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Non-invasive Brain Imaging and Stimulation in Post-stroke Motor Rehabilitation: A Review

Hui Chang, Yixuan Sheng, Jinbiao Liu, Hongyu Yang, Xiangyu Pan, and Honghai Liu*, *Fellow, IEEE*

***Abstract*—Motor dysfunction is the common sequela of stroke, which seriously affects the patients' daily life. Brain imaging is primarily employed to reconstruct the brain's structural and functional networks to assess motor function during motor rehabilitation. Non-invasive brain imaging techniques have been widely used due to the non-surgical advantages. Electroencephalography (EEG) and magnetoencephalography (MEG) are measurements of electromagnetic field changes during brain activity. At the same time, functional magnetic resonance imaging (fMRI) and functional near-infrared spectroscopy (fNIRS) are measurements of hemodynamic state during brain activity. Brain network consisting of functional connectivity and effective connectivity could be established based on brain imaging. Multimodal imaging can overcome the limitation of single-mode, making the motor function assessment more comprehensive and accurate. Mathematical models are required for studying connectivity and relationships among brain areas. Brain activity can be modulated through brain stimulation to enhance motor rehabilitation based on motor function assessments. Although not yet included in clinical guidelines, transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) have been shown in numerous clinical trials to promote bilateral brain balance. Brain network reorganization guides therapeutic strategies integrating brain stimulations. Although brain imaging and brain stimulation on stroke motor rehabilitation are well-studied forms, a thorough between imaging-based motor assessment and stimulation-based rehabilitation strategy is still lacking. This narrative review aims to summarize the methods of motor function assessment using brain imaging and interventions for motor function rehabilitation using brain stimulation after stroke, which would be helpful to establish a closed-loop rehabilitation approach.**

***Index Terms*—Stroke, Motor function assessment, Motor rehabilitation, brain imaging, brain stimulation.**

I. Introduction

STROKE has become the "second killer" worldwide, with high morbidity, mortality, and disability rates [1]. Thrombolytic drugs administered within hours of a stroke can save infarcts of brain tissue but do not eliminate the sequelae of loss of function. As a result, the medical burden due to stroke is expected to increase in the future [2]. Most of the functional loss caused by stroke is permanent and mainly motor function impairment [3]. The manifestations of motor impairment post-stroke were different from acute, subacute to chronic stage. Therefore, different degrees and stages require different rehabilitation therapies. At present, the methods to improve motor function after stroke can be divided into training intervention (such as constraint-induced movement therapy), technological intervention (such as virtual reality training), pharmacological intervention (such as cerebrolysin), and brain stimulation intervention [4]. Brain stimulation, as a potential method to change the brain's plasticity, has become a very precious research direction.

Brain stimulation, also known as neuromodulation, refers to the stimulation of the brain by various electrical, magnetic, optical, and ultrasonic technologies to change abnormal neural activity, which can be classified into two types: invasive and non-invasive. The usual methods of invasive brain stimulation are deep brain stimulation (DBS) [5], and cortical electrical stimulation (CES) [6]. Due to the need for craniotomy, the clinical application of invasive brain stimulation is difficult. Non-invasive brain stimulation includes TMS [7], tDCS [8], transcranial ultrasound stimulation (TUS) [9] and transcranial photobiomodulation (tPBM) [10]. This review focuses on TMS and tDCS because many studies have proved that TMS and tDCS have good effects. In the brain stimulation of stroke patients, it is necessary to locate the abnormal brain areas accurately. Otherwise, the brain stimulation can not play its due role and even produce adverse effects. Brain imaging technology can help "see" the inside of the brain, which can navigate brain stimulation.

Brain imaging technology can be divided into structural imaging and functional imaging based on brain tissue imaging and neural activity imaging [11]. Structural imaging techniques such as magnetic resonance imaging (MRI) [12], diffusion tensor imaging (DTI) [13], and computed tomography (CT) [14] can reveal the anatomical structure and morphology of the brain. Functional imaging is the focus of this paper, and the main methods include fMRI [15], fNIRS [16], MEG [17] and EEG [18]. These techniques have their advantages in spatial resolution and temporal resolution. EEG and MEG have good temporal resolution, while fMRI and fNIRS have outstanding spatial resolution. The brain imaging of stroke patients hopes to obtain both spatial and temporal information of abnormal neural activity, so clinical studies will use the combination of two or more technologies. In addition to the internal use of brain imaging techniques, brain-muscle coupling, which combines EEG or MEG information with a patient's muscle signals (electromyography, EMG) to analyze

*corresponding author

Hui Chang, Hongyu Yang, Xiangyu Pan, and Honghai Liu are with the State Key Laboratory of Robotics and Systems, Harbin Institute of Technology (Shenzhen), Shenzhen, China (e-mail: hui.chang@stu.hit.edu.cn, 20s053004@stu.hit.edu.cn, 15634400498@163.com, honghai.liu@icloud.com).

Yixuan Sheng is with the State Key Laboratory of Mechanical System and Vibration, Shanghai Jiao Tong University, Shanghai 200240, China (e-mail: 018020210008@sjtu.edu.cn).

Jinbiao Liu is with the Artificial Intelligence Research Institute, Research Centre for Augmented Intelligence, Zhejiang Laboratory, Hangzhou, China (e-mail: liujinbiao1518@zhejianglab.com).

motor dysfunction, is also currently a hot topic.

The twofold purposes of this paper are twofold: to summarize the current research progress of non-invasive theory and technology on brain imaging and brain stimulation, further shed light on breakthroughs of establishing feasible brain imaging-stimulation solutions to motor rehabilitation after stroke. The remaining of this review is organized as follows: Section II presents the progress of the generally used brain imaging methods and the multi-technique coupling analysis methodology. Section III digests the principle and improvement of brain stimulation methods. Section IV overviews the applications of brain imaging and brain stimulation in stroke and their combined effects. Finally, we discuss the challenges of stroke rehabilitation and the potential applications of brain imaging and brain stimulation techniques in the end.

II. Brain Imaging Methods

Brain imaging is an important achievement of modern science, and it is thriving. The increased depth of the observed brain, the increased temporal and spatial resolution, and the continuous fusion of multiple modes make brain imaging outstanding to study brain science and brain diseases. This section introduces the application of EEG, MEG, fMRI, fNIRS, and multimodal imaging in motor function assessment of stroke. Figure 1 shows the equipment for the four imaging modalities and the preliminary visualization results of the collected data.

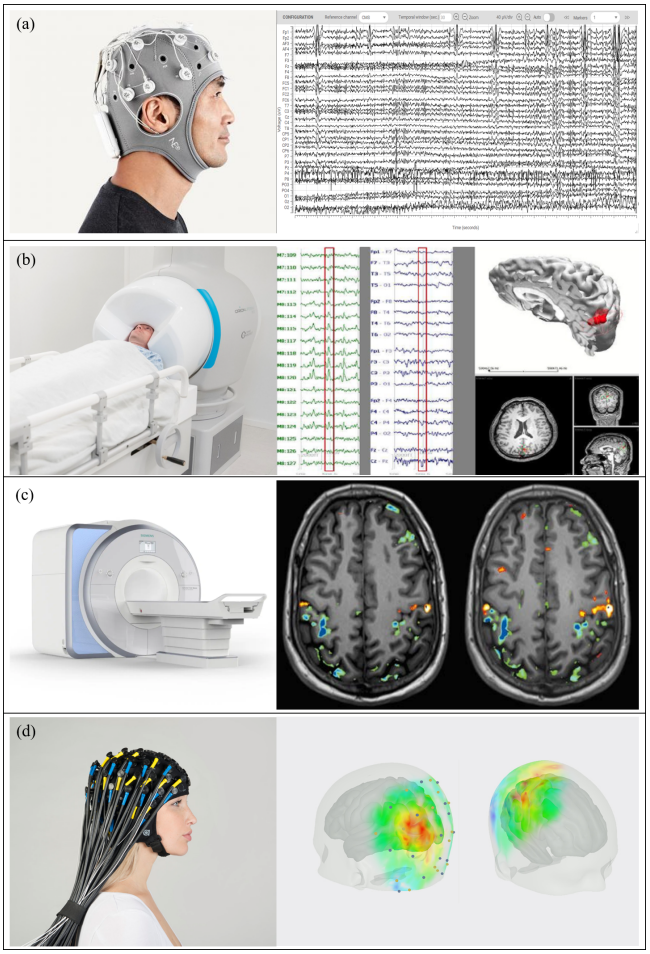

Fig. 1: Equipment and preliminary data visualization of four non-invasive brain imaging methods. (a) EEG: Enobio system, Neuroelectrics, Spain. (b) ORION LIFESGAN MEG system, Compumedics, Germany. (c) 3.0T Magnetom Skyra, Siemens Healthineers, Germany. (d) fNIRS: OxyMon system, Artinis Medical Systems, Netherlands.

A. Electroencephalogram

EEG is a general reflection of the electrical activity of brain nerve cells in the scalp [19]. With a time resolution of milliseconds, it can record faster brain activity [11]. However, the spatial resolution of EEG is limited because it is necessary to place an electrode with a diameter of about 1 cm on the scalp [20]. With the development of high-density EEG and source location technology, EEG has shown unique advantages in the field of diagnosis and evaluation of brain diseases [21], [22]. EEG electrode positioning is based on the standard 10-20 system, which currently achieves up to 256 channels [23]. Before a further state analysis, source localization analysis (SLA) of raw EEG signals is required, that is, inverse estimation of the location, direction, and intensity of neural activity sources in the brain. SLA software includes Matlab plugins such as Brainstorm, EEGLAB, FieldTrip, NutMeg, and SPM, as well as independent analysis software such as MNE, OpenMEEG, and NeuroFEM [24].

In recent years, with the development of quantitative analysis techniques, EEG has been widely used in the assessment of stroke rehabilitation [25], [26]. The Power Spectral Densities (PSD) of the delta, theta, alpha, and beta bands in EEG signals and the Relative Power Ratio (RPR) are commonly used for stroke detection, or classification [27]. Acute ischemic stroke can be confirmed or detected by the presence of slow waves (delta-theta) in the EEG signals [28]. Trujillo et al., [29] found that PRI (power ratio index: ratio of delta plus theta to alpha plus beta) can be used as an effective indicator to predict exercise rehabilitation by analyzing the relationship between EEG quantitative indicators and Fugl-Meyer Assessment. Aminov et al. [30] calculated the frequency band power and the ratio of single-channel EEG signals in stroke patients and found that delta-Theta ratio (DTR) could well reflect the cognitive performance after stroke, which was consistent with the 90-day MoCA (Montreal Cognitive Assessment) Scores. Bentes et al., [31] used mean Fast Fourier Transform to calculate EEG power to predict post-stroke performance. Results showed that delta-theta to alpha-beta ratio (DTABR) and alpha relative powers were good predictors of post-stroke functional performance. The alpha band showed the most significant correlation for the assessment of motor learning performance [32]. Delta-alpha ratio (DAR) exhibited the optimal classifier accuracy with a threshold of 3.7 in discriminating between acute ischaemic stroke and healthy subjects [28]. Partial least squares (PLS) models of delta or beta power across the whole brain are significantly associated with the National Institutes of Health Stroke Scale (NIHSS) score in measuring brain function [18]. The above work indicates that qEEG is an effective indicator

for quantitative assessment of motor function after stroke and is highly consistent with the results of the clinical assessment scale.

Brain Symmetry Index (BSI) is another indicator commonly used to assess the outcome of stroke rehabilitation based on EEG signals. Poor functional performance is often associated with high BSI values [33], [34]. Furthermore, there was a significant correlation between early BSI and Fugl-Meyer score later in rehabilitation, which indicates that BSI can be used to assess motor function after stroke [35]. Sheorajpanday et al. [36] demonstrated the predictive value of EEG by analyzing the correlation between pdBSI (pairwise derived BSI) and DTABR ((delta + theta)/(alpha + beta) ratio) of EEG signals in stroke patients and their mRS (modified Rankin Scale) and NIHSS scores after six months.

In addition to traditional statistical analysis methods, machine learning is increasingly used in the identification and evaluation of stroke patients [37]. With PSD of each frequency band as input, KNN was used to classify the degree of stroke, and the classification accuracy of more than 85% could be achieved [38]. Altan et al., [39] used a deep belief network to classify the brain activities of slow cortical potentials (SCP) training in stroke patients, and the accuracy rate could reach more than 90%. Djamal et al., [40] used fast Fourier transform (FFT) and one-dimensional convolutional neural network to detect EEG data of stroke patients, achieving 100% accuracy in the training set and 80.3% accuracy in the test set. Wavelet transform is more effective than FFT in the data extraction of non-stationary EEG signals. The accuracy of EEG emotion classification based on wavelet transform can be improved from 72% to 87% [41]. The accuracy of 93.33% was achieved by using wavelet transform to extract EEG frequency band, PCA to reduce dimension, and one-dimension CNN to classify stroke degree [42]. Using qEEG as a network input provides better classification or detection results than raw EEG as input. Using DAR, DTABR, and BSI as inputs, the accuracy, sensitivity, and specificity of Extreme Learning Machine (ELM) for stroke classification were over 72% [43]. The accuracy of stroke classification can be achieved 97.3% using PSD of EEG bands for 50 convolutional filters with 1x120 kernel size [44].

B. Magnetoencephalogram

MEG records neural activity by measuring changes in the brain's magnetic field using a sensitive magnetometer with a spatial resolution better than EEG [45]–[47]. However, MEG is expensive and easily interfered with by environmental magnetic fields when measuring small magnetic field changes [48]. MEG has become a means of stroke assessment or other brain disease detection because the spatial resolution has been further improved with the increase of the number of sensors, and the source location algorithm has also been extensively developed [17]. More than 250 channels of MEG signal can be collected simultaneously. MEG and EEG are different manifestations of the same signal, so analysis software is common to both. The difficulty of collecting MEG signals is that the magnetic field generated by brain activity is the pT degree, more than 100 times weaker than the Earth's magnetic field. MEG's recording was made possible by the invention of a sensitive magnetic flux detector called superconducting quantum interference device [49].

With the development of data acquisition and source localization technology, MEG has shown its unique value in stroke motor rehabilitation evaluation [50]. MEG signals are susceptible to the cortical abnormalities associated with stroke [51]. Event-related desynchronizations and synchronizations(ERDs/ERSs) of beta and gamma oscillations have been shown to correlate with motor performance in stroke patients. They can be used to assess rehabilitation progress [52], [53]. The movement-related beta desynchronization (MRBD) in the contralateral primary motor cortex of stroke patients is lower than control subjects, and MRBD is smaller in those with more motor impairment [54]. Beta rhythm rebound, another indicator that is thought to reflect decreased motor cortex excitability, was weak in the affected hemisphere of stroke patients and increased with the recovery process [55]. Abnormal low-frequency magnetic activity (ALFMA) can reflect the size of the lesion and is detected around the lesion in the affected hemisphere of some stroke patients. The lesion size was significantly larger in patients with ALFMA. The strength of 10Hz around oscillations in temporoparietal in the affected hemisphere was increased during recovery compared with unaffected side [56]. Quantitative MEG can be used to detect and localize perilesional dysfunction in stroke, same to qEEG. The beta relative power spectrum was decreased in perilesional tissue as well as a reduction in multiscale entropy (MSE) [57]. Accurate localization of the lesion can provide an anchor point for non-invasive brain stimulation therapy. The principle and analysis method is consistent with EEG. However, the research on MEG started late, and its application in the assessment of stroke still needs to be further explored.

C. Functional Magnetic Resonance Imaging

fMRI is a non-radioactive technique that looks at brain activity based on blood oxygenation level-dependent (BOLD) and has been widely used in neuroscience [58]. Changes in movement-related BOLD activation patterns during stroke rehabilitation provide evidence for the use of fMRI in rehabilitation assessment [59]. The prediction of motor rehabilitation combined with fMRI showed an increase in explanation compared to the FM score alone [60]. Interhemispheric activation balance (IHAB) in motor-related cortex changes with the rehabilitation process and laterality indexes (LIs) before and after the improvement of motor function can be a good measure of IHAB [61], [62]. The equation LIs = (ipsilesional activation - contralesional activation) / (ipsilesional activation + contralesional activation). LIs range from -1 to 1, with +1 representing complete ipsilesional activation and -1 representing exclusively contralesional activation. Contralaterality index (CI) is essentially the same indicator as LIs, and its equation CI = (contralesional - ipsilesional) / (contralesional + ipsilesional), which is used in some reports [63]. fMRI analysis in kinematics showed that a larger area of the cortex was activated when the patient performed ankle dorsal plantar-flexion movements one month after the rehabilitation evaluation [64].

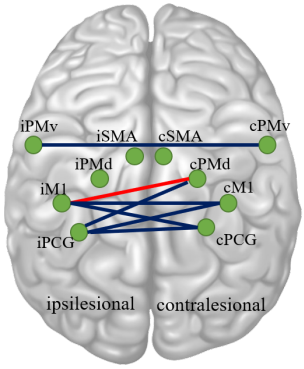

Fig. 2: Motor functional connectivity different between groups. Blue lines: FC different between healthy subjects and stroke patients. Red lines: FC different between stroke patients with favorable and unfavorable outcomes. Adopted from Chi et al [70]. (PMv: ventrolateral premotor cortex. PMd: dorsolateral premotor cortex. PCG: postcentral gyrus.)

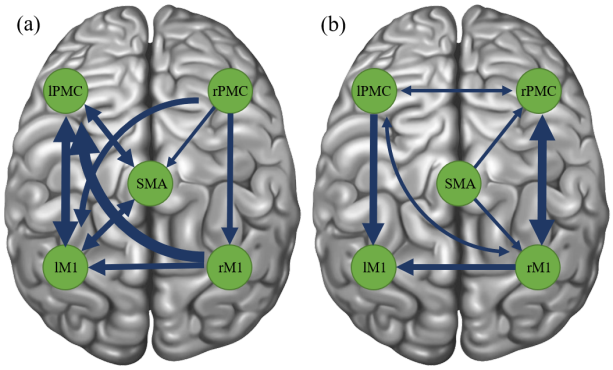

Fig. 3: EC within the cortical motor network in healthy subject (a) and stroke patients (b). Adopted from Wang et al [71].

After 6 months of rehabilitation, the activation balance in the patient's primary motor cortex shifted to the affected hemisphere [65]. Longitudinal evaluation of brain activation balance changes from onset to several months post-stroke by fMRI can effectively evaluate the rehabilitation therapy [66], [67]. Two weeks after treatment with constraint-induced movement therapy, fMRI activation in the sensorimotor area increased significantly, and the magnitude was greater in ipsilesional than contralesional [68].

fMRI-based functional connectivity (FC) and effective connectivity (EC) have been proven to be effective methods for assessing the status of exercise rehabilitation in stroke patients. FC measures functional interaction between different brain regions, or hemispheres, while EC provides directional information about the influence of one region on another [69].

Changes in the FC network were associated with stroke rehabilitation. At the onset of stroke, the FC in the motor area of the ipsilesional is weakened while in the contralesional is strengthened, as showed in figure 2 [70]. Resting-state fMRI can reflect FC from another perspective, and tracking longitudinal changes can better evaluate the clinical efficiency of rehabilitation strategies. Table 1 lists some reports of FC longitudinal changes via fMRI. Since stroke can lead to loss of balance of activation in both hemispheres, enhancing primary motor cortex (M1) activation in ipsilesional and constraining M1 activation in contralesional may promote motor function recovery [72], [73]. In addition to M1, activity in the prefrontal cortex and cerebellum has also been shown to contribute to exercise rehabilitation [74].

Stroke patients usually show weakened EC on the ipsilesional and enhanced on the contralesional, as showed in figure 3 [71]. The interaction between M1, premotor cortex (PMC), and supplementary motor area (SMA) could best reflect the state of motor function of patients [79]. When the movement of the paretic hand, some patients show additional inhibition from contralesional M1 activity on the ipsilesional M1 activity [80]. There may be that there are compensatory mechanisms in the body. The contralesional hemisphere takes on more to deal with the tasks to protect the ipsilesional from further damage. As with FC, the tracking of EC changes from acute stroke to chronic have more re for the assessment of rehabilitation status [69]. In the acute phase of stroke, EC of the ipsilesional SMA and PMC with the ipsilesional M1 decreased significantly [59]. After 3-6 months of rehabilitation treatment, EC between these areas increased as motor function improved. At the same time, after entering the subacute phase, the healthy side M1 began to show positive effects on the affected side M1, which is very beneficial to the improvement of sports performance [59], [81]. For methods to construct EC, many mathematical models are established. Granger causality is the most commonly used method to analyze interactivity [71], [82], [83]. EC can be set using structural equation modeling (SEM) [84]for resting-state fMRI data, and time-varying vector autoregression (TV-VAR) [85] for motor-tasks fMRI data. fMRI effectively assesses brain reorganization, changes in activation patterns, functional connectivity, and effective connectivity and is consistent with clinical evaluations. However, these conclusions need to be confirmed by future studies.

D. functional Near Infrared Spectroscopy

fNIRS is an emerging brain imaging technology in recent years. Its principle is similar to fMRI, that is, neural activity in the brain can lead to changes in hemodynamics [86]. Oxygenated hemoglobin (oxy-Hb) and deoxygenated hemoglobin (deoxy-Hb) in brain tissue have different absorption rates of near-infrared light to varying wavelengths of 600-900nm, which can be deduced to the brain activity according to the Beer-Lambert law [87]. Furthermore, the spatial resolution of fNIRS as fMRI is far superior to that of EEG and MEG. Meanwhile, the time sampling rate of fNIRS can reach about 10Hz, which is higher than that of fMRI [88].

Moreover, fNIRS has the characteristics of high experimental flexibility and strong anti-motion artifact ability, which can be more suitable for patients in different states [89], [90]. However, the limitation of fNIRS is that its detection depth is only about 1.5cm, which can only detect the activity of the outer cerebral cortex [91]. Its temporal resolution is only about 0.1s [92]. Based on these characteristics, fNIRS has become an effective method to study neurological diseases such as stroke [93].

TABLE I: Longitudinal changes of barin functional connectivity

Study	time span	Sample	changes of FC
Wang et al. (2010) [75]	1 year	10 Ps and 9 Cs	FC significantly increased between IP motor cortex and CP motor areas.
Park et al. (2011) [67]	6 months	12 Ps and 11 Cs	FC of CP M1 and occipital cortex decreased.
Golestani et al. (2013) [66]	3 months	51 Ps and 15 Cs	recovered patients exhibited normal motor connectivity in motor cortices.
Zhang et al. [76]	1 month	17 Ps and 15 Cs	FC increased between IP-M1 and CP-M1. FC decreased between IP-M1 and IP-SMA.
Tang et al. [77]	8 months	30 Ps and 37 Cs	FC reduced between CP-CPL and IP-PG, IFG, IPL, MTG and thalamus.
Lin et al. [78]	1 year	31 Ps and 20 Cs	FC between motor regions improved, but mostly within the first 3 months.

Ps: patients. Cs: controls
IP: ipsilesional. CP: contralesional
SMA: supplementary motor area. CPL: cerebellum posterior lobe. PG: precentral gyrus. IFG: inferior frontal gyrus. IPL: inferior parietal lobule. MTG: middle temporal gyrus.

Based on its imaging principles, fNIRS can assess brain reorganization after stroke, and functional recovery during rehabilitation [94]. Same as fMRI, FC [95] and EC [96]are commonly used to measure connection-based changes in stroke patients. Resting-state functional connectivity (rsFC) analysis showed a weakened connection of the ipsilesional, whereas a strengthened contralesional after stroke. Longitudinal studies have demonstrated improved connectivity between the primary motor area, somatosensory area, and premotor areas of the ipsilesional as rehabilitation progresses [97]. This result is consistent with the previous fMRI-based analysis results [69]. Direct assessment of hemodynamic patterns is also a way to assess the status of motor rehabilitation. LI was used to characterize interhemispheric balance, and the result was in good agreement with FMA for motor assessment of stroke patients [98]. Although fNIRS technology has not been developed for a long time, it has shown a specific application potential in the detection of neural activity related to motor tasks [99]. In the future, with the continuous improvement of equipment and the constant verification of clinical studies, fNIRS will become a good supplement in the assessment of stroke rehabilitation [100].

E. Multimodal method

Each imaging method has its advantages and disadvantages, and multimodal imaging can complement these advantages to provide a more comprehensive and accurate assessment of changes in brain structure and function [101]. We examined research reports from the last decade and found that the most popular multimodal combinations are EEG-fMRI [102] and EEG-fNIRS [103], [104]. EEG-MEG [48] and fMRI-fNIRS [105] combined studies have also been performed, but few studies have explored motor function assessment after stroke. EEG or MEG and EMG coupling analysis is another popular multimodal analysis method that can establish a correlation between brain activity and muscle behavior, which has unique advantages in assessing motor loss caused by abnormal neural activity after stroke [106]. This subsection focuses on applying EEG-fMRI coupling, EEG-FNRIS coupling, and EEG-EMG coupling in motor function assessment of stroke.

1) EEG-fMRI coupling: Simultaneous EEG and fMRI collection can assess the correlation between electrophysiological activity and hemodynamic changes in the brain [107]. Simultaneous resting-state EEG-fMRI and simultaneous task-related EEG-fMRI have different meanings and are used in different experimental paradigms. Simultaneous resting-state EEG-fMRI is mainly used to construct brain connectivity networks [108]. In contrast, while simultaneous task-related EEG-fMRI is used primarily to study functional brain activation under specific tasks [109]. The analysis of functional and effective connectivity for single-mode signals has been introduced. Multimodal functional network connectivity is a fusion method of EEG and fMRI in network space [110]. The basic steps are as follows: firstly, spatial independent component analysis (sICA) is used to extract functional network from a single-mode; Then, granger causality analysis is performed on functional networks of EEG and fMRI, respectively, to establish directed connections between networks; Finally, the functional networks of EEG and fMRI are matched by network source localization [111].

Changes in multimodal functional network connectivity in patients after stroke and during rehabilitation, as well as EEG signal-based hemispherical balance analysis described above, can be used to more comprehensively assess motor rehabilitation after stroke. A study evaluating bCI-guided robot-assisted training for stroke rehabilitation showed that training effect was significantly correlated with functional connectivity (derived from fMRI) between ipsilesional M1 and contralesional Bradman area 6. Meanwhile, the training effect significantly correlated with information flow change from contralesional PMA to ipsilesional M1 and from SMA to ipsilesional M1 [112]. Related studies from the same team have shown a correlation between increased motor area connectivity and a reduction in interhemispheric asymmetry in the central brain region covering the motor area, both associated with improved FMA scores [113].

In addition, synchronous EEG-fMRI imaging makes neurofeedback more effective for stroke rehabilitation [114]. Bimodal EEG-fMRI neurofeedback can provide the patient with more information to help him achieve faster and more specific self-regulation [115]. Off-line fMRI analysis revealed that motor activations were stronger under EEG-fMRI neurofeedback than that under single-mode neurofeedback [115], [116]. It is worth emphasizing that EEG-fMRI neurofeedback has the potential to induce an augmented activation of ipsilesional motor areas [117].

2) EEG-fNIRS coupling: As mentioned above, both EEG and fMRI signals are susceptible to motion artifacts, and a combination of EEG and fNIRS is an excellent solution to overcome this limitation [118]. Simultaneously EEG-fNIRS can provide comprehensive brain electrical and hemodynamic images. The development of wearable, integrated EEG-fNIRS

technology became the basis for multimodal assessment of brain function [103]. An fNIRS-informed EEG source imaging method was used to assess cortical activity and functional connectivity [118], [119]. The results showed that task-evoked Theta strength in the ipsilesional primary somatosensory was significantly lower in stroke patients than in healthy controls. After 4 weeks of rehabilitation, with better motor function recovery, the ipsilesional PMC theta strength increased, and the connection between bilateral M1 was strengthened [118]. Asymmetrical indicators based on EEG-fNIRS are commonly used to assess the progression of motor function rehabilitation in stroke patients. Inter-hemispheric sample entropy (IHI-En) and inter-hemispheric Oxygenated hemoglobin (IHI-Hbo) were extracted and compared, and significant differences were observed between stroke patients and healthy controls [120]. Simultaneously EEG-fNIRS analysis focusing on EEG-derived event-related desynchronization and oxygenated and deoxygenated hemoglobin concentrations provide a new basis for evaluating neurofeedback training effect [121]. Muchmore, EEG-fNIRS-based assessment of transcranial direct current stimulation on stroke rehabilitation has also been widely used, which will be discussed in the next section [122].

3) EEG/MEG-EMG coupling: There is a certain degree of information transmission and interaction between the cerebral cortex and the muscles during limb motion [106]. Corticomuscular coupling (CMC) is a quantitative assessment method that can reflect cerebral cortex information and motor muscle state [123]. CMC reveals the functional connectivity between the cerebral cortex and muscles by quantifying the synchronization between electromyography (EMG) and electroencephalogram (EEG) [124], or magnetoencephalography (MEG) [125]. The corticomuscular coupling phenomenon between the central nervous system and the periphery nervous system is essential for the neural control of movement. This functional coupling between the brain and muscle originates from the neural signal afferent and efferent process [126]. The brain transmits control commands to the peripheral nervous system in electrical charges through interconnected synapses and neuronal cells and then controls the contraction or extension of various muscle groups. The afferent process is a reverse process, and the feedback signal comes from the proprioceptors of muscles or joints and the mechanoreceptors of the skin [127]. Based on the complex interaction between the cortex and muscles at different coupling levels, CMC can be roughly divided into linear coupling and nonlinear coupling. Linear coupling analysis methods are mainly based on amplitude squared coherence, short-time Fourier time-frequency coherence, wavelet coherence, Granger causality, partial directed coherence, etc. The nonlinear coupling analysis method is mainly based on nonlinear Granger causality, mutual information, cross-spectral coherence, multi-spectral phase coherence, transfer entropy estimation, etc.

Coherence and mutual information (MI) are two basic methods of CMC, and the other methods are extensions of these two methods. Coherence-based CMC linearly evaluates the information interaction between the brain and innervating muscles and is currently the most widely used classical linear coupling analysis method [128]. Coherence-based CMC is essentially calculating the correlation in the frequency domain. The calculation formula is as follows:

$$Coh_{XY}(f) = \frac{|P_{XY}(f)|^2}{|P_{XX}(f)| \times |P_{YY}(f)|} \tag{1}$$

Where, $P_{XY}(f)$ is cross-spectrum density of EMG and EEG, $P_{XX}(f)$ and $P_{YY}(f)$ are the auto-power spectral density of EMG and EEG, respectively. The value range of CMC is 0 to 1, approaching 1 indicates high interdependence. Coherence-based CMC can analyze the control of the nerve signals of stroke patients on the muscle state under a specific movement paradigm from the time series and quantify the degree of rehabilitation of their motor function [106]. Generally, cerebral injury and muscle atrophy after stroke significantly decrease in CMC values and CMC increases during motor recovery. In addition, the amplitude of CMC on the contralesional of stroke patients was significantly higher than that on the ipsilesional, both in the acute stage and the post-acute stage [128]. Beta and Gamma band CMC can best reflect the dynamic changes of the motor system in stroke patients during rehabilitation [129], [130]. More specific studies indicate that the beta band CMC correlates with static force output and the Gamma band CMC correlates with dynamic force output [131]. Symmetry degree between contralesional CMC and ipsilesional CMC can also be used to assess stroke severity and recovery progress [132]. Belardinelli et al., [133] tested the CMC value of 8 stroke patients before and after four weeks of upper limb exercise rehabilitation, and all patients had a significant increase in beta band CMC.

Mutual Information is a measure of the amount of information that a random variable contains another random variable [134]. Suppose the joint distribution of two random variables (X, Y) is p(x, y), the marginal distribution is p(x) and p(y), and the mutual information I(X, Y) is the joint distribution and marginal distribution Relative entropy defined as follows:

$$I(X;Y) = \sum_{x \in X} \sum_{y \in Y} p(x,y) \log \frac{p(x,y)}{p(x)p(y)} \tag{2}$$

Jin et al., [135]proposed a model-free method based on time delay mutual information (TDMI) linear and nonlinear information flow, which can simultaneously detect the linear and nonlinear information components from the cortex to the muscle. Moreover, this method can also determine the flow of information. The difference NI(X, Y) between TDMI(X, Y) and TDMI(Y, X) represents the net flow of information, which can be interpreted as the flow of information between them. If NI(X, Y) is positive, information flows from X to Y; if NI(X, Y) is negative, information flows from Y to X. The calculation formula is as follows:

$$\begin{aligned} &TDMI(X,Y) = TDMI(x(t), y(t+\tau)) \\ &= -\sum_{n} p(X(t), Y(t+\tau)) \log \tfrac{p(X(t),Y(t+\tau))}{p(X(t))p(Y(t+\tau))} \\ &TDMI(Y,X) = TDMI(y(t), x(t+\tau)) \\ &= -\sum_{n} p(Y(t), X(t+\tau)) \log \tfrac{p(Y(t),X(t+\tau))}{p(Y(t))p(X(t+\tau))} \end{aligned} \tag{3}$$

Transfer entropy (TE) is a coupling analysis method based on mutual information, which has advantages in judging information flow and has been favored by researchers in recent

years [136], [137]. The transfer spectrum entropy (TSE) can reveal the coupling state between two signals in the local frequency band [138]. Directed coherence is also a directional coupling analysis method that is often used in studies to explore whether the brain sends information to or receives feedback from the muscles [139], [140]. Although CMC is a relatively new research direction, good results have been obtained, and more studies are needed to evaluate its clinical effects in the future.

III. Brain Stimulation Methods

Brain stimulation has evolved from invasive electrode stimulation to implantable and non-invasive stimulation. In recent years, with the development of non-invasive brain stimulation (NIBS) [141], the clinical application of TMS [142] and tDCS [143] has achieved good results in the stroke motor rehabilitation. The mechanism of how TMS and tDCS contribute to stroke motor rehabilitation has yet to be confirmed. Feasible mechanisms include hemispheric interaction inhibition [144], change of neuronal membrane potential polarity [145] and brain plasticity [146]. The TMS and tDCS affect not only the target areas of the motor cortex but also affect the networks of the brain and spinal cord that are connected at a distance [147]. In this section, we will review the research on the application and mechanism of TMS and tDCS in stroke motor rehabilitation within the last ten years.

A. Transcranial magnetic stimulation

TMS is painless stimulation of the cerebral cortex or peripheral nerves divided into single pulse TMS and repetitive TMS (rTMS). Single-pulse TMS is usually used in combination with other imaging methods to assess motor function after stroke, while rTMS is used for motor rehabilitation treatment [148]. The magnetic field passes unattenuated through high-impedance tissues such as the skull and scalp, causing the cerebral cortex to generate induced currents. Induced currents change the membrane potential of cells, increasing or inhibiting the excitability of neurons. Changes in neuronal excitability can affect synaptic plasticity and promote motor learning and motor function recovery after stroke [142]. According to the size of stimulus frequency, rTMS can be divided into low-frequency stimulation ($\leq 1Hz$) and high-frequency stimulation ($>1Hz$). Low-frequency rTMS can reduce the excitability of the target cortex, while high-frequency rTMS can improve it [149].

1) Mechanism of rTMS in stroke motor rehabilitation: Current studies generally believe that the mechanism of rTMS for stroke rehabilitation is reflected in the modulation of hemispheric interaction [150] and enhancement of brain plasticity [151]. It has been shown in the previous section that stroke can lead to disruption of the activation balance between the cerebral hemispheres. The excitability of the motion-related areas on the ipsilesional hemisphere decreased, but the contralesional hemisphere's excitability increased. In addition, when the affected hand performed motor tasks, the contralesional hemisphere inhibited the ipsilesional hemisphere. High-frequency TMS can improve the excitability of the motor cortex of the ipsilesional, but low-frequency TMS can inhibit the excitability of the motor cortex of the contralesional, thus realizing the regulation of cerebral hemisphere interaction [152], [153]. After treatment with rTMS, the lateralization of power spectral density and information transmission efficiency between bilateral hemispheric central cortexes was significantly changed. In other words, rTMS can modulate hemispheric lateralization, which may be an important neural mechanism to improve motor function [154].

Neuroplasticity refers to the characteristic that the nervous system can change its structure and function in the activity and maintain it for some time to actively adapt to and reflect various changes in the internal and external environment. Because synapses are needed for information transmission, processing, storage, and retrieval between neurons, the most basic and essential aspect of neuroplasticity is synaptic plasticity [155]. In synaptic plasticity, there are two essential types: Long-Term Potentiation (LTP: enhancement of synaptic strength due to continuous high-frequency synaptic activity that can last for hours or even days) and Long-Term Depression (LTD: continuous inhibition of synaptic strength due to constant low-frequency synaptic activity) [156], [157]. In general, LTP can be induced by TMS higher than 5Hz, and LTD can be generated by TMS at low-frequency [153].

2) Application of rTMS in stroke motor rehabilitation: It had been approved that rTMS positively affects motor function rehabilitation after stroke, especially in subacute patients. In a meta-analysis of 392 patients, only 4 showed adverse reactions to rTMS, while the rest improved motor function [158]. The progress of the ability to complete fine movements of the upper limbs and the improvement of the walking function of the lower limbs are the urgent needs of stroke patients. Fortunately, rTMS has shown effectiveness in rehabilitating both the upper and lower limbs. A meta-analysis summarized 8 reports of 273 patients with positive changes in finger movement and hand function after rTMS treatment [159]. Jin et al. recruited 127 subacute stroke patients with upper limb motor dysfunction. After two weeks of rTMS treatment, the cortical latency of motor evoked potentials and central motor conduction time were significantly lower than in the previous treatment. The motor score was improved considerably [154]. A study divided 13 stroke patients into the sleep group (7 patients) and the situation group (6 patients) for rTMS treatment. After 15 days of hospitalization, the increase of Action Research Arm Test (ARAT) score in the sleep group was significantly higher than that in the awake group, which may provide a new idea for the treatment of rTMS [160]. To evaluate the effect of rTMS on lower extremity motor rehabilitation in stroke patients, a meta-analysis involving eight studies 169 patients revealed that rTMS significantly improved lower limb motor function, lower limb activity, and motor evoked potentials. Subgroup analysis demonstrated that rTMS could improve walking speed along with FMA score [161]. In addition, it has been shown that TMS applied to the motor cortex induces a motor evoked potential (MEP) in the target muscle, which is recorded by surface EMG [162].

Either applying low frequency rTMS (LF-rTMS) to the contralesional alone, applying high frequency rTMS (HF-

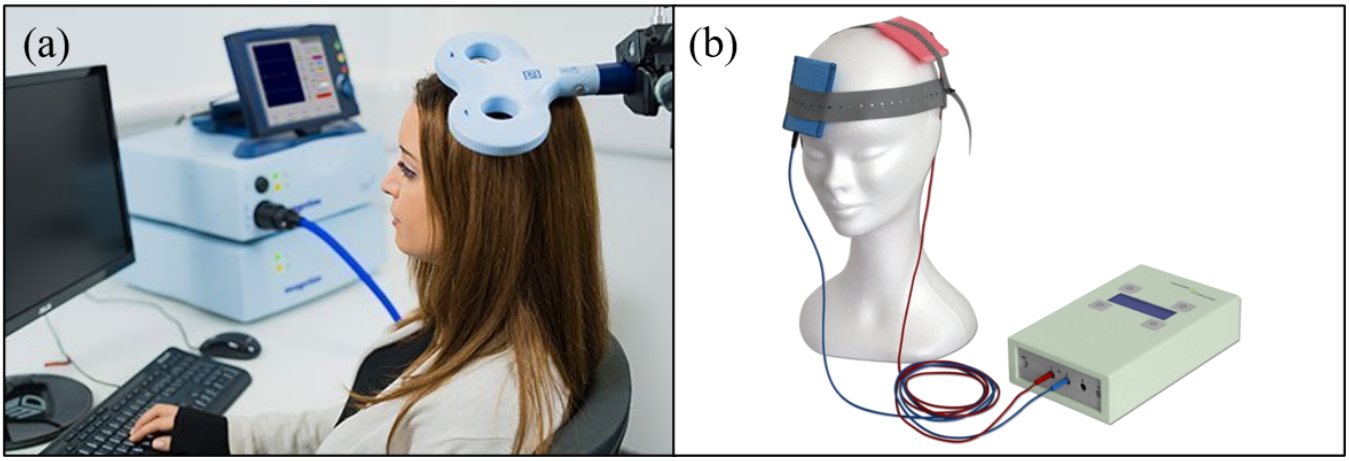

Fig. 4: Equipment of TMS and tDCS. (a)TMS: Magstim Rapid2, Magstim Company, UK. (b) tDCS: DC-STIMULATOR, NeuroConn, Germany.

rTMS) to the ipsilesional, or using LF-rTMS and HF-rTMS at the same time, both can improve motor function [149], [163]–[166]. But other studies have pointed out that stimulation of low-frequency rTMS on the healthy side may be more beneficial than stimulation of high-frequency rTMS on the affected side [158]. At the same time, rTMS also performed well in long-term effects, which are critical for clinical treatment [167]. Some literature suggests that intermittent theta-burst stimulation (iTBS) of the affected side is a useful rehabilitation therapy [158], [168], but more research is needed to approve.

Since there is currently no clinical guideline for rTMS, we summarize the stimulus paradigm used in the current study with good rehabilitation outcomes (see Table 3) to help future studies specify effective treatment regimens. Commonly used low frequency is 1Hz, high frequency is 3Hz or 10Hz, and a single treatment contains 500-1500 pulses.

Although rTMS is effective in stroke rehabilitation, studies of stimulation and outcomes are heterogeneous, and routine use of a specific stimulus paradigm cannot be recommended. Future research and evaluation of the most promising protocols will be needed to determine the stimulus paradigm for clinical treatment [142].

B. Transcranial direct current stimulation

tDCS is a type of transcranial electrical stimulation (tES) that regulates the excitability of neurons by applying a weak direct current to the cerebral cortex [174]. tDCS can be divided into anodal tDCS and cathodal tDCS according to the polarity of the electrodes applied to the target stimulated brain region. In general, anodal tDCS can enhance the excitability of the target area, while cathodal tDCS can inhibit it [175]. The current ranging from 0.5mA to 2mA poses no risk to the human body, with a single session lasting from 7 to 40 minutes. Common electrode pads are $15-35cm^2$ in size, so the current density is about $0.04-0.06mA/cm^2$. Typically, the moderating effects of tDCS last from a few minutes to several hours after the stimulation [145], [176]. After a single session of 20 to 30 minutes, the effect can last about 90 minutes. After five consecutive days of stimulation, the aftereffect lasted for three months. Compared to rTMS, tDCS is more portable and safe, with less patient discomfort, and can be easily combined with other peripheral therapies [143].

1) Mechanism of tDCS in stroke motor rehabilitation: tDCS has been increasingly used as an adjunct therapy for motor rehabilitation, but its potential application is limited because of the unclear mechanism of action [177]. The current explanation for the means of tDCS can be summarized as changing the polarity of neuronal membrane potential and regulating synaptic plasticity. The underlying mechanism of tDCS has been studied since the 1960s, and it was proved that tDCS could change cortical excitability by detecting the change of motor-evoked potential (MEP) through TMS in 1998 [178]. When weak direct current is applied to the scalp, the resting membrane potential and spontaneous discharge rate of neurons are modulated, leading to plasticity [145]. Anodal tDCS causes neurons membrane to depolarize, leading to an increase in the excitability of the cortex, while cathodal tDCS causes neurons membrane to polarize to decrease excitability [179]. The membrane potential polarization state change may be the mechanism of immediate effect after tDCS. tDCS can induce long-lasting changes in synaptic excitability in the motor cortex, and the biological agent is LTP and LTD phenomena at the cellular level [157]. Some studies suggest that tDCS induces synaptic plasticity by altering changes in neurotransmitter concentration [178]. Moreover, some studies have shown that anodic tDCS can reduce gamma-aminobutyric acid (GABA) in the cortex and enhance cortical excitability. On the contrary, cathode tDCS reduced glutamate concentration and thus reduced cortical excitability [180]. In addition, changes in dopamine, acetylcholine, and serotonin may also be involved, but more research is needed to confirm this [178].

2) Application of tDCS in stroke motor rehabilitation: The underlying assumption of tDCS in motor rehabilitation is that post-stroke maladaptive interhemispheric interactions affect motor function. tDCS can regulate interhemispheric excitability, reduce the inhibition of the contralesional hemisphere to the ipsilesional hemisphere, and promote the balance of hemispheric interaction [181]. EEG measurement revealed

TABLE II: Summary of rTMS experimental paradigm

Study	Samples	Experimental paradigm	Motor assessment scales
Khedr et al. (2010) [167]	48 patients (16 HF-1 group, 16 HF-2 group, 16 control group)	HF-1: 3 Hz, 5s, 50 trains, 750 pulses, 130% rMT on CP. HF-2: 10Hz, 2s, 37 trains, 750 pulses, 100% rMT on CP. Control: sham, parameters same with HF-1, coil angled away from head.	NIHSS and mRS
Avenanti et al. (2012) [169]	30 patients (8 group A, 8 group B, 7 group C, 7 group C)	Group A: real rTMS-PT. Group B: PT-real rTMS. Group C: sham rTMS-PT. Group D: PT-sham rTMS. (Real rTMS: 1Hz, 1500 pulses, total 25 min, 90% rMT on CP. Sham rTMS: no current induced)	JHFT and NHPT and B&B
Sasaki et al. (2013) [170]	29 patients (9 HF group, 11 LF group, 9 control group)	HF group: 10Hz, 10s, interval 50s, 1000 pulses, 90% rMT on IP. LF group: 1Hz, 30min, 1800pulses, 90% rMT on CP. Control group: sham, parameters same with LF group, coil rotated 90°.	NIHSS and BRS
Sung et al. (2013) [168]	54 patients (16 group A, 13 group B, 14 group C, 15 group D)	Group A: course 1 (1 Hz rTMS, on CP M1, 10 sessions), course 2 (iTBS, on IP M1, 10 sessions). Group B: course 1 (sham, 1 Hz rTMS, on CP M1, 10 sessions), course 2 (iTBS, on IP M1, 10 sessions). Group C: course 1 (1 Hz rTMS, on CP M1, 10 sessions), course 2 (sham, iTBS, on IP M1, 10 sessions). Group D: course 1 (sham, 1 Hz rTMS, on CP M1, 10 sessions), course 2 (sham, iTBS, on IP M1, 10 sessions). (rTMS: 5s, interval 5s, 600 pulses, 90% rMT. iTBS: 3 pulses at 50 Hz repeated at 200-ms intervals for 2 seconds, train interval 10s, 600 pulses)	FMA and MRC
Galvão et al. (2014) [171]	20 patients (10 experimental group, 10 control group)	Experimental group: 1 Hz, 60s, interval 120s, 1500 pulses, 90% rMT on CP, 1 session per day, 10 consecutive sessions. Control group: sham, coil disconnected.	MAS and FMA
Du et al. (2016) [172]	69 patients (23 HF group, 23 LF group, 23 control group)	HF groups: 3 Hz, 10s, interval 10s, 40 trains, 1200 pulses, 80%-90% rMT on IP, 5 consecutive days. LF groups: 1Hz, 30s, interval 2s, 40 trains, 1200 pulses, 110%-120% rMT on CP, 5 consecutive days. Control groups: sham, parameters same with LF, coil rotated 90°, 5 consecutive days.	FMA and MRC
Rastgoo et al. (2016) [173]	14 patients (7 AS group, 7 SA group)	AS group: 5 daily sessions active rTMS, 1 week after, 5 daily sessions sham rTMS. SA group: 5 daily sessions sham rTMS, 1 week after, 5 daily sessions active rTMS. (Active rTMS: 1Hz, 1000 pulses, total 20min, 90% tibialis anterior MT on CP. Sham rTMS: audio coil replace magnetic coil)	MMAS and FMA

rMT: resting motor threshold. aMT: active motor threshold
HF: high frequency. LF: low frequency.
CP: contralesional. IP: ipsilesional.
MAS: Modified Ashworth scale. MRC: Medical Research Council. MMAS: Modified Modified Ashworth scale. BRS: Brunnstrom Recovery Stage. JHFT: Jebsen-Taylor Hand Function Test. NHPT: Nine-Hole Peg Test. B&B: Box and Block Test.

the functional connectivity of the brain network, and it is found that anodal tDCS treatment enhanced the functional connectivity of the ipsilesional motor cortex [182], [183]. A review of 19 studies summarized the upper limb recovery performance of 388 patients who received tDCS [184]. 124 patients with acute or post-acute stroke received cathodal tDCS on the contralesional, and 28 patients had significantly improved motor performance. The motor performance of 28 chronic patients was improved after receiving cathodal tDCS. 169 acute or post-acute patients received anodal tDCS on ipsilesional, and 48 showed significant improvement in movement. 67 chronic patients who received anodal tDCS showed improvement in motor performance. 54 patients who received bilateral tDCS showed improved motor performance [184]. A meta-analysis summarized lower limb motor function recovery after tDCS in 194 patients from 10 studies. Mobility and muscle strength were significantly improved while walking speed, walking endurance, and balance function was not significantly changed [145]. And other studies have cast doubt on the long-term effects of tDCS. In an analysis of 15 studies involving 315 patients, Marquez et al. indicate that tDCS improved motor function only in the short term [184], [185]. FMA scores showed that the combination of tDCS and functional electrical stimulation (FES) was more effective than FES alone [186].

Given the current controversy over the effectiveness of tDCS, there are still no clinically guided treatment paradigm and parameters. Nevertheless, We summarized some studies with sound rehabilitation effects on diverse stimulus configu-

ration (see Table 4), which can provide a reference for relevant studies. The usual current intensity is 1-2 mA, the electrode area is $15 - 35cm^2$, and the single stimulation time is 10-30 minutes.

There is not enough evidence to determine whether cathode or anode treatment is more effective [184], [185]. Compared with unilateral stimulation, simultaneous stimulation of the motor cortex (anodal tDCS on IP and cathodal tDCS on CP) can produce a superposition effect, which is a more effective treatment strategy [191], [192]. There is a consensus that tDCS and motor training is better for rehabilitation. The reason may be that tDCS increases the excitability of the cortex during motor learning [185].

Traditional rehabilitation methods, such as exercise training, mostly require some residual motor capacity, rTMS and tDCS can be applied to survivors with varying impairment levels [193]. It is important to note that both rTMS and tDCS have after-effects, which may pave the way for them to become clinical treatment options [194]. Although rTMS and tDCS have been proved to be effective for stroke motor rehabilitation, the parameters of stimulation and clinical trial design characteristics remain to be clarified, and the mechanism of stimulation remains to be explored [195]. In addition, safety parameters for stroke patients must be further evaluated, especially for exploring the future use of high-frequency rTMS and high-current tDCS.

IV. Discussions

1) Post-stroke Motor funciton assessment with brain imaging: The use of brain imaging provides a more accurate solution to the precise assessment of motor function post-stroke, which is the basis of navigated rehabilitation. To better characterize brain function networks, high spatial and temporal resolution imaging techniques are required. Multimodal imaging can make up for the defect of single-mode and will become the mainstream research direction in the future. EEG-fMRI and EEG-fNIRS have attracted much attention and obtained some research results, and can further explore their potential in the future. CMC is a novel evaluation method that can get information about muscle states and brain states. It provides a correlation between the brain and muscles (which reflects the brain's ability to control muscles) and provides time delay information (which reflects changes in information transmission), which is helpful for assessing motor function after stroke. Graph theory can supplement traditional statistical analysis and is very important for building brain networks. A number of features can be extracted that are more indicative of change before and after treatment, which are essential for quantifying recovery progress. The evaluation method based on brain imaging can well supplement the deficiency of clinical qualitative evaluation scale.

2) Post-stroke Motor rehabilitation with clinical brain stimulation: Although rTMS and tDCS are effective in rebuilding motor function post-stroke, there are no guidelines for clinical use. The safe range of brain stimulation parameters should pay attention, which is crucial to whether patients accept treatment. Effective stimulation processes and paradigms need to be explored, which is the focus of current research. Brain stimulation combined with training interventions proved to be more effective and more acceptable to stroke patients. With the realization of accurate evaluation, it is necessary to apply different stimulation parameters to other brain regions, which requires high spatial and temporal resolution of brain stimulation technology. New TMS and tES devices and methods are also being investigated, such as high-definition tDCS and the Heaed TMS coil. In addition to tDCS, the effects of transcranial alternate current stimulation and transcranial random noise stimulation on stroke rehabilitation are also being explored. Meanwhile, NIBS and brain imaging techniques combined can document large-scale stimulus-induced restructuring of structural and functional networks during rest or task-related activities.

3) Close-loop solutions to post-stroke motor rehabilitation: This paper emphasizes the importance of assessment for rehabilitation, and the combination of non-invasive brain imaging and brain stimulation is the future direction. After accurate assessment of the cerebral functional network, hemispheric balance index, and CMC characteristic values of stroke patients, the brain stimulation paradigm formulation can improve rehabilitation efficiency. At present, the popular combination studies of brain imaging and brain stimulation in stroke rehabilitation include rTMS-fMRI [196], tDCS-EEG [197], tDCS-CMC [198], etc. Multimodal assessment and multimodal rehabilitation have potential application value in stroke rehabilitation.

4) Factors affecting post-stroke motor rehabilitation: Exercise rehabilitation after stroke is affected by socio-demographic characteristics (such as age, gender, race, etc.), clinical factors (such as stroke type, co-morbidities, rehabilitation therapeutics, etc.), and genetic factors [199]. As a result, there is a significant difference in stroke patients, which requires the establishment of individualized rehabilitation therapies. More effective than scale assessment, brain imaging technology can be used to establish the state of the individual brain functional network for each patient so that personalized brain stimulation rehabilitation therapy can be built. Fatigue is a common syndrome after stroke, which will directly affect the results of motor function assessment and intervention. Fatigue manifestations in stroke patients include brain fatigue and muscle fatigue. Taking fatigue into account when constructing a patient's brain functional network is a grand challenge, as in brain stimulation treatment. The assessment and treatment of post-stroke fatigue have attracted the attention of researchers, and brain imaging and brain stimulation techniques can also become effective means.

V. Conclusion

This paper summarizes state of art in brain imaging and stimulation, exploring potential solutions to post-stroke motor rehabilitation. The principle, advantages, limitations, and analytical methods of EEG, MEG, fMRI, and fNIRS brain imaging were presented with the intent of demonstrating the benefits of brain imaging in motor function assessment of stroke. We summarized the application of rTMS and tDCS in

TABLE III: Summary of tDCS experimental paradigm

Study	Samples	Experimental paradigm	Motor assessment scales
Kim et al. (2010) [175]	18 patients (6 A-group, 5 C-group, 7 S-group)	common parameters: 2 mA, electrode $25cm^2$, 10 sessions (5 times per week for 2 wks). A-group: anodal tDCS, 20 min, on IP M1. C-group: cathodal tDCS, 20 min, on CP M1. S-group: : sham tDCS, 1 min (20 min period), on IP M1.	FMA and MBI
Lindenberg et al. (2010) [187]	20 patients (10 Exp group, 10 S-group)	common parameters: 1.5 mA, electrode $16.3cm^2$. Exp group: real bilateral tDCS (anodal tDCS on IP M1 and cathodal tDCS on CP M1), 30 min. S-group: sham tDCS, 30s (30 min period).	UE-FM and WMFT
Nair et al. (2011) [188]	14 patients (7 C-group, 7 S-group)	common parameters: 1 mA, electrode $25cm^2$, 5 consecutive days. C-group: cathodal tDCS, 30 min, on CP M1. S-group: sham tDCS, 30-60 s (25 min period), on IP M1.	UE-FM
Khedr et al. (2013) [189]	40 patients (14 A-group, 13 C-group, 13 S-group)	common parameters: 2 mA, electrode $35cm^2$, 6 consecutive days. A-group: anodal tDCS, 25 min, on IP M1. C-group: cathodal tDCS, 25 min, on CP M1. S-group: sham tDCS, 2 min (25 min period), on IP M1.	NIHSS, OMCASS, and BI
Di et al. (2014) [157]	14 patients (7 Exp group, 7 S-group)	common parameters: 2 mA, electrode $35cm^2$, 5 consecutive days. Exp group: real bilateral tDCS, 40 min. S-group: sham tDCS, 30 s (40 min period).	ARAT, 9HPT, MAL, and NIHSS
Viana et al. (2014) [190]	20 patients (10 Exp group, 10 S-group)	common parameters: 2 mA, electrode $35cm^2$. Exp group: real bilateral tDCS, 13 min. S-group: sham tDCS, 30s (13 min period).	FMA, MAS and SSQOL

A-group: anodal group. C-group: cathodal group. S-group: sham group
OMCASS: Orgogozo MCA scale. BI/MBI: Barthel index/ modified BI. ARAT: Action Research Arm Test. 9HPT: 9 Hole Peg Test. MAL: Motor Activity Log Rating Scale. UE-FM: Upper Extremity Fugl-Meyer. WMFT: Wolf Motor Function Test. MAS: modified Ashworth scale. SSQOL: stroke specific quality of life scale.

stroke rehabilitation, the setting of stimulus parameters, and their mechanism. More studies are needed in the future to demonstrate its effectiveness in motor rehabilitation and to identify clinical stimulation paradigms. Finally, we discussed the prospects of combining brain imaging with brain stimulation in stroke rehabilitation, which we believe will be the direction of future research. Based on the summary of motor rehabilitation of stroke, there are typical problems in motor impairment caused by neurological diseases such as spinal injury and epilepsy. It is expected that this paper would facilitate researchers and practitioners with a better understanding of non-invasive brain imaging and brain stimulation and their development on solutions to post-stroke motor rehabilitation.

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