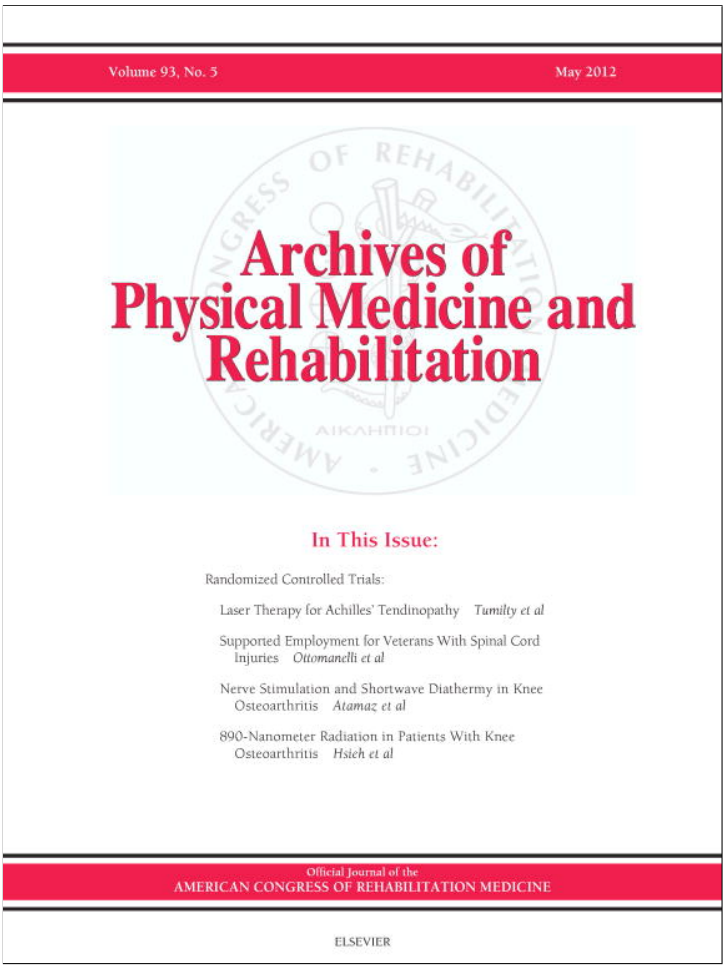

CLINICAL IMPLICATIONS OF BASIC RESEARCH

Feasibility and Test-Retest Reliability of an Electroencephalography-Based Brain Mapping System in Children With Cerebral Palsy: A Preliminary Investigation

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ABSTRACT. Lee NG, Kang SK, Lee DR, Hwang HJ, Jung JH, You JH, Im CH, Kim DA, Lee JA, Kim KS. Feasibility and test-retest reliability of an electroencephalography-based brain mapping system in children with cerebral palsy: a preliminary investigation. Arch Phys Med Rehabil 2012;93:882-8.

Objective: To investigate the feasibility and test-retest reliability of a novel electroencephalography (EEG)-based brain mapping system in healthy children and children with cerebral palsy (CP).

Design: Correlation statistics.

Setting: University brain mapping and neurorehabilitation laboratory.

Participants: A convenience sample of children (N=12; 5 healthy children, mean ± SD, 12.6±0.89y; 7 children with CP, mean ± SD, 9.71±1.1y) participated in the study.

Interventions: Not applicable.

Main Outcome Measures: Mu band (8–12Hz) power values in event-related spectral perturbation maps during reach and grasp hand movements were repeatedly measured on 2 separate occasions (2h apart). Intraclass correlation coefficient ($ICC_{1,2}$) tests were computed to determine test-retest reliability at the standard level of significance ($P<.004$). In addition, the feasibility of the system was determined by evaluating potential differences in the cortical activation areas obtained from topographical maps during actual reach and grasp motor tasks between healthy children and children with CP.

Results: The test-retest reliability results showed excellent reliability between the repeated measures, ranging from .93 ($P=.000$) to .99 ($P=.000$). Our EEG brain mapping system was capable of distinguishing differences in the cortical activity power (mu band power spectra) between healthy children and children with CP.

Conclusions: To our knowledge, this study is the first evidence demonstrating the feasibility and reliability of the EEG brain mapping system. Clinically, this system provides important insights into neuroplasticity associated with motor recovery after treatment and can also be used as real-time neurofeedback or noninvasive neuromodulation in the course of neurologic rehabilitation.

Key Words: Brain mapping; Cerebral palsy; Electroencephalography; Rehabilitation.

RECENTLY, THANKS to the superior temporal resolutions of electroencephalography (EEG) compared with other neuroimaging techniques including transcranial magnetic stimulation, positron emission tomography (PET), functional magnetic resonance imaging (fMRI), and diffusion tensor tractography,[1,2] it has been used to investigate human brain rhythmic activity at various frequency bands that closely represent neuronal signals or information encoding in the brain regions of interest (ROIs).[3-5] Specifically, the EEG cortical rhythmic patterns recorded during the suppression of bar-pressing motor behavior in animals ranged from 12 to 20Hz, which was topographically localized to the sensorimotor cortex (SMC). Sterman[6] first termed this localization the sensorimotor rhythm. Similarly, the cortical activity of the mu band (10 and 20Hz) was associated with electrical stimulation–induced thumb movements in healthy adult subjects.[4] Salmelin and Hari[4] suggested that the 10-Hz signals were related to somatosensory activation during thumb movements, whereas the 20-Hz sig-

List of Abbreviations

CP	cerebral palsy
EEG	electroencephalography
ERD	event-related desynchronization
ERS	event-related synchronization
ERSP	event-related spectral perturbation
fMRI	functional magnetic resonance imaging
GMFCS	Gross Motor Function Classification System
ICC	intraclass correlation coefficient
MACS	Manual Abilities Classification System
PET	positron emission tomography
POA	parieto-occipital area
PPC	posterior parietal cortex
ROI	region of interest
SMA	supplementary motor area
SMC	sensorimotor cortex

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nals represented somatomotor activation. Moreover, it has been well established that the imagination of each left and right hand movement results in the event-related desynchronization (ERD) of mu band power in the contralateral SMC areas in healthy adult subjects.[7,8] This mu band cortical activity also occurred during actual hand movements in healthy adults.[9]

Advanced neuroimaging techniques have also been used to evaluate cortical activation and associated motor recovery. While fMRI neuroimaging provides excellent spatial resolution for neural substrates,[10] networks associated with motor imagery,[11,12] and real movement based on correlation statistics,[13] important issues have been raised about the validity of this claimed homology. For example, 1 major shortcoming is related to the blood-oxygen-level dependence response time.[10,14] The fMRI contrast of blood deoxyhemoglobin response peaks approximately 5 seconds after neuronal potentials are evoked in the brain area. This suggests that it is difficult to discriminate between the target blood-oxygen-level dependence responses and other surrounding or different neuronal activities or events that can be observed within a short time window.[14] Another limitation is that in children with poor compliance, it is often extremely difficult to implement motor tasks in a closed fMRI system, and motion artifacts are produced.[15]

To overcome this challenge, we recently developed an EEG-based real-time brain mapping system to ascertain the neural mechanisms that underpin motor planning during actual movement execution (ie, reach and grasp motor tasks) in healthy children and children with cerebral palsy (CP). This novel real-time multichannel EEG brain mapping system was used to measure cortical activity organization (temporal and spatial characteristics).[16] In brief, this real-time EEG system has a capability to instantly display the topographical maps on the computer monitor. The specific aim of this study was, therefore, to establish the test-retest reliability of the mu band cortical activity and also to examine the feasibility to discriminate potential differences in the cortical activation areas obtained from topographical maps during actual reach and grasp motor tasks between healthy children and children with CP.

METHODS

Participants

A convenience sample of 15 children (7 children with CP; mean ± SD, 10.4±1.0y; 5 healthy children; mean ± SD, 12.4±1.3y) was recruited from the National Rehabilitation Hospital and a local community in this study, respectively. All informed consents were obtained from parents prior to the participation. The institutional review board approved the experimental protocol. Of those 15 children, 3 children were excluded because they met the exclusion criteria. The inclusion criteria for children with CP were (1) functional ability to sit independently while performing a reach and grasp task with the affected upper limb; and (2) cognitive ability to understand and follow the instruction. Exclusion criteria included severe cognitive impairment, visual-perceptual impairment, sensory deficit or hearing dysfunction, severe spasticity and contracture in both upper limbs (Modified Ashworth Scale >3), or seizure medications that could affect the experimental tests. The sample size was not computed in this experiment because this study was a preliminary investigation. Based on this preliminary investigation, the sample size for future studies will be determined.

Experimental Tasks and Procedure

Each child was instructed to sit in a quiet room in a comfortable armchair with neutral shoulder position and the elbow at 90° flexion in front of a personal laptop computer located at a distance of approximately 65cm (fig 1). Each child practiced a reach and grasp motor task, which involved random reaching and grasping of a small ball while avoiding any undesirable body movements such as head and trunk movements.[17] The motor task experiment consisted of a total of 40 trials (20 left and 20 right) within a 9-second period. As depicted in figure 2, the child was initially presented with a fixation cross at the center of the computer monitor. A beep tone sounded at 2 seconds, and at 3 seconds an arrow appeared at the center of the monitor for 1.25 seconds, pointing to either the left or the right. The child was asked to perform the reach and grasp hand movement with the hand indicated by the direction of the arrow. The interval between arrow cue stimuli was at least 9 seconds. The EEG data recorded for 3 seconds (during the interval from 4.25 to 7.25s) were used for further data analysis. All children rested as needed for 3 to 5 minutes between the different tasks or trials to avoid mental fatigue.[18]

In addition, test-retest reliability by an identical experimental procedure as that detailed above was established for the mu frequency band during the reach and grasp hand movements on 2 separate occasions (2h apart) to ensure the repeatability or consistency of the measurements. For reliable assessment, all the testing conditions including the tester, procedures, time of day, interval, and testing environment (lighting and temperature) were kept as consistent as possible.

EEG Data Acquisition

A 32-channel EEG system (WEEG 32[a]) along with a customized EEG-based real-time brain mapping software was used to acquire data on the cortical activity in the ROIs in the bilateral hemispheres during the reach and grasp motor task. Specific locations of scalp electrodes (Ag-AgCl) were determined according to an extended 10-20 system (fig 3).[19] ELE-FIX conductive adhesive electrode paste[b] was used because it is a highly conductive gel with low impedance and does not require scalp preparation. Thirty-two electrodes were attached on the subject's scalp. Among the 32 electrodes or channels, the EEG signals were recorded from 30 electrodes to determine the reorganization patterns of cortical rhythmic activity in the ROIs in the bilateral hemispheres. Two other electrodes were attached to the bilateral extensor carpi radialis muscles[20] to ensure that a child started moving his or her hand at the proper time during the motor task. A ground electrode was attached to

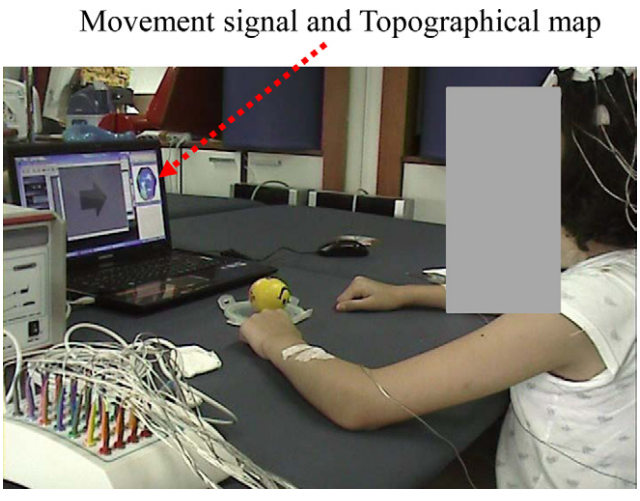

Fig 1. Experimental setup.

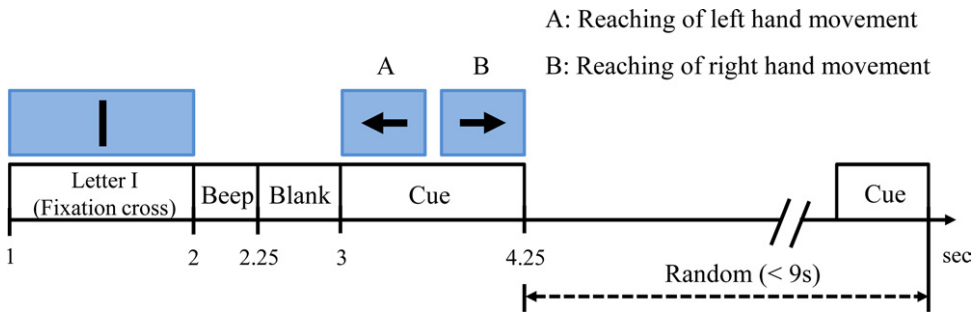

Fig 2. The experimental paradigm used for EEG recording: after presenting a letter I at the center of the monitor for 2 seconds, a black arrow cue appeared randomly on either the left or right side of the screen for the next 1.25 seconds, which signaled the child to initiate either left or right hand motor execution. The sequence of left and right hand movement tasks and the resting period between consecutive trials were randomized. The EEG data recorded for 3 seconds (4.25–7.25s interval) were used for the data analysis.

the forehead and a reference electrode was placed on the left mastoid. The ROIs included SMC and supplementary motor area (SMA) in the bilateral hemispheres, in which activity was recorded at the C1, C2, C3, C4, CP1, CP2, CP3, CP4, FC1, FC2, FC3, and FC4 electrodes.[21] These ROIs were chosen because these areas have been reported to have neuroplastic recovery potential.[22,23]

EEG Data Analysis

We used event-related spectral perturbation (ERSP), which measures the average change in spectral power (ie, ERD and event-related synchronization [ERS]) related to the tasks over time to an experimental event, to examine changes in cortical electrical activity selectively engaged in the brain ROIs. Our real-time EEG system can instantly display the topographical maps on the computer monitor, but the recorded EEG data were analyzed offline. The ERSP analysis was implemented in EEGLAB (http://sccn.ucsd.edu/eeglab/),[24] which is a well-known MATLAB toolbox.[c] For ERSP analysis, a time segment of 7 seconds was extracted for each epoch in which the first 2 seconds of EEG data were taken from 0 to 2 seconds before the onset of the cue as the reference period. The frequency bands selected ranged from 6 to 40Hz and included the mu and beta bands, which are related to limb movements. In addition, topographical power maps were displayed to examine spatial perturbations in the ROIs as the tasks were performed. We used previously calculated power values for the mu band (8–12Hz) in ERSP maps to map the power distribution topographically because the mu rhythm data for all subjects showed significant patterns of brain activity associated with arm movements. The mu band power values recorded from 0 to 5 seconds after the onset of the cue were averaged for each electrode position, and the average values were displayed in the predefined color map. Relative mu rhythm values derived from power spectrum data were determined by dividing the mu band spectrum values by the power spectrum values ranging from 4 to 50Hz because of large individual variability. This power spectrum range is considered to be the maximal EEG signal range that can be obtained from human brain electrical signals; any undesirable signals, which were the delta band associated with eyelid and EEG cable movements, were discarded. The relative mu data were calculated using Telescan version 2.92.[a]

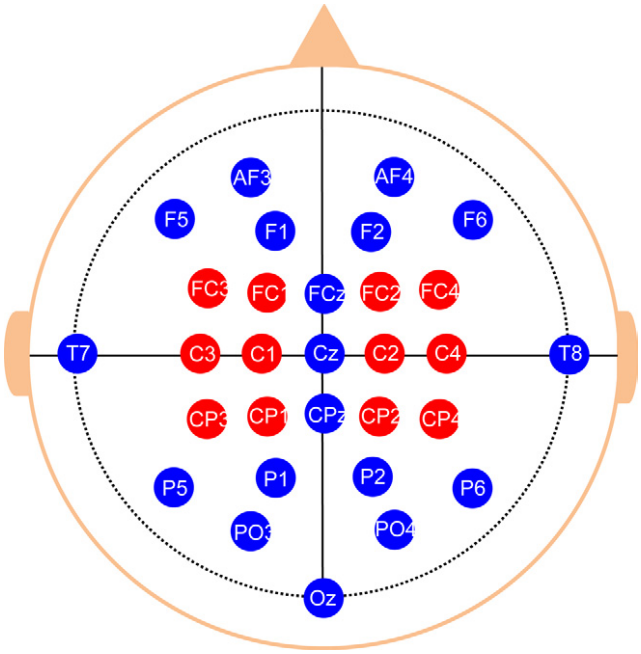

Fig 3. Electrode placement according to an extended 10-20 system and representative brain mapping areas of ROIs (red color).

Statistical Analysis

Descriptive analysis included means and SDs calculated for continuous scale variables and proportions for categorical variables. Intraclass correlation coefficient ($ICC_{1,2}$) tests were computed to determine test-retest reliability. Specifically, ICC values between the repeatedly measured relative mu rhythm data in the mu bands were assessed for the bilateral ROIs over the SMC and SMA.[22,23] To account for type I error, a correction for multiple comparisons in the ICC analysis was adjusted by dividing the number of correlation comparisons by .05. Hence, the significance level was set at $P<.004$ in all cases. We used the SPSS, Windows version 12.0[d] for statistical analysis.

RESULTS

Demographic and Clinical Characteristics of Subjects

Table 1 presents a summary of the demographic and clinical details of the children with CP. The clinical characteristics included previous medical history, clinical diagnosis, Gross Motor Function Classification System (GMFCS), Manual Abilities Classification System (MACS), and handedness. Children with CP were classified at GMFCS level I (n=3), level II (n=0), level III (n=3), or level IV (n=1). MACS was used to

Table 1: Demographic and Clinical Characteristics of Healthy Children and Children With CP (N=12)

Subject No.	Sex	Age (y)	History	Clinical Description	GMFCS	MACS (R/L)	Handedness
1	G	13	Healthy gestation	NA	NA	NA	R
2	B	10	Healthy gestation	NA	NA	NA	R
3	B	13	Healthy gestation	NA	NA	NA	R
4	B	13	Healthy gestation	NA	NA	NA	R
5	G	13	Healthy gestation		NA	NA	R
6	B	10	PB 36wk, BW 2800g	Spastic diplegia	3	3/3	R
7	G	11	PB 29wk	Spastic diplegia	3	2/3	R
8	B	10	PB 30wk, strabismus	Spastic diplegia	3	2/1	L
9	B	10	PB 21wk, BW 1100g	Ataxic quadriplegia	1	2/3	R
10	G	12	PB 32wk	Right hemiplegia	1	2/1	L
11	B	11	PB 30wk, strabismus	Spastic quadriplegia	4	3/3	R
12	B	9	PB 28wk, BW 930g	Right hemiplegia	1	2/1	L

Abbreviations: B, boy; BW, body weight; G, girl; L, left; NA, not applicable; PB, premature baby; R, right.

categorize an ability to manipulate objects in daily activities, and handedness was determined by asking "which hand does the child use in writing or eating?" (see table 1).

Test-Retest Reliability

Rhythmic EEG activity representing the functional characteristics of the relative mu rhythm was identified in all subjects. The test-retest reliability analysis revealed that ICC values for relative mu rhythm in the bilateral ROIs including C1-2, C3-4, CP1-2, CP3-4, FC1-2, and FC3-4 during each right and left hand movement were excellent, ranging from .93 (P=.000) to .99 (P=.000). Excellent test-retest reliability suggests that our EEG-based real-time brain mapping system can be used to provide consistent measurements of cortical electrical activity during active hand motor tasks in both healthy children and children with CP (tables 2 and 3).

Comparison of Topographical Brain Mapping Images Between Healthy Children and Children With CP

ERD/ERS topographical maps allow visualization of the cortical activation area (visual- and motor-related areas) during reach and grasp motor tasks. Figures 4A and 4B illustrate 2 representative topographies for a healthy child and a child with hemiplegic CP, respectively. Table 4 presents the cortical activation area (close to the electrode position) during reach and grasp motor tasks in individual subjects. In healthy children (subjects 1–5), the EEG cortical activity pattern was primarily localized over the SMC (electrodes close to C3, C4, CP3, and CP4). However, in children with CP (subjects 6–12), the distinctive pattern of EEG cortical activity was presented over the SMC (electrodes close to C3 and C4), SMA (electrode close to F2), posterior parietal cortex (PPC) (electrodes close to P1, P2, and P5), and parieto-occipital area (POA) (electrodes close to PO3 and PO4) (see table 4).

DISCUSSION

This study sought to determine the feasibility and test-retest reliability of the proposed EEG-based real-time brain mapping system during reach and grasp movements. Our test-retest reliability study demonstrated excellent reliability in the mu frequency band for reach and grasp hand movements ($ICC_{1,2}$=.93–.99) recorded on 2 separate occasions (2h apart). These results suggest that the EEG-based brain mapping system is highly reliable for the detection of mu rhythm (or relative mu rhythm) in both healthy children and children with CP.

To our knowledge, the present study is the first attempt that investigated the test-retest reliability of the sensorimotor EEG mapping. Only 1 cognitive EEG study examined test-retest reliability within sessions and between sessions (interval of 7d) during cognitive memory tasks (working memory task and psychomotor vigilance task).[25] This study showed relatively good test-retest reliability for the frontal midline theta, posterior theta, and slow and fast alpha recorded at Fz (midpoint between F1 and F2) and Pz (midpoint between P1 and P2), which ranged from .83 to .99.[25] However, because the study focused on the cognitive aspect of EEG neural activation in a healthy adult population, it was difficult to compare this previous result with our present EEG findings.[25]

Clinical feasibility of sensorimotor EEG mapping was determined by our EEG brain mapping system. Our EEG brain mapping data demonstrated different cortical areas involved between healthy children and children with CP during the motor task. For instance, the cortical activity pattern was primarily localized over the SMC in healthy children, whereas in children with CP the cortical activation areas such as SMC, SMA, PCC, and POA are more diversified. Certainly, these findings suggest that our EEG brain mapping system is capable of discriminating cortical activation patterns between healthy

Table 2: Test and Retest Reliability for Measuring the Relative Mu Rhythm During Right Hand Movement

ROIs	C1	C2	C3	C4	FC1	FC2	FC3	FC4	CP1	CP2	CP3	CP4
Mean relative mu rhythm ± SD												
Test	0.19±0.03	0.18±0.04	0.18±0.04	0.19±0.05	0.18±0.03	0.17±0.03	0.17±0.04	0.17±0.04	0.20±0.04	0.19±0.04	0.20±0.04	0.20±0.04
Retest	0.20±0.04	0.19±0.04	0.19±0.04	0.20±0.05	0.18±0.03	0.18±0.04	0.18±0.03	0.18±0.04	0.21±0.05	0.21±0.05	0.21±0.06	0.22±0.05
$ICC_{1,2}$	0.96	0.97	0.97	0.96	0.99	0.97	0.97	0.93	0.97	0.98	0.96	0.97
P	.00*	.00*	.00*	.00*	.00*	.00*	.00*	.00*	.00*	.00*	.00*	.00*

*$ICC_{1,2}$ was performed to determine test-retest reliability by comparing the mean relative mu rhythm data in healthy children and children with CP at 2 consecutive days at P<.004.

Table 3: Test and Retest Reliability for Measuring the Relative Mu Rhythm During Left Hand Movement

ROIs	C1	C2	C3	C4	FC1	FC2	FC3	FC4	CP1	CP2	CP3	CP4
Mean relative mu rhythm ± SD												
Test	0.19±0.04	0.18±0.03	0.19±0.05	0.18±0.04	0.18±0.03	0.17±0.03	0.17±0.03	0.17±0.03	0.21±0.05	0.20±0.05	0.20±0.05	0.20±0.05
Retest	0.19±0.04	0.18±0.04	0.19±0.05	0.18±0.04	0.17±0.03	0.17±0.03	0.17±0.03	0.17±0.03	0.21±0.05	0.20±0.05	0.21±0.06	0.20±0.05
$ICC_{1,2}$	0.99	0.98	0.98	0.96	0.98	0.94	0.98	0.93	0.98	0.98	0.96	0.97
P	.00*	.00*	.00*	.00*	.00*	.00*	.00*	.00*	.00*	.00*	.00*	.00*

*$ICC_{1,2}$ was performed to determine test-retest reliability by comparing the mean relative mu rhythm data in healthy children and children with CP at 2 consecutive days at $P<.004$.

children and children with CP. Similarly, Pfurtscheller and Neuper[26] showed that desynchronization in the mu and beta bands was observed over the contralateral SMC during both actual and imagined movement in healthy adults. Other EEG studies[9,27] have examined mu and beta cortical rhythm activity during actual movement and motor imagery. McFarland et al[9] reported significant mu rhythm desynchronization from subdural electrodes over the SMC during actual movement and motor imagery. Schupp et al[27] demonstrated that both actual object manipulation and imagination of manipulation resulted in desynchronization in the 8- to 12-Hz band with heterogeneous cortical characteristics in ERD topographical maps.

The degree of similarity in the cortical activation patterns associated with actual movement detected by the EEG-based brain mapping system and those recorded by current neuroimaging techniques (PET or fMRI) has been well-established.[1,2,28,29] Advanced neuroimaging techniques, such as PET and fMRI, have been employed to probe cortical reorganization and associated motor recovery. Recent fMRI studies[28,29] involving upper extremity (hand, finger) motor recovery have suggested that in healthy subjects, contralateral SMC activation is primarily responsible for hand motor tasks, whereas in recovered stroke patients, the ipsilateral SMC and the premotor cortex assume the role served by the contralateral motor tract prior to stroke in the production of movement in the paretic hand. We previously evaluated the hand motor function of a right hemiparetic patient with schizencephaly using a combination of fMRI and transcranial magnetic stimulation.[30] Only the contralesional SMC was activated during either affected or unaffected hand movements. In the same study, evoked motor potentials with similar characteristics were obtained simultaneously from both abductor pollicis brevis muscles when stimulating the contralesional motor cortex.[30] A subsequent study of a child with hemiparetic CP showed that cortical activation during affected elbow movement was adaptively reorganized from the aberrant bilateral SMCs along with the bilateral primary motor cortices (M1s) and primary sensory cortices (S1s) and the ipsilateral SMA (before intervention) to the contralateral SMC (after intervention), which accounted for significant decreases in voxel volumes in the ipsilateral hemisphere.[31] Deiber et al[32] also observed increased PET activations in inferoparietal, premotor, and prefrontal sites during imagined movement and additional cortical activations in the motor cortex and cerebellum during actual hand movement. Taken together, our EEG brain mapping data appear to be consistent with both our previous fMRI data[31] and other findings from neuroimaging investigations,[29,30,32] indicating that our EEG brain mapping method is feasible to highlight different cortical activation regions between healthy children and children with CP.

Study Limitations

Our EEG-based brain mapping system is portable and offers the capability to collect real-time data with excellent time resolution for brain mapping during active movement. It enables clinicians to localize cortical electrical activation areas on a consistent basis, a feature that is not afforded by other neuroimaging techniques (ie, fMRI and PET) and is particularly useful for children who may need to be anesthetized to minimize movement artifacts. Furthermore, the system can be used to probe neuroplastic changes associated with motor recovery or improvement and provide powerful real-time cortical activation neurofeedback, thereby facilitating motor relearning or motor imagery training in the course of neurorehabiliation for individuals with neurologic impairments. One major shortcoming that the system shares with fMRI and PET is related to motion artifacts during eye or head-neck motion, which can contribute to fatigue during motor tasks. An additional weakness of the EEG system relates to its ability to provide accurate estimates at the activation site due to inherent issues of spatial resolution. Further studies should determine neuroplastic changes after neurorehabilitation or motor imagery using this EEG-based brain mapping system with higher spatial resolution. Finally, it would be of great interest to examine differences in cortical activation quantitatively and statistically with more homogeneous and age-matched groups. However, these

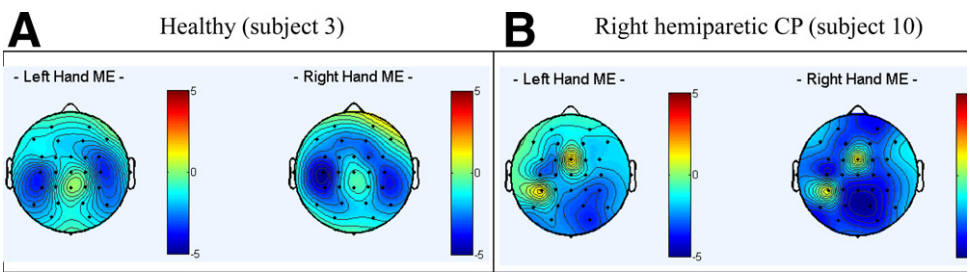

Fig 4. ERS/ERD maps of (A) a healthy child and (B) a child with hemiparetic CP. The color scale is adjusted according to the maximum and minimum power spectra value for each subject. The maximum band power increase (ERS) and the maximum band power decrease (ERD) are coded in dark red and blue, respectively. Positive and negative deflections of longitudinal time graphs indicate a band power increase (ERS) and decrease (ERD), respectively. Abbreviation: ME, movement execution.

Table 4: Cortical Activation Areas (close to the electrode position) During Reach and Grasp Motor Tasks in Individual Subjects

Subject No.	Right	Left
1	SMC (CP3, C4)	SMC (CP3, C4)
2	SMC (C3)	SMC (C1, C2, C3)
3	SMC (C3, C4, CP4)	SMC (C3, C4, CP3)
4	SMC (C4)	SMC, SMA (C1, FC1, C4, FC4)
5	SMC, PPC (C4, CP3, CP4, P1)	SMC, PPC (C4, CP4, P1)
6	SMC (C3, C4)	SMC, SMA (C4, F2)
7	PPC, POA (P1, PO3)	SMC (CP1, CP2, CP3, CP4)
8	POA (PO4)	SMC, POA (CP4, PO3, PO4)
9	SMC (CPz, CP1)	SMC (CPz, CP1)
10	PPC (P2)	POA (PO4)
11	SMC (CP2, CP4)	SMC (CP2, CP4)
12	SMC, PPC (C3, C4, CPz, P1, P2)	SMC, PPC (C3, P5)

differences in demographic characteristics between groups were unlikely to have influenced our test-retest correlation outcomes.

CONCLUSIONS

Given the status of the real-time EEG-based brain mapping system as a new technology, examination of its potential efficiency in rehabilitation has only just begun. Nevertheless, our brain mapping system can be used as an alternative neuroimaging vehicle to probe underlying neural recovery mechanisms. In fact, this system was feasible to record movement-related cortical activation patterns in both healthy children and children with CP. In addition, it can provide a new horizon for a powerful real-time neurofeedback program for neurologic populations with CP and stroke to enrich their motor relearning and skill reacquisition.

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