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The Transformation of Dynamic Network State in Ischemic Stroke

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ABSTRACT

Ischemic stroke is a common disease of the nervous system, which poses a serious threat to human health due to its high disability rate and mortality rate, among which ischemic stroke occupies the first place. According to the Chinese National Stroke Registry Study, the crude and standardized prevalence of stroke in people over 40 years of age is 2.0% and 1.9%[1]. Because of its high disability rate and mortality, it is very important to accurately evaluate the disease condition and prognosis in the early stage of the disease. There are many methods to judge the severity of stroke patients, and the most widely used ones are clinical scale and imaging examination. In order to detect the onset of ischemic stroke early, it is important to identify specific electroencephalogram (EEG) dynamics and resting state fMRI for the transformation of brain activity during the onset of ischemic stroke. In this study, we investigated the transition of brain activity from interseizure to preseizure states, combining EEG networks at different frequency bands and cluster analysis combined with resting state fMRI to consider changes in patients' brain networks. These findings may provide useful insights into the pathogenesis of ischemic stroke and can also be used for prediction and subsequent intervention of ischemic stroke onset.

KEYWORDS

Ischemic stroke; EEG; Resting state fMRI; Brain network

1. INTRODUCTION

The brain is a networked system of interconnected units that shift dynamically through various activation states supporting cognitive function, and its various parts interact dynamically on multiple temporal and spatial scales. This network property is the basis of neuroplasticity, allowing for the acquisition of new skills (e.g., learning) as well as functional recovery after brain injury (e.g., stroke). Understanding the mechanisms and processes that give rise to these trajectories through state space is critical to intervening in ischemic stroke disease to restore cognitive function.

EEG (electroencephalogram) is a non-invasive method for recording the electrical activity of the brain. It can reflect neuronal activity by measuring electrical changes in the cerebral cortex. In research, scientists have been exploring the possibility of using EEG to predict ischemic stroke. Some studies have suggested that specific EEG patterns or changes may be associated with stroke risk. For example, some studies have found that people who have had an ischemic stroke may show specific patterns of electrical brain activity before the attack. By analyzing the spectral characteristics of EEG signals, the researchers were able to reveal the spatio-temporal dynamics of brain activity and the interactions between different frequency components. This information is crucial for understanding brain function, the organization of neural networks, and mental processes such as cognition, emotion, and behavior. These patterns may include abnormal increases or decreases in electrical activity, or specific changes in certain frequency bands

In this study, we analyzed the dynamic network of EEG electrical signals in different frequency bands of ischemic stroke, and cluster analysis was then applied to the EEG network to capture the transition of brain activity from the onset to the pre-onset state, as well as the dynamics of the pre-onset EEG network connections in ischemic stroke. Based on frequency characteristics, EEG signals are typically divided into five main frequency bands: delta, theta, alpha, beta, and gamma. These frequency bands correspond to different functional states and cognitive processes of the brain, providing rich data for the study of cerebral network in ischemic stroke. With variation in recovery time after stroke, increased interhemispheric homologous integration and intrhemispheric dissociation appear to be fundamental principles for the restoration of associative/higher cognitive functions (e.g., attention, language) as quantified by the restoration of normal modular organization [2].

In fact, the role of time in complex networks has recently been modified to model and analyze fundamental variables that show the phenomenon of world connectivity [3]. By introducing time, new higher-order properties emerge that cannot be captured by static network or graph methods. In a temporal network, two disconnected nodes can still interact if there is a chronological sequence of links connecting their adjacent points.

This way of rethinking networks naturally extends standard topological properties with purely temporal concepts such as latency, persistence, or the formation of connection patterns or patterns. At the same time, the inherent ability of temporal topological measures to characterize dynamic brain networks to predict future behavior is increasingly being demonstrated in the context of human neuroscience [5-10].

2. MATERIALS AND METHODS

2.1. PARTICIPANTS

All patients were required to read and sign informed consent forms prior to EEG monitoring, a dataset consisting of electroencephalogram (EEG) data from 50 (subject 1-subject 50) participants, aged 30 to 77 years. Participants included 39 men and 11 women. The time after stroke varies from 1 to 30 days. Twenty-two participants had hemiplegia in the right hemisphere and 28 in the left. All participants were initially right-handed. In this study, to eliminate the effects of anti-stroke medications, all patients were asked not to take anti-stroke medications before starting 24-hour EEG monitoring.

2.2. EEG RECORDING

All EEG data sets were based on the Grael series digital video EEG of Computer Medicine in Australia, with a sampling frequency of 500Hz. According to the international 10/20 system, 29 Ag/AgCl electrodes (FP1, FP2, Fz, F3, F4, F7, F8, FCz, FC3, FC4, FT7, FT8, Cz, C3, C4, T3, T4, CP3, CP4, TP7, TP8, Pz, P3, P4, T5, T6, Oz, O1 and O2) is positioned on the scalp. At the same time, single or dual cameras were used to monitor the clinical behavior of patients with epilepsy during EEG recording.

2.3. EEG DATA ANALYSIS

In addition, before building the EEG network, all of the data sets were preprocessed, including average reference, dimpled filtering to remove power frequency interference, which typically refers to 50Hz (or 60Hz) power line noise that might be present in the EEG signal, and the application of reverse filters to allow the dimpled filter to pass through and weaken signals outside the frequency band. Band-pass filtering is used to extract signals in the 0.5 to 80Hz band offline, while filtering signals in other frequency ranges. Through this kind of data processing, EEG data can be filtered effectively, so as to reduce the influence of noise such as power frequency interference and baseline drift on analysis results. We then exclude segments with absolute amplitudes greater than 100uV that are considered artifacts.

In order to study the change of stroke state before the onset of ischemic stroke, the EEG network was constructed by using coherence. Coherence is a statistical measure that describes the consistency or synchronicity of two signals over the frequency domain. It reflects the strength of the relationship between two signals in a certain frequency range, and is a common method for defining components of synchronization between two signals at a specific frequency [11]. The coherence formula is usually defined based on the spectral density of the signal. For example, in a frequency-selective channel, the coherence between two signals can be calculated from their power spectral density. In this case, if the power spectral densities of two signals are similar in a certain frequency range, the coherence between them will be higher. At this point, considering the two variables x(t) and y(t) in each segment, let Pxx(f)and Pyy (f) be the self-spectral density at the frequencies f of x(t) and y(t), respectively, and Pxy (f) be the corresponding cross-spectral density, then the coherence is formulated as follows:

$$C_{xy}(\mathrm{f}) = \frac{|P_{xy}(f)|}{P_{xx}(f)P_{yy}(f)} \tag{1}$$

Where Cxy (f) is the frequency-dependent measure. Since a number of studies have demonstrated the EEG dynamics of ischemic stroke attacks in different frequency bands. Then, we constructed correlated EEG networks over five frequency bands, namely delta(1-4Hz), theta(4-8Hz), alpha(8-13Hz), beta(13-30Hz), and low gamma(30-45Hz) [12]. For each specific frequency band, the EEG network is obtained by averaging Cxy over its frequency range. In this coherence definition, the corresponding spectral densities Pxx(f) and Pyy (f) and Pxy (f) are basically calculated from the fast Fourier transform (FFT) rather than the wavelet transform. The final constructed network is a graph where the nodes/vertices represent brain regions and the edges are region-to-region coherence.

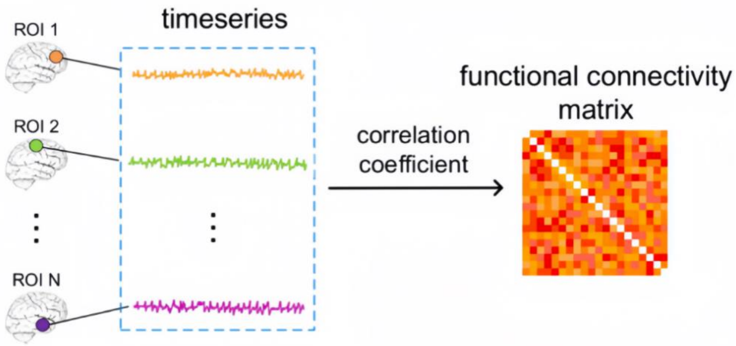

Figure 1. The procedure of brain FC network construction

Four weighted network attributes, namely clustering coefficient (CC), characteristic path length (CPL), local efficiency (LE), and global efficiency (GE) corresponding to the weighted network were used to quantitatively evaluate the dynamic response of EEG network synchronization to ischemic stroke. Weighted network in this study, the four attributes in the following definition for the formulation, and by using the brain connection toolkit (brain connectivity toolbox, BCT http://www.nitrc.org/projects/bct/) further calculation.

2.4. Time-frequency Analysis

Time-frequency analysis is a general-purpose technique used to study brain fluctuations over time and in different frequency bands. Here the time frequency of the central region (electrodes C3 and C4) is highlighted. During MI, the alpha band (8-15HZ) and beta band (15-30HZ) display power decreases. A continuous wavelet transform is a function that can capture both time and frequency information, which can be used for time-frequency analysis. The specific calculation steps are as follows: (1) Select the wavelet basis function (Morlet wavelet), (2) decompose the signal, (3) calculate the wavelet coefficient, (4) calculate the energy or amplitude, and (5) create a time-frequency graph.

Electrical Activity Mapping (BEAM) To study activation in the motor region, we calculated the average power distribution in the alpha and beta bands and plotted it on a topographic map based on channel location. Mapping maps generated from data during the left - and right-handed MI tasks show a clear pattern of ERD in the contralateral motion area. As shown in Figure 2, in terms of the 8-30HZ power of C3 and C4 channels, in most subjects, the power of C3 channel was consistently higher than that of C4 channel during left-handed MI (23/50=46%), and the grasp of C4 channel was consistently higher than that of C3 channel during right-handed MI. (21/50=42%) showed a more significant contralateral advantage. According to the clinical characteristics of the 50 patients, contralateral EEG activity during MI was more pronounced in patients with mild and moderate hemiplegia. However, when performing right-handed MI, some subjects had higher power at C3 than C4 at 8-30 Hz. Further analysis is needed to determine if this finding is relevant to the hemiplegic side.

Previous studies have shown that EEG α rhythm background slows down or disappears in patients with ischemic stroke, β activity decreases, θ and δ slow activity increases, and amplitude increases. In the trial expectation, after brain tissue injury in stroke patients, the connectivity of brain functional network is damaged, and there should be a variety of local network indicators with different degrees of decline, in addition, affected by a variety of factors such as symptoms, symptoms, etc., there are certain differences in different brain areas and indicators.

2.5. Changes in Intra - and Inter-network Connections of Brain Functional Networks

According to Yeo's 7-17 brain network template, the brain network is divided into seven major brain networks. Some scholars have proposed that these seven brain networks can be divided into three categories according to the main functions of each network: Primary sensorimotor networks (including SMN and VN), higher cognitive function networks (including DMN, DAN, ECN, and SN), and limbic system networks (including LN). The higher cognitive function network can be divided into task-positive network (TPN) and task-negative network (TNN). Task negative Network mainly

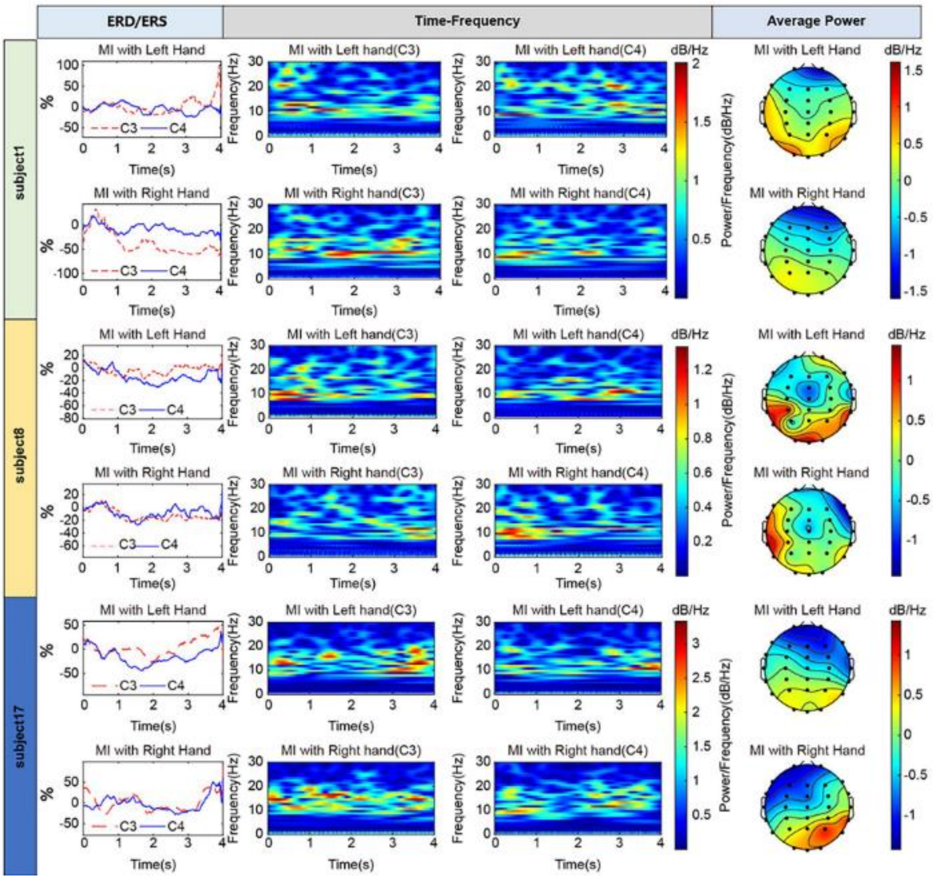

Figure 2. ERP,time-frequency,and averge power results(on topographical maps) of three subjects

Refers to DMN, which is responsible for the cognitive function of internal orientation, while SN and ECN belong to the Frontoparietal Control Network (FPCN), which is mainly responsible for the allocation of attention resources. In general, according to the previous theory, FPCN sends signals to regulate the functional activities of other brain regions, and its regulatory regions are all less interconnected networks. The limbic network mainly regulates emotion and is related to visceral movement.

2.6. Changes in Connectivity Within Functional Brain Networks

Compared with the normal control group, patients with acute ischemic stroke showed significantly reduced internal connectivity of DMN, ECN, and DAN, all of which are part of the higher cognitive function network but have their own functions. In general, the most serious and typical clinical symptom in stroke patients is a change in limb motor function, which is controlled by SMN. The MRIcorn software was used to manually delineate the contour of the abnormal part of the T2-weighted image signal layer by layer, obtain the focal mask of the patient, and standardize the T2-weighted image onto the MNI space. The patient's lesion mask was summed up to obtain the lesion superposition map.

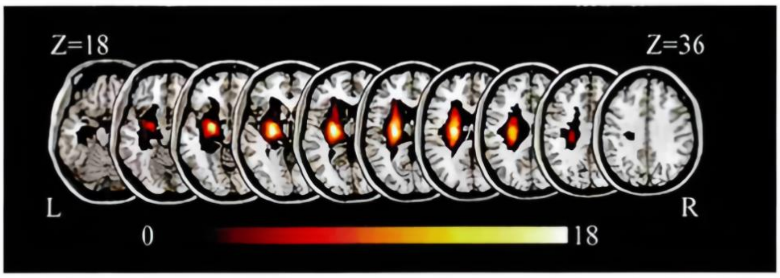

Figure 3. Patient lesion distribution

According to ICA, the relationship between the distribution of sensorimotor network brain region and the position of M1 region, which represents the hand motor function, was constructed. The sensorimotor network spatial map of healthy people was obtained by single-sample detection (FDR, $P < 0.005$, cluster size > 100) of the sensorimotor network selected by the subjects. Sensorimotor network and functional connection analysis were simultaneously superimposed on M1 region and presented on the standard template, and the position distribution relationship between the network space map and M1 was observed.

2.7. ICA Analysis Results

ICA automatically estimates 48 components, sensorimotor network was extracted, including dorsal sensorimotor network (dSMN), ventral Sensorimotor network (ventral sensorimotor network), dorsal sensorimotor network (DSMN). vSMN), left sensorimotor network (lSMN), and right sensorimotor network (rSMN) (as shown in Figure 4). dSMN is mainly distributed in bilateral anterior central gyrus, posterior central gyrus, auxiliary motor cortex, anterior cuneus and middle cingulate gyrus. vSMN was mainly distributed in bilateral ventral anterior central gyrus, posterior central gyrus, bilateral auxiliary motor cortex, insula and bilateral cerebellum. The lSMN is mainly distributed in the left primary sensorimotor cortex (including paracentric lobules), premotor cortex, auxiliary motor cortex, middle cingulate gyrus, subparietal lobules, parietal lobules, and suproccipital gyrus, as well as the right anterior cerebellar, posterior central and superior frontal gyrus. rSMN was mainly distributed in the right primary sensorimotor cortex (including paracentral lobules), premotor cortex, auxiliary motor cortex, middle cingulate gyrus, subparietal lobules, and parietal lobules, as well as the left anterior cerebellum, posterior central gyrus, and middle temporal gyrus.

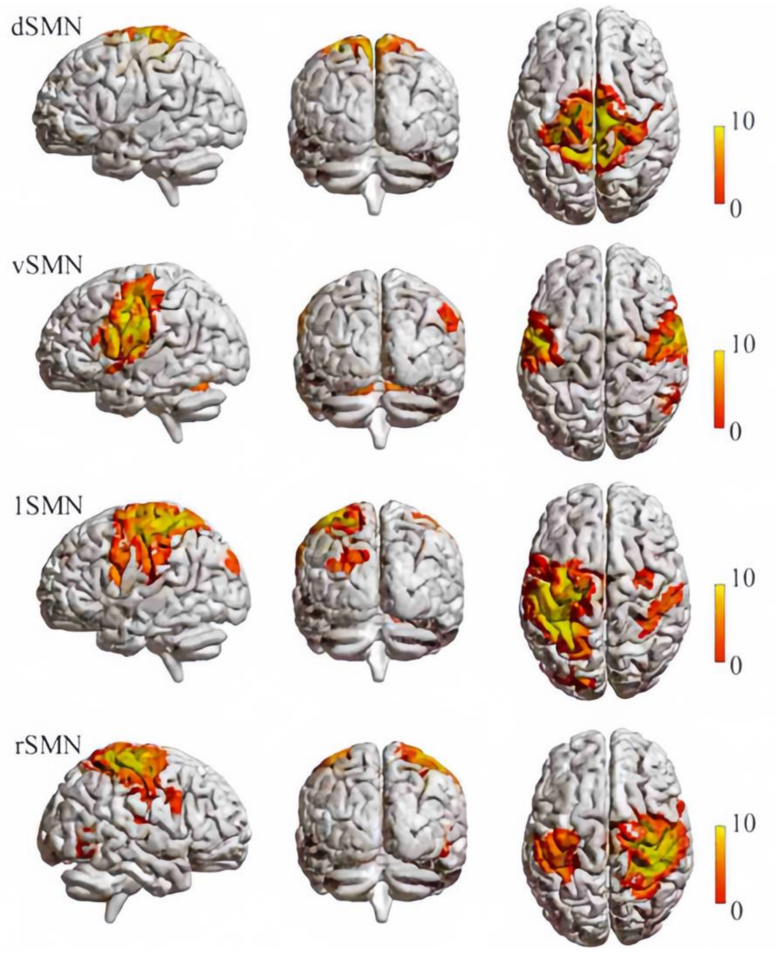

Figure 4. Four sensorimotor networks resolved by ICA

2.8. Results of Statistical Analysis of Sensorimotor Network Differences Between Groups

Compared with the healthy control group, all four sensorimotor networks in the patient group showed significantly reduced functional connectivity (FC) in the brain region, but not significantly increased functional connectivity in the brain region. The main brain areas involved are: left anterior central gyrus and right posterior central gyrus in dSMN, left posterior central gyrus in vSMN, left auxiliary motor cortex and right posterior central gyrus in lSMN, and left anterior and posterior central gyrus in rSMN. (As shown in Figure 5, Table1)

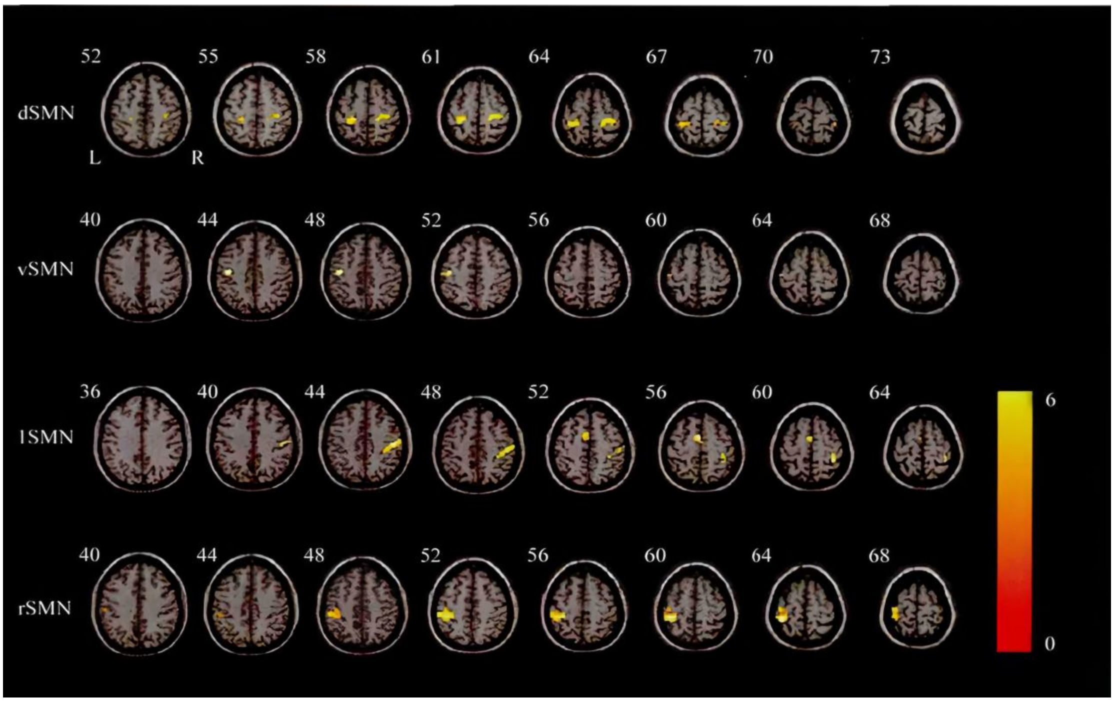

Figure 5. Stroke Functional connectivity reduced

Table 1. Stroke lower functional connections in the sensorimotor network than normal

Network	Brain region	The Brodman subdivision	Voxel value	T value	Peak coordinate		
					x	y	z
dSMN	Left posterior central gyrus	3	66	5.33	-24	-33	57
	Right anterior central gyrus	4	68	4.75	18	-33	57
vSMN	Left posterior central gyrus	3	45	4.03	-42	-15	45
lSMN	Right posterior central gyrus	2/3	146	4.98	51	-21	42
	Left side auxiliary motor area	6	56	4.94	-3	0	57
rSMN	Left posterior central gyrus Left anterior central gyrus	3/2/4	249	5.81	-39	-36	

3. CONCLUSION

In this study, ICA method was used to perform functional connection analysis on a group of stroke EEG data and resting fMRI data, and EEG data was used to propose whether the sensorimotor effects of stroke patients were related to the hemiplegic side. Further analysis results showed that, the sensorimotor networks (dorsal, ventral, left and right sensorimotor networks) extracted by ICA showed a significant decline in the functional links of the inner brain regions, indicating that stroke lesions caused multi-range comprehensive damage to the sensorimotor system of patients with hemiplegia.

The spatial distribution of dSMN in normal and healthy subjects showed left-right symmetry, mainly involving the dorsal primary sensorimotor cortex and auxiliary motor cortex. This network is highly stable and is one of the most stable networks in ICA studies. Therefore, dSMN is the main research network in ICA studies to investigate the abnormality and recovery mechanism of stroke network with impaired motor function [13]. The functional connectivity of bilateral sensorimotor cortices in dSMN was significantly reduced in the patient group compared with the normal control group. According to the fine localization relationship of the anterior central gyrus of the human brain, dSMN should be responsible for the sensorimotor functions of the human body's bilateral neck, trunk, and lower limbs [14]. The results suggest that the sensorimotor functions of the brain that govern the corresponding body parts are impaired. In addition, we found a significant decline in functional connections in the left posterior central gyrus in the vSMN, which may indicate that stroke lesions have a negative impact on the sensory functions of the face, including the jaw and tongue, which are the main operators of this network.

At present, many studies take M1 as the study area to consider the abnormal network connection pattern of patients with impaired motor function after stroke. The results show that unilateral subcortical stroke will lead to changes in the functional connection between the two hemispheres of the brain, and it is generally found that the functional connection of the M1 on the diseased side and the sensorimotor network on the healthy side is reduced. For example, Park et al. confirmed in a longitudinal study that the functional connection between ipsilateral M1 and contralateral primary sensorimotor cortex of stroke patients with motor disorders decreased after the onset of the disease, and the abnormal functional connection would be restored with the improvement of motor function [14].

More and more functional connectivity studies have shown that sensorimotor network is the core network vulnerable to stroke lesion attack. The higher cognitive regulatory networks related to sensorimotor function, such as frontoparietal network, executive control network and motor attention network, also have functional impairment or compensation, which is called functional reorganization. Multiple networks were constructed based on the combination of EEG and resting state fMRI analysis, and the appropriate networks were selected to observe the network changes caused by stroke lesions, and even the interaction between these networks could be further clarified. It provides a new and effective way to comprehensively understand the damage of multiple sensorimotor functional connection networks in hemiplegia patients.

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