

Interhemispheric Reorganization of Motor Hand Function to the Primary Motor Cortex Predicted With Functional Magnetic Resonance Imaging and Transcranial Magnetic Stimulation

ABSTRACT

The objective of this study was presurgical assessment of reorganization of motor hand function in an 11-year-old girl with intractable epilepsy and a right-sided hemiplegia resulting from an extensive perinatal left hemispheric stroke. Prior to a left functional hemispherectomy, functional magnetic resonance imaging (MRI) showed that both nonparetic and paretic motor hand function predominantly activated the right primary motor cortex, whereas no activation was found in the left hemisphere. Transcranial magnetic stimulation of the right central area yielded responses in both the nonparetic and the paretic hand, whereas no responses were obtained after stimulation of the affected hemisphere. Both techniques indicated that motor function was mediated by corticospinal fibers originating from the undamaged (primary) motor cortex and predicted no further loss of motor hand function after surgery. Indeed, subsequent functional hemispherectomy induced no new sensorimotor deficits. Functional MRI was repeated 22 months after surgery and matched preoperative sensorimotor functional MRI findings, confirming reorganization of the primary motor cortex. No additional reorganization was introduced by surgery. (*J Child Neurol* 2002;17:292-297).

Patients who are candidates for neurosurgical resection of epileptogenic brain areas meet strict preoperative criteria to ensure that surgery reduces or abolishes epileptic seizures while sensorimotor and cognitive functions remain unaffected. In some of these patients, cerebral functions have reorganized as a consequence of the epileptogenic lesion (ie, have shifted from their normal cortical localization to other brain areas).¹ Identification of these patterns of reorganization, and subsequent prediction of functional impact of the planned resection, would be of great clinical benefit.

Motor recovery that follows extensive unilateral brain injury in early life can be impressive, often allowing children to reach and grasp with their affected hand and walk with only a mild hemiparetic limp. In patients who have undergone a cerebral hemispherectomy, sensorimotor functions can be served by only a single hemisphere.² However, mechanisms and constraints of reorganization are largely unknown. Individual patterns of intra- and/or interhemispheric reorganization depend on at least several variables such as age, lesion size, and topography and integrity of surrounding brain areas.²⁻⁴ Vining et al documented that of 58 hemispherectomies performed in children, motor function worsened in 17%, improved in 33%, and remained unchanged in 50%.¹

Both functional magnetic resonance imaging (MRI) and positron emission tomography (PET) provide detailed individual brain activity maps by measuring local cerebral blood flow patterns induced by changes in neural activity.⁵ Several studies have investigated postlesional organization of motor functions using functional MRI or PET. Most studies found pronounced activation of sec-

ondary sensorimotor areas in the lesional and, to a lesser extent, contralesional hemisphere, as well as in areas not directly involved in motor control (parietal and prefrontal cortices).⁶⁻¹¹ Occasionally, additional activation of the contralesional primary motor cortex has been reported.¹²⁻¹⁶ However, it remains largely unknown to what extent these techniques can accurately predict postoperative motor function as only a few studies have been performed prior to introduction of a (surgical) lesion.^{14,16,17} Moreover, brain activity maps rely heavily on data analysis procedures and statistical methodology.

In patients who are candidates for functional hemispherectomy, the amobarbital (Wada) test is regarded as the gold standard for the prediction of postoperative motor function following hemispherectomy. There is, however, a need for less invasive alternatives as several potential risks and disadvantages limit use of the Wada test for this purpose (eg, it only allows for lateralization of function). Two promising noninvasive techniques to predict postoperative motor hand function prior to a functional hemispherectomy are functional MRI and transcranial magnetic stimulation. Transcranial magnetic stimulation directly stimulates cortical areas and is thought to identify only those areas that are directly linked to descending corticospinal projections.¹⁸ Recent studies have suggested that transcranial magnetic stimulation can be used complementary to functional MRI in the preoperative assessment of motor function as it may aid in the differentiation between critical and noncritical motor areas detected with functional MRI.^{13,16,19} In the current study, we applied both techniques, as well as the Wada test, to determine which brain areas mediated motor function in a patient with severe unilateral brain damage. To assess whether surgical resection altered the representation of sensorimotor hand function, functional MRI was repeated 2 years after surgery.

Case Report

An 11-year-old girl underwent a left functional hemispherectomy, aiming at the relief of medically intractable seizures. Gestation had been uncomplicated, and there were no adverse perinatal events. Shortly after birth, a spastic right-sided hemiparesis was noted. A computed tomographic scan at the age of 5 months showed a large cyst in the left hemisphere, suggesting a perinatal stroke. Complex partial epileptic seizures started at the age of 9 months. Since that time, the patient has never been free of seizures, despite various antiepileptic medication. Psychomotor development was retarded: walking at 2 years and talking at 4 years. In the years before surgery, her IQ declined from 70 to 45 (Wechsler Intelligence Scale for Children-Revised [WISC-R]), presumably owing to an increase in seizure frequency. At the time of presurgical evaluation, the patient showed strong involuntary movements of the nonparetic hand (with intentional movements of the paretic hand) and mild mirror movements of the paretic hand (with intentional movements of the nonparetic hand). Motor strength testing (Medical Research Council scale) yielded a grade 3 strength for the proximal and distal muscles of the right arm. For the right leg, there was a grade 4 proximal and grade 1 to 3 distal strength. Left-sided motor strength was normal (Medical Research Council grade 5). No sensory deficits were found. Despite her right hemiparesis, the patient could walk and ride a bicycle unaided. Preoperative MRI indicated severe left hemispheric abnormalities: a large porencephalic cyst, severe atrophy of the caudate nucleus and thalamus, and cortical atrophy (Figure 1).

Wada Test

Wada testing involved injection of 125 mg of amobarbital in the left internal carotid artery to assess the functional status of the right hemisphere (ie, memory, language, and motor function). A slight reduction in right hand motor strength was observed following injection of amobarbital. Muscle tone was unchanged, and the patient kept voluntary control over both arms and

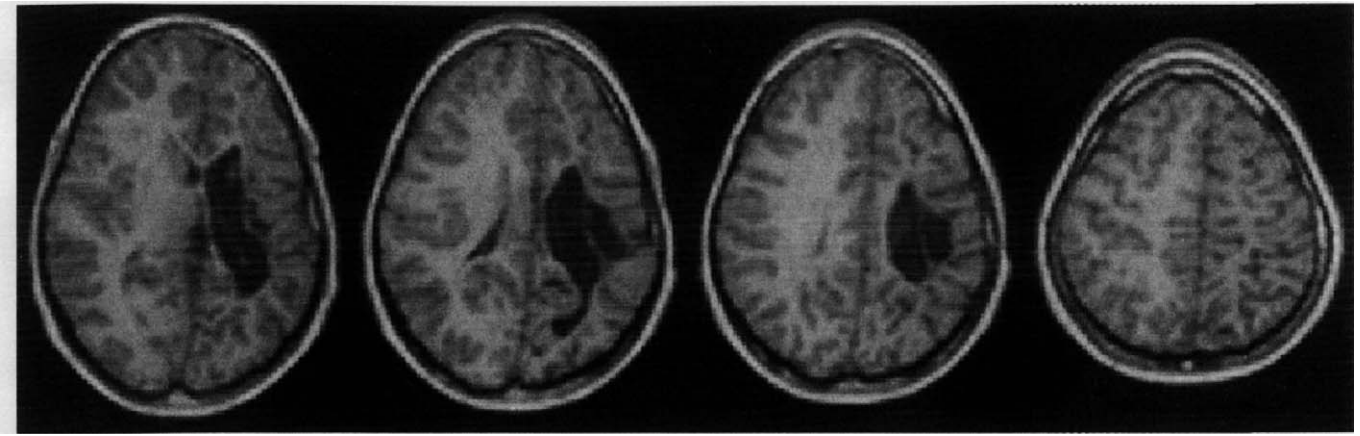


Figure 1. Preoperative magnetic resonance image demonstrating a cyst in the smaller left hemisphere, severe atrophy of the left caudate nucleus and thalamus, and left cortical atrophy.

legs. This suggested that at least part of the critical motor areas that controlled the paretic extremities was located in the ipsilateral healthy right hemisphere. Neuropsychologic testing yielded adequate short-term memory function and revealed no dysphasia, indicating that critical language functions resided in the right hemisphere.

Preoperative Functional Magnetic Resonance Imaging

One month prior to surgery, functional MRI¹ was performed using a three-dimensional BOLD technique (navigated PRESTO sequence, TE/TR 30/24.5 ms, flip angle 10 degrees, matrix 52*64*22, FOV 183*225*77 mm, voxel size 3.51 mm isotropic, scan time 7.25 s), implemented on a Philips ACS-NT 1.5-Tesla scanner (Philips Medical Systems, Best, The Netherlands) with P1000 gradients.^{20,21} Following functional MRI scans, an anatomic image was acquired (three-dimensional-FFE, TE/TR 4.6/30 ms, flip angle 30 degrees, FOV 256*256*130, voxel size 1 × 1 × 1.2 mm). Functional scans were aligned roughly perpendicular to the course of the central sulcus and included the frontal and parietal lobes.

Four tasks were used in the scanner—movement of the right and left hand and tactile stimulation of the right and left hand—and were practiced extensively beforehand. Eighty-four functional MRI scans were acquired per task, during which periods of activity (ie, movements or tactile stimulation) were alternated with rest periods (22 seconds' duration each). In the scanner room, one of the authors (G.-J.M.R.) instructed the patient before each block and monitored patient performance. During the motor task, a green or red dot was projected on a screen that the patient could see via a mirror that was mounted on the headcoil. The active condition consisted of squeezing a sponge in pace with the flashing green dot (1 Hz). The red non-flashing dot indicated the rest condition. For tactile stimulation, light brushing of the palm of the hand was used (paced at 1 Hz).

Prior to statistical analysis, coregistration of functional and anatomic scans was performed.²¹ No functional scans were excluded from analysis. Statistical maps for each task were obtained using multiple regression analysis, which included detrending, resulting in a value for each voxel.²² No smoothing of functional scans was applied. Statistical maps were stringently thresholded ($T_{\text{critical}} = 4.5$, corresponding to $P < .05$ after Bonferroni correction for the number of comparisons, ie, the number of voxels in the scanned volume) to minimize the occurrence of false-positive brain activation.

Patient performance was excellent during both motor and sensory tasks, and no epileptic seizures were observed. Functional MRI results for the motor and sensory tasks are depicted in Figure 2. The central sulcus was localized according to the method described by Yousry et al.²³ Movement of the nonparetic left hand activated the right primary motor cortex and premotor cortex. Movement of the paretic right hand activated the ipsilateral (ie, right) primary motor cortex, close to the central sulcus, but no activation was detected in contralateral motor areas in the affected hemisphere. Sensory

stimulation of the nonparetic left hand yielded a large area of activation in the right primary sensory and motor cortex and a smaller area of activation in the left and right premotor cortex, right supplementary motor area, right superior parietal lobe, and right secondary somatosensory cortex. Sensory stimulation of the paretic right hand yielded no active brain areas in either hemisphere; when statistical threshold was lowered to $T_{\text{critical}} = 4.0$, only activation in the right superior parietal lobule emerged for this task.

Postoperative Functional Magnetic Resonance Imaging

Twenty-two months after hemispherectomy, functional MRI was again performed. Procedures and experimental design (including tasks and timing) were identical to those in the preoperative functional MRI experiment. Owing to an upgrade of MRI hardware (P6000 gradients), three times as many volume scans were acquired in the same amount of time (ie, 252 instead of 84 volume scans per task), whereas the number of slices increased from 22 to 26. Functional scan volume and orientation of slices were adjusted to match settings in the preoperative functional MRI experiment.

Both movement of the nonparetic (left) hand and the paretic (right) hand yielded activation in the same convolutions as in the preoperative functional MRI experiment (compare Figures 2A and 3A). The results from the sensory hand tasks also closely matched preoperative functional MRI findings (compare Figures 2B and 3B).

Transcranial Magnetic Stimulation

Focal transcranial magnetic stimulation was carried out with a “figure-of-eight” coil (diameter 70 mm per coil, peak magnetic field strength 2.2 Tesla) and a magnetic stimulator generating a monophasic pulse (Magstim Company, Whitland, UK). The center between the coils was held at the desired scalp position.²⁴ At least four stimuli were given at each of the scalp positions, F1, F2, C3, and C4, of the International 10-20 system. Motor evoked potentials were recorded simultaneously from the left and right abductor pollicis brevis muscles using 1.0-cm diameter Ag/AgCl surface electrodes in a belly-tendon montage connected to an electromyograph (Viking IV, Nicolet, standard motor nerve conduction settings). We obtained recordings without and with facilitation (slight abduction of the thumb).

Focal transcranial magnetic stimulation of the right central region (C4) resulted in motor evoked potentials in the left and right abductor pollicis brevis (Figure 4). No motor evoked potentials were obtained after stimulation of the left central region (C3) or the frontal regions (F3 and F4). Facilitation yielded motor evoked potentials with shorter latency and larger amplitude (facilitation: left abductor pollicis brevis 17.7 ms, 1.9 mV; right abductor pollicis brevis 18.3 ms, 0.9 mV; no facilitation: left abductor pollicis brevis 22.4 ms, 0.7 mV; right abductor pollicis brevis 21.6 ms, 0.5 mV).

Surgery and Follow-up

The patient underwent a left functional hemispherectomy. Postoperatively, there was a slight increase in the right-hand paresis that recovered within a few weeks to the level of preoperative findings. Sensory functions remained

¹BOLD = blood oxygen level dependent; PRESTO = principle of echo shifting with a train of observations; TE = echo time; TR = repetition time; FFE = fast field echo.

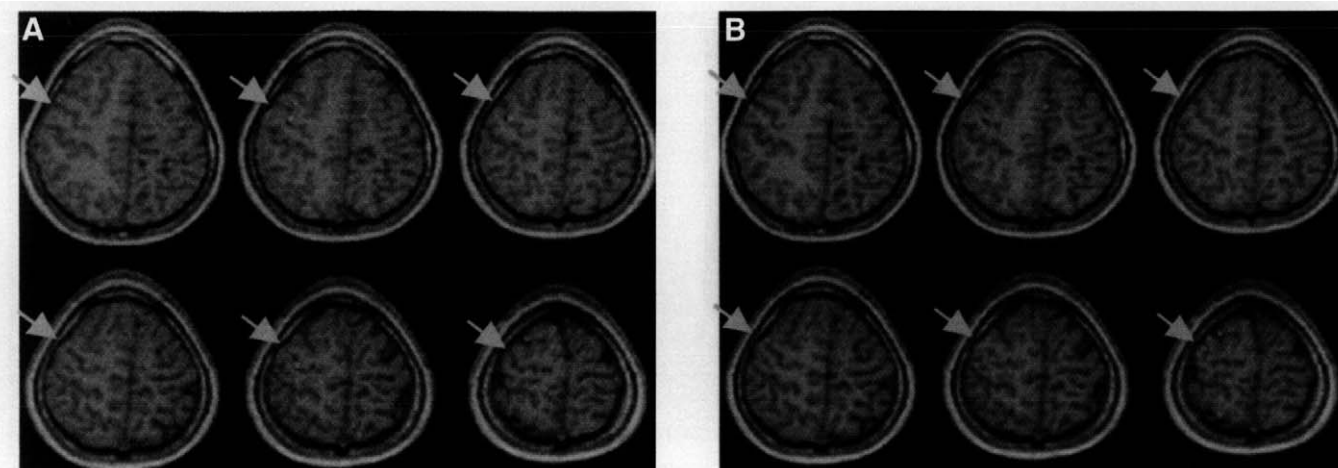


Figure 2. Preoperative functional magnetic resonance images demonstrating cortical activation elicited by motor (A) and sensory (B) hand tasks. Statistical maps ($P < .05$, Bonferroni corrected) are superimposed on preoperative anatomic images. Axial slices are shown in radiologic orientation (ie, the right hemisphere is depicted on the left side and vice versa). The arrow indicates the location of the central sulcus. A, Movements of both the nonparetic left hand (green voxels) and the paretic right hand (orange voxels) activated the right primary motor cortex. In addition, nonparetic hand movements activated the right premotor cortex. B, Tactile stimulation of the nonparetic hand (green voxels) yielded activation in the right primary sensory and motor cortex, premotor cortex, supplementary motor area, and superior parietal lobule. Stimulation of the paretic hand yielded no activation; lowering of the threshold to $T_{\text{critical}} = 4.0$ yielded activation only in the right superior parietal lobule (not shown).

unaffected. The extent and intensity of the mirror movements remained unchanged. Two years after surgery, the patient is still free of seizures and has dramatically improved in social functioning. She has experienced no worsening of language deficits. Her IQ has increased from 45 to 59.

Discussion

In this study, presurgical functional MRI and transcranial magnetic stimulation correctly predicted functional outcome of hand motor function after a left functional hemispherectomy in an 11-year-old patient. We were able to demonstrate that interhemispheric reorganization of right-hand motor function (to the right, ie, ipsilateral, primary motor cortex) was not the result of the sur-

gical intervention but was present before surgery, most likely resulting from the severe perinatal left hemispheric lesion and medically intractable epilepsy.

Lesion studies and intraoperative electrocortical stimulation mapping have typically located critical hand motor function within the contralateral "hand knob," the posteriorly curved part of the middle genu of the precentral gyrus that can reliably be identified via anatomic landmarks.^{23,25} In functional imaging studies of normal volunteers, ipsilateral activation is usually not found with a simple motor hand task (such as the one used in our study) or is present only in addition to considerably larger contralateral acti-

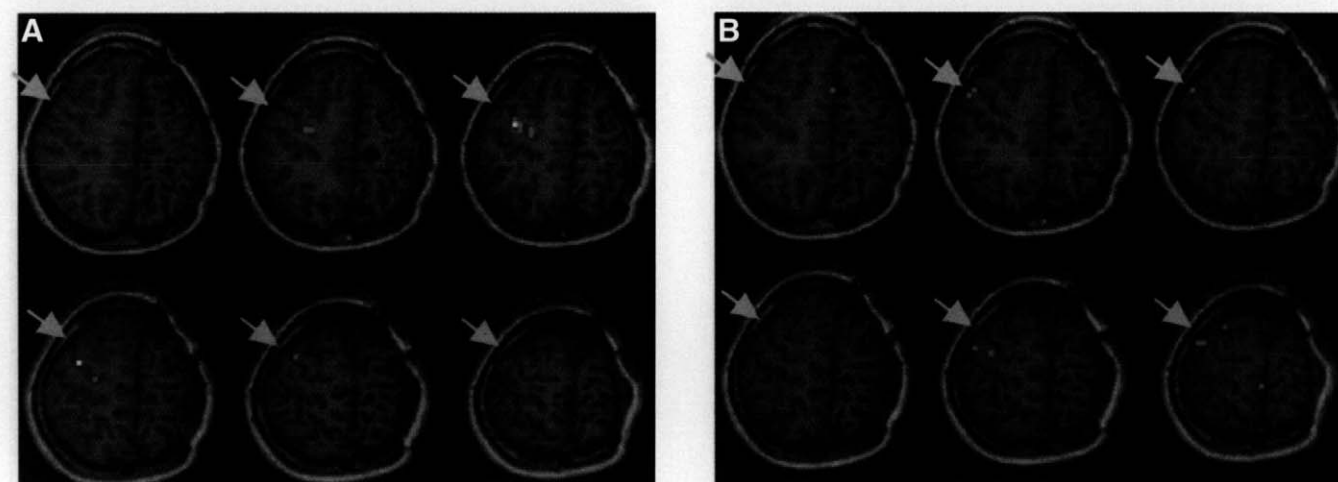


Figure 3. Postoperative functional magnetic resonance images demonstrating cortical activation elicited by motor (A) and sensory (B) hand tasks. Statistical maps ($P < .05$, Bonferroni corrected) are superimposed on postoperative anatomic images. Axial slices show approximately the same anatomic volume as in Figure 1. The arrow indicates the location of the central sulcus. A, Movements of both the nonparetic left hand (green voxels) and the paretic right hand (orange voxels) activated the right primary motor cortex. In addition, nonparetic hand movements activated the right premotor cortex. White voxels were active in both tasks. B, Tactile stimulation of the nonparetic hand yielded activation in the right primary sensory and motor cortex, premotor cortex, supplementary motor area, and secondary somatosensory cortex (green voxels). Stimulation of the paretic hand yielded activation in the right superior parietal lobule (orange voxels).

vation.^{26,27} Several observations supported the fact that reorganization of motor function involved the contralesional (right) primary motor cortex and corticospinal tract: (1) both pre- and postsurgical functional MRI demonstrated a representation of paretic (right) and nonparetic (left) hand motor function in the middle genu of the precentral gyrus of the healthy (right) hemisphere, whereas no activated areas were found in the damaged (left) hemisphere; (2) transcranial magnetic stimulation indicated that these representations were directly involved in motor hand control via the corticospinal tract as stimulation resulted in symmetric short-latency motor evoked potentials in the left and right abductor pollicis brevis muscles, whereas no motor evoked potentials were obtained from stimulation of the central region in the left hemisphere; and (3) left functional hemispherectomy did not affect long-term motor hand function (there was a temporary slight decrease in motor hand function during the first postoperative weeks). As pre- and postoperative functional MRI yielded similar brain activation maps, it can be concluded that no (additional) reorganization of function was induced by surgery.

A consistent finding in our study was that tactile stimulation of the paretic hand (in which the patient did not report sensory deficits) did not activate the ipsilateral or contralateral primary sensorimotor cortex with functional MRI, whereas stimulation of the unaffected hand robustly activated the contralateral primary sensorimotor cortex. This agrees with the results from previous functional MRI studies in which tactile stimulation of the affected hand in patients who had undergone hemispherectomy failed to activate the primary sensorimotor cortex.^{7,8} Bittar et al⁷ and Graveline et al⁸ found that for stimulation of the affected hand, the ipsilateral superior parietal lobule (Brodmann area 7) was a common area of activation in these patients, consistent with our findings. This suggests that a different form of reorganization has taken place for sensory hand function than for motor hand function.

Mirror movements, as observed in our patient, are the consequences of reorganization of motor function and are seen especially when brain injury occurs before 1 year of age.²⁸ Several studies have demonstrated that in a subset of children with striking mirror movements and hemiplegia following early-life hemispheric damage, transcranial magnetic stimulation induces bilateral and short-latency motor evoked potentials from the healthy hemisphere, whereas no responses are obtained from the lesioned hemisphere.^{4,29,30} These studies have suggested that in these patients, the corticospinal fibers that originate from the undamaged motor cortex have branched and now project to motoneuron pools on both sides of the spinal cord, leaving the healthy hemisphere in control over both sides of the body.^{4,13,16,29} Such a model can account for the mirror movements observed in our patient.⁴ Unmasking of ipsilateral corticospinal axons from the healthy hemisphere is a less likely explanation for reorganization as these fibers tend to be relatively slow conducting and do not normally make direct corticomotoneuronal connections.^{4,31} The neighbouring and partly overlapping representations of both hands in the primary motor cortex as found with functional MRI are consistent with previous neurophysiologic studies in healthy subjects and animals. Sanes et al showed that different finger movements are controlled by overlapping brain areas in the human primary motor cortex.^{32,33} Schieber et al showed with electrical recordings of motor cortex neurons

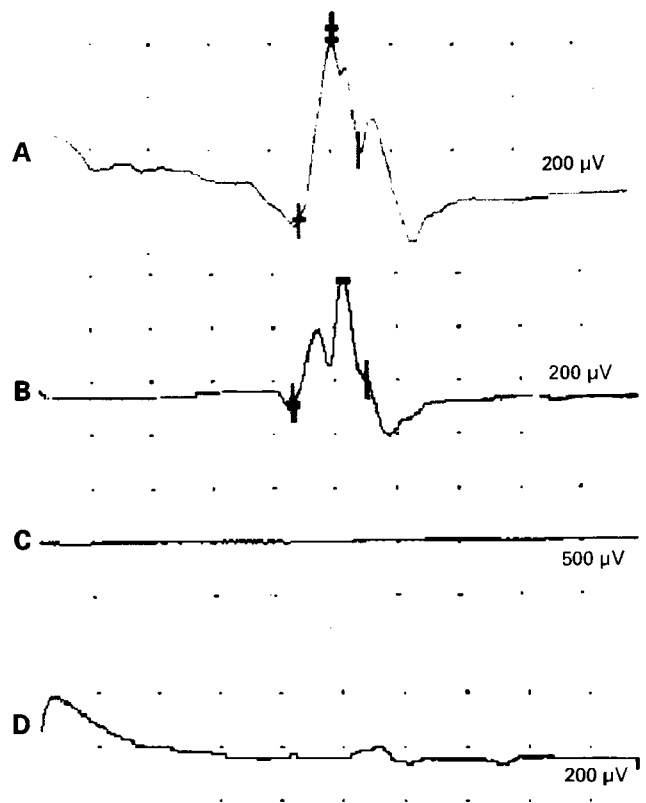


Figure 4. Preoperative findings from transcranial magnetic stimulation of the right and left central region. Stimulation of the right central region (C3) resulted in symmetric short-latency motor evoked potentials in both the left (A) and right (B) abductor pollicis brevis muscle. Stimulation of the left central region (C4) did not result in motor evoked potentials in the right (C) or left (D) abductor pollicis brevis muscle.

in monkeys that cortical representations of different movements can coexist in the same area and can be activated independently by different inputs.³⁴

The use of a stringent statistical threshold in functional MRI analysis resulted in correct assessment of hemispheric lateralization of motor hand function, in accordance with recent studies in which use of a high threshold improved localization of critical brain areas.³⁵ However, a high threshold also lowers detection power for brain activity. This might explain the absence of robust activation in secondary motor areas (premotor areas and SMA), although it is known that the "simple" motor hand task that was used in our experiment does not consistently show activation in these areas in normal volunteers.³⁶ It is important to realize that the presence of functional MRI activation in a particular brain area does not imply that this area plays a critical role in the performance of a particular function. To distinguish critical from non-critical motor areas that were indicated with functional MRI, we additionally used transcranial magnetic stimulation. A combination of both techniques could become a useful and noninvasive presurgical technique to predict postoperative motor function.¹⁶

In children with unilateral brain injury, motor functions seem to have a more limited potential for postnatal interhemispheric plasticity than language functions.⁶ This may be associated with the early

ontogenesis of the corticospinal tract, which ends before 30 weeks' gestation.^{37,38} Most functional imaging studies of patients with damage to the primary motor cortex have suggested a certain "resistance" of cortical motor control to shift to its homologous area in the contralesional hemisphere.^{6,8-12,17} However, the current study, in which results obtained from functional MRI, transcranial magnetic stimulation, the Wada test, and behavioral observations converged, presents strong evidence for interhemispheric reallocation of motor hand function to the primary motor cortex and corticospinal tract. As predicted with these techniques, particularly with functional MRI, functional hemispherectomy did not result in additional loss of sensorimotor function.

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Ictal Electroencephalography in a Case of Benign Centrottemporal Epilepsy

ABSTRACT

The purpose of this research was to publish a complete ictal electroencephalographic (EEG) record of a child with benign centrottemporal epilepsy. The record includes a brief description of the patient's epilepsy syndrome, analysis of interictal and ictal EEG records, and a description of corresponding clinical ictal events. Ictal EEG activity appeared over the right rolandic cortex and spread to adjacent sites. Initial rhythmic activity was followed by bilateral series of sharply contoured slow waves. The electric field of the seizure discharge changed during the seizure. Tangentially oriented dipolar field was found in the middle part of the seizure. Evolution of clinical seizure phenomena roughly corresponded to propagation of the ictal discharge. In terms of topography and electromorphology, this ictal record was similar but not completely identical with those reported previously. Collection of further ictal records in benign rolandic or centrottemporal epilepsy of childhood and other epilepsy syndromes is necessary. (*J Child Neurol* 2002;17:297–300).

Benign rolandic or centrottemporal epilepsy of childhood is a genetically determined condition with variable contribution of acquired and pathoplastic factors.¹ Its characteristics have been summarized in excellent reviews.^{2–5} In most cases seizures are rare, diagnosis and treatment are easy, and there is no need for repeated or long-term electroencephalographic (EEG) monitoring. Hence, ictal EEGs have been recorded very rarely. Unillustrated descriptions of ictal EEG^{6,7} reports of subclinical electrographic seizures^{8–10} or status epilepticus^{11,12} are available in the literature. Only a few articles contain EEG records of typical clinical seizures.^{13,14} In this article, we demonstrate a complete ictal EEG of a typical seizure of a child with typical benign rolandic or centrottemporal epilepsy.

Case Report

The patient, an 8-year-old right-handed Caucasian girl, had an unremarkable family history. Pregnancy, delivery, and developmental milestones were normal, and she did very well at school. At the age of 8 years, she had three

unprovoked seizures, which occurred when falling asleep or when awakening. Initial seizure symptoms were guttural sounds, drooling, and irregular respiration followed by mild rhythmic clonic movements on the left side or bilaterally. After about 30 seconds, the cloni slowed down, and the girl was hypotonic and unarousable. A few minutes later, she awakened and complained of a headache and colic. We investigated the case after her third seizure. The results of pediatric and neurologic investigation were normal. Her intelligence was above average. Blood chemistry and hematology were normal. Her EEG was characteristic of benign rolandic or centrottemporal epilepsy, and her cranial computed tomogram was normal. Anticonvulsive treatment (300-mg carbamazepine daily) was introduced. During follow-up (from September 1998 to April 2001), no further seizures were observed, and no adverse event occurred. Cognitive performances remained excellent, and no psychologic problems emerged.

Electroencephalography

An EEG investigation was done by means of Brain Quick (Micromed, Mestre, Italy) digital EEG equipment. Electrodes were placed according to the International 10–20 system, and a 19-channel EEG was recorded against linked ears reference (both ear lobes were connected via a 20 kOhm impedance). Montage reformatting and off-line parameter resetting were possible. Standard EEG showed regular alpha background activity, and neurometric scores of waking background activity showed no statistically significant alterations. Sharp waves showed a dipolar potential field with negative voltage maximum at the right midtemporal (T4) electrode and positive maximum right frontally (F4). Spontaneous sleep activated trains of sharp and slow waves (Figure 1A). In stage 2 sleep, sharp waves and sleep patterns suddenly ceased, and 8-Hz rhythmic activity emerged in the right midtemporal-central region (Figure 1B). A few seconds later, both EEG and artifacts indicated arousal (Figure 1C). In the first 70 seconds of the electrographic seizure, morphology of the ictal rhythm did not change, but its voltage increased, and its frequency slowed down to 6 Hz. Rhythmic ictal activity gradually spread to adjacent sites (Figure 1C–E). Thereafter, right-sided rhythmic activity became irregular. At the same time, sharply contoured high-voltage rhythmic 2-Hz activity emerged in the left hemisphere (Figure 1E–F). The final part of the seizure was characterized by bilateral rhythmic delta activity with higher voltage on the left side and superposition of faster rhythms on the right (Figure 1G–H). The electrographic seizure was followed by postictal flattening. Electroencephalographic depression was greater in the right hemisphere than in the left (Figure 1J–I). Referential and bipolar montages were used for phase analysis. In-phase activity was recorded between F4, C4, and T4 electrodes at the beginning of the seizure discharge. After 20 seconds, phase reversal occurred between F4, C4 and T4, T6 electrodes. The following electrographically irregular part of the seizure showed no consistent phase relations. Bihemispheric in-phase delta activity characterized the terminal phase of the electrographic seizure.

Electroclinical correlation could be analyzed based on the notes of the technician. Seizure onset and electrographic arousal were associated with small body movements. Evolution and propagation of the seizure discharge were coupled with drooling and mild clonic movements (laterality not specified by the technician), whereas bilateral rhythmic delta was associated with atonia and unresponsiveness. Exact matching of clinical and EEG data was not possible because this seizure was recorded by chance, without video. For the same reason, no ictal and postictal testing of cerebral functions was carried out.

Discussion

In benign rolandic or centrottemporal epilepsy, motor and sensory seizure symptoms localize seizure onset to the upper or lower part of the precentral and/or postcentral gyrus.¹⁵ Also, analysis of interictal sharp waves¹⁶ and magnetoencephalographic discharges^{17,18} pointed to these areas of the cortex. The coexistence of the irritative zone and the symptomatogenic zone¹⁹ was supported by the observation that the first seizure symptoms and EEG interictal spikes concordantly pointed to the rostral or caudal part of