The time-varying networks of the wrist extension in post-stroke hemiplegic patients

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Abstract
Hemiplegia is a common dysfunction caused by the brain stroke and leads to movement disability. Although the lateralization of movement-related potential, the event-related desynchronization, and more complicated inter-regional information coupling have been investigated, seldom studies have focused on investigating the dynamic information exchanging among multiple brain regions during motor execution for post-stroke hemiplegic patients. With high temporal-resolution electroencephalogram (EEG), the time-varying network is able to reflect the dynamical complex network modalities corresponding to the movements at a millisecond level. In our present study, the wrist extension experiment was designed, along with related EEG datasets being collected. Thereafter, the corresponding time-varying networks underlying the wrist extension were accordingly constructed by adopting the adaptive directed transfer function and then statistically explored, to further uncover the dynamic network deficits (i.e., motor dysfunction) in post-stroke hemiplegic patients. Results of this study found the effective connectivity between the stroked motor area and other areas decreased in patients when compared to healthy controls; on the contrary, the enhanced connectivity between non-stroked motor areas and other areas, especially the frontal and parietal-occipital lobes, were further identified for patients during their accomplishing the designed wrist extension, which might dynamically compensate for the deficited patients’ motor behaviors. These findings not only help deepen our knowledge of the mechanism underlying the patients’ motor behaviors, but also facilitated the real-time strategies for clinical therapy of brain stroke, as well as providing a reliable biomarker to predict the future rehabilitation.

Keywords EEG · Time-varying networks · Network properties · Post-stroke hemiplegia

Introduction
Stroke, also known as cerebrovascular accident, is a disease of brain damage caused by the sudden burst of cerebral blood vessels or the block of blood vessels, including hemorrhagic and ischemic stroke. Stroke has high morbidity, disability, and mortality rates, and 40% of stroke survivors still live with various disabilities. After a stroke, multiple functions are seriously impaired, and the most common one is post-stroke contralateral limb hemiplegia (Winstein et al. 2016). Such a wrist or upper limb dysfunction usually lasts a lifetime. Wrist extension is an essential part of hand touching object movement. Severe wrist paralysis is still a considerable challenge in clinical practice, which impacts the patients with their activities of daily living functions and the quality of life.

Symptoms of post-stroke limb disorders depend on the location of the brain in the left or right hemisphere. The stroke of the dominant left hemisphere may behave communication disorder and paralysis of the right hand and foot. In comparison, lesions in the right hemisphere might lead to the impairment of perception (visual impairment) and the paralysis of the left hand and foot. Compared with the right hemisphere stroke, the dysfunction caused by the left hemisphere stroke is usually easier to be identified and diagnosed on time. In this study, we mainly took middle-aged and older people as the subjects to investigate the differences in time-varying network architectures between patients with unilateral stroke and the control group during wrist extension.

The implementations of the motor behaviors in healthy controls (HCs) are usually achieved by simultaneous
activation of multiple motor-related brain regions, including supplementary motor area (SMA), sensorimotor area, primary motor area, prefrontal lobe, and bilateral dorsal anterior motor area, etc. (Vry et al. 2012; Xie et al. 2021; Zhang et al. 2019). The changes in the ipsilateral motor cortex of the stroked hemisphere are usually more complicated for post-stroke hemiplegic patients (Li et al. 2020). For example, after analyzing the changes in bilateral primary motor areas' functional connectivity, Li et al. found the decreased functional connectivity in stroke patients (Li et al. 2016b), and Zhao et al. used independent component analysis to explore related functional networks of stroked patients and found connectivity within and between motor-related networks were both abnormal, especially the decline in the dorsal attention network and the overcompensation of the executive control network (Zhao et al. 2018). Moreover, the increased activation of frontal and parietal regions and motor areas in stroke patients has also been associated with the motor behaviors and those non-motor areas such as the occipital lobe (Marshall et al. 2000; Puh et al. 2007; Ward et al. 2003).

Concerning the electrophysiological characteristic, the brain activity in the sensorimotor rhythm of 8–30 Hz has been widely studied, and electroencephalogram (EEG) is usually used to investigate the sensorimotor rhythm related to the motor behaviors, as well as its application in stroke (Wiese et al. 2005). Meanwhile, as demonstrated previously, the brain is a complex network (Bertolero and Bassett 2020; Luo et al. 2021), and the multi-regional interaction completes the completion of motor execution. Stroke patients also include multiple motor and non-motor regions to achieve limb movement (Rehme et al. 2012). In recent decades, researchers have explored the motor oscillations, event-related desynchronization, and motor-related networks when accomplishing related motor behaviors (Park et al. 2011; Ramoser et al. 2000), especially the dynamic resource allocation. For example, in the previous study, by modeling the corresponding brain networks within the early, middle, and late periods of the hand-gripping fatigue task, the temporal evolution of the network dysconnectivity was accordingly observed (Deshpande et al. 2009). Moreover, by focusing on the dynamic information propagation, our previous study has detailedly explored the time-varying networks before (motor preparation), during (motor imagery), and after (short rest) task, and identified the dynamic network reconﬁgurations that help guarantee the individual task achievement (Li et al. 2019). Unfortunately, fewer efforts had been put on exploring the time-varying network modalities related to the movements for the post-stroke hemiplegic patients.

In fact, the investigation of the time-varying networks during motor execution helps understand the motor dysfunction in stroke patients. Given the EEG has a relatively high time resolution, we can further explore the dynamic interactions among different brain regions in milliseconds. Previously, the adaptive directed transfer function (ADTF) was developed based on the multivariate adaptive autoregressive (MVAAR) model to mine the causality relationships (i.e., information flows) among signals. It had been applied to explore the time-variant propagation of seizures and interictal spikes, which reported similar results with the clinical assessments of neurologists (Wilke et al. 2008). As ADTF takes advantage of the high temporal resolution of EEG signals, it can quantitatively measure the effective connectivity in milliseconds and thus facilitates the construction of time-varying networks on each time point, which provides the huge potential for capturing the dynamic transition related to the movement effectively. In our previous study, based on the ATDF approach, distinct information processing stages related to the P300 (Li et al. 2016a) and decision-making (Si et al. 2019) had also been investigated.

To better investigate the differences in dynamic network architectures between the stroke patients and HCs during the motor execution, in our present study, we applied the ADTF in three subject groups, i.e., HCs, post-stroke hemiplegic of the left arm (PL), and post-stroke hemiplegic of the right arm (PR), to construct their time-varying networks related to the wrist extension. Thereafter, the potential differences concerning the three groups were further investigated from the dynamic network topology and property perspective to better understand the motor dysfunction that occurred in post-stroke hemiplegic patients.

**Methods**

**Participants**

The study protocol was approved by the ethics committee of the First Affiliated Hospital of Sun Yat-sen University. Twenty-seven participants were recruited in the present study, which included 9 PL patients (7 males, age 56.1 ± 10.7 years), 7 PR patients (6 males, age 55.7 ± 8.8 years), and 11 HCs (5 males, age 52.8 ± 7.6 years). Herein, the stroke patients’ inclusion criteria were: (1) first-time onset stroke patient, diagnosed by a neurologist and confirmed by a CT or MRI imagine test; (2) unilateral hemiplegia was presented as the main dysfunction; (3) upper limb Brunnstrom stage ≥ II; (4) patients with stable vital signs to withstand and complete the event-related potential (ERP) tests. While, the patients’ exclusion criteria were: (1) patients with cognitive dysfunction who cannot understand and perform experimental
tasks; (2) with upper limb muscular-skeletal diseases and cannot perform required movements; (3) a previous history of mental illness or taking any antipsychotic drugs; (4) patients with collapse syndrome who cannot endure the ERP experiment room; (5) severe lateral neglect syndrome. Following the inclusion and exclusion criteria depicted above, these patients were recruited. In fact, concerning the three groups, to guarantee their experimental behaviors, those who had a history of mental illness or taking any antipsychotic drugs were first excluded. Thereafter, before starting the ERP test, all participants were further informed of the study protocol, along with the signed informed consent forms. Meanwhile, no further medication was reported from all subjects, and the sufficient cognitive function, as well as matched education level, was also controlled.

**Experiment procedure**

E-prime 2.0 software (Psychology Software Tools, Inc, USA) was used to present the visual directions or cues in the study. The paradigm of the Instruction Response Movement (IRM) was adopted to present a solid arrow picture pointing either to the left or the right (regarded as “GO” signals in this study). Accordingly, the subjects were requested to perform the unilateral (i.e., left or right forearm) wrist extension. In each IRM trial (Fig. 1), a white cross in the center of a black screen serves as an attention point, which lasted for a duration ranging from 1000 to 2000 ms randomly. The left or right “GO” signal then appeared randomly at the screen for a duration of 3000 ms, and the subject started to perform the required motion when they noticed the presence of the “GO” signal. After finishing the movement, subjects rested their arms on the table, and a black screen lasting for 2000 ms was presented for a short rest. Herein, the left or right arrow was presented randomly, with 40 trials on each side movement, and the total duration of the experiment would last from 480 to 560 s, as the duration of the attention screen was randomly set with [1000, 2000] ms. Meanwhile, before data recording, subjects would also practice the required movement for 1 min to 2 mins to get familiar with our experiments.

**EEG recording**

All of the experiments were conducted in a shielded room, which provided insulation from electromagnetic signals and background noise distractions. An observation window was also designed to allow the experimenter to visually monitor the behavioral responses of the subject during the whole experiment. During the tests, the subjects sat in front of a 17-inch computer screen, 75 cm apart on eye level, and their forearms were also placed on the table to maintain a stable sitting position. A BrainAmp 32-channel amplifier from Brain Products (Munich, Germany) was used to record EEG. All of the 32 Ag/AgCl electrodes were placed according to the 10–20 international system. The online digital sampling rate is 1000 Hz, and electrodes FCz and AFz were used as the reference and ground, respectively. Electrooculogram (EOG) was measured by two extra electrodes, one above the middle point of the right brow to record the EOG vertically, and the other was placed 2 cm aside from the outer corner of the right eye to record the EOG horizontally. To guarantee reliable data quality, throughout the experiment, the impedance for all electrodes was kept below 5 kΩ.

**EEG data analysis**

In this study, the recorded EEG was first pre-processed to acquire the artifact-free trials and then used to construct the corresponding time-varying effective connectivity networks. The details were further depicted in the following sections.

**EEG data pre-processing**

The corresponding EEG preprocessing was carried out using MATLAB v2014a (The MathWorks Inc., Natick, MA). Concretely, the EEG was first band-pass filtered within a frequency range of [1, 30] Hz, and based on the independent component analysis (ICA) approach, the ocular was then corrected semi-automatically. Thereafter, the EEG was re-referenced to a neutral reference of the Reference Electrode Standardization Technique (REST) [16, 17]. In the meantime, [−1000, 2000] ms range (0 ms corresponds to the stimulus onsets) data segmentation and [−1000, −800] ms baseline correction was further performed. Herein, to guarantee the data quality, a threshold of ±75 μV (Li et al. 2015) was applied when performing
artifact removal procedure. Moreover, to further eliminate those unexpected artifacts, the researchers were also required to visually inspect the remaining trials to exclude those that still contain residual artifacts. The nearby electrodes acquire a similar contribution from cortical sources and also capture a similar activity. In this study, to reduce the effect of volume conduction on EEG networks, as well as focusing more on the brain activity at the motor area, the following protocols applied in previous studies (Si et al. 2020; Xu et al. 2014), the sparse electrodes (i.e., 24 out of 32 channels, Fp1/2, Fz/3/4/7/8, FC1/2, T7/8, Cz/3/4, CP1/2, Pz/3/4/7/8, and Oz/1/2) are extracted and then used in our present study.

Timing-varying network

To unveil the dynamic network pattern underlying the required motion, the ADTF was used to construct corresponding time-varying networks of this motion that were further statistically compared to identify the group-wise differences of dynamic network patterns between PL, PR, and HC groups. In specific, for each subject, the remaining artifact-free trials were down-sampled to 100 Hz, resulting in the 10 ms interval between two neighboring sample points, and based on the trial-by-trial ADTF, the time-varying networks were then constructed.

1. Multivariate adaptive autoregressive model

For each trial time series, the MVAAR model was defined and then calculated with the following equation,

\[ X(t) = \sum_{i=1}^{P} A(i,t)X(t-i) + E(t) \]  

(1)

where \( X(t) \) denotes the artifact-free EEG vector at time point \( t \), \( A(i,t) \) denotes the matrix of the MVAAR model coefficients estimated by the Kalman filter algorithm (Arnold et al. 1998), \( E(t) \) is the multivariate independent white noise, and \( P \) is the optimal MVAAR model order automatically determined by the Akaike Information Criterion (Eq. (2) (Lütkepohl 2005),

\[ AIC(P) = \ln(\text{det}(\Sigma)) + 2M^2P/N \]  

(2)

where \( M \) is the number of EEG channels, \( N \) is the time point, and \( \Sigma \) is the covariance matrix of noise. The observation and state equations were then solved by the recursive least squares algorithm with the forgetting factor (Campi 1994). Herein, considering the accurate estimation of MVAAR model was attributed to the optimal model order \( P \), when performing the trial-by-trial ADTF, the corresponding \( P \) was determined separately, that was, \( P \) varied from trial to trial, to guarantee the corresponding time-varying network constructions.

2. Adaptive directed transfer function

After acquiring the MVAAR model coefficient \( A(i,t) \), its transformation in the frequency domain, \( H(f,t) \), would also be obtained, and the \( H_{ij} \) element of \( H(f,t) \) represents the directed information flow from the \( j \)-th to the \( i \)-th element for each time point \( t \) at frequency \( f \). And accordingly, Eq. (1) is then further transferred to the frequency domain as

\[ A(f,t)X(f,t) = E(f,t) \]  

(3)

\[ X(f,t) = A^{-1}(f,t)E(f,t) = H(f,t)E(f,t) \]  

(4)

where \( A(f,t) = \sum_{p} A(i,t)e^{-j2\pi ftk} \) and \( A(i,t)_{k=0} = I \). \( X(f,t) \) and \( E(f,t) \) are the transformations of \( X(t) \) and \( E(t) \) in the frequency domain, respectively.

The normalized ADTF, which describes the directed information flow from the \( j \)-th channel to the \( i \)-th channel at frequency \( f \) and time \( t \), is defined with a range of \([0, 1]\) as,

\[ \gamma_{ij}^2(f,t) = \frac{|H_{ij}(f,t)|^2}{\sum_{m=1}^{n} |H_{im}(f,t)|^2} \]  

(5)

And the integrated ADTF is finally defined as the average of the normalized ADTF over the interested band \([f_1, f_2]\) at time \( t \). Herein, considering both \( \mu \) ([8, 12] Hz) and \( \beta \) ([13, 30] Hz) rhythms had been validated to be consistently and closely correlated with motor imagery (Li et al. 2019; Ren et al. 2020), the interested frequency band \([f_1, f_2]\) was thus defined within a fuse range of \([8, 30]\) Hz.

\[ a_{ij} = \Theta_{ij}^2(t) = \frac{\sum_{k=f_1}^{f_2} \gamma_{ij}^2(k,t)}{f_2 - f_1} \]  

(6)

After acquiring the ADTF adjacency matrix for each artifact-free motion trial, the trial-average of the ADTF matrices was obtained to define the final time-varying networks for each subject. When exploring the group-wise differences, the time-varying weighted networks of the PL, PR, and HC groups were first binarily thresholded into the time-varying binary networks with a connectivity cost of 5% to illustrate the intrinsic network architectures. Thereafter, these time-varying networks were also statistically compared by using the non-parametric Wilcoxon rank-sum test, which was carried out using related functions in MATLAB v2014a. And the corresponding \( p \)-values were further multiply corrected by false discovery rate (FDR) under a significance level of 0.05 (\( p < 0.05 \)).

Network properties

Based on graph theory, the time-varying global efficiency (GE) was calculated by using the brain connectivity
toolbox (BCT, http://www.nitrc.org/projects/bct/) (Rubinov and Sporns 2010), which was still based on the constructed time-varying weighted networks. The $G_E$ describes the ability of the time-varying networks to process information.

\[
G_E = \frac{1}{M \sum_{i=1}^{m} \sum_{\Psi} \left( \frac{\sum_{a_{ij} \in \Psi_{i,j}} a_{ij}}{M - 1} \right)^{-1}}
\]  

(7)

where $M$ denotes the channel number, $\Psi$ denotes the set of all network channels, and $g_{i-j}$ denotes the weighted directed shortest path from channels $i$-th to $j$-th.

### Power spectral density

For each subject, the power spectral density (PSD) of each electrode was first estimated using the pWelch also within the same frequency range of $[8, 30]$ Hz. When exploring the group differences, the PSD of the PL, PR, and HC groups were statistically compared by using the non-parametric Wilcoxon rank-sum test, whose $p$-values were also multiply corrected by FDR ($p < 0.05$).

### Results

#### PSD

The corresponding PSD of the three groups was first obtained, and as illustrated in Fig. 2, the electrodes whose statistical $p$-values pasted the test were marked out. The scalp topographies exhibiting stronger PSD for the PL subjects were found to locate at the parietal and occipital areas compared to HC subjects when executing the left-hand wrist movement (Fig. 2a, $p < 0.05$), while no differences were revealed between PR and HC groups when performing the right-hand wrist extension (Fig. 2b, $p > 0.05$).

#### Differential time-varying network patterns

To investigate the time-varying patterns of brain networks in HC, PL, and PR groups during wrist extension, the effective connectivity at each time point was averaged across subjects and then sparsed with 5% sparseness (i.e., the connection edge with the strongest weight remaining 5%) to display the transient network topology. As shown in Fig. 3, for the HC subjects (Fig. 3a), the electrodes C3 or C4 served as the crucial hub to control the right or left-hand wrist extension at first, which was then transferred to the joint control from bilateral C3 and C4 electrodes. However, for the PL subjects (Fig. 3b), the motor area of the stroked hemisphere (i.e., right hemisphere) showed seldom connectivity when starting to perform the left-hand wrist extension, but the contralateral F3 and C3 electrodes (i.e., at the left hemisphere) extended to the occipital lobe showed the stronger connectivity architectures; while for the PR subjects (Fig. 3c), the crucial hubs were found to be located at the contralateral C4 and P4 and ipsilateral P3, when performing the right-hand wrist extension.

To further explore the differential dynamic network patterns between post-stroke hemiplegic patients and healthy people during motor execution, Fig. 4 further displays the corresponding statistical network topologies. When comparing the PL and HC subjects (Fig. 4a), the electrodes having stronger information flow in the PL group transferred from the occipital lobe (e.g., Oz) to the left frontal lobe (e.g., F7); however, for the PR subjects (Fig. 4b), this transmission occurred from occipital lobe (e.g., Oz) and left frontal lobe (e.g., F7) to the right temporal lobe (e.g., T6).
The time-varying $GE$ of all subjects in PL, PR, and HC groups at different time points were averaged, as illustrated in Fig. 5a. During the wrist extension, the $GE$ increased along with the motion. And when quantitatively measuring the potential differences, Fig. 5b further illustrated that only when performing left-hand wrist extension, the $GE$ of the PL group was greater than that of the HC group ($p < 0.05$).

**Discussion**

Stroke is one of the most important diseases that threaten our lives and further leads to motor impairments in stroke survivors. Compared with healthy people, the interaction among different brain regions is more complicated in post-stroke patients when accomplishing the movements. Hence, in the current study, we proposed to adopt the ADTF to investigate the dynamic network architectures of movement-related activity during the wrist extension in post-stroke hemiplegic patients and healthy people.

Before applying the ADTF, the different PSD topographies were first investigated, as displayed in Fig. 2, although the stronger activities at the left primary motor
areas (e.g., C3) and right parietal and occipital lobes (e.g., P4 and O2) were found for the PL group compared to the HC group, no differences were found for the PR group. This result suggested that the contralateral brain areas corresponding to the stroked hemisphere of PL patients were strongly activated than that of healthy people to compensate for the damaged lateral brain areas. Unfortunately, the PSD failed to uncover the detailed interactions among different brain areas related to the wrist extension, which seemed to be more helpful for our understanding of the post-stroke motion.

To explore the dynamic interaction in post-stroke hemiplegic patients (i.e., PL and PR groups) and healthy people (i.e., HC group) across different brain regions, time-varying network topologies of the left- and right-hand wrist extension were calculated and then illustrated in Fig. 3. As displayed in Fig. 3a, when the “GO” signal appeared, the networks of earlier motor execution stage (i.e., networks of 0 ms to 800 ms) for the HC subjects showed strong contralateral connectivity coupling among right motor area concerning the left-hand wrist extension. In contrast, the left motor area showed significantly stronger connectivity during right-hand movement, which then switched to a bilateral connectivity architecture (i.e., networks of 0 ms to 1600 ms) with C3 or C4 as the hub. Previous studies have demonstrated that medial frontal gyrus, parietal lobe, primary motor cortex, and SMA are highly involved during motor execution and exhibit contralateral hemispherical responses corresponding to the moving hand (Raffin et al. 2012; Sharma and Baron 2013), and similar to the motor imagery, during the posterior of the required motion, this contralateral hub would be transferred to the bilateral hubs to accomplish this motion (Li et al. 2019), which was consistent with our current findings. Moreover, in our previous study (Li et al. 2018), when looking at the motor potential (MP) and mu event-related desynchronization of HC individuals, along with the movement execution, these electrophysiological features presented no significant difference between C3 and C4 electrodes, but become bilaterally symmetrical, which further validated the joint role of bilateral C3 and C4 in controlling the required motor behaviors.

However, since the stroke occurred in PL and PR subjects, our previous study first identified the deficit motor function of these patients, as lesional cortices were found to consume more energy and experienced larger excitatory MP during movement, and then clarified the compensation of related contralateral cortices (Li et al. 2020). Herein, as expected, the network patterns of PL and PR patients were found to be different from that of healthy people, and the site and severity of stroke did affect the degree of neural plasticity related to the motor-related network architecture (Park et al. 2011). Specifically investigating Fig. 3(b), when performing the left-hand movement (i.e., networks of 0 ms to 800 ms), stronger functional coupling existed between F3/C3 and parietal-occipital lobe, while seldom connectivity of the stroked right hemisphere was observed, which might account for the deficits in the left-hand wrist extension of the PL subjects. The frontal lobe is activated to be responsible for the control of body movements and to compensate for the deficits brought by the stroked right hemisphere. The ipsilateral hemisphere then provides the functional compensation for the body movements (Li et al. 2020; Li et al. 2018). After that, hubs transferred from F3 and C3 to bilateral motor areas (i.e., C3 and C4, networks of 800 ms to 1600 ms), similar to that of the HC subjects. While concerning the right-hand movement of the PR subjects, as displayed in Fig. 3c, stronger flows (i.e., networks of 0 ms to 800 ms) directed from F3 were observed, as well as the bilateral parietal lobe at 1600 ms whose hubs were P3 and P4, which might further clarify that besides the participation of the contralateral motor area of the stroked hemisphere, the other non-motor areas in the injured hemisphere that were responsible for the high-level cognition, such as motor planning and attention, may also be involved.

To further explore the impaired effective connectivity in PL and PR patients, Fig. 4 then illustrated the different patterns of time-varying networks between PL/PR and HC groups during hand movement. The PL patients exhibited enhanced connectivity to frontal-parietal and motor areas starting from Oz compared with the HC group, which is bottom-up architecture (i.e., networks of 0 ms and 400 ms). The occipital lobe is responsible for visual information processing. After receiving the “GO” signal...
(i.e., 0 ms), the upper limb dyspraxia in stroke patients led to the delayed movement, the enhanced bottom-up connectivity might then intensify the motion intention of the required wrist extension (Rowe et al. 2002), and during the later motion stage (i.e., from 800 to 1600 ms), the hub gradually transferred from Oz to F7 (Fig. 4a). The top-down modulation starting from F7 to the bilateral parietal-occipital lobe is significantly enhanced. As illustrated above, frontal and parietal regions play an irreplaceable role in motion planning and decision-making associated with motor regulation (Andersen and Cui 2009). When planning the motion, the parietal lobe is regulated by the prefrontal lobe. That is, their cooperation helps complete the assigned tasks (Buschman and Miller 2007). However, the stroke in PL patients destroyed the high-level regulations involved in movement execution. To compensate for the completion of the wrist execution, our previous studies did find the activation of bilateral brain areas in accomplishing the required movements (Li et al. 2020), in the meantime, our present study further found the enhanced connectivity in the contralateral frontal-occipital lobe of the stroked hemisphere for the PL subjects. Concerning the PR patients (Fig. 4b), the hubs transferred from the occipital lobe (e.g., Oz) and left frontal lobe (e.g., F7) to the right temporal lobe (e.g., T6), and although the stroke resulted in the dysfunction of the patients’ motor network, more contralateral hemispheric and ipsilateral non-motor regions were included to compensate for the wrist extension. Accordingly, the enhanced time-varying network architectures connecting related areas facilitated the stroked patients with their motion.

Moreover, GE is the average efficiency of the related brain network and is usually applied to estimate the potential for functional integration among brain areas. Besides the above network architecture, just as illustrated in Fig. 5, during the wrist extension, the time-varying GE of the HC, PL, and PR groups increased along with the execution. We speculated that due to the plasticity changes between different brain regions after stroke, patients with post-stroke hemiplegic activated more other brain regions as compensation, and the increased interaction could dynamically compensate for the injured hemisphere to complete our required movement. And indeed, in our present study, when performing the left-hand wrist extension, the average GE of the PL group was significantly larger than that of the HC group (Fig. 5b).

The possible limitation would be the small subject number enrolled. Given the limited sample size, findings of our present study should be considered with caution; in our future study, more subjects would be recruited to participate in our experiments, and related external intervention based on transcranial magnetic stimulation, etc., would also be considered, to further validate our findings.

**Conclusion**

In conclusion, by using the ADTF, we investigated the time-varying network patterns of the PL, PR, HC groups when they were performing the required wrist extension. We found the control hub’s obvious transition from the contralateral to the bilateral hemisphere for the HC subjects. However, concerning the PL and PR patients, when performing the wrist extension, the effective connectivity between stroked motor area and others was weaker while that between non-stroked motor area and others was enhanced for the motor planning and regulation, especially the frontal and parietal-occipital lobes, to compensate for the dysfunction of the motor behaviors for the stroked patients. These findings help us better understand the network mechanism underlying the motor dysfunction of the patients with post-stroke hemiplegic and might also serve as a reliable biomarker applied to the future rehabilitation of stroke patients.

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**Declarations**

**Conflicts of interest** The authors declare that they have no competing interests.

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