Hemispheric Activation during Planning and Execution Phases in Reaching post Stroke

A consort study

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Abstract: Enhanced activation in the non-lesion hemisphere in stroke patients was widely observed during movement of the affected upper limb, but its functional role related to motor planning and execution is still unknown.

This study was to characterize the activation in the non-lesion hemisphere during movement planning and execution by localizing sources of high-density electroencephalography (EEG) signal and estimating the source strength (current density [A/m^2]).

Ten individuals with chronic stroke and shoulder/elbow coordination deficits and 5 healthy controls participated in the study.

EEG (64 channels) was recorded from scalp electrodes while the subjects performed a reach task involving shoulder flexion and elbow extension of the affected (patients) or dominant (controls) upper extremity. Sources of the EEG were obtained and analyzed at 17 time points across movement preparation and execution phases. A 3-layer boundary element model was overlaid and used to identify the brain activation sources. A distributed current density model, low-resolution electromagnetic tomography (LORETA) L1 norm method, was applied to the data pre-processed by independent component analysis.

Subjects with stroke had stronger source strength in the sensorimotor cortices during the movement compared with the controls. Their contralesional/lesional activation ratio (CTLR) for the primary motor

cortices was significantly higher than that of the controls during the movement-planning phase, but not during the execution phase. The CTLR was higher in planning than in the execution phase in the stroke group.

Excessive contralesional motor cortical activation appears to be more related to movement preparation rather than execution in chronic stroke.

Abbreviations: BEM = boundary element model, CDR = current density reconstruction source model, CTLR = contralesional/lesional activation ratio, CWS = center of the workspace, ECD = equivalent current dipole model, EEG = electroencephalography, fMRI = functional magnetic resonance imaging, ICA = independent component analysis, M1 = the primary motor cortex, MEPs = ipsilateral motor evoked potentials, MMT = Manual Muscle Test, TMS = transcranial magnetic stimulation.

INTRODUCTION

Motor recovery after stroke is at least partly attributed to cortical plasticity and reorganization, during which the normal locus for impaired motor function can be assumed by the perilesional cortical regions or homologous areas on the contralesional hemisphere.[1–3] A functional magnetic resonance imaging (MRI) (fMRI) study suggested that after stroke, there are changes in the hemispheric lateralization of cortical activation during movements of paretic extremities. In the acute stage, there is greater activation in the lesioned hemisphere. In the sub-acute and early chronic stages, there is greater activation in the contralesional hemisphere. Finally, in the chronic stage, there is greater activation in the lesioned hemisphere again.[4] This changing pattern of hemispheric lateralization suggests a *temporary* role of the contralesional hemisphere activation in movement control during the subacute/early chronic stroke stage.

Many studies have suggested that enhanced contralesional activation may compensate for the impaired function by activating the uncrossed pathway.[5,6] However, more recent studies have indicated that functional corticomuscular coupling measured by brain–muscle signal coherence originates mainly from the lesioned hemisphere,[7] and contralesional transcranial magnetic stimulation (TMS) failed to elicit responses in the paretic hand in well recovered subjects.[8] The authors[8] hypothesized that instead of being involved into direct corticospinal recruitment, enhanced contralesional activities observed in well-recovered stroke patients might be related to higher level cortical processing of movement preparation, such as selection of movement trajectory and programming of multi-joint activities, in order to facilitate the relatively difficult motor control process for stroke patients, in a manner similar to that of the extended cortical activation observed in controlling complex movements in healthy individuals.[9,10] Nevertheless, there is no

direct evidence to support this hypothesis. Primate studies suggested that a distinct population of neurons only fire phasically *before* muscle contraction, whereas other neuron populations fire tonically *during* the contraction, indicating different neural populations may be involved in motor planning and execution.[11,12] Moreover, motor planning influences the subsequent motor execution, for example, excitability of the corticospinal pathway, which is an important predictor of the outcome of motor recovery post stroke.[13–17] To understand the exact role of the enhanced contralesional cortical activation related to motor planning and execution in stroke is thus warranted.

The source localization method based on high-density scalp EEG data has showed validity in locating focal cortical activities during upper-limb movements post stroke.[18,19] The EEG source reconstruction method has the advantage of higher temporal resolution compared with some other imaging methods such as fMRI; the source localization approach allows investigators to examine brain activities in various sources at different temporal phases of motor control. The current study estimated sources of scalp EEG recorded from stroke patients and healthy controls during an upper extremity-reaching task. Reaching is a fundamental upper extremity function and more than 70% of stroke patients admitted to rehabilitation services are unable to reach successfully while sitting.[20] Because of high temporal resolution of the EEG signals, brain activities before and after the movement onset can be localized in order to distinguish cortical activities related to both motor planning (movement preparation) and motor execution (corticospinal pathway activation). The purpose of this study was to investigate the functional role of abnormally elevated contralesional hemisphere activation, based on the high-resolution EEG sources in motor planning and execution of the reach movement.

METHODS

Subjects

Participants in the study were 10 stroke patients with persistent ($\geq$12 months, 37.10 ± 29.59 months, range 12–94

months) dyscoordination of the upper limb (Table 1; mean age, 63.50 ± 12.44 years; range, 39–78 years; 8 male) and 5 healthy controls (mean age, 62.40 ± 8.91 years; range, 52–71 years; 4 male; all right-hand dominant). The controls were screened for neurological and musculoskeletal conditions to ensure their sensorimotor function was not affected. The lesion sites of the stroke patients are listed in Table 1. This study was performed under the oversight of the Institutional Review Board of Cleveland VA Medical Center. All subjects gave informed consent prior to their participation. Exclusion criteria included more than one stroke, presence of other intracranial pathology, normal performance of the reach task, medications that might interfere with the neuromuscular system and motor function recovery, muscle tone (spasticity) of finger, wrist and elbow flexors >3 (Ashworth Scale), and other neuromuscular lesions/diseases that impair motor function. To assess motor function, the Fugl-Meyer score (upper limb) and Manual Muscle Test were evaluated (Table 1).

Data Recording

Motor Task Apparatus

A de-activated shoulder/elbow robot (no assistance or resistance to movement was provided; InMotion2; Interactive Motion Technologies, Inc., Cambridge, MA) was used to support the subject's forearm and hand, standardize the shoulder/elbow reach task on a horizontal plane, and acquire kinematic data (Figure 1). The apparatus supported the fingers and wrist, allowing movements only at the elbow and shoulder joints. Prior to performing each reach movement, the subject's hand was placed at the center of the workspace (CWS) and a target was displayed on a PC monitor; hitting the target with the cursor on the screen required an accurate 14-cm linear movement of the manipulandum away from the subject, in a horizontal plane, as the result of shoulder flexion and elbow extension. At the end of the reach movement, an experimenter assisted in returning the patient's hand to the original CWS. Visual feedback was provided for each trial, via the monitor showing the progress of

TABLE 1. Demographic Information of Stroke Patients

| Subject | Age | Sex | Months Post Stroke | Lesion Location | | Dominant Hand | Stroke Type | Fugl Meyer | Manual Muscle Test | Lateral Deviation |
				Lesion Site	Dominance Hemisphere					
S1	76	M	24	R basal ganglia	No	R	Ischemia	32	1.7	0.9489
S2	77	M	12	L post limb internal capsule	Yes	R	Ischemia	49	3.3	0.1271
S3	71	M	58	L corona radiata	Yes	R	Ischemia	32	4.5	1.08
S4	39	F	94	R cerebral aneurysm*	No	R	Hemorrhage	44	4.5	0.91
S5	60	F	24	L lower pons	Yes	R	Ischemia	27	0	0.76
S6	61	M	35	L basal ganglia	Yes	R	Ischemia	14	2.7	0.48
S7	61	M	16	R frontal parietal internal capsule	No	R	Ischemia	27	0	0.754
S8	78	M	79	L mid-pons	Yes	R	Ischemia	39	3.7	0.36
S9	61	M	16	R basal ganglia	Yes	L	Ischemia	31	2.7	0.5
S10	51	M	13	L internal capsule	Yes	R	Ischemia	36	3.7	0.46

Fugl Meyer indicates the upper extremity FM scores; elbow extension strength was tested by the Manual Muscle Test, data is in the unit of kg; the unit of lateral deviation is cm, which indicating the deviation of subject's trajectory from the direct connection between start and end points. *Cerebral aneurysm at the anterior division of the M-2 segment of the right MCA, detailed lesion location is unclear as MRI data was not available, most likely this subject had infarcts in M1 and S1; no infarct in or near M1 or S1 was found through examining MRI images for other subjects.
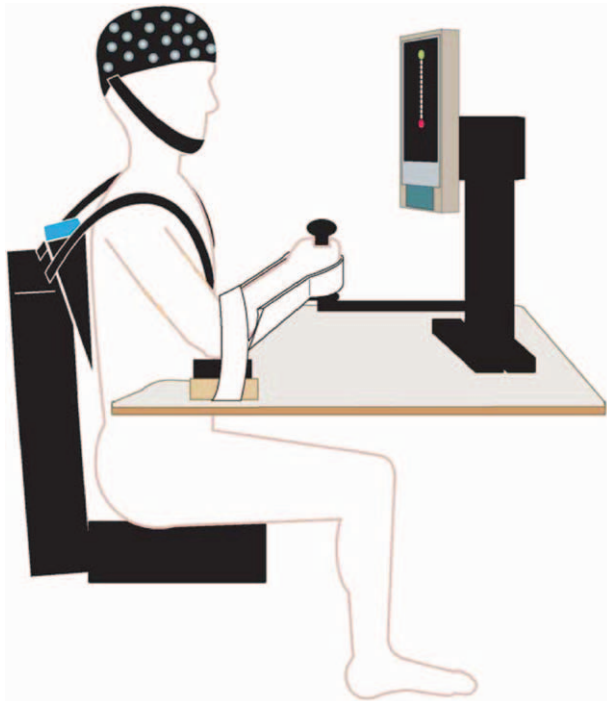
FIGURE 1. Experimental setup. Subjects were seated in a chair with only the unilateral (affected side in stroke and dominant side in controls) shoulder and arm moveable. The elbow, forearm, and hand were cradled and supported. A target and the start position were displayed on a screen, and subjects needed to move the manipulandum forward to reach the target point, by flexing the shoulder and extending the elbow. No assistance or resistance was provided by the robot.

the cursor movement toward the target. Five sets of 10 repetitions were performed with a 2-minute rest between sets (each inter-trial interval was about 20 s) to avoid fatigue. A customized goniometer was attached to the upper and lower robot arms to acquire elbow joint angle information during the reach movement.

EEG Recording

A 64-channel NeuroScan EEG system (NeuroScan Labs, El Paso, TX) was used to acquire surface EEG signals. A Quik-Cap elastic cap that holds 64 surface electrodes was placed on the scalp for EEG data recording. The configuration of the electrode arrangement on the cap was based on the International 10–20 System.[21] All the 64-channel EEG signals were referenced to the common-linked earlobes. Impedance for all the electrodes was monitored at a level below $10,000\,\Omega$ prior to the initiation of data collection. All channels of the EEG signals were amplified ($\times75,000$), filtered ($0.3–50\,Hz$), and digitized (1000 sample/s) using the NeuroScan Labs software.

The elbow angle signal sensed by the potentiometer in the goniometer was also acquired (1000 samples/s) by the NeuroScan (EEG) systems. A trigger signal was generated at each movement onset in each trial when a $2°$ change in elbow angle was detected by the potentiometer for the subsequent trigger averaging of the EEG.

Motor Performance Data

The robot acquired position data of the manipulandum at 200 Hz during the movement, as the subject attempted to move the manipulandum (represented by the cursor on the monitor) from the start position (CWS) to the target. The position data were used to calculate a measure of the ability to maintain the desired movement trajectory to the target (lateral deviation). Detailed calculation method can be found in our previous work.[22] In this study, the stroke patients exhibited greater lateral deviation (poorer motor performance) than controls during the reach movements (Figure 6).

Data Processing and Analysis

Estimation of Current Densities Using LORETA

LORETA uses the so-called inverse solution to estimate electrical sources in the brain that produce the EEG signals measured by the electrodes on the scalp. With the inverse approach, there is an unlimited number of sources or combinations of sources per signal. These sources are modeled as current density reconstructions (CDRs) on a volume conductor model, which can be a head model based on the MRI data. Current density is defined as dipole moment per volume ($\mu Amm/mm^3$) and is modeled as a 3D grid of dipoles. The goal is to find the dipole moments for the grid nodes. CDRs assume simultaneous activity across sources and LORETA assumes these sources to be of similar strength to each other. LORETA uses a goodness-of-fit of about 1/signal-to-noise ratio (SNR) to help estimate the sources from the current density model.

The raw EEG data were visually inspected and trials with artifacts due to eye blinks or head movements were excluded. Both EEG data preprocessing and LORETA current density estimation were performed using the Curry software package (version 4.5, Neuro Scan Labs, VA, USA). The individual trials of EEG data were segmented and then all the segments were aligned with the movement onset (detected by the potentiomenter/goniometer) before they were averaged. The averaged EEG data were baseline corrected using baseline data from -2891 to $-2391\,ms$ (prior to movement onset). Subsequently, an independent component analysis (ICA) was applied to the data. Only the main components (SNR > 1) were chosen for the source reconstruction. To overlay the sources, we used a 3-layer (conductivities of the scalp and brain: 0.033 S/m, and the skull: 0.0042 S/m) triangle-node, boundary element model.[23,24] Based on the Montréal Neurological Institute (MNI) brain MRI, distributed current density model (LORETA), with L1 norm method, was applied to the ICA-preprocessed data. In addition, the sources were constrained to the reconstructed layer of the folded cortex with 6926 nodes using a rotating model (Curry user guide, 1999).[25,26]

Current Density Data Analysis – Post Processing

Source localization was analyzed at 17 different time points (planning phase: -2000, -1900, -1800, -750, -600, -450, -300, -150; 0 ms [movement onset]; execution phase: 150, 300, 450, 600, 750, 1800, 1900, 2000 ms) throughout the planning and execution phases of the reaching movement for each subject. Since each source needed to be identified at its anatomical location under Talairach coordinate for further analysis, several steps were taken to transform CurryV4.5 coordinate to Talairach coordinate. First, transformation of the SPM99/MNI (X, Y, Z) coordinates from the Curry coordinates (x, y, z) was obtained as follows (the MNI image dataset has a 1.8-mm voxel size in Curry V4.5, while the MNI brain

originally had a voxel size of 2 mm):

$$X = (120 \text{ mm} - x) \times 2/1.8$$
$$Y = (102 \text{ mm} - y) \times 2/1.8$$
$$Z = (z - 100 \text{ mm}) \times 2/1.8$$

Second, transformation of the SPM99/MNI coordinates (X, Y, Z) to the Talairach coordinates (X', Y', Z') was performed: (http://www.mrc-cbu.cam.ac.uk/Imaging/Common/mnispace.shtml)

Above the anterior commissure (AC) ($Z \geq 0$):

$$X' = 0.9900X$$
$$Y' = 0.9688Y + 0.0460Z$$
$$Z' = -0.0485Y + 0.9189Z$$

Below the AC ($Z < 0$):

$$X' = 0.9900X$$
$$Y' = 0.9688Y + 0.0420Z$$
$$Z' = -0.0485Y + 0.8390Z$$

Third, after establishing the position of each source on the Talairach coordinate, the anatomical label was obtained through the Talairach Daemon search for each source location. Thus, all the current densities in the Brodmann area 4 (primary motor cortex), and areas 3, 1 and 2 (primary sensory cortex) were identified and vector-averaged (we chose these Brodmann areas based on their well-known role in modulating muscle activities). The overall averaged current densities of these areas in lesioned and contralesional hemispheres were used to calculate a contralesional/lesional activation ratio (CTLR) in stroke patients. For controls, the ipsilateral/contralateral (ipsilateral hemisphere is on the same side of movement hand) ratio was calculated. The CTLR was calculated and displayed in both planning and execution phases, respectively, to compare the activation ratio of the two hemispheres during each of the two motor control phases.

Statistical Analysis

The Mann–Whitney test was performed to compare control and stroke patients, according to the overall current density averaged across each of the 17 time points covering movement preparation and execution (Figure 4). Similarly, control and stroke patients were compared according to the CTLR during planning and execution phases (Figure 5A); and CTLR of the control and stroke subjects was compared for planning versus execution phases (Figure 5B). A 2-way ANOVA was also applied to CTLR results with the two factors of subject group (stroke or control) and movement phase (planning or execution). Significance level was $P \leq 0.05$.

RESULTS

Figure 2 shows the EEG source signals of a stroke subject overlaid on the MNI brain from 1000 ms before to 900 ms after the movement onset. Each image represents average source activities over 100 ms. The time 0 (movement onset) occurred within the time window represented by the 11th image (3rd image from left on 3rd row from top). The left hemisphere (left side of each brain image) was the lesioned side and right hemisphere the nonlesioned side. Abnormally elevated contralesional (right hemisphere) activation was observed before and at movement onset. After movement onset began, the activation in the non-lesion hemisphere diminished.

The average source (current density) data at 17 time points during the motor task are presented for both stroke and control groups (Figure 3, time 0 indicates movement onset). The control group showed almost no activation in the right hemisphere (ipsilateral to the moving limb) while the patients exhibited substantial contralesional hemisphere activation especially before movement onset (Figure 3C, D). Although the results for the lesioned hemisphere (left [contralateral] for controls) were mixed, there was a tendency for the stroke patients to have a higher level of activation than controls (Figure 3A, B).

Figure 4 shows the results of the quantitative comparisons of stroke versus control, according to the source strength averaged throughout the task (from 2000 ms before to 2000 ms after the movement onset). The results show clear differences in signal strength between the stroke and control groups in the right or non-lesioned hemispheres (Figure 4, data bars C and D; $P = 0.03$; $P = 0.03$, respectively). In the left or lesioned hemisphere, the P values for stroke versus controls suggested a trend toward abnormally elevated values for source strength ($P = 0.12$ and 0.24, respectively) (Figure 4, data bars A and B).

The CTLR was calculated and comparisons are showed in Figure 5 between stroke and control groups (Figure 5A) and between planning and execution phases (Figure 5B). CTLR is the ratio of activation in the right or non-lesion hemisphere versus left or lesioned hemisphere. The controls had a CTLR ratio below 1 (greater activity in the left hemisphere, contralateral to the moving arm, which is as expected [Figure 5A, blue bars]); in contrast, stroke patients exhibited a >1 non-lesioned to lesioned hemisphere ratio, especially in the planning phase (Figure 5A, red bars). The CTLR for stroke was significantly higher than the controls in the planning phases in area 4 and areas 3, 1, 2 ($P = 0.03$ and 0.04, respectively). However, in the execution phase, the difference was not significant ($P = 0.34$ and 0.24, respectively; Figure 5A). Within the stroke group (Figure 5B, first data bar group), the CTLR was significantly higher in the planning than execution phase for the Brodmann area 4 ($P = 0.04$); and in the areas 3, 1, and 2 the comparison did not reach significance ($P = 0.27$). For the control group, the CTRL values for the planning versus execution phases were similar (Figure 5B).

Previous literature indicated that hemispheric dominance might influence the cortical activation pattern in that dominant hand movement is associated with more contralateral hemisphere activation than non-dominant hand. To evaluate the possible influence of handedness on the results, a sub-sample of stroke subjects was studied. CTLR was compared between 5 right-handed controls and 7 stroke subjects (S2, 3, 5, 6, 8, 9, 10) with lesion in the dominant hemisphere (Figure 5C, D). The results of comparison between hemispheric dominance matched sub-groups are similar to Figure 5A and B. The CTLR for stroke was significantly higher than that for the controls in the planning phases in area 4 and areas 3, 1, 2 ($P = 0.02$ and 0.04, respectively). However, in the execution phase, the difference was not significant ($P = 0.39$ and 0.32, respectively; Figure 5C). In addition, for the stroke group, there was a significant difference between planning and execution phases in area 4 ($P = 0.04$, Figure 5D), which is consistent with the observation for the whole stroke group (Figure 5B).

The two-way ANOVA analysis of CTLR with the two factors of group (stroke and control) and movement phase (planning and execution) indicated that subject group had a significant effect on the CTLR ($P = 0.02$) whereas movement phase did not ($P = 0.30$). And there was a tendency the difference
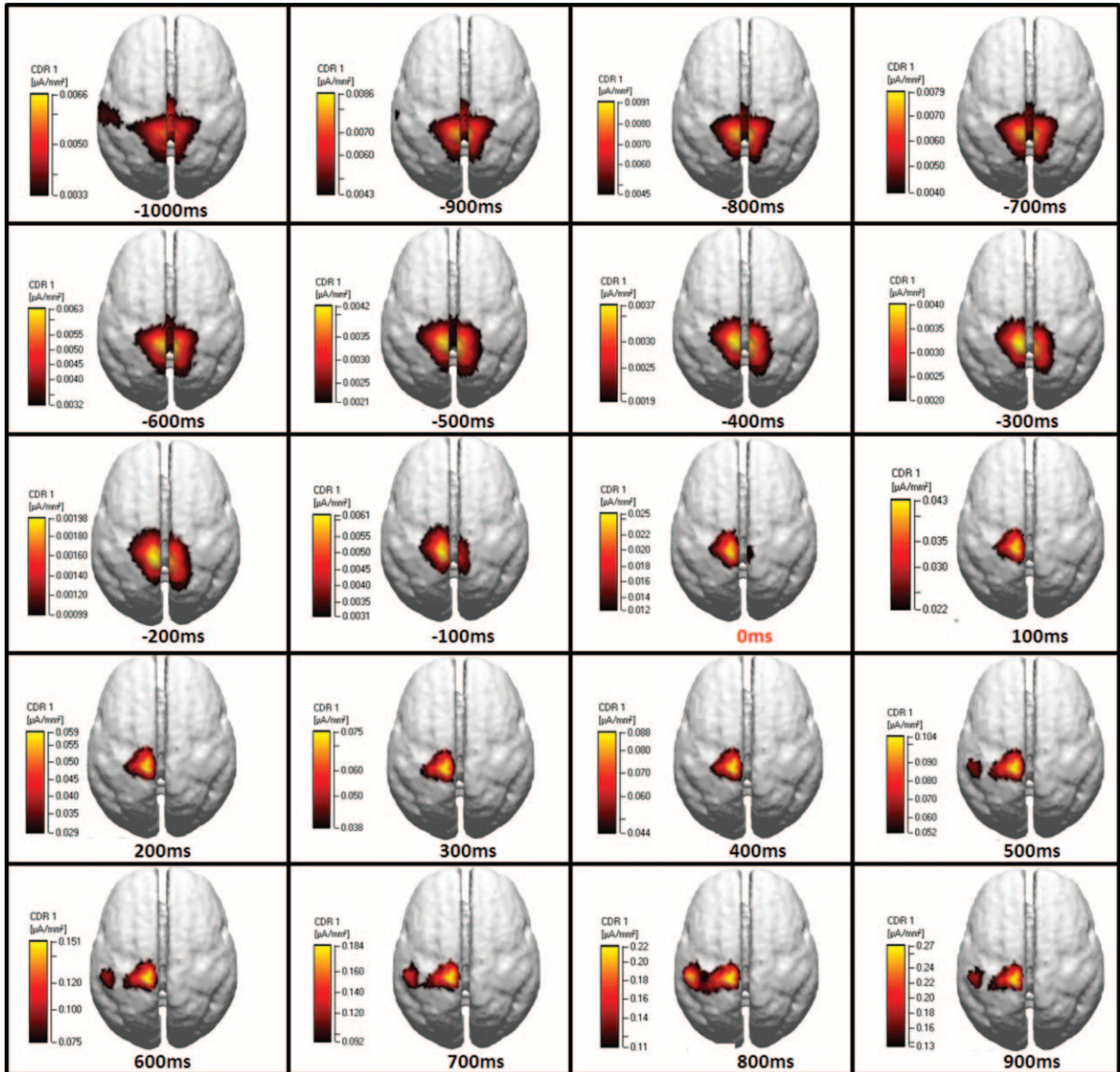
FIGURE 2. Sources localized using Curry in a stroke subject during the reach movement with the paretic right arm, with brain maps beginning from 1000 ms before the movement onset, and continuing to 900 ms during the movement. Each image represents 100-ms data. The time 0 was movement onset (indicated by the red color), and occurred within the time window represented by the 11th image. Lesional area is on the left hemisphere. The patient had abnormally elevated right or contralesional activation during the motor planning phase and it diminished soon after the movement onset.

in the CTLR between stroke and control groups was influenced by the movement phase (planning or execution) as the interaction between subject group and movement phase had a P value of 0.17.

DISCUSSION

Cortical Activation

Our results suggest that the overall cortical activation of stroke subjects, as measured by EEG source strength, especially in the contralesional hemisphere, was abnormally higher than healthy controls (Figures 3 and 4). This finding is consistent with our previous investigations that quantified movement-related cortical potential in the two hemispheres[22,27]; and

current finding is also consistent with previous neuroimaging studies by others in that greater activation was observed in the contralesional hemisphere in stroke.[2,5] With damage in the cortical network caused by stroke, it is expected that greater voluntary effort was needed for the stroke patients to perform the motor task,[22] which may have been reflected by an overall higher brain activation level in stroke compared with control subjects.

The CTLR of the stroke patients was higher than the controls in the planning phase; however, this significant difference between stroke and controls was not seen in the execution phase (Figure 5A). A higher CTLR in the planning phase means more contralesional motor cortex participation in pre-movement preparation for the stroke patients. This CTLR result is
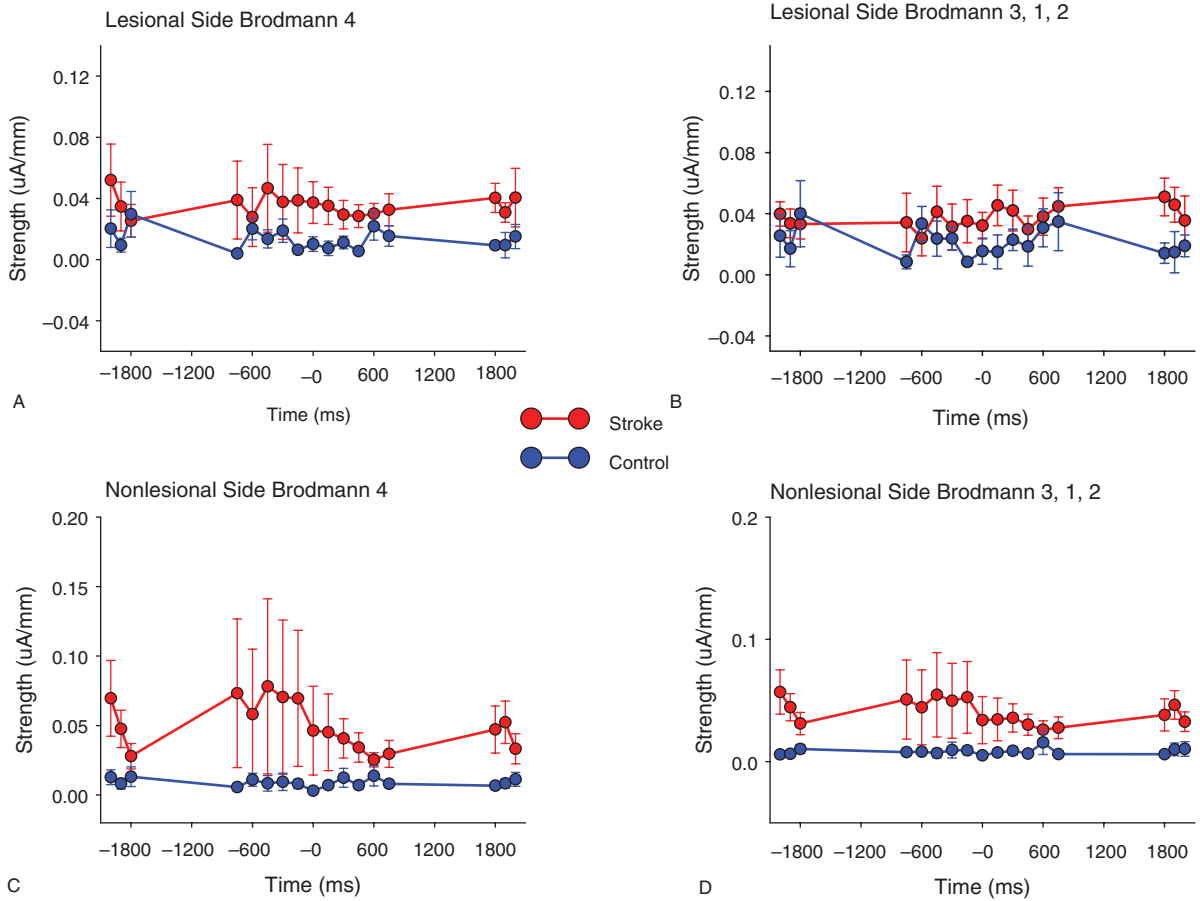
FIGURE 3. Group averaging of source strength (current density) for stroke and control subjects for each of the 17 time points at lesional and nonlesional sides in Brodmann area 4, and areas 3, 1, 2. A: lesional side (contralateral side for controls) Brodmann area 4; B: lesional side Brodmann areas 3, 1, and 2; C: nonlesional side (ipsilateral side for controls) Brodmann area 4. D: nonlesional side Brodmann areas 3, 1, 2. Red: Stroke group; Blue: Control group.
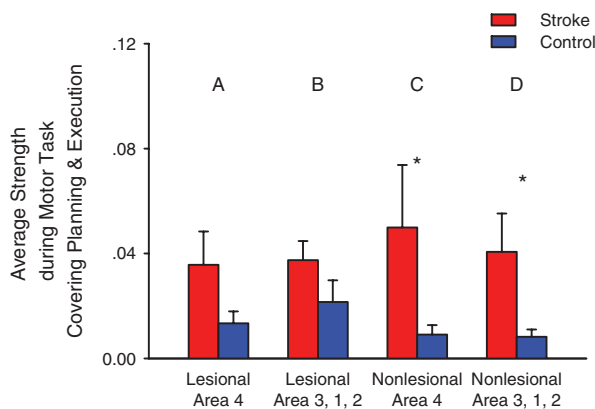

FIGURE 4. Comparisons of stroke versus controls, according to the source strength (current density) averaged across the 17 time points covering the planning and execution phases. The nonlesional side source strength was significantly higher for stroke than control subjects ($P = 0.03$ [C] and $P = 0.03$ [D]). A similar tendency, although not significant, was seen on the lesional side ($P = 0.12$ [A] and $P = 0.24$ [B]). Red: Stroke group; Blue: Control group.

consistent with previous laterality index studies.[28,29] Many previous studies investigated activation patterns of ipsilesional and contralesional hemispheres and the results have been mixed. None of these studies, however, separated the activation patterns into the two distinct phases of planning and execution. Based on the high time resolution that the EEG source signals afford, our study contributes to the literature by demonstrating a greater CTLR in the planning phase but not the execution phase.

Previous studies suggested that the ipsilateral hemisphere could be activated during *both the planning and execution phases*, under certain conditions such as strong stimulation and increased task difficulties. About 8% to 10% of pyramidal axons do not decussate,[30] offering the possibility for ipsilateral activation of the uncrossed pathway, together with corticoreticulospinal or corticopropriospinal pathways.[31] Ziemann et al[31] found that ipsilateral motor evoked potentials could be elicited from healthy people with high intensity TMS with active target muscle; and bilateral activation of prefrontal areas was observed with additional demands in a working memory task.[32] Thus it appears a reasonable possibility that compensatory activation of the neural network in the contralesional hemisphere could assist stroke patients regain movement ability.[5,28]

Recent studies of corticomuscular coherence measurement[7] and of contralesional TMS stimulation,[8] however, suggest that the corticospinal connection mainly originates from
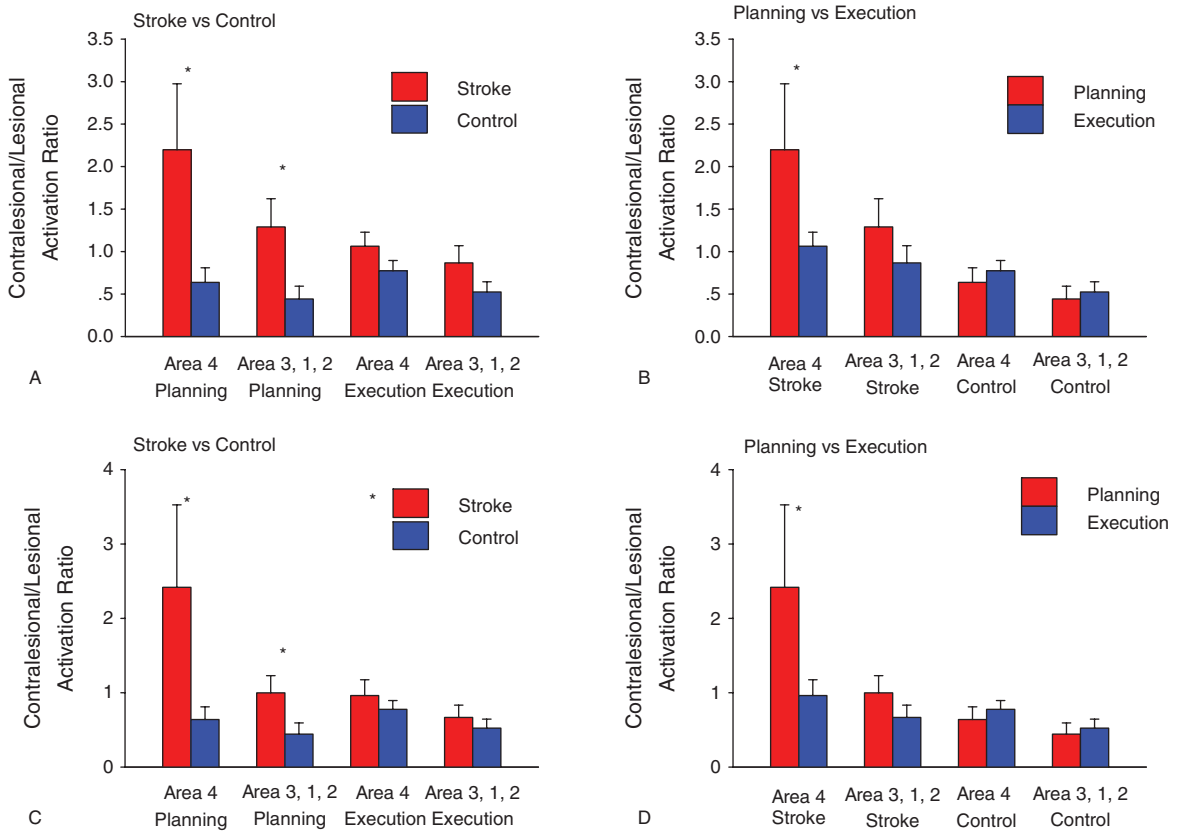
FIGURE 5. Comparisons of CTLR between the stroke and control groups (A); between planning and execution phases (B); and between the stroke and control groups (C) and between planning and execution phases (D) in subgroups of stroke and control subjects with same hemispheric dominance. A: the CTLR was significantly higher in stroke than control groups only for the planning phase in both the motor (area 4, $P = 0.03$) and sensory (areas 3,1,2, $P = 0.04$) cortices. The CTLR was not significantly different between the two groups for the execution phase, although a trend of higher CTLR in stroke was seen. Red: Stroke; Blue: Control. B: the CTLR was significantly greater during the planning versus execution phase for area 4 in stroke group only ($P = 0.04$). Red: Planning; Blue: Execution. C: seven stroke subjects with lesion on the dominant hemisphere were compared with control groups for the CTLR. The results are similar to A. D: The CTLR of controls and 7 seven-stroke subjects with lesion on the dominant hemisphere was also compared between planning and execution phases. The results are similar to B.

ipsilesional hemisphere in well-recovered stroke subjects. And although there is no significant corticospinal connection originating from the contralesional hemisphere to the paretic extremities, activation from contralesional hemisphere was still
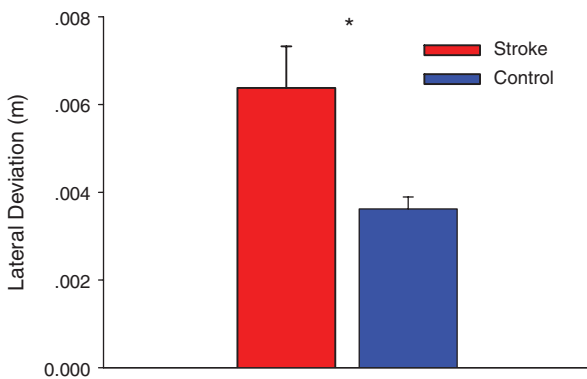

FIGURE 6. Comparison of lateral deviation during reaching between stroke patients and controls. The lateral deviation was significantly greater in the patient group.

observed during motor tasks.[1,8] Further, it is suggested that such observed contralesional activation is not related to mirror movements, since in both studies, EMG activities of the unaffected extremities were well monitored. Gerloff et al[8] suggest that instead of being directly involved in corticospinal commands, elevated contralesional hemisphere activities might be related to higher level cortical processing, such as movement direction selection and movement preparation, to facilitate the motor control of stroke patients in a manner similar to that of the extended networks involved in controlling a complex movement in healthy controls. For voluntary movement in healthy adults, prominent activation of ipsilateral primary motor area was observed during challenging and difficult unimanual motor tasks, or a simple task performed by the nondominant hand.[9−10] The underlying mechanisms might be similar for ipsilateral activation of the intact (contralesional) hemisphere in stroke patients, since motor difficulty is a common phenomenon for stroke patients, suggested by their prolonged motor planning time and increased effort level.[22,27] Consistent with this speculation is the observation that contralesional activation is enhanced in response to motor skill challenge in chronic strokes.[3]

The current study specifically separated the movement control process into planning and execution phases to determine

whether the abnormally elevated contralesional hemisphere activation in stroke was motor phase dependent. Our results indicated that the CTLR was higher in planning than execution phase in the Brodmann area 4, the primary motor cortex (M1) (Figure 5). The M1 region is generally regarded as necessary for controlling voluntary movement execution; however, it is also involved in higher-order function such as movement planning for direction selection or programming multi-joint activities.[33,34] It has been suggested that both the contralateral and ipsilateral M1 regions participate in coding sequences of complex motor tasks.[6,35] A large population of trajectory-specific cells was found in M1.[36,37] Because the current study observed greater contralesional M1 activation only in the planning phase, it is reasonable to speculate that the contralesional M1 in stroke could be involved in high-order level processing related to movement preparation and scheduling before movement onset, as suggested by Gerloff et al.[8] Schaechter and Perdue[3] found that activation in the contralesional hemisphere increased even in well-recovered stroke patients, in response to greater challenge in motor task skill, and that ''increased cortical processing related to the planning and somatosensory guidance of coordinated movement.'' Wisneski et al[38] observed that affected hand movements of stroke patients were associated with contralesional hemispheric electrophysiological changes (measured by intracranial ECoG) that occurred earlier than the changes that were associated with contralateral hand movements, in which ''the timing of signal alteration supports the role of ipsilateral cortex in planning of movements.'' Our results, with higher activation level in the contralesional M1 during planning phase, are supportive of the hypotheses of these previous studies.[8,38]

Source Localization Method

To the best of our knowledge, only a few studies have employed the CDR source model to analyze motor-related source signal.[19,39] Most previous motor control research involving this topic used the equivalent current dipole model (ECD).[40,41] The general strategy of ECD model is to place dipoles in the known motor cortical areas and then fit amplitudes, positions and orientations within certain limits. Usually, principle components analysis or functional MRI activation map was used to determine the number of dipoles. However, it has been reported that the ECD methods cannot determine accurate locations of all the sources even if the number of dipoles were correct.[26] No prior information of source locations is needed for the CDR method. Nevertheless, several methodological limitations associated with the CDR should be mentioned. All steps in the process of solving the inverse problem should be taken carefully to avoid or reduce biased results.

First, a consistent SNR is necessary for a reliable reconstruction result. A SNR value above 8 is preferable in source location studies.[42] When the SNR is below 8, the quality of the reconstruction results declines. However, SNR of scalp EEG associated with motor tasks is usually below 8. Also, choosing a correct regulation parameter, λ, to account for the noise is very important. Higher levels of noise usually need a bigger regularization value (λ), which can be determined using χ^2 and L-curve methods.[26] Unfortunately, the CURRY program (version 4.5) does not provide this function for LORETA L1-norm. Therefore, a fixed value ($\lambda = 1$) was used in this study. For this reason over-fitting or underestimating the data might happen for the extremely small or extremely high SNR data. Although the values of SNR for the data of each subject were within a reasonably small range, it may still be one of the reasons that the results had relatively large inter-subject variation.

For the head model used in this study, it is desirable to co-register each subject's anatomical MRI with the individual's EEG electrode location. But using MNI averaged MRI brain image is also a choice that does not lose substantial resolution[24,43], while at the same time this method can decrease the computation load.[23,43] The conductivity value of the head (especially the skull conductivity) is also one of the factors that can influence the performance of the inverse solutions.[44–46] Unfortunately, the real value of skull conductivity is still unknown and the direct measurement results have shown large variation across different studies.[44,47,48] We used the default values in CURRY for the MNI brain.

The study only had 10 stroke patients and 5 control participants. The relatively small sample size for each group is an apparent limitation for drawing more definite conclusions. However, the small sample size of the participants was compensated by a large number (sample size) of performance trials (50) by each participant. The number (5) of control subjects was smaller than the number (10) of patients and this may have also contributed to variation of the data. Finally, the EEG data in this study reflect only the cortical activities but muscle activation producing the reaching movement could be, to some extent contributed by subcortical control centers such as basal ganglia, cerebellum, and brain stem nuclei.

In summary, our results showed that stroke patients exhibited overall abnormally elevated cortical activation, specifically in the contralesional hemisphere. We examined the motor planning and execution phases separately, and found that the CTLR in stroke was significantly higher than controls for the planning phase only. Furthermore, within the stroke group, the CTLR was higher in the planning than execution phase. Excessive contralesional motor cortical activation seems to be more related to movement preparation rather than execution in chronic stroke. Many methods (eg, rTMS, tDCS, BCI, mental practice, etc.) have recently been employed as supplementary treatments to influence cortical plasticity in patients with stroke to facilitate motor recovery. These treatments aiming at facilitating cortical plasticity for functional recovery require a better understanding of the roles of altered cortical activation patterns (such as abnormally high level contralesional hemisphere activation) post stroke. Our results indicate that greater contralesional activation occurs only during planning rather than execution phase during upper extremity reaching in stroke. This finding is potentially useful for guiding development of more targeted therapies.

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