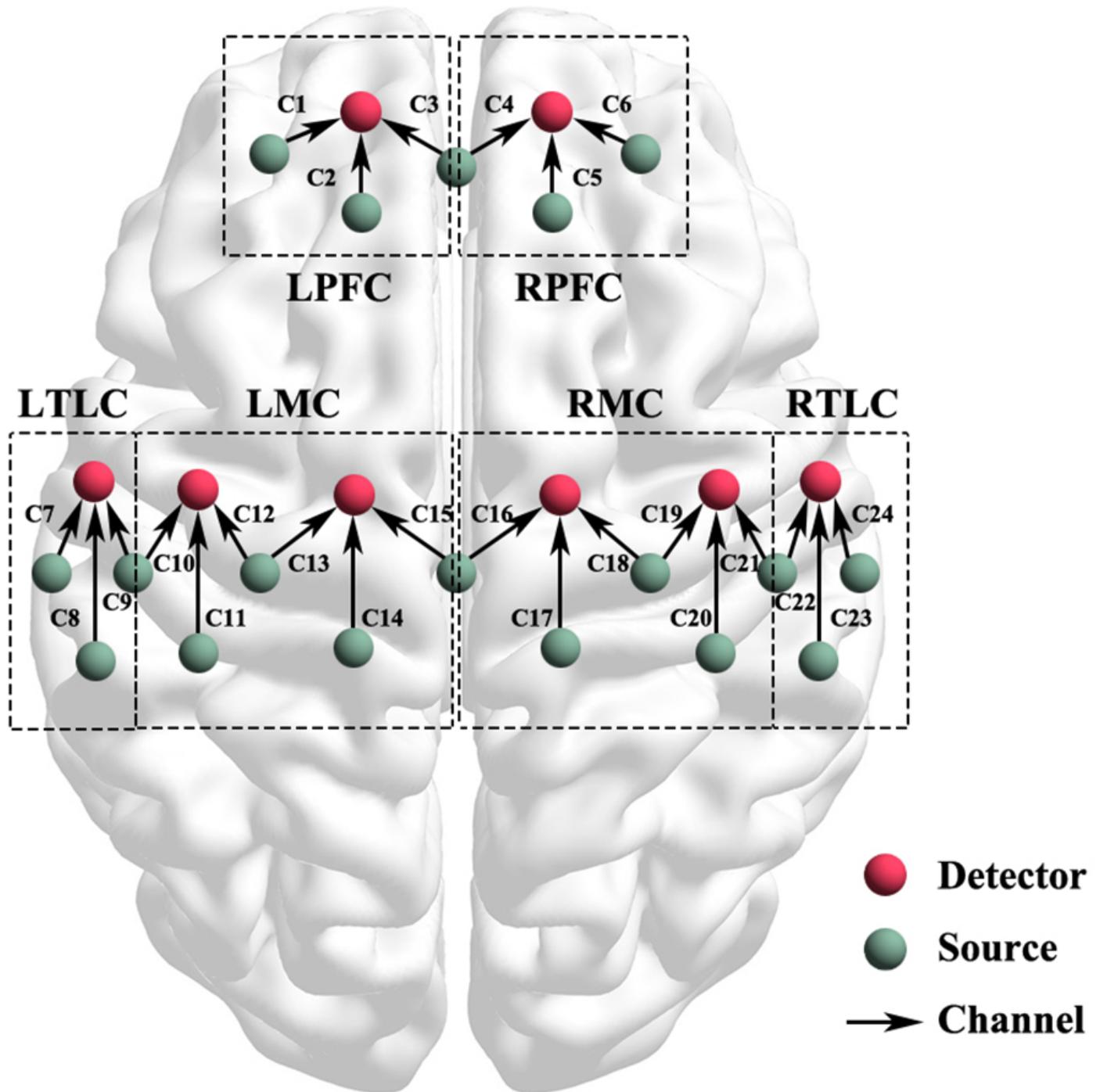
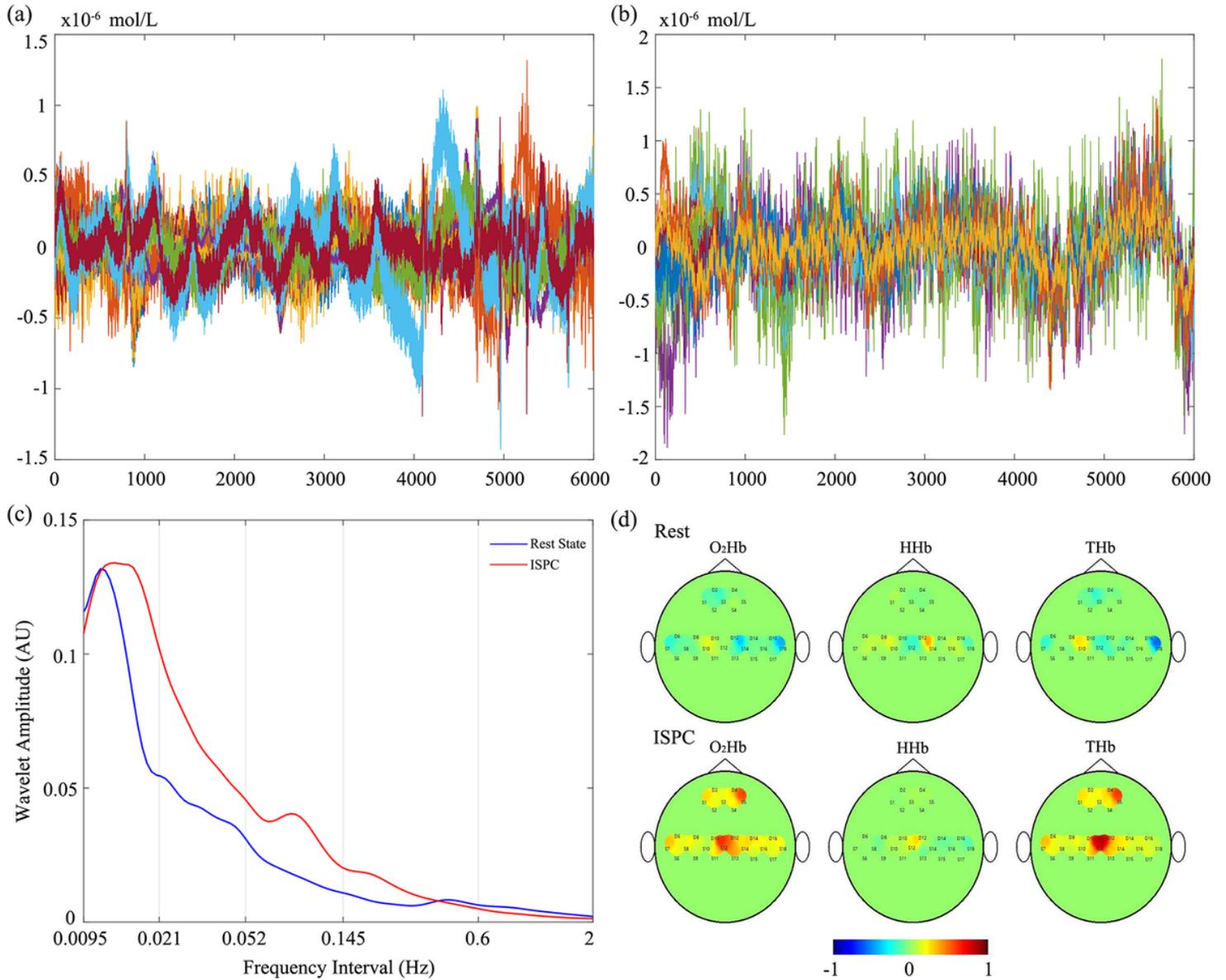


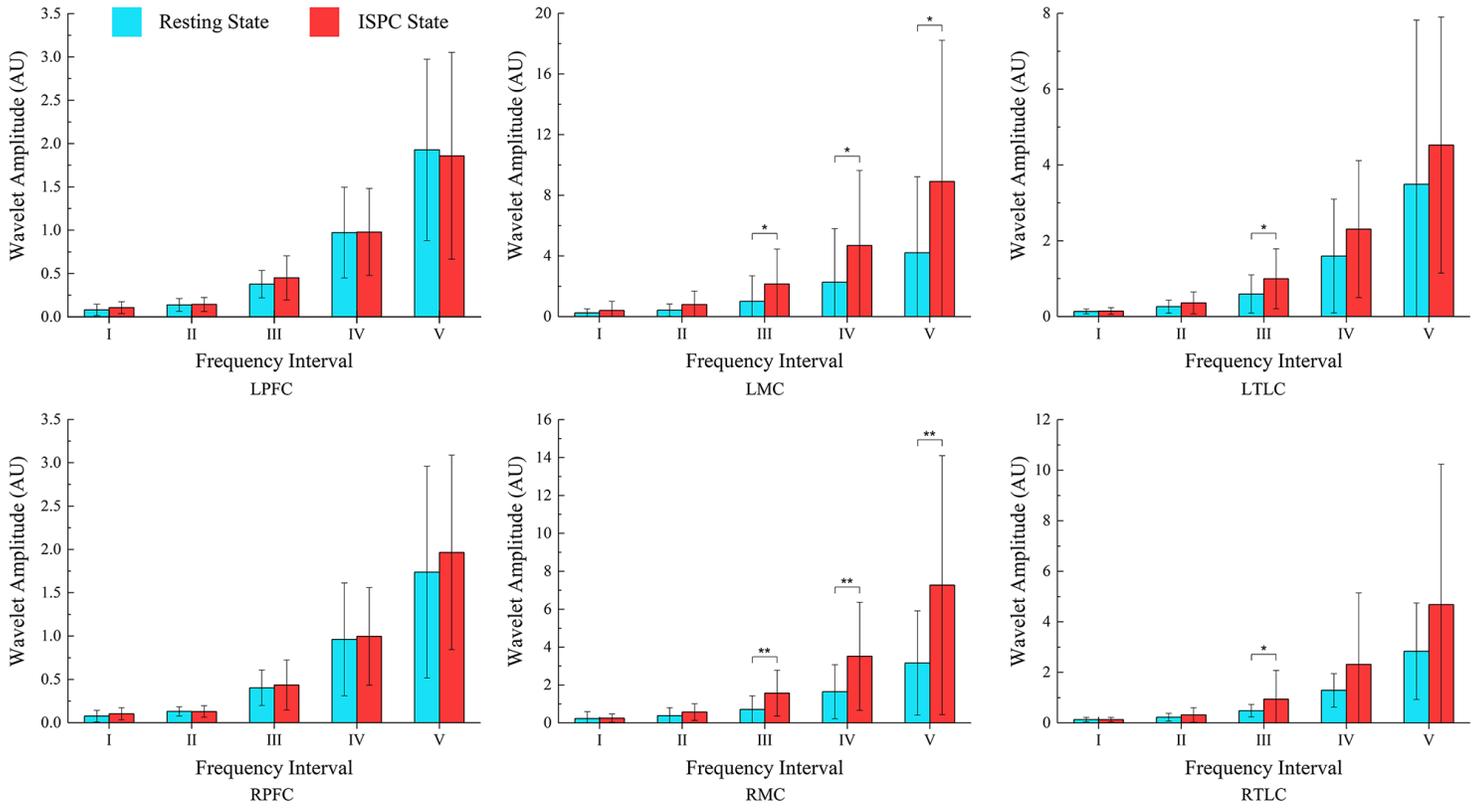
Figure 1

Schematic diagram of the experimental setup. Configuration of 18 source optodes, 8 detector optodes and 24 measurement channels.



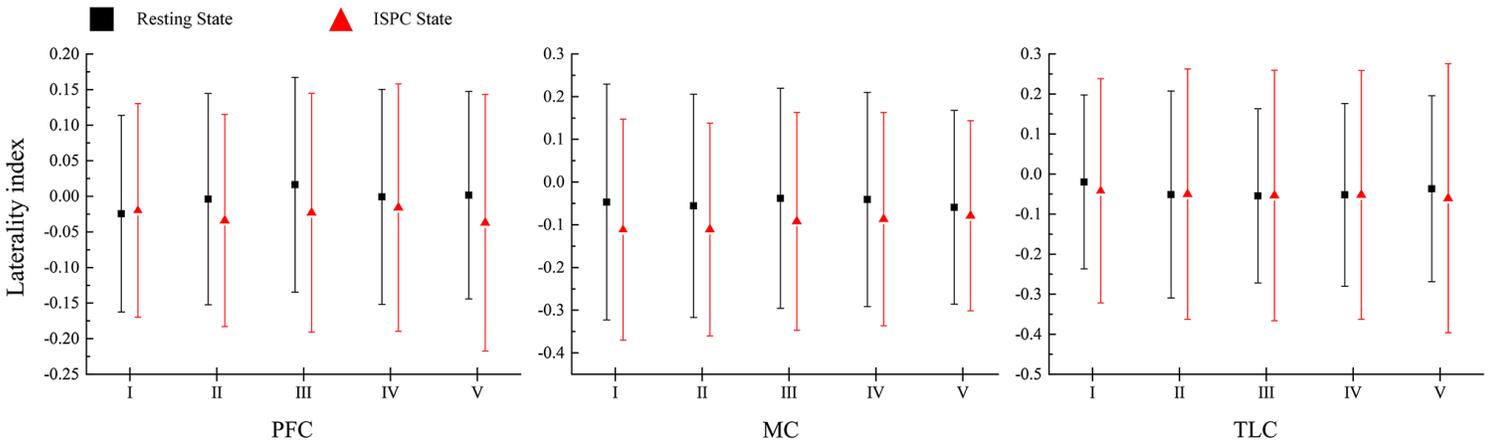
**Figure 2**

Cerebral oscillations changes in different states. The original signal during the resting (a) and ISPC (b) states and the WA in the five frequency intervals after wavelet transform (c). The cortical intensities during the two states are shown in (d), in which the letters indicate the position of the light source and detector. The color bar number range on the right-hand side of the image represents the activation in the six brain regions. The red color represents higher activation than the blue color.



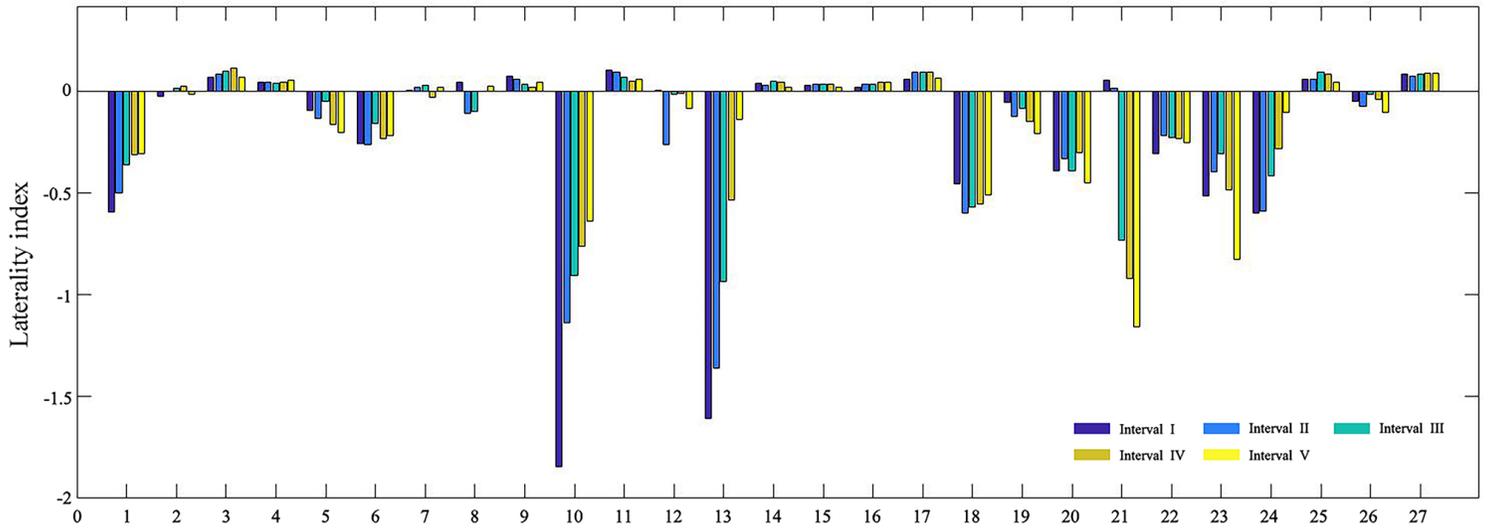
**Figure 3**

Comparative results of the WA values between resting and ISPC states in the six regions. \*,  $p < 0.05$ ; \*\*,  $p < 0.001$ .



**Figure 4**

The changes in laterality index in each brain region under the resting and ISPC states.



**Figure 5**

The individual LI values of each patients with stroke after 0.03 Hz ISPC application.

## Supplementary Files

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