Xavier De Tiège, M.D.
Neurosciences Unit,
University College London
Institute of Child Health,
London, United Kingdom

Alan Connelly, Ph.D.
Radiology and Physics Unit,
University College London
Institute of Child Health,
London, United Kingdom

Frédérique Liégeois, Ph.D.
Developmental Cognitive
Neuroscience Unit,
University College London
Institute of Child Health,
London, United Kingdom

William Harkness, F.R.C.S.
Department of Neurosurgery,
Great Ormond Street Hospital for
Children NHS Trust,
London, United Kingdom

Chris A. Clark, Ph.D.
Radiology and Physics Unit,
University College London
Institute of Child Health,
London, United Kingdom

Wui K. Chong, M.D.
Department of Neuroradiology,
Great Ormond Street Hospital for
Children NHS Trust,
London, United Kingdom

David G. Gadian, Ph.D.
Radiology and Physics Unit,
University College London
Institute of Child Health,
London, United Kingdom

J. Helen Cross, Ph.D.
Neurosciences Unit,
University College London
Institute of Child Health,
London, United Kingdom

Reprint requests:
Xavier De Tiège, M.D.,
Neuroscience Unit,
UCL Institute of Child Health,
30 Guilford Street,
London WC1N 1EH, UK.
Email: xdetiege@ulb.ac.be

Received, December 6, 2007.
Accepted, December 9, 2008.

Influence of Motor Functional Magnetic Resonance Imaging on the Surgical Management of Children and Adolescents with Symptomatic Focal Epilepsy

OBJECTIVE: To determine the clinical value of motor functional magnetic resonance imaging (fMRI) in the presurgical evaluation of a large group of children and adolescents with epilepsy caused by lesions close to the central sulcus.

METHODS: Forty-three patients (19 males; mean age, 13 years) with lesional focal epilepsy underwent motor fMRI as part of a multidisciplinary standardized presurgical evaluation between 2000 and 2006. fMRI data were analyzed using statistical parametric mapping (SPM2) and screened for the presence of movement-related artifacts. The ways in which the results of motor fMRI influenced the decision-making process were reviewed.

RESULTS: The success rate of motor fMRI was 93% and data were of high quality in 67.5% of the patients. Together with other clinical considerations, motor fMRI results contributed to the surgical management of 32 patients (74%). They helped 1) to determine the type of surgery in 23 patients (72%; 12 cases with and 11 cases without invasive functional mapping), 2) to indicate a reduced benefit-risk ratio with the consequence that surgery was not further considered in 5 patients (16%), and 3) to indicate that surgery was not an appropriate option because of the high risk of motor function deficit in 4 patients (12%).

CONCLUSION: Motor fMRI can be performed with a high degree of success and good data quality in this population of patients. It has an important additive role in the discussion of the feasibility of resective surgery contributing to the decision-making process for children with epilepsy caused by brain lesions close to the central sulcus.

KEY WORDS: Children, Decision-making process, Epilepsy surgery, Functional magnetic resonance imaging, Motor functional magnetic resonance imaging

Neurosurgery 64:856–864, 2009 DOI: 10.1227/01.NEU.0000343741.54200.58 www.neurosurgery-online.com

The primary aims of the presurgical evaluation of children with intractable lesional epilepsy are to define whether the lesion is responsible for seizures and to address its anatomic relationship to functionally eloquent cortex to determine likely functional risk when resected (5). In the first stage, such evaluation is based on a noninvasive and multidisciplinary approach that includes clinical assessment, video-electroencephalogram monitoring, structural and possibly functional cerebral imaging (5, 6). Neuropsychological and neuropsychiatric assessments also form an integral part of the assessment (5, 6). A multidisciplinary discussion, balancing the benefits against the risk of surgery based on the results of noninvasive evaluation, determines the eligibility of the children for resective surgery. Surgery might not be a worthwhile option if there is sufficient evidence that functional deficits will inevitably result from the extent of resection required to alleviate seizures (5, 19). In cases whereby the noninvasive approach fails to provide the required information, invasive monitoring using subdural or depth electrodes is required to accurately localize the area of seizure onset and determine its proximity to functional cortex (5).

Functional magnetic resonance imaging (fMRI) of the brain is a noninvasive neuroimaging technique that has progressively been transferred from research to clinical practice and is

ABBREVIATIONS: fMRI, functional magnetic resonance imaging; **IFM**, invasive functional mapping; **PSMC**, primary sensorimotor cortices; **SPM**, statistical parametric mapping

now used routinely in the presurgical evaluation of children with intractable epilepsy (12). fMRI has mainly been used to locate functional language and sensorimotor cortices in relation to a lesion (12, 19). Thus, in cases whereby resective epilepsy surgery might compromise motor function and therefore significantly affect the patient's quality of life, fMRI can aid surgical decision-making by providing accurate localization of primary sensorimotor cortices (PSMC) and establishing their anatomic relationships with brain lesions (3, 4, 8, 17). In addition, fMRI can provide information about possible reorganization of function, which may be of particular interest when determining the surgical strategy (11, 14, 19). Although numerous studies have validated and highlighted the important role of motor fMRI in the presurgical evaluation of patients with epilepsy, reports describing how motor fMRI can actually influence the surgical management of patients with extratemporal brain lesions are rare and principally focused on adults (2, 17, 19).

To determine the clinical value of motor fMRI in the presurgical evaluation of children and adolescents with extratemporal symptomatic epilepsy, we reviewed how motor fMRI contributes to the surgical management of a large group of children with epilepsy caused by the presence of a lesion or lesions close to the central sulcus.

PATIENTS AND METHODS

Patients

The epilepsy surgery program at Great Ormond Street Hospital for Children NHS Trust has been in existence since 1992. Children included in the present study had complex epilepsy and were referred for assessment of possible epilepsy surgery between July 2000 and August 2006.

Forty-three patients (19 males and 24 females; mean age, 13 years; range, 7 to 18 years) with lesional focal epilepsy underwent motor fMRI as part of a multidisciplinary standardized presurgical evaluation at Great Ormond Street Hospital for Children NHS Trust over this time period. The decision to perform motor fMRI was based on presumed proximity of the lesion to the PSMC. Children younger than 7 years old were not referred for fMRI because of the high likelihood of poor compliance. Other investigations undertaken for the presurgical evaluation included clinical review, interictal and ictal electroencephalogram with or without single-photon emission computed tomography, optimized structural magnetic resonance imaging, neuropsychological and neuropsychiatric evaluations. After evaluation, surgery feasibility was discussed in a multidisciplinary meeting considering results of all investigations, and a decision was made about whether to offer surgery. For patients who underwent surgery, we categorized the type of surgical procedure (invasive monitoring, focal resection, disconnection, biopsy) and the postoperative outcome (seizure frequency according to the Engel Classification of Postoperative Outcome [9] and neurological deficit). For each patient, data were retrieved from medical records.

Clinical details of the patients are summarized in Table 1. Seven children had lesions acquired during the first 2 years of life (patients 1–7). Six children had vascular malformations (patients 8–13). Five children had tumors (patients 14–18). Twenty-three children (patients 19–41) had malformations of cortical development (1), and 2 children had other types of brain lesions (patients 42 and 43). Nine patients (21%) had motor deficits. Three other patients had motor coordination problems of the affected hand associated with a parietal lesion. Twenty-eight patients (65%) had mild to severe learning and/or behavioral difficulties.

fMRI Data Acquisition

Magnetic resonance imaging investigations were performed between July 2000 and February 2005 (32 patients) on a Siemens Magnetom Vision 1.5 T system (Erlangen, Germany) and from October 2005 until August 2006 (11 patients) on a Siemens Magnetom Avanto 1.5 T system. Anatomic images used for the localization of activated voxels were obtained from T1-weighted fast low-angle shot images. fMRI data were acquired using whole-brain echo planar imaging. The parameters used for structural and fMRI data acquisition have been described in detail elsewhere (7, 18, 19).

Experimental Paradigm

Each run consisted of the acquisition of 125 echo planar imaging volumes (14, 19). The first 5 volumes were discarded to ensure magnetization equilibrium. In the 120 remaining volumes, a block design was used, consisting of 24 alternating blocks of rest and motor task with 5 volumes in each block (14, 19). During rest periods, children were asked to close their eyes, relax, and make no movements. The motor task consisted of active or passive flexion-extension of all fingers simultaneously (approximately 1–2 Hz) (19). For each patient, 2 runs for the hand contralateral to the brain lesion (the affected hand) were obtained. One run was also obtained for the hand ipsilateral to the brain lesion (the nonaffected hand) in 30 patients (70%) to compare with the activation map obtained with the affected hand. In patient 22, foot movement–related activations were used instead of the hand, using the same paradigm except that the motor task consisted of movements of flexion-extension of the ankle. Each child practiced the task outside the scanner before fMRI data acquisition. Task performance during the scanning procedure was closely monitored.

fMRI Data Preprocessing and Analyses

Because the fMRI data used for the surgical discussion and decision-making processes were acquired over a 6-year period, the need for contemporaneous surgical decision-making meant that the images were preprocessed and analyzed using different versions of the statistical parametric mapping (SPM) software (SPM99 for the earlier studies and SPM2 for the later studies; Wellcome Department of Imaging Neuroscience, London, UK; http://www.fil.ion.ucl.ac.uk/spm). The images were first realigned to the first image of the first run to correct for head movements (post hoc realignment). Structural images were then coregistered to the mean echo planar image. fMRI data were then smoothed to 3 times the original voxel size (14, 19). The statistical analyses compared motor task with rest in a block design (14, 19). The results were considered significant at $P < 0.05$ corrected for multiple comparisons.

Finally, to assess fMRI data quality in this group of children at the end of the 6-year period, all data were preprocessed and reanalyzed in SPM2 using the same methodology.

Assessment of Motor fMRI Data Quality

Motor fMRI paradigms can be associated with sudden head movements or head motion synchronized with the motor task condition. This is a well recognized confounding factor that can impair the quality of fMRI data and produce regions of false apparent activation (10, 13, 16). This could be particularly true in this population of children and adolescents with pharmacoresistent lesional epilepsy because 65% of them had mild to severe learning and/or behavioral difficulties. To evaluate in this group of patients the impact of head movements on the quality of motor fMRI data after post hoc realignment, fMRI results that were reanalyzed in SPM2 were screened for the presence of motion-related artifacts, which typically appear in the form of a corona of activation at the edges of the brain (13, 16). The fMRI studies of each patient were then

TABLE 1. Clinical details of the patients[a]

Patient no.	Age (y)/sex	Hand	Lesion type	Motor deficit	Epilepsy onset	Current seizure
1	7/F	L	L Fr-Pa atrophy	R hemiparesis	3 d	CPS
2	11/M	L	L Te-Oc porencephalic cyst	No	1 d	SPS
3	15/M	R	R Pa-Oc atrophy	L hemiparesis	2 y	CPS
4	15/M	R	R hemispheric atrophy	L hemiparesis	5 y	CPS
5	17/F	L	L Fr-Pa atrophy	R hemiplegia	3 d	SPS
6	18/F	L	L Fr porencephalic cyst	R hemiparesis	4 mo	SPS
7	18/M	R	R Fr-Pa-Te atrophy	L hemiparesis	8 y	SPS ± SG
8	10/F	R	L Fr-Pa AVM	No	4 y	CPS
9	10/M	R	R Pa pial angioma	No	3 y	CPS
10	11/F	R	R Pa AVM	No	11 y	SPS
11	12/F	R	R Pa-Oc pial angioma	No	10 y	SPS
12	13/M	R	R Fr cavernoma	No	10 y	CPS
13	16/F	R	R Fr-Ce cavernomas	No	14 y	SPS
14	10/M	R	L Pa-Oc pilocytic astrocytoma	R dyspraxia	7 y 6 mo	SPS
15	11/M	R	R Fr-Ce meningiomatosis	No	6 y	SPS
16	12/M	R	R Fr-Pa meningiomatosis	No	12 y	SPS
17	12/F	R	L Fr meningioangiomatosis	No	8 y	SPS ± SG
18	16/F	R	L Fr-Pa anaplastic astrocytoma	No	9 y	SPS
19	8/F	R	R Pa-Ce DNET[b]	No	4 y	SPS
20	9/F	R	R Fr DNET	No	3 y	CPS
21	10/F	R	R Te-Pa FCD	No	7 mo	CPS
22	10/F	L	L Pa-Oc FCD	No	2 y 5 mo	CPS
23	10/M	R	L Pa DNET	No	8 y	SPS
24	12/F	R	L Fr-Ce DNET[b]	No	1 y 6 mo	SPS
25	12/F	R	R Fr-Pa FCD[b]	L hemiparesis	1 y 7 mo	SPS, CPS ± SG
26	12/F	R	L Fr DNET	No	11 y	CPS
27	12/M	R	R Fr FCDb	No	7 mo	CPS ± SG
28	12/M	R	R Pa DNETb	No	12 y	CPS
29	12/F	R	L Fr FCDb	No	5 y	CPS
30	12/F	R	R Fr FCD	No	2 y	CPS
31	13/F	R	L Pa DNET	R dyspraxia	10 y	CPS
32	14/F	L	L Pa DNET	No	8 y	CPS
33	14/M	R	L Pa-Te FCD[b]	No	2 y	SPS
34	14/M	L	L Fr and L Pa FCD[b]	No	9 y	CPS
35	15/M	L	R Fr DNET	No	10 y	SPS
36	15/M	L	L Fr FCD	R hemiparesis	3 mo	CPS
37	15/M	L	R Fr DNET	No	11 y	CPS
38	16/F	R	R Pa DNET[b]	No	3 mo	SPS
39	16/F	L	L polymicrogyria	R hemiparesis	11 y	CPS
40	17/F	L	L Pa FCD	R dyspraxia	6 mo	CPS
41	17/F	R	L insular FCD	No	1 y	SPS
42	14/M	R	L HS (L Fr epileptic focus)	No	3 y 5 mo	CPS ± SG
43	14/M	R	L Pa-Te hemorrhage, L HS, L Te atrophy	No	9 y	SPS

[a] Age, age at the time of motor functional magnetic resonance imaging; hand, handedness; L, left; Fr, frontal; Pa, parietal; R, right; CPS, complex partial seizures; Te, temporal; Oc, occipital; SPS, simple partial seizures; SG, secondary generalization; AVM, arteriovenous malformation; Ce, central; DNET, dysembryoplastic neuroepithelial tumor; FCD, focal cortical dysplasia; HS, hippocampal sclerosis.
[b] Based on radiology.

rated according to a classification adapted from Hoeller et al. (13): "no motion-related artifacts" (Grade 1), "mild to moderate motion-related artifacts" (Grade 2), or "severe motion-related artifacts" (Grade 3).

We searched for the existence of a significant association between the presence of movement-related artifact (Grades 2 and 3) and the age at the time of fMRI using the unpaired t test. The χ^2 test was used to search for significant association between the presence of movement-related artifact (Grades 2 and 3) and the presence of focal motor deficit or learning and/or behavioral difficulties. For χ^2 tests, the Yates correction was used when the number of patients per cell was less than 5. Results were considered significant at $P < 0.05$.

Influence of Motor fMRI Data on the Surgical Management

Reports of the epilepsy surgery meeting and medical records were reviewed to determine in what ways motor fMRI data influenced the surgical management of each patient. Reanalysis of data did not contribute to this part of the study.

The surgical management of children with symptomatic epilepsy is typically based on a multidisciplinary approach and can be influenced by multiple factors (5). Therefore, to determine the specific contribution of motor fMRI in surgical management, we considered separately the influence of motor fMRI data on 2 key stages: the discussion of surgery feasibility (discussion process) and the final surgical management (decision-making process). Indeed, even if some children were considered eligible for surgery based on fMRI after the discussion process, motor fMRI data may not have directly influenced the final surgical management because other factors dominated the final decision.

During the discussion of the results of the multidisciplinary standardized presurgical evaluation performed at Great Ormond Street Hospital for Children NHS Trust, fMRI results were used to help determine the surgery feasibility in consideration of the risk to motor function by localizing function and determining its anatomic relationship to the brain lesions being considered for resection. Therefore, the ways in which the results of motor fMRI influenced the discussion process were grouped into 3 categories: 1) there was no risk of impairment of motor function, 2) invasive functional mapping (IFM) was required because of the close anatomic relationship between motor cortex and the brain lesion, 3) surgery was not an option because of the high risk to motor function.

Then, the information provided by motor fMRI was integrated with other results of the noninvasive presurgical evaluation to balance the benefits against the risk of surgery and decide whether the children were eligible for resective surgery. The ways in which the motor fMRI results influenced this decision-making process were grouped into 4 categories: 1) it influenced the type of surgery (with or without IFM; surgical technique), 2) surgery was not considered because of a poor benefit-risk ratio, 3) surgery was not performed because of the high risk to motor function, and 4) the final decision to perform surgery was dominated by factors other than the risk to motor function. Each patient was classified according to these categories. A reduced benefit-risk ratio for surgery meant that, considering the overall clinical picture of the patient at the time of evaluation and the potential risk to motor function, it was better to not perform surgery. For example, this might be the case for a patient with a benign lesion and a low seizure frequency or nondisabling seizures. Surgery was not considered an appropriate option when the risk to motor function was clearly too high, whatever the seizure frequency or type.

RESULTS

fMRI Results

fMRI analyses showed significant predominant activation of the PSMC contralateral to the affected hand (or foot) in 38 patients (88%), significant activation only in the PSMC ipsilateral to the affected hand in 2 patients (5%, patients 5 and 18) (Fig. 1), and no significant activation in 3 patients (7%, patients 8, 11, and 29). We found significant activation in the PSMC contralateral to the unaffected hand in 93% of the 30 patients who had a motor fMRI examination for this hand.

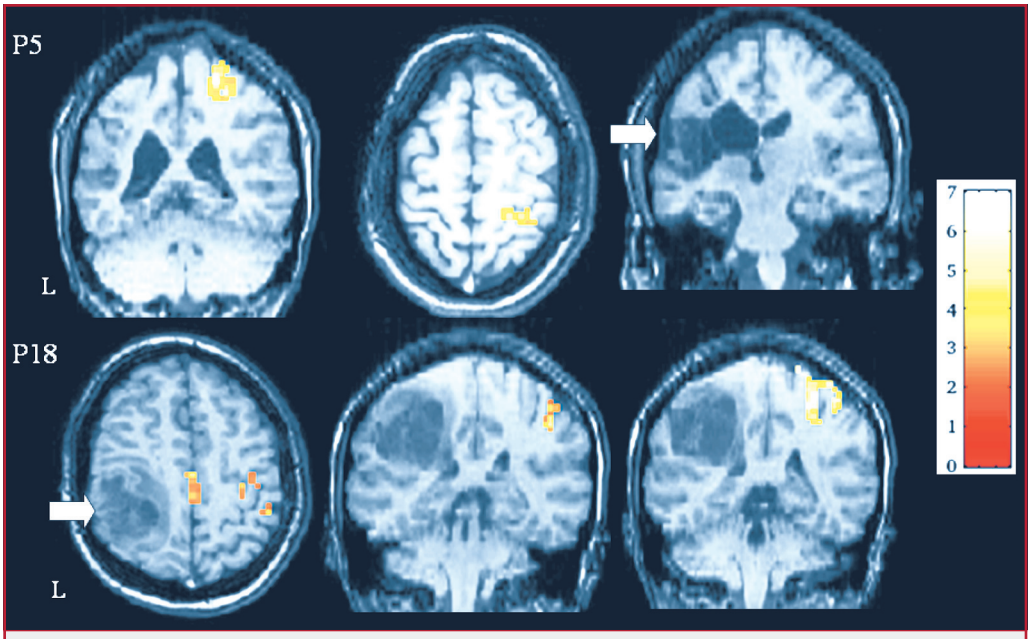

FIGURE 1. *Predominant activations found in the primary sensory-motor cortex (PSMC) ipsilateral to the affected hand in patients 5 and 18 (P5 and P18) suggesting the occurrence of functional reorganization related to the brain lesion. Red–white scale indicates the level of significance of the BOLD (blood oxygen level dependent) signal increase (Z score). Motor functional magnetic resonance imaging (fMRI) results are superimposed on structural magnetic resonance imaging (MRI) scans (T1-weighted image). Brain lesions are highlighted by a white arrow. For both patients, movement of the affected right hand induced significant activation only in the right PSMC. In P5, the atrophy of the left hemisphere as a result of perinatal stroke can be seen. This patient did not have a motor fMRI scan of the nonaffected hand. In P18, movement of the nonaffected hand induced significant activation that colocalized with those of the affected hand (right). The left frontoparietal astrocytoma can be seen on the structural MRI scan. L, left.*

Quality of Motor fMRI Data

fMRI data that were reanalyzed in SPM2 were screened for the presence of motion-related artifacts. Twenty-nine patients (67.5%) had Grade 1 motion-related artifacts, 10 (23.5%) had Grade 2 motion-related artifacts, and 4 (9%) had Grade 3 motion-related artifacts (Fig. 2). In these latter 4 patients, motion-related artifacts resulted from head motion of small amplitude synchronized with the motor condition as evaluated by post hoc realignment (Fig. 2). The presence of motion-related artifacts did not prevent the localization of the PSMC with regard to the lesion.

No significant association was found between the presence of movement-related artifact and age at the time of fMRI ($P = 0.23$), the presence of focal motor deficit (χ^2, 0.1851; $P = 0.667$), or the presence of learning and/or behavioral difficulties (χ^2, 0.07; $P = 0.793$ with the Yates correction).

No significant activation was observed in 3 of the 43 patients. The absence of significant activation in the PSMC in patient 29 was attributable to frequent sudden head movements of high amplitude (>10 mm for translation movements and >15 degrees for rotation movements) as evaluated by post hoc realignment. The absence of significant activation in the other 2 patients (patients 8 and 11) was not attributable to head movements as assessed by post hoc realignment.

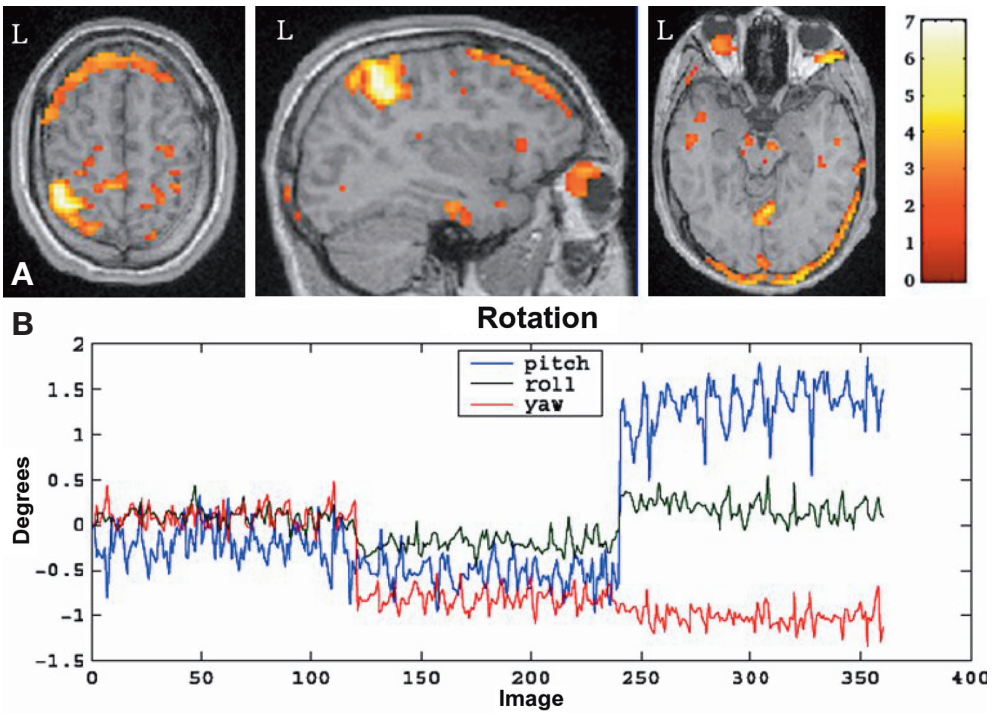

FIGURE 2. *Movement-related artifact observed in patient 33, classified as "severe" (Grade 3) as defined by Hoeller et al. (13).* **A**, *motor fMRI results superimposed on the patient's structural MRI scan (T1-weighted image) showing the activation in the left primary sensory-motor cortex and movement-related artifacts that appear in the form of a corona of activation at the edges of the brain. A red–white scale is shown, as in Figure 1.* **B**, *results of the post hoc realignment (3 rotation parameters) showing that the movement-related artifacts were the result of head motion of small amplitude synchronized with the motor condition. Note that the movement data display the results from 3 separate acquisition runs, each of 120 image data sets (24 alternating blocks of rest and motor task with 5 whole-head data sets in each block), producing the relatively large shifts evident at images 120 and 240. L, left.*

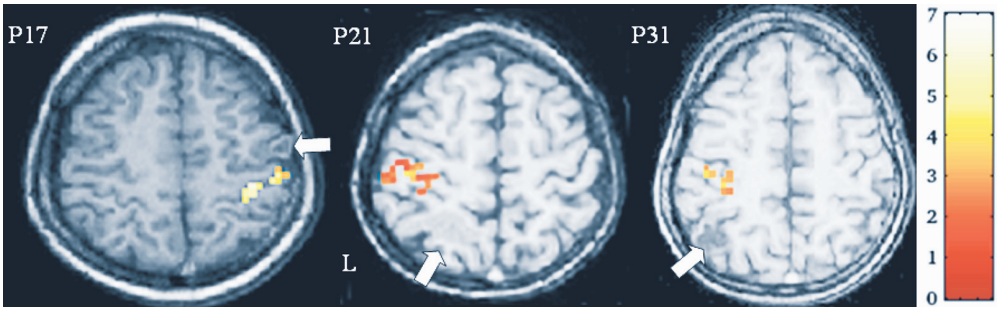

FIGURE 3. *Motor fMRI results of patients 17, 22, and 31 (P17, P22, and P31) superimposed on their structural MRI (T1-weighted) scans. Motor fMRI confirmed that the surgical procedure posed little functional risk in these patients and that invasive functional mapping was not required. Brain lesions are highlighted by a white arrow. Red–white scale as in Figure 1. L, left.*

Influence of Motor fMRI Data on the Surgical Management

The ways in which motor fMRI data influenced the discussion of surgery feasibility based on the risk for motor function (discussion process) and the final surgical management (decision-making process) were determined for the 40 patients with significant PSMC activations.

During the discussion process, motor fMRI indicated that there was no risk to motor function in 17 patients (42.5%) (Fig. 3);

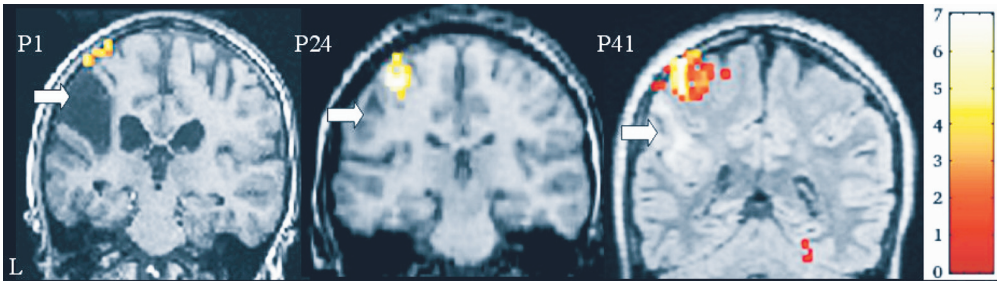

FIGURE 4. *Motor fMRI results of patients 1, 24, and 41 (P1, P24, and P41) superimposed on their structural MRI scans (T1-weighted image for P1 and P24, FLAIR [fluid-attenuated inversion recovery] for P41). Motor fMRI confirmed that the surgical procedure was of high functional risk in these patients and that invasive functional mapping was required. Brain lesions are highlighted by a white arrow. Red–white scale as in Figure 1. L, left.*

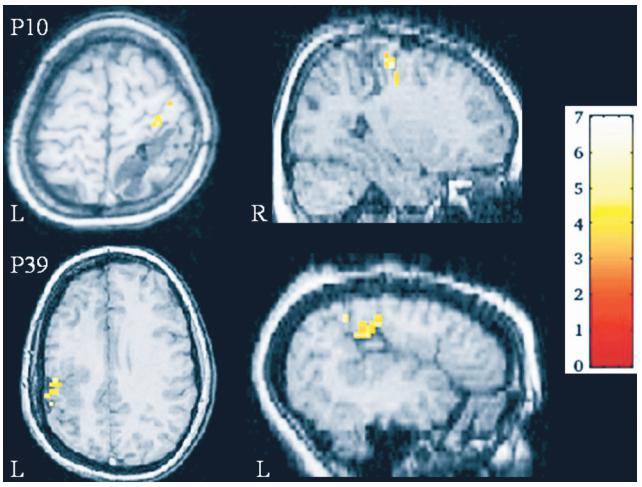

FIGURE 5. *Motor fMRI results of patients 10 and 39 (P10 and P39) superimposed on their structural (T1-weighted) MRI scans. Motor fMRI confirmed that the surgical procedure was probably not an option in these patients because risk to motor function was too high. The motor fMRI for patient 39 showed that the polymicrogyric cortex was functionally active and did not show any significant activation in the ipsilateral primary sensory-motor cortex. Red–white scale as in Figure 1. L, left; R, right.*

that IFM was required in 19 patients (47.5%) (Fig. 4); and that surgery was probably not an option because of the high risk to motor function in 4 patients (10%) (Fig. 5).

In the 17 patients for whom it was concluded that fMRI indicated a negligible risk to motor function, 11 patients were finally selected for surgery without IFM. In the other 6 children, motor fMRI data did not directly influence the final surgical management because other factors dominated the final decision: surgery was finally refused by the parents and/or the child in 2 cases despite the absence of risk to motor function (patients 2 and 5); surgery was finally not performed because seizures were well controlled by antiepileptic drugs at the time of surgical decision and the lesion was nonprogressive in 2 children (patients 27 and 33); and surgery was performed with invasive monitoring for localization of seizure onset in 2 patients (patients 21 and 43).

In the 19 patients for whom fMRI identified the need for IFM, 13 patients were finally selected for surgery with IFM, but 1 of them required an emergency operation without IFM (patient 18). Five other patients were not considered further for surgery because of the potential risk to motor function and the fact that seizures were relatively well controlled by antiepileptic drugs (decreased benefit-risk ratio). In 1 case, surgery was finally not offered because of the poor chance of surgical success (seizure onset not localized electroclinically, diffuse pial angioma).

In the 4 patients for whom fMRI identified that surgery was probably not an option, surgery was not offered, in order to spare motor function.

Therefore, in this population of 43 children, motor fMRI results were not considered for the final surgical management in 11 patients (26%, 3 with no significant fMRI results and 8 for whom motor fMRI did not directly influence the final surgical management); motor fMRI results, together with other clinical considerations, influenced the final surgical management in 32 patients (74%). In these 32 children, motor fMRI contributed to determining the type of surgery in 23 patients (72%, 11 cases without IFM and 12 cases with IFM), indicated a reduced benefit-risk ratio with the consequence that surgery was not further considered in 5 patients (16%), or indicated that surgery was not an option because of the high risk to motor function in 4 patients (12%).

Surgical Outcome

Among the 23 children in whom motor fMRI helped in the final surgical decision, 22 had surgery. One adolescent (patient 41) was referred to an adult center for surgery, and no surgical data are available. The surgical outcome of the patients is summarized in Table 2. Among the 22 children who underwent a surgical procedure, 2 had IFM but did not undergo resective surgery because of a close relationship between the motor cortex and the epileptic focus as assessed by IFM. In the 20 remaining cases, only 1 had a motor deficit after surgery, which was transient. Regarding seizure outcome, 65% were free from disabling seizures (Engel Class I), 10% had rare disabling seizures (Engel Class II), 15% had a worthwhile improvement (Engel Class III), and 10% had no worthwhile improvement (Engel Class IV).

DISCUSSION

This study shows that motor fMRI can have an important additive role in the discussion of the feasibility of resective surgery and the final decision-making process for children with epilepsy caused by a brain lesion or lesions close to the central sulcus.

TABLE 2. Surgical outcomes of the patients[a]

Patient no.	Operation	Pathology	PO deficit	Engel class
3	IM + R Te-Oc dysC	NA	Unchanged	IA
4	IM + R Te FR	Hypoxic-ischemic changes	Unchanged	IA
12	R Fr FR	Cavernoma	No	IA
14	L Pa-Oc FR	Pilocytic astrocytoma	Unchanged	IA
15	L Fr FR	Meningiomatosis	No	IA
16	R lesionectomy	Meningiomatosis	No	IA
17	L Fr FR	Meningioangiomatosis	No	IVB
19	IM + R Pa-Ce FR	DNET	No	IIIA
20	IM + R Fr FR	DNET	No	IIIA
22	L Pa-Oc FR	FCD	No	IA
23	L Pa FR	DNET	No	IA
26	L Fr FR	DNET	No	IA
28	IM + R Pa FR	DNET	No	IB
30	IM + R Fr FR	FCD	No	IA
31	L Pa FR	DNET	No	IIIA
32	IM + L Pa FR	DNET	No	IIA
33	L Te lobectomy	Nonspecific	No	IA
35	IM + R Fr FR	DNET	L transient hemiplegia	IIA
36	IM + L Fr FR	FCD	Unchanged	IVB
37	R Fr FR	DNET	No	IA
38	IM	NA	No	NA
42	IM	NA	No	NA

[a]PO, postoperative; IM, invasive monitoring; R, right; Te, temporal; Oc, occipital; dysC, disconnection; FR, focal resection; Fr, frontal; L, left; Pa, parietal; Ce, central; DNET, dysembryoplastic neuroepithelial tumor; FCD, focal cortical dysplasia; NA, not applicable.

This study also demonstrates that motor fMRI can be performed with a high degree of success and high data quality in children and adolescents with pharmacoresistent extratemporal epilepsy, even in the presence of learning or behavioral disorder. Indeed, in our group of 43 children, the success rate was 93% and data were of high quality in 67.5%, despite the fact that 65% of the patients had mild to severe cognitive or behavioral impairments. In 32.5% of patients, we found moderate to severe motion-related artifacts that did not, however, prevent the localization of the sensorimotor cortex. According to our results, the presence of movement-related artifact was not associated with a younger age at the time of fMRI, the presence of motor deficit, or learning and behavioral difficulties. The referral of children for motor fMRI should therefore not be limited. The severe motion-related artifacts were attributable to small-amplitude head motions synchronized with the motor condition, which is a well recognized confounding factor that can produce regions of false activation (10, 13, 16).

In 2 patients, fMRI showed predominant activations in the ipsilateral PSMC. Although we cannot rule out the existence of false-negative fMRI results in the contralateral cortex because of cerebral hypoperfusion or lack of vascular autoregulation caused by the brain lesion, these results may suggest the existence of a shift of motor function from the contralateral to the ipsilateral PSMC. In these 2 cases, fMRI did not directly influence the final surgical management. Nevertheless, they highlight the potential role of fMRI to reveal possible functional reorganization in children with brain lesions. However, to validate the existence of motor reorganization as suggested by fMRI, the functional evaluation of such patients could be combined with other investigations such as neurophysiological evaluation (motor evoked responses, transcranial magnetic stimulation).

At the time of surgical discussion, fMRI contributed to determining that the brain lesion was adequately distant from the motor cortex (IFM not required) in 42.5% of the children. In 47.5% of the patients, it highlighted the need to perform IFM because of the close anatomic relationship between the lesion and the motor cortex. Finally, in 10%, the lesion was shown to lie in the motor cortex and surgery was, therefore, not considered a possible therapeutic option, in order to spare motor function. In 1 of these patients, fMRI showed that the polymicrogyric cortex was functionally active. This was crucial information when the feasibility of extensive resective surgery was considered and discussed. This case illustrates, as previous studies have shown,

the major role of fMRI in the functional assessment of large malformations of cortical development before surgery (15, 20–22).

In the group of 43 children we studied, motor fMRI influenced the final surgical decision (decision-making process) in 74% of cases. In these 32 patients, by helping in the evaluation of the risk to motor function, fMRI contributed to determining the type of surgery (with or without IFM) in 72% of the children and had a major impact in 28% of the patients by leading to the decision to reject surgical treatment. However, it must be stressed that it is very difficult to try to quantify the specific contribution of fMRI in the surgical decision-making process, because the decision is based on a multidisciplinary approach that is affected by multiple factors.

Although it is not possible to compare our data with what would have been the postoperative outcome without the use of motor fMRI, our data do suggest that the use of motor fMRI in noninvasive presurgical evaluation can contribute to postoperative prognosis. Indeed, by contributing to determining the benefit-risk ratio for resective surgery, considering the results from motor fMRI is likely to decrease the number of patients who would undergo IFM without resective surgery. Moreover, it helps to select patients who will have the best chance for a good neurological outcome after surgery. This statement is consistent with the very good postoperative outcome obtained in the 20 children who underwent resective surgery.

In our institution, in view of the potential risks from inferring functional eloquence solely from anatomic landmarks based on anatomic variability, anatomic displacement induced by the lesion, and plasticity phenomena, motor fMRI is now performed in all children with epilepsy aged 7 years or older who are being considered for surgery and who have lesions close to the central sulcus. Motor fMRI is used to provide additional information to determine the localization of the motor cortex. Even when motor fMRI "only" confirms the location of the motor cortex as suggested by structural magnetic resonance imaging, these results substantially increase the confidence level in discussing the feasibility of surgery, and they help in determining the benefit-risk ratio of resective surgery at the individual patient level. Considering the noninvasiveness of fMRI, its increasing availability, and its potential to contribute substantially to surgical management, our data suggest that this investigation should be considered in all children with epilepsy caused by a lesion close to the central sulcus who are candidates for resective surgery.

CONCLUSION

This study shows that motor fMRI is a very useful imaging technique in the surgical management of children with symptomatic epilepsy caused by the presence of a lesion close to the central sulcus. By identifying the pattern of motor activation at the individual level (anatomic location, functional involvement of pathological cortex, cerebral reorganization), fMRI helps to outline the overall clinical picture of each patient, guide the final surgical decision, and contribute to the postoperative outcome. fMRI is therefore useful in counseling parents and children, and in improving the process of informed consent for resective surgery.

Disclosure

XDT is funded by the European Federation of Neurological Society Fellowship 2005, the Fonds de la Recherche Scientifique (FRS-FNRS, Belgium), and the M.E. Horlait-Dapsens Foundation (Belgium). This work was undertaken at Great Ormond Street Hospital for Children NHS Trust and UCL Institute of Child Health, which received a proportion of funding from the Department of Health's NIHR Biomedical Research Centers funding scheme.

REFERENCES

1. Barkovich AJ, Kuzniecky RI, Jackson GD, Guerrini R, Dobyns WB: A developmental and genetic classification for malformations of cortical development. **Neurology** 65:1873–1887, 2005.
2. Bartsch AJ, Homola G, Biller A, Solymosi L, Bendszus M: Diagnostic functional MRI: Illustrated clinical applications and decision-making. **J Magn Reson Imaging** 23:921–932, 2006.
3. Bittar RG, Olivier A, Sadikot AF, Andermann F, Reutens DC: Cortical motor and somatosensory representation: Effect of cerebral lesions. **J Neurosurg** 92:242–248, 2000.
4. Carpentier AC, Constable RT, Schlosser MJ, de Lotbinière A, Piepmeier JM, Spencer DD, Awad IA: Patterns of functional magnetic resonance imaging activation in association with structural lesions in the rolandic region: A classification system. **J Neurosurg** 94:946–954, 2001.
5. Cross JH: Epilepsy surgery in childhood. **Epilepsia** 43 [Suppl 3]:65–70, 2002.
6. Cross JH, Jayakar P, Nordli D, Delalande O, Duchowny M, Wieser HG, Guerrini R, Mathern GW; International League against Epilepsy, Subcommission for Paediatric Epilepsy Surgery; Commissions of Neurosurgery and Paediatrics: Proposed criteria for referral and evaluation of children for epilepsy surgery: Recommendations of the Subcommission for Pediatric Epilepsy Surgery. **Epilepsia** 47:952–959, 2006.
7. De Tiège X, Laufs H, Boyd SG, Harkness W, Allen PJ, Clark CA, Connelly A, Cross JH: EEG-fMRI in children with pharmacoresistant focal epilepsy. **Epilepsia** 48:385–389, 2007.
8. Dymarkowski S, Sunaert S, Van Oostende S, Van Hecke P, Wilms G, Demaerel P, Nuttin B, Plets C, Marchal G: Functional MRI of the brain: Localisation of eloquent cortex in focal brain lesion therapy. **Eur Radiol** 8:1573–1580, 1998.
9. Engel JJ, Van Ness P, Rasmussen T, Ojemann L: Outcome with respect to epileptic seizures, in Engel JJ (ed): *Surgical Treatment of the Epilepsies*. New York, Raven Press, 1993, ed 2, pp 609–621.
10. Field AS, Yen YF, Burdette JH, Elster AD: False cerebral activation on BOLD functional MR images: Study of low-amplitude motion weakly correlated to stimulus. **AJNR Am J Neuroradiol** 21:1388–1396, 2000.
11. Hertz-Pannier L: Brain plasticity during development: Physiological bases and functional MRI approach [in French]. **J Neuroradiol** 26:S66–S74, 1999.
12. Hertz-Pannier L, Chiron C, Véra P, Van de Morteele PF, Kaminska A, Bourgeois M, Hollo A, Ville D, Cieuta C, Dulac O, Brunelle F, LeBihan D: Functional imaging in the work-up of childhood epilepsy. **Childs Nerv Syst** 17:223–228, 2001.
13. Hoeller M, Krings T, Reinges MH, Hans FJ, Gilsbach JM, Thron A: Movement artefacts and MR BOLD signal increase during different paradigms for mapping the sensorimotor cortex. **Acta Neurochir (Wien)** 144:279–284, 2002.
14. Holloway V, Gadian DG, Vargha-Khadem F, Porter DA, Boyd SG, Connelly A: The reorganization of sensorimotor function in children after hemispherectomy. A functional MRI and somatosensory evoked potential study. **Brain** 123:2432–2444, 2000.
15. Janszky J, Ebner A, Kruse B, Mertens M, Jokeit H, Seitz RJ, Witte OW, Tuxhorn I, Woermann FG: Functional organization of the brain with malformations of cortical development. **Ann Neurol** 53:759–767, 2003.
16. Krings T, Reinges MH, Erberich S, Kemeny S, Rohde V, Spetzger U, Korinth M, Willmes K, Gilsbach JM, Thron A: Functional MRI for presurgical planning: Problems, artefacts, and solution strategies. **J Neurol Neurosurg Psychiatry** 70:749–760, 2001.
17. Lee CC, Ward HA, Sharbrough FW, Meyer FB, Marsh WR, Raffel C, So EL, Cascino GD, Shin C, Xu Y, Riederer SJ, Jack CR Jr: Assessment of functional MR imaging in neurosurgical planning. **AJNR Am J Neuroradiol** 20:1511–1519, 1999.
18. Liégeois F, Connelly A, Cross JH, Boyd SG, Gadian DG, Vargha-Khadem F, Baldeweg T: Language reorganization in children with early-onset lesions of the left hemisphere: An fMRI study. **Brain** 127:1229–1236, 2004.

19. Liégeois F, Cross JH, Gadian DG, Connelly A: Role of fMRI in the decision-making process: Epilepsy surgery for children. **J Magn Reson Imaging** 23:933–940, 2006.
20. Marusic P, Najm IM, Ying Z, Prayson R, Rona S, Nair D, Hadar E, Kotagal P, Bej MD, Wyllie E, Bingaman W, Lüders H: Focal cortical dysplasias in eloquent cortex: Functional characteristics and correlation with MRI and histopathologic changes. **Epilepsia** 43:27–32, 2002.
21. Müller RA, Behen ME, Muzik O, Rothermel RD, Downey RA, Mangner TJ, Chugani HT: Task-related activations in heterotopic brain malformations: A PET study. **Neuroreport** 9:2527–2533, 1998.
22. Pinard J, Feydy A, Carlier R, Perez N, Pierot L, Burnod Y: Functional MRI in double cortex: Functionality of heterotopia. **Neurology** 54:1531–1533, 2000.

Acknowledgment

We thank Donald Tournier, Ph.D., for help in the preprocessing of the fMRI data acquired on the Vision magnetic resonance imaging system.

COMMENTS

De Tiège et al. have described their approach to using motor functional magnetic resonance imaging (fMRI) in the preoperative evaluation of a small cohort of 43 young patients with focal epilepsy caused by lesions in proximity to the central sulcus. Specifically, this study targets the issue of how motor fMRI may meaningfully contribute to the surgical management of these patients.

The authors' main finding is that the implementation of motor fMRI, in the context of other clinical considerations, may be useful in as many as 75% of cases. Also, their results suggest that motor fMRI helps in the decision to pursue invasive, intraoperative functional mapping, aids in identifying a decreased "benefit-risk ratio" of surgical intervention, and helps eliminate surgery as an option in high-risk patients who are susceptible to developing a postoperative motor deficit.

Importantly, this article captures the necessity to develop technologies such as motor fMRI, and other applications that extend beyond this technique, for the preoperative assessment of epileptic patients who are about to undergo surgical treatment. In fact, it is often difficult to identify a specific epileptogenic focus for resection, either in focal (i.e., lesional) or generalized (i.e., nonlesional) epilepsy. Fortunately, techniques such as motor fMRI are welcomed and encouraged in clinical practice to help identify eloquent cortex that might otherwise be at risk during resection. These noninvasive tools are quickly applied and easily interpreted, and they often provide additional information such as potential functional reorganization of neural pathways. Ultimately, it is in the best interest of the patient to collect as much data as possible before pursuing resective surgery, and it is for this reason that motor fMRI should be included in any physician's armamentarium of diagnostic tools for epilepsy, in addition to video-electroencephalography, standard imaging studies (e.g., magnetic resonance imaging), single-photon emission computed tomography, neuropsychological examination, and Wada testing. De Tiège et al. have produced an elegant study discussing some details inherent to the motor fMRI technique, which will likely continue to become increasingly refined over time.

Demitre Serletis
James T. Rutka
Toronto, Canada

This is a retrospective study of how motor fMRI data influenced decision making for children potentially undergoing epilepsy surgery. The authors were able to obtain good-quality studies in a large percentage of patients, although some sort of reprocessing and reanalysis was evidently performed for purposes of this study. It is unclear how this after-the-fact reanalysis impacts the decision making, which was obviously done at the time of the original study.

These types of studies are difficult to perform. One cannot really ascertain the true value of the study, since we do not know how these patients would have done without this study being performed. In a sense, there is a self-fulfilling prophecy: if the fMRI looked problematic, the patient was not offered surgery, so we do not know what would have happened had the surgery actually been performed. The best that one can conclude is that the fMRI influenced the decision-making process, but we cannot determine whether it was for better or worse.

Leslie N. Sutton
Philadelphia, Pennsylvania

In this study, the authors were able to obtain reliable fMRI data in most children imaged, even though many were uncooperative and moved their heads during the sequences. The authors' success will encourage others to pursue fMRI studies in similar patients.

To me, discrete lesion surgery is different from seizure surgery. In this group of 22 patients, there were 11 discrete lesions, 9 dysembryoplastic neuroepithelial tumors, 1 cavernoma, and 1 pilocytic astrocytoma. I am not quite certain where to place the 3 with focal cortical dysplasia. If one removes the lesion, and not the surrounding brain, the seizures stop or are significantly diminished in the majority of cases. Even if abnormal electrical activity were present in the adjacent parenchyma, I would not excise the area. Thus, I question the usefulness of fMRI in this subgroup of the authors' series. In those discrete lesions that are enlarging and/or producing a progressively difficult-to-control seizure disorder, there would be little reason not to operate, irrespective of the results of fMRI.

In their series, only 1 patient had a transient neurological deficit. This would indicate that the selection of patients was excellent, that their surgical technique was very good, or that they were overly conservative. The reality is probably a combination of these factors.

J. Gordon McComb
Los Angeles, California

This is a large and important report of motor fMRI in children as young as 7 years of age who were considered candidates for epilepsy surgery. Although it is not possible to prove the precise benefit of fMRI from this study, there are sufficient anecdotes to show that the information was useful to support moving forward with this noninvasive technology, especially if it informs more definitive evaluations, such as cortical stimulation mapping through grid electrodes. It is encouraging that effective images could be obtained both from active motor tasks and passive finger flexion/extension, as it gives opportunities to map even the less cooperative patients.

fMRI has been accepted too slowly by the neurosurgical community, perhaps because it is expected to give "the" functional map, as opposed to being one of several indications of functional localization in the presurgical evaluation of the (pediatric) epilepsy patient. The relatively easy analysis stream and acquisition time described in this article should encourage future use of this method. I think the authors should be more aggressive with regard to the youngest ages for which they will try to perform fMRI. Our group has successfully imaged children as young as 5.1 years of age with careful, frequent practice and desensitization, including using a mock scanner before the study. Interestingly, our work was almost cancelled, at the last minute, by the radiology department because the child was "too young" for an fMRI. The capacity of young children to cooperate for studies should not be dismissed.

Jeffrey G. Ojemann
Seattle, Washington