Electroencephalography-based functional brain network analysis according to lesion location and motor function in stroke patients

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Research

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Abstract

Background. While numerous studies have investigated changes in brain activation after stroke, limited information exists on the association between functional brain networks and lesion location in stroke patients.

Methods. We compared the characteristics of brain networks among patients with cortico-subcortical lesions (n = 5), subcortical lesions (n = 7), and age-matched healthy controls (n = 12) during the execution of hand movements. Functional brain networks were analyzed based on network parameters in beta frequency electroencephalography (EEG) bands.

Results. Our results indicated that while the healthy control group had appropriate compensatory patterns on the brain network with an aging effect, the two stroke lesion groups exhibited different hyper-connected characteristics in the brain network within the sensorimotor regions, particularly the contralesional M1, during motor execution. In addition, the betweenness centrality on the contralesional motor area was identified as a promising biomarker for motor functional ability associated with stroke. Our findings further allowed us to identify the characteristics of the stroke lesion that could not be found with EEG power by using the EEG brain network on the cerebral cortex.

Conclusions. We anticipate that our study will improve the understanding of the complex changes that occur in the brain network as a result of stroke, and support the development of more effective and efficient rehabilitation programs based on lesion location for stroke patients.

Background

The restoration of motor functions in stroke patients is associated with brain plasticity and reorganization of the motor cortex. Several research groups have utilized neuroimaging to investigate the mechanisms underlying recovery, which has led to improved rehabilitation approaches [1, 2, 3, 4, 5, 6]. For example, Grefkes et al. (2008) argued that motor deficits in stroke patients are due to pathological interhemispheric interactions among key motor regions in a functional imaging study [2]. In addition, Kim et al (2015). demonstrated that stroke has different mechanisms according to the different motor tasks in the electroencephalography (EEG) brain network [7]. Furthermore, previous studies have investigated brain activation following stroke based on lesion location, which can be roughly categorized as either cortico-subcortical or subcortical [8, 9]. A cortico-subcortical lesion (CL) refers to a supratentorial lesion with primary motor cortex involvement, whereas a subcortical lesion (SL) refers to a supratentorial lesion without primary motor cortex involvement or an infratentorial lesion. Shelton and Reding (2001) argued that motor recovery of the affected upper limb following stroke can be predicted based on the degree of primary motor cortex involvement [10]. Additional studies have further revealed that facilitatory repetitive transcranial magnetic stimulation following stroke produces significantly different responses between CL and SL patients [11]. A functional magnetic resonance imaging (fMRI) study by Luft et al. (2004) demonstrated that SL patients exhibit stronger activation in the ipsilesional primary motor cortex compared with CL patients during movement of the affected hand [12]. Liepert et al. (2005) reported that patients with lesions of the primary motor cortex exhibit greater changes in excitability within the ipsilesional primary motor cortex compared with SL patients during transcranial magnetic stimulation [13]. Recently, Park et al. (2016) demonstrated that hemispheric asymmetry and event-related desynchronization (ERD) patterns in the beta frequency band differ based on the location of the stroke lesion. Indeed, the authors observed significant differences among patients with supratentorial lesions including primary motor cortex damage, with supratentorial lesions excluding primary motor cortex damage, and with infratentorial lesions [14]. These findings highlight the need to focus on these differences related to stroke lesions.

The majority of these previous studies have investigated brain activity only in stroke patients, which is not sufficient for interpreting the mechanisms underlying motor dysfunction in stroke. To appropriately analyze the mechanisms associated with motor function in stroke, various additional approaches are necessary. To this end, some studies have characterized the mechanism of motor recovery in the brain from a network perspective [15, 16]. These studies have suggested that brain connectivity can provide a greater understanding of the mechanism of motor recovery as well as important changes associated with the pathophysiology of motor impairment after stroke [17, 18]. In their review, Calautti and Baron (2003) proposed that the reconstruction of damaged brain networks represents a compensatory mechanism that enhances motor recovery following stroke [19]. The authors reported that patient motor ability can be improved through compensatory enhancements in activity even within the disconnected network, without having to perfectly replace the original motor network. In addition, Grefkes and Fink (2011) observed different patterns of brain connectivity during hand movement between stroke patients and healthy controls, suggesting that pathological interactions between the contralesional and ipsilesional motor areas may represent a key pathophysiological component of motor impairment in stroke patients [20]. Furthermore, a recent study by Liu et al. (2016) revealed that patients with stroke exhibit functional impairment with regard to information transmission and weak cortical functional connectivity compared with healthy controls [21]. Therefore, the motor characteristics of stroke need to be identified not only by neuro-activity but also through the brain network.

In the present study, we utilized EEG to investigate the characteristics of the brain networks associated with motor function and dysfunction following stroke. In addition, we employed graph theory to obtain information regarding the mechanisms of recovery in stroke patients [22]. EEG was utilized to investigate brain connectivity by the graph theory in healthy controls and two groups of patients with different stroke lesion locations.

For this study, we had two hypotheses. Our first hypothesis was that the two stroke subgroups would exhibit apparent differences in connectivity with regard to the sensorimotor regions during motor execution [23]. Second, we hypothesized that the network characteristics for the subcortical lesion group without damage to the motor cortex would be similar to those of the healthy group but different from those of the cortical lesion group with motor cortex damage.

Methods

Participants

Eleven stroke patients exhibiting chronic, unilateral motor impairment of the upper limb participated in the present study. We categorized the patients into CL (n = 5, 52.6 years) and SL groups (n = 6, 53 years). The healthy control (HC) group was composed of 12 healthy (male = 8), age-matched individuals with a mean age of 52.8 years. We included patients who had survived more than 3 months following a stroke and were between 40 and 70 years of age. Patients with pacemakers, claustrophobia, pain associated with EEG electrodes, and those who could not understand instructions due to decreased cognitive function were excluded. The present study was approved by the institutional review boards (IRB) of the Korea Institute of Science and Technology (KIST) and the Samsung Medical Center (SMC) (KIST IRB; KIST 2013-009, SMC IRB; SMC 2013-02-091). All experiments were performed under IRB guidance and all participants provided written informed consent prior to participation in the study. In addition, the participants provided permission to publish their individual experimental data. The datasets generated and analyzed during the current study are not currently publicly available; however, they are available from the corresponding authors upon reasonable request.

Table 1. Demographics of the study participants.

Experimental designs

Following a cue, all stroke patients performed a grasp-and-pull task with their affected hand using a robot device to support the hand movement. In contrast, the HC participants performed a grasping motor task with their non-dominant hand to mimic the grasping movement of patients in the stroke group. The experimental design is described in detail in our previous studies [7,24]. Briefly, the experimental protocol included the following three motor tasks: an active task to be executed by a voluntary movement; a passive task to be executed using a robotic device; and a motor imagery task in which participants were instructed to imagine their movement without any physical movement. Each task involved 42 trials. For each trial, participants fixed their gaze on the monitor for 2 or 3 s, after which they performed the motor task for 2 s after the visual and auditory cues. Participants maintained their grasping movement for 1 s, after which they were asked to release the handle while the robotic device returned it back to its starting position.

In this study, data from the active task were analyzed to determine what characteristics of brain connectivity were dependent on lesion location during the voluntary movement. The robotic device, which was controlled by a digital signal processor, had several functions, including storing the data from the executed hand movement, assisting in the movement during the passive task, and synchronizing with the

Flash^{TM} software to provide participants with instructions. The Flash^{TM} software was also connected to an EEG system (Active-two, Biosemi^{TM}, Amsterdam, Netherlands).

Analysis of EEG signals

EEG signals were recorded at a sampling rate of 2,048 Hz using a 64-channel active EEG electrode system. For preprocessing, the EEG data were down-sampled at 256 Hz and band-pass-filtered at 1–80 Hz. Electrooculography and electromyography signals were then removed via independent component analysis using the EEGlab toolbox [25]. The common average reference value was then applied to improve the quality of the signal-to-noise ratio, and we investigated the relationships between the patterns of activity in the EEG brain networks (beta band, 13–30 Hz) [26].

Next, in order to obtain additional indices of functional impairment following stroke, we analyzed the functional connectivity based on mixed EEG signals from various brain sources [17,27]. To analyze the functional connectivity among the different regions of each brain network, we utilized the phase locking value(PLV), which quantifies the frequency-specific synchronization of two regions [28]. Data were then extracted from 0.25 to 1.25 s (the period of motor execution) and graph theory was used to characterize the estimated network parameters [22,26].

In the present study, we sought to identify meaningful characteristics that could be used to determine whether a particular brain lesion influenced the pattern of network connectivity during upper limb movement. To elucidate which channels represented the motor characteristics of functional connectivity based on stroke lesion location, we analyzed the brain network by global and local parameters using the Brain Connectivity Toolbox [29]. In addition, we analyzed the characteristics of the brain networks based on both local graph parameters (betweenness, nodal clustering coefficient, and local efficiency) and global parameters (characteristic path length, clustering coefficient, global efficiency).

Betweenness is a local (small-scale) parameter that represents the centrality and is defined as the percentage of shortest paths that pass through a given node. The nodal clustering coefficient is essentially the degree of the node that is connected to neighbors of each other, thus representing the tendency to cluster together. The local efficiency is a basic parameter of small-worldness at the local network level and represents the informative efficiency of each node within its own subnetwork.

As a global (large-scale) parameter, the characteristic path length commonly represents the functional integration of the network. The clustering coefficient, known as the transitivity, is the mean nodal clustering coefficient. This parameter is the normalized nodal clustering coefficient. The global efficiency is characterized as the average inverse shortest path length and is the most common measurement for the functional integration of the network.

In this study, we focused on the motor task-related difference in local network parameters between pre-/post- motor task as follows:

$$\text{The motor task} - \text{related difference} = \frac{post\ task - pre\ task}{pre\ task} * 100$$

Analysis of covariance (ANCOVA) was used to analyze the difference in graph parameters of the brain functional connectivity from pre- to post motor execution among the two stroke lesion groups and the HC group. For multiple comparison correction, the Fisher's least significant difference procedure was applied as the post-hoc test. In this study, we also applied stepwise regression to find a causal relationship between the motor function ability for the stroke and the brain network features that demonstrated significant differences among the stroke subgroups and the healthy control group.

Results

Threshold

Based on the global efficiency, which is commonly measured for the connection in the network, we calculated the significant threshold points among each group to determine the variance in global efficiency between pre- and post- motor execution using ANCOVA (Figure 1). As the result, we obtained a significant threshold point at 70 percent of the total functional connection (the post-hoc test by Fisher's least significant difference, p-value < 0.05). Using the post-hoc test, this threshold point had a significant difference among each stroke lesion group and the HC group.

Figure 1. Significant threshold points among each group for their variance of the global efficiency between pre- and post- motor execution using ANCOVA.

Characteristics of the network

In this study, we identified the characteristics of the brain network using both local and global parameters [29]. To this end, we analyzed the motor task-related differences between pre- and post- motor execution to focus on network changes during the motor task.

Global parameters

To identify the whole functional integration for the brain network, we analyzed global parameters, including the global efficiency, which measures the integration on the disconnected network, the global clustering coefficient, which represents the functional segregation for densely interconnected regions, and the characteristic path length, which is the average shortest path length among all nodes.

From the global parameters, stroke had the motor task-related change (Figure 2), which was evident by a decreased global efficiency and an increase in the clustering coefficient and characteristic path length in the injured brain. Depending on the stroke lesion location, the CL group with damage to the motor cortex had motor task-related patterns, with a decrease in both the global efficiency and clustering coefficient and an increase in the characteristic path length. The SL group, which was characterized by a disconnected path from the subcortical lesion to the cortex, had the motor task-related change on the network, with an increase in both the global efficiency and clustering coefficient and a decrease in the characteristic path length. In the HC group with no damage to the brain, only nominal changes in the global parameters for the motor task were observed.

Figure 2. Motor task-related changes in the global parameters. (a) The global efficiency. (b) The clustering coefficient. (c) The characteristics path length.

Local parameters

Next, we identified the local characteristics that were dependent on the stroke lesion location using the local network parameters, including the betweenness, which represents the centrality measurement, the local clustering coefficient, and the local efficiency for the small-worldness. In addition, we analyzed EEG power, which represents brain activity, in order to compare with the local network patterns. To identify motor task-related changes, we expressed the local network characteristics during the motor task on a topoplot in comparison with the baseline.

Our results indicated that the betweenness centrality for the stroke, without considering the lesion, decreased on the ipsilesional M1 and increased on the peripheral regions. On the ipsilesional M1, the stroke had a decreasing effect on the local clustering coefficient, while increasing the information efficiency by the local efficiency for the motor task. EEG power as a comparative feature represented the ERD patterns on the bilateral M1.

The CL group with motor cortex damage demonstrated a decrease in the betweenness centrality, local efficiency, and clustering coefficient, which was centered on the ipsilesional M1, while they demonstrated ERD patterns on the contralesional M1.

In contrast, the SL group, with the disconnected pathway between the cortex and subcortex, demonstrated a decrease in the betweenness centrality on bilateral M1, while their local efficiency and clustering coefficient were increased. As the control EEG feature, the EEG power of the SL group represented the ERD patterns on the bilateral M1 centered on the ipsilesional M1.

The HC group demonstrated an increased centrality, local efficiency, and clustering coefficient on the contralateral M1. In addition, the EEG activity in this group had the ERD patterns on the bilateral M1 centered on the contralateral M1.

From these results, we determined that the stroke groups had lesion-related network characteristics, whereas the HC group had motor task-related patterns on the contralateral M1. In addition, we found that each lesion group had contrary patterns that were dependent on the characteristics of their lesion location.

In this study, we found that the stroke lesion groups were significantly different with relation to the motor task-related brain network (ANCOVA test, p-value < 0.05). In addition, we determined that the contralesional M1 of the betweenness centrality represented the significant difference among the stroke lesion and HC groups by post-hoc test (Fisher's least significant difference, p-value < 0.05; significant differential areas: FC5, AF4, FC4, C4).

Figure 3. Motor task-related changes in local parameters.

Predicting stroke motor function ability by using brain network features

In this study, we confirmed that the betweenness centrality is an important feature of the brain network because there were significant differences among the stroke lesion groups using the ANCOVA test (Figure 4.a). Based on these results, we can provide a new biomarker for stroke motor function ability (the upper-Fugle–Mayer Assessment). We next examined the stroke motor regression model using stepwise regression to train only the significant network features among the local betweenness features in this study. As a result, we found that the motor function ability of the stroke and the betweenness centrality on the contralesional motor area (AF4, FC4, and C4) had a strong causal relationship (adjusted r-value = 0.7961, p-value = 0.0287; Figure 4.b).

Figure 4. (a) Betweenness centrality on the contralesional motor area demonstrating a significant difference among the stroke lesion groups using the ANCOVA test (*p < 0.05, S: stroke; SL: subcortical; CL; cortico-subcortical; HC: healthy control). (b) Stroke motor regression model for motor function ability (the upper-Fugle–Mayer Assessment) by stepwise regression using the brain network properties (betweenness centrality on the contralesional motor area).

Discussion

Different characteristics were observed between stroke patients and HCs

In this study, we identified the damaged brain network for stroke patients through the comparison with HCs. Considering the properties of the network, we assumed that the HC group had an efficient network and light workload during motor execution [30, 31].

The HC group without any brain injury had entirely different results from those of the stroke patients, displaying patterns for the motor task-related global parameter. The healthy pattern observed for the HC group was similar to that observed from the motor tasks in our previous studies [32]. This characteristic for the HC group was the result of a non-injured brain network that needed no detoured connections and had a low workload for the motor task by a single trial. In addition, these results are related to our previous study, which showed the characteristics of the task-related global parameters, including an increase in the clustering coefficient and a decrease in both the global efficiency and path length, because of the reconstructed network by the task [32].

In the local parameter, the HCs showed that they had an intact motor pathway and a smooth transference of motor information through the increase in the centrality local clustering coefficient and local efficiency on the contralateral motor area. Our results are supported by previous studies such as those of Gresfkes et al. (2008) and Volz et al. (2015), and showed the significant network patterns on the sensorimotor area during upper limb movement between stroke patients and HCs [2, 33]. In addition, Grefkes et al. (2008) and Pool et al. (2013) argued that there is smooth information transmission to the primary motor cortex from the premotor area (PMA) for the normal brain network during upper limb movement [34, 35]. Although these studies represent just the coupling strength between two regions, our results on the contralateral motor area indicated that the HCs had a light workload and a high efficiency network compared with the stroke patients during motor execution. Furthermore, our results are related to previous studies showing that that the HC group has a compensatory effect on the ipsilateral motor area for the contralateral primary motor cortex with an aging effect [36, 37, 38]. In this study, in particular, the local efficiency and clustering coefficient on the ipsilateral PMA of the HCs represented a significantly increased pattern in comparison with the stroke patients, and this pattern indicated that the HCs on the ipsilateral PMA had a strong compensatory effect through the smooth transmission of information. On the other hand, the local efficiency and clustering coefficient on the ipsilateral primary motor cortex for HCs decreased significantly in comparison with the stroke patients, although the centrality on the ipsilateral primary motor cortex increased. The elderly commonly shows brain activation on the bilateral motor area during motor tasks [36, 37, 39]. Thus, we assumed that these characteristics of the HC group represented a compensatory effect on the normal brain network. The decreased local efficiency and clustering coefficient on the ipsilateral motor area of the HC group may also indicate non-transmission of the motor information to the next stage even though they were over-connected on the ipsilateral primary motor cortex by the compensatory effect by aging.

Unlike the HC group, the stroke patients had the characteristics of a damaged network on the ipsilesional motor area. To activate the abnormal network, we assumed that the peripheral motor area constructed the over-connected network by the increased workload for the stroke. In addition, this damaged network for the stroke may have bad characteristics regarding information transmission by the decreasing efficiency. The increased centrality of the stroke patients observed in this study is supported by previous results. Indeed, Fridman et al. (2004) and Cramer et al. (1997) argued that there is over-activation on the ipsilesional motor area through the increased workload on the peripheral motor area for the damaged region after stroke [30, 31]. These results were also shown in our previous study, in which Kim et al. (2015) analyzed the motor task-related network properties for chronic stroke that represented increased centrality and the bilateral primary motor cortices and decreased local efficiency on the contralesional motor area [7]. These previous works indicated that stroke results in significant brain activation on the contralesional motor area by a compensatory effect [5, 40], and the dendritic growth on the undamaged motor area supports the construction of a network on the contralesional hemisphere by adaptive plasticity [41]. Furthermore, Kim et al. (2003) and Honda et al. (1997) argued that the contralesional motor pathway is one of the main mechanisms for stroke recovery [4, 42]. In this study, we found more specific characteristics of the brain network for the compensatory effect using graph theory. Although the contralesional motor area had brain activation for the compensatory effect, we showed that these brain activities had a low efficiency regarding information transmission by the damaged network. In particular, the stroke patients had a lower local efficiency than the HCs on the contralesional PMA. These results were related to previous studies such as that of Jiang et al. (2013), which showed that the compensatory effect of stroke does not have normal information propagation compared with HCs [18].

Stroke has different characteristics of the task-related brain network by lesion location

We hypothesized that stroke patients would have differences in brain network characteristics based on whether the brain lesion included the primary motor cortex or not. To test this hypothesis, we analyzed the motor task-related brain network patterns for each stroke lesion group.

In the damaged brain, the more the damaged brain area, the more the clustering coefficient is increased in order to find detour pathways [43]. In addition, stroke has different global characteristics by lesion location unlike the HCs, which demonstrated a reconstructed subnetwork centered on the related area during the motor task [32].

For the global parameters, the CL group had typical, chronic hyper-connectivity patterns. This hyper-connectivity of the brain is known as a compensation effect in order to repair the damage to the cerebral cortex [43]. These patterns, which include the increasing path length and the decreasing clustering coefficient and global efficiency, were caused by the reconstructed network to avoid the lesion location. In contrast, the SL group, which had damage to the inner connection between the subcortical area and the cortex, demonstrated hyper-connected network patterns. We assumed that these network characteristics were caused by the detour pathways to avoid the inner lesion. Moreover, we considered that the SL group had an increased connection to the cortex but a decreased clustering coefficient by the disconnected connections between the subcortex and cortex [44].

For the local parameters, stroke patients showed motor task-related network properties, including increased centrality and local efficiency and decreasing local clustering coefficient on the ipsilesional M1. As a comparative method, EEG power, which is a typical EEG feature, indicated different patterns depending on the stroke lesion. While stroke patients had ERD patterns on the bilateral M1, the CL group had ERD patterns centered on the contralesional M1, while the SL group had features centered on the ipsilesional M1. These characteristics for the lesion groups were more likely in the local parameters of the brain network. The CL group with involvement of the primary motor cortex had different network properties on the ipsilesional motor area in comparison with the SL group. In addition, the CL group represented the task-related characteristics, including the increased centrality and decreased local efficiency and clustering patterns. The SL group had increased centrality, local efficiency, and clustering coefficient centered on the ipsilesional M1 in different patterns to the CL group. Based on these results, we determined that there were significantly different characteristics of the brain network on the ipsilesional primary motor cortex depending in the sublesion group. These results may indicate that the CL group had more damage in the ipsilesional motor area than the SL group because their lesions involved the primary motor cortex. Furthermore, the task-related increased efficiency and clustering characteristics on the ipsilesional motor area of the SL group support previous results indicating that brain activation on the ipsilesional primary motor cortex of the SL group is larger than that of the CL group [12].

Based these differences between the two sublesion groups, we confirmed that the CL group had the motor task-related stronger over-connected network, but had a decreased efficiency of information transmission and clustering patterns on the ipsilesional motor area in comparison with the SL group.

Next, we assumed that the contralesional motor area of the SL group had a low workload for the motor task by having a low increase in centrality in comparison with the CL group [32]. Because the SL group had less damage to the cerebral cortex, this group may not need more of the workload (centrality) of the peripheral motor area as a compensatory effect for the ipsilesional motor area given that they had task-related high local efficiency and clustering coefficient.

Although the ipsilesional primary motor cortex of the SL group was less influenced by the damaged cerebral network, the compensatory effect of this group might be caused by the workload involving in searching for detour motor pathways for transmitting motor information from the contralesional motor area to the ipsilesional motor area [45].

Furthermore, the CL group had network characteristics on the contralesional M1 by a compensatory effect; however, their patterns differed from those of the SL group. The CL group had increased motor task-related betweenness on the contralesional M1 as compensation, but they had little increase in the local efficiency and clustering coefficient by the cerebral damage. Based on these results, we confirmed that the two sublesion groups had different network properties on the contralesional motor area by the compensatory effect. We determined that the network characteristics on this area had a difference among the lesion groups and the HC group. Because these network characteristics for the stroke had high correlation with their motor function ability, we expect that these brain network features will be further developed in the stroke rehabilitation field as a new biomarker.

The CL group had a more over-connected network as a compensatory effect, but this was not considered efficient. In contrast, the SL group showed weak over-connected characteristics of the brain network, which were effective. Based on these results, we can better understand the characteristics of the brain network of each lesion as opposed to the brain activity patterns.

In this study, we hypothesized that the SL group would have similar patterns on the brain network as the HC group because we analyzed EEG signals, which measure activity on the cortex. Similar to this hypothesis, the EEG power represented similar ERD patterns for the SL group and HC group. However, the SL group had different characteristics from the HC group with regard to the brain network. In our study, the SL group exhibited a completely different network pattern from the CL group and had similar characteristics to the HC group. However, for the brain network, the SL group had different characteristics from both the HC and CL groups. The SL group had the network characteristic of a hyper-connection on the cortex (increasing connection and decreasing clustering coefficient), while the HC group had patterns characterized by the reconstructed subnetwork for the motor task. Based on these results, we identified that the SL group is not similar with the HC group with regard to the brain network.

Conclusions

In this study, we compared the characteristics of the brain motor network according to the stroke lesion in comparison with HCs using the graph theory. We sought to reveal the more detailed differences in the motor-related mechanisms between the stroke patients and HCs or the stroke’s subgroups for lesion location during motor execution than the results from previous studies. While these previous studies have indicated differences in brain activation and connectivity strength in various motor areas between stroke patients and HCs, we demonstrated in this study the detailed differences in the mechanisms of the motor area for upper limb execution between normal and abnormal networks.

In addition, we found differences in the contralesional motor area according to the characteristic of the stroke lesion. However, there was a limitation in terms of statistical analysis to determine the network characteristics of each group because of the small number of participants in each lesion group. To solve this problem, we plan to analyze the overall brain network, including global and local-scale network characteristics, of stroke patients and HCs by recruiting more participants based on this study.

Collectively, our findings may aid in the design of therapies and programs of rehabilitation for patients with stroke by inducing neuroplasticity in comparison with the normal healthy brain network. While previous studies have analyzed characteristics of stroke by fMRI or EEG power, we represented the brain network characteristics for stroke lesion on the cortex by EEG. As a result, we were able to quickly identify new features of stroke lesion in comparison with fMRI and EEG power. Our results may also help to assess the progress of therapy and rehabilitation for stroke depending on each lesion group by understanding the complex interactions in the damaged brain network after stroke as a new biomarker.

Declarations

Ethics Approval and Consent to Participate

We obtained EEG data for the stroke and healthy control groups. Therefore, we have included the names of the ethics committees and their reference numbers in the Methods section, as follows: “The present study was approved by the institutional review boards (IRB) of the Korea Institute of Science and Technology (KIST) and Samsung Medical Center (SMC) (KIST IRB; KIST 2013-009; SMC IRB; SMC 2013-02-091), and all experiments were performed under IRB guidance.”

Consent for Publication

All participants provided written informed consent prior to participation in the study and provided permission to publish their individual experimental data.

Data Availability

The EEG datasets generated and analyzed during the current study are not publicly available due to privacy concerns, but are available from the corresponding authors upon reasonable request. Interested parties may request the data from one of the co-corresponding authors (laehyunk@kist.re.kr) for individual, case-by-case access.

Conflicting Interests

The authors declare no potential conflicts of interest with respect to the research, authorship, or publication of this article.

Authors' contributions

DHK participated in the design of the study, performed the statistical analysis, and wrote the manuscript. GHK, WP, and YHK participated in the experimental design, selection of the clinical population, and protocol adaptation for patients. SWL and LK conceived of and coordinated the study, and helped to draft the manuscript. All authors read and approved the final manuscript.

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Abbreviations

EEG
electroencephalography
S
Stroke
CL
Cortico-subcortical lesion
SL
Subcortical lesion
HC
Healthy control
ERD
Event-related desynchronization
PLV
Phase locking value
ANCOVA
Analysis of covariance
Ipsi. M1
Ipsilesional primary motor cortex
Contra.M1
Contralesional primary motor cortex

PMA
premotor area

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Tables

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Figures

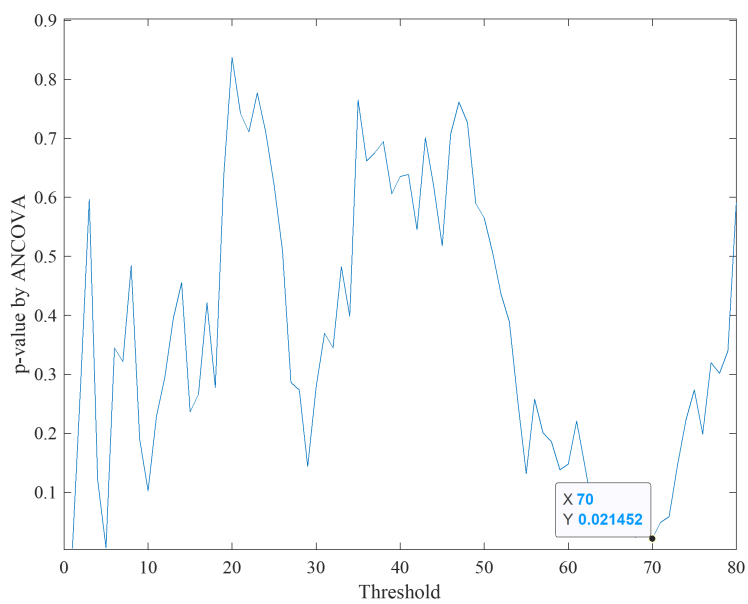

Figure 1

The significant threshold points among each group for their variance in the global efficiency between pre- and post- motor execution using ANCOVA.

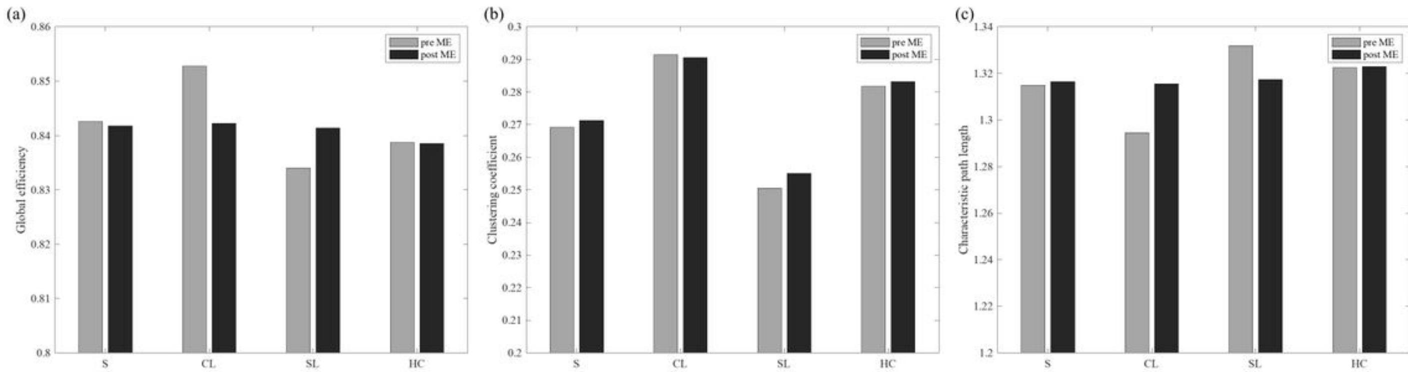

Figure 2

Motor task-related changes in the global parameters. (a) The global efficiency. (b) The clustering coefficient. (c) The characteristics path length.

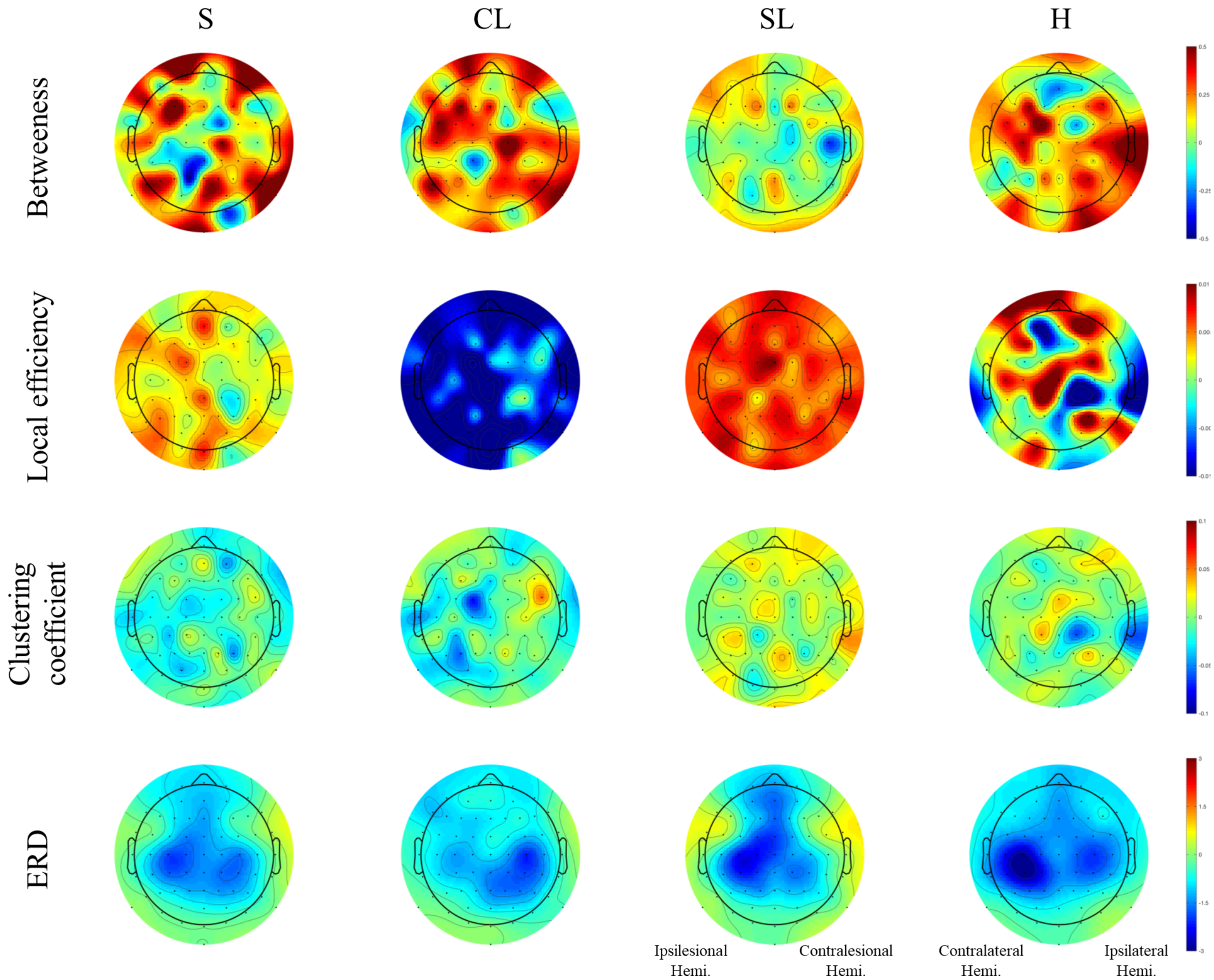

Figure 3

Motor task-related changes in the local parameters.

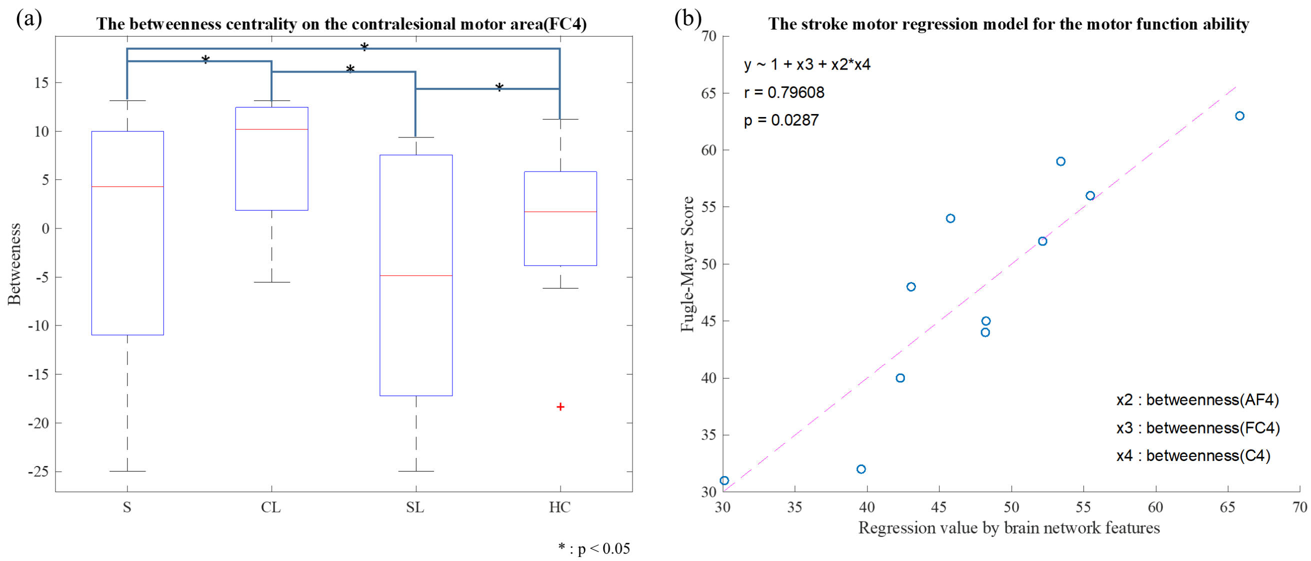

Figure 4

(a) The betweenness centrality on the contralesional motor area demonstrating a significant difference among stroke lesion groups using the ANCOVA test (*p < 0.05, S: stroke; SL: subcortical; CL; cortico-subcortical; HC: healthy control). (b) The stroke motor regression model for the motor function ability (the upper-Fugle–Mayer Assessment) by stepwise regression using the brain network properties (betweenness centrality on the contralesional motor area).

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