Invited Review

Role of fMRI in the Decision-Making Process: Epilepsy Surgery for Children

Frédérique Liégeois, PhD,[1,2]* J. Helen Cross, PhD,[3,4] David G. Gadian, DPhil,[5] and Alan Connelly, PhD[5]

Functional MRI (fMRI) is increasingly being used to evaluate children and adolescents who are candidates for surgical treatment of intractable epilepsy. It has the advantage of being noninvasive and well tolerated by young people. By identifying important functional regions within the brain, including unpredictable patterns of functional reorganization, it can aid in surgical decision-making. Here we illustrate this using a number of case studies from the pediatric epilepsy surgery program at our institution. We describe how fMRI, used in conjunction with conventional investigative methods such as neuropsychological assessment, MRI, and electrophysiology, can 1) help to improve functional outcome by enabling resective surgery that spares functional cortex, 2) guide surgical intervention by revealing when reorganization of function has occurred, and 3) show when abnormal cortex is also functionally active, and hence that surgery may not be the best option. Altogether, these roles have reduced the need for invasive procedures that can be both risky and distressing for young people with epilepsy. In our experience, fMRI has significantly contributed to the decision-making process, and improved the counseling and management of young people with intractable epilepsy.

Key Words: fMRI; pediatric epilepsy; epilepsy surgery; brain plasticity; language; motor
J. Magn. Reson. Imaging 2006;23:933–940.
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FUNCTIONAL MRI (fMRI) can be used in a number of different ways to investigate brain disease in pediatric patients. The most extensive clinical applications to date have been in the context of neurosurgical treatment. Within this context, an important application has been the treatment of epilepsy. Individuals with this condition are prone to recurrent seizures, and it affects up to 1% of children. Approximately 25% of children with epilepsy will not respond to antiepileptic medication, and as a result some may become candidates for neurosurgical treatment. The presurgical evaluation of candidates for epilepsy surgery is a multidisciplinary process involving clinical assessment, video EEG monitoring, MRI, neuropsychological assessment, and neuropsychiatric evaluation. In some children, it is not possible to define the spatial relationship between the epileptogenic focus and functional cortex, and traditionally this has required invasive EEG recording, which involves the placement of subdural electrodes on the surface of the brain.

fMRI has a number of possible roles in the assessment of children with epilepsy. It can be used in some cases to help identify brain regions that are associated with ictal (during seizure) or interictal (between seizures) activity and may therefore be target areas for surgical resection (e.g., Refs. 1 and 2). It can be used to identify critical motor, speech and language, or memory areas as an aid to surgical planning (e.g., Refs. 2 and 3). In addition, from a more neuroscientific perspective, it may be used to investigate the reorganization of brain function that may occur as a result of brain damage and/or seizure activity (4–6). In some respects, these different roles for fMRI are interrelated; for example, in relation to presurgical planning, the need to avoid resection of eloquent cortical areas should be considered along with the possibility that reorganization of function may have occurred. It is important to note in this context that rendering a patient seizure-free is not the sole criterion for determining the optimum surgical intervention in patients with epilepsy. In many cases, a crucial consideration is the likely functional outcome, and surgical decision-making requires a judgment to be made regarding the quality-of-life balance between reduction of seizures and maintenance of function. At one extreme, this may result in a decision to not proceed to surgery when there is sufficient evidence that significant functional deficits will result from the extent of resection required to alleviate seizures.

[1]Developmental Cognitive Neuroscience Unit, UCL Institute of Child Health, London, United Kingdom.
[2]Harrison Research Centre, Children's Trust, Tadworth, United Kingdom.
[3]UCL Neurosciences Unit, Institute of Child Health, London, United Kingdom.
[4]Great Ormond Street Hospital for Children NHS Trust, London, United Kingdom.
[5]Radiology and Physics Unit, UCL Institute of Child Health, London, United Kingdom.
Contract grant sponsors: Wellcome Trust.
*Address reprint requests to: F.L, Developmental Cognitive Neuroscience Unit, Institute of Child Health, UCL, 30 Guilford Street, London WC1N 1EH, UK. E-mail: F.Liegeois@ich.ucl.ac.uk
Received July 6, 2005; Accepted February 17, 2006.
DOI 10.1002/jmri.20586
Published online 28 April 2006 in Wiley InterScience (www.interscience.wiley.com).

In our own studies we have used fMRI in many of the different ways mentioned above (2–6). Here we focus on our fMRI investigations of sensorimotor and language functions in the evaluation of children who are candidates for epilepsy surgery. We discuss the additive role that fMRI plays in the context of the many other procedures that influence neurosurgical decision-making, and how, in practice, it fits into the decision-making process.

With regard to language function, it should be noted that in contrast to their adult counterparts, children with focal brain injury to the left hemisphere rarely show pronounced speech and language impairments (e.g., Ref. 7). This sparing of function has been attributed to the impressive plasticity of the immature brain, which enables language functions to reorganize to other brain regions. However, studies of adults (8) and children (6,9) with intractable epilepsy have indicated that language lateralization cannot be reliably predicted in this population from structural imaging and clinical data alone. This is presumably because numerous factors contribute to plasticity processes, including the size and site of the lesion, etiology, and age at onset of habitual seizures. Thus language function may remain lateralized within a typical network, reorganize within the damaged left hemisphere and recruit atypical brain regions, reorganize to homotopic regions of the right hemisphere, or recruit both hemispheres. Therefore, when children with focal lesions become candidates for resection of epileptogenic cortex, fMRI can contribute to the decision-making process by identifying the patterns of language reorganization that may have occurred.

Reorganization of sensorimotor functions may likewise be unpredictable. For instance, motor fMRI activation contralateral to hand movement but within the abnormal hemisphere has been observed in individuals with congenital (pediatric case (10)) or early acquired (adult case (11)) pathologies, but has also been seen to reorganize to the ipsilateral intact hemisphere in patients with congenital hemiparesis (12). A variety of patterns of motor function reorganization were also evident in some of our earlier studies of sensorimotor function, in which we reported on the use of fMRI in conjunction with somatosensory evoked potential (SEP) measurements to investigate children who had undergone hemispherectomy for relief from epilepsy (4). We found that not all of the patients who exhibited ipsilateral SEP or fMRI responses had residual sensorimotor function in the hemiplegic hand. Ipsilateral sensorimotor responses were demonstrated both in patients with congenital disease and in those with acquired disease, which suggests that other factors, in addition to etiology and age at injury, may influence the degree of residual sensorimotor function and cerebral reorganization.

Another important point highlighted by functional imaging studies is that pathological cortex can be functionally active, especially in the case of developmental pathologies (10,13–15). This further illustrates the difficulty of predicting patterns of cerebral organization following brain injury, and adds to the argument for carrying out fMRI investigations in the course of neurosurgical planning.

Although the important role of fMRI in epilepsy surgery has been highlighted in both adult (16–18) and pediatric (19) populations, illustrative examples of how fMRI results are used in the decision-making process are rare and focus mainly on adult single cases (e.g., Refs. 8, 11, and 20; but see Ref. 21 for a pediatric case). Here we report on a number of case studies arising out of the pediatric epilepsy surgery program at our institution. These cases illustrate the role that fMRI can play in identifying patterns of cerebral activation in young patients with epilepsy, and how fMRI can be used in conjunction with conventional investigative methods to contribute to the neurosurgical decision-making process.

MATERIALS AND METHODS

Participants

Between November 2000 and February 2005, 44 children and adolescents who were candidates for surgical resection of epileptogenic cortex were referred for fMRI of language, motor function, or both, as part of their presurgical evaluation. Language fMRI (31 cases) was requested either for cortical mapping of language regions when lesions were nearby or encroaching on classic language areas, or to provide additional evidence for assessing lateralization of language functions in candidates for temporal lobectomies or focal resections. Motor fMRI (22 cases) was requested in cases in which it appeared that the lesion was nearby or encroached on primary or secondary sensorimotor regions.

The patients were 7–18 years old and suffered from acquired (ischemia, $N = 4$; Rasmussen's syndrome, $N = 3$; mesial temporal sclerosis, $N = 3$) or developmental (cortical dysplasia, $N = 11$; dysembryoplastic neuroepithelial tumour, $N = 16$) pathology, or unknown/other pathology ($N = 7$). Their cognitive abilities, as measured by standardized neuropsychological assessment, ranged from high average to the extremely low range. In the present study we report six illustrative cases from this series, as well as an additional case studied before 2000 (case 1).

fMRI Investigations

fMRI investigations were performed on a 1.5 T Siemens Vision system. Anatomical images were obtained from multislice T1-weighted fast low-angle-shot (FLASH) images (TR = 31 msec, TE = 11 msec, flip angle = 40°, matrix size = 256 × 256 × 64, voxel size = 0.75 × 0.75 × 3 mm). fMRI data were acquired using a whole-brain 3D EPI sequence (TR = 87 msec, TE = 40 msec, flip angle = 30°, matrix = 64 × 64 × 64, 3-mm isotropic voxels). The total acquisition time for each 3D data set was 5.6 seconds.

For the motor studies, 120 images were acquired that consisted of 12 rest/task cycles with five images per state in each cycle. In patients with sufficient motor function to perform the required movements, the task consisted of flexion-extension of all fingers and thumb simultaneously at a rate of approximately 2 Hz. In a small number of patients with impaired motor ability, a passive movement task was used in which the patient's hand was moved by one of the investigators in a manner similar to that described for the active motor task. Two runs were performed for the affected hand, and one was run for the unaffected hand as a reference. The scanning time was 12 minutes per run, and the total study (including acquisition of anatomical and functional images) lasted ~40 minutes.

For the language studies we used a covert verb generation task, since such tasks have been reported to show good correlations between lateralization of fMRI activation and language lateralization as determined with invasive techniques (5,22–24). In our pilot work we had tested other tasks that did not prove to be appropriate, for different reasons. Passive listening to stories did not provide reliable lateralization results in control participants, and generating multiple words (semantic association or phonemic fluency tasks) proved too difficult even outside the scanner for patients with learning/word-finding difficulties and literacy/phonological limitations. These difficulties are not uncommon in patients with long-lasting epilepsy. Single verb generation was selected because it proved to be the most reliable task and could be carried out by children of all ages and with a wide range of cognitive abilities (as shown in the present series).

Our protocol has been described previously (5,6). Briefly, two consecutive runs of 120 three-dimensional data sets were collected. Each run consisted of 10 task/rest cycles with six data sets in each state. The presentation of the first stimulus of each cycle was triggered automatically by the first image in that cycle. During the task period, participants were asked to generate covertly (i.e., silently) single verbs to concrete nouns (one to three syllables long) presented via earphones every 2.8 seconds (~12 nouns per task period). The interstimulus interval was increased to four seconds for those patients who, prior to scanning, had not managed to perform overt generation of verbs to nouns within three seconds. During the rest period, bursts of amplitude-modulated noise were presented at the same rate as the nouns. The scanning time was 12 minutes per run, and the total study (including acquisition of anatomical and functional images) lasted ~40 minutes.

The images were analyzed using Statistical Parametric Mapping (SPM) software (SPM99 and subsequently SPM2; Wellcome Department of Imaging Neuroscience, London, UK., http://www.fil.ion.ucl.ac.uk/spm). The images were realigned, coregistered, and then smoothed to three times the original voxel size. The statistical analysis involved the comparison of task vs. rest in a block design.

Assessment of Hemispheric Dominance for Language

Hemispheric dominance was based on cortical activation in the inferior frontal regions.

The results were presented at a multidisciplinary surgery meeting, during which findings from seizure semiology, neurology, electrophysiology, radiology, neuropsychology, and neuropsychiatry were also discussed. fMRI results were qualified depending on whether results were replicated in both independent runs (stronger degree of certainty) or not. The degree of hemispheric dominance was also communicated. Strong dominance was concluded if inferior frontal activation was seen in only one hemisphere at the lowest possible statistical threshold ($P = 0.05$, uncorrected for multiple comparisons). Bilateral activation with dominance was concluded if activation was seen in both hemispheres ($P = 0.05$, uncorrected for multiple comparisons), with, however, a higher statistical level of significance in one hemisphere relative to the other. Bilateral language representation was concluded if activation in both hemispheres was seen at a similar statistical threshold. In the majority of cases, qualitative evaluation of lateralization was made on visual examination of the individual fMRI results, as described above.

In cases in which lateralization was ambiguous, and the lesions were small enough to not affect normalization parameters, the data were normalized to the default adult SPM99 template and lateralization maps were computed (5). Lateralization maps enable identification of the loci where activation in a region (in this case the inferior frontal gyrus) is statistically higher than activation in the homotopic region of the opposite hemisphere, and therefore provide an objective means of assessing hemispheric dominance.

Postsurgical Outcome

Seventeen patients underwent invasive EEG monitoring, and one underwent intraoperative stimulation in addition to fMRI. No patient in this series underwent Wada testing. In all cases, concordance between fMRI and invasive results was found (as previously reported in Ref. 5, and consistent with Refs. 22–24). When motor and/or language functional cortex was identified within the lesioned hemisphere, this region was spared during surgery. Lobectomies were performed only in cases in which lateralization of language was in the opposite hemisphere. Forty patients underwent surgery (three hemispherectomy and 37 focal resection), and none presented with clinically noticeable deterioration of language or motor functions postoperatively.

Case Reports

In this section we present a number of cases that illustrate the ways in which we have used fMRI to help in the assessment of candidates for epilepsy surgery.

Case 1

We begin with a previously reported (3) case of an 18-year-old right-handed girl, who presented with a history of partial motor seizures involving an alternating rhythmic grasping and releasing motion of her right hand. During these seizures, which occurred on a daily basis and lasted several hours, there was no alteration of her conscious level, but she could not use her right hand. Her seizures were refractory to medical treatment. She lived in an area of Portugal that is endemic for cysticercosis, and neuroimaging revealed a small focus of calcification within the left central sulcus. fMRI studies of right-hand motor function showed a region of activation 9 mm distant from the calcified lesion (see

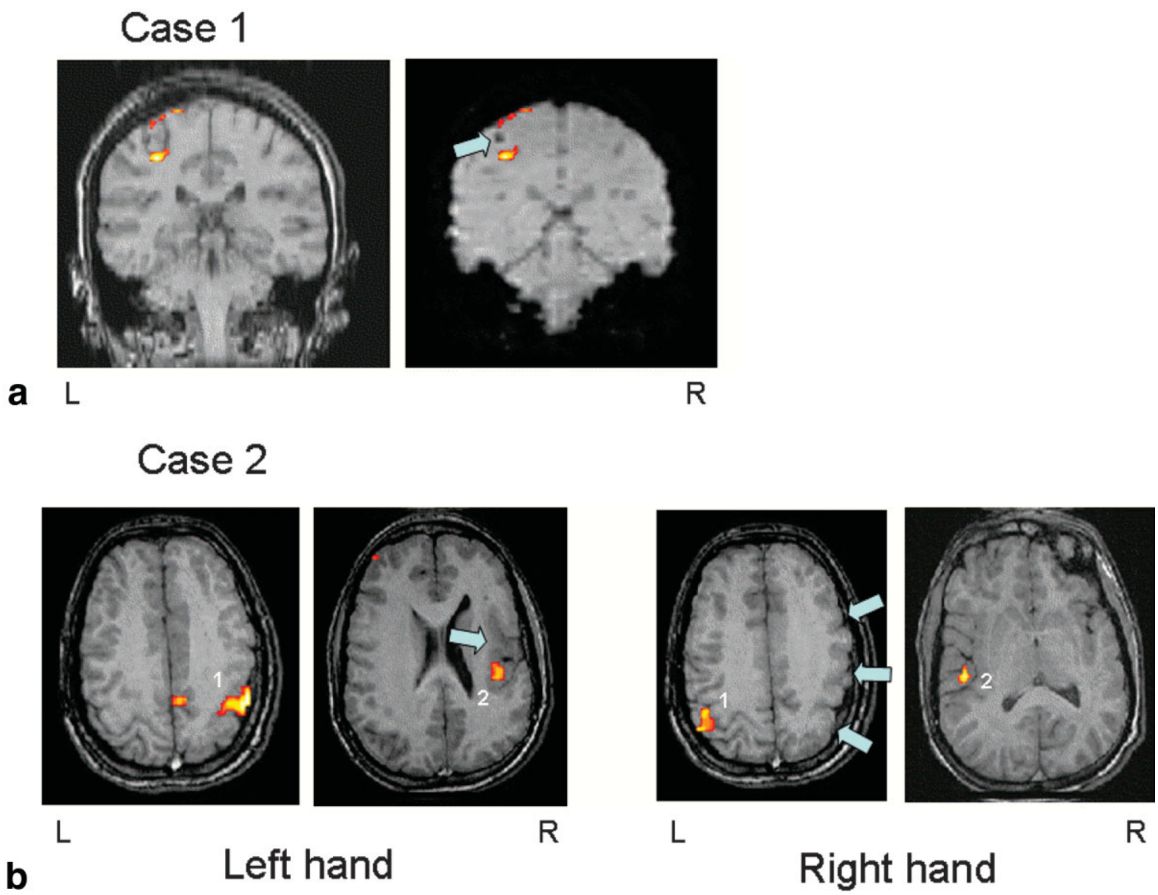

Figure 1. Illustrative examples of fMRI activation during hand movement. L: left hemisphere; R: right hemisphere. **a:** Case 1. Motor activation following right-hand movement is displayed superimposed on coronal T1-weighted structural (left) and echo-planar (right) images. The arrow indicates the position of a calcified lesion. Reprinted from Holloway V, Chong WK, Connelly A, Harkness WH, Gadian DG. Somatomotor fMRI in the pre-surgical evaluation of a case of focal epilepsy. Clin Radiol 1999;54:301–303 with permission from the Royal College of Radiology. **b:** Case 2. Extensive regions of polymicrogyria are evident in the right hemisphere (arrows). fMRI activation is seen in the contralateral primary sensorimotor cortex (labeled 1) and the second somatosensory region (S-II) (labeled 2) following passive hand movement of both the left (impaired) and right (normal) hands. Note that on left-hand movement, activation is seen within regions of severely abnormal-appearing cortex.

Fig. 1a), and deeper within the central sulcus. This suggested that minimal resection of part of the motor cortex would be required in order to achieve minimal loss of hand function.

To confirm that the radiologically visible lesion was the epileptogenic focus, presurgical invasive EEG monitoring, using a subdural grid, was carried out. Invasive corticography was also performed, with the subdural grid used to stimulate the cortex. Subsequent intraoperative cortical stimulation showed that the area of cortex immediately around the lesion did not serve any motor function. Moreover, after removal of the lesion, stimulation of the deep cortical region that showed activation on fMRI resulted in a grasping movement of the right hand. Thus there was strong concordance between the fMRI and invasive cortical stimulation findings in a region that would not have been accessible intraoperatively until resection of the lesion had been achieved.

After the lesion was removed, the patient suffered a transient loss of facility of her right hand, but without loss of power, which lasted for less than one week after surgery. This was attributed to postoperative edema, and she subsequently showed no deficit and remained seizure-free. In this patient, fMRI helped to identify functional cortex in a location that could not have been identified by surface cortical stimulation.

Case 2

Case 2, a boy, presented at the age of 22 months with macrocephaly and developmental delay. He had a mild left hemiplegia and cutaneous stigmata of neurofibromatosis type 1 (NF1). There was a strong family history of NF1 (mother, aunt, cousin, uncle, grandmother, great aunt, and great uncle). His first seizure occurred at the age of two years when he was febrile, with twitching of the limbs for 15 minutes. Subsequently he experienced further afebrile episodes involving rolling of the eyes and associated twitching of the mouth. Secondary generalized seizures emerged at the age of four years. These continued, predominantly nocturnally, at a frequency of one to three per month, with more frequent episodes of behavioral arrest and unresponsiveness

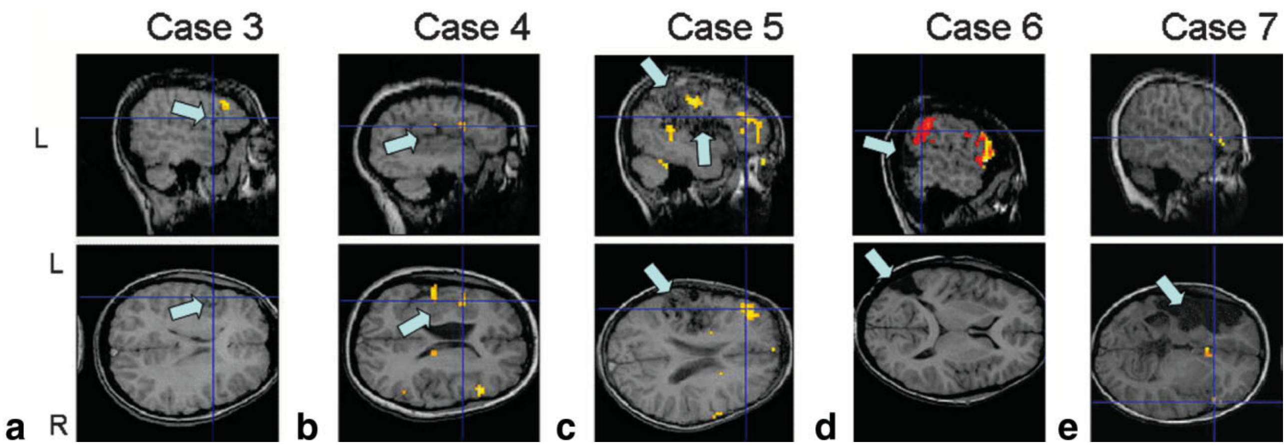

Figure 2. a–e: Illustrative examples of fMRI activation during covert verb generation for cases 3–7, respectively. Top row: sagittal images; bottom row: corresponding axial images for each patient. L: left hemisphere; R: right hemisphere. Arrows indicate lesions/areas of abnormality. The crosshair is centered on the locus of maximum activation near the lesion, except in case 3, where it is centered on the lesion, with the activated region shown anterior and superior to the lesion. Note that in case 7 the activation is located in the opposite hemisphere. a and c: Reprinted from Liégeois F, Connelly A, Cross JH, et al. Language reorganization in children with early-onset lesions of the left hemisphere: an fMRI study. Brain 2004;127:1229–1236, with permission from Oxford University Press.

that were also thought to be seizural in origin. These all proved to be resistant to multiple epileptic drugs. MRI revealed right hemipolymicrogyria. Neuropsychological testing at 14 years revealed a generally below-average score, with evidence of decline over the previous year. With the observed extensive hemispheric abnormality, the operation of choice to treat his epilepsy would have been hemispherectomy. However, his left-hand function was relatively good and therefore it was believed that hemispherectomy could lead to considerable reduction in function if the abnormal-appearing cortex were to be functionally active. fMRI for left-hand motor function revealed activation within the region of polymicrogyria in the right hemisphere (see Fig. 1b). The patient underwent invasive subdural grid recording for further localization of seizure onset within the polymicrogyria, to determine whether a focal resection avoiding the motor cortex was possible. Intraoperative stimulation confirmed that the cortex responsible for hand function was within the abnormal area of brain, with a similar distribution to that seen on fMRI. Limited cortical resection (guided by seizure onset according to the subdural recording) was therefore performed, following which the pathology was confirmed as polymicrogyria. Postoperatively, a 75% reduction in seizures was noted without loss of hand function, which represents a good outcome in this particular patient. In this case, fMRI contributed significantly to the decision-making process—not only in revealing that the dysplastic region remained functional, but also in indicating the need for intraoperative investigation with a subdural grid.

Case 3

Case 3, a girl, was evaluated at the age of 12 years for possible surgery for the management of her epilepsy. She had an uneventful birth and early developmental history. She had chickenpox at three years of age, during which she had an encephalopathic episode, with recurrent focal seizures requiring hospitalization. Subsequently her first seizure occurred when she was six years old (she was observed standing in a room, unresponsive, and smiling for 30 seconds). These became recurrent episodes and then evolved into episodes involving a warning that allowed her to lie down, after which she would become stiff and stare, remaining unresponsive, for up to a minute. After these episodes she would lose the ability of speech for up to 20 minutes, although she could communicate by signing. The sei-

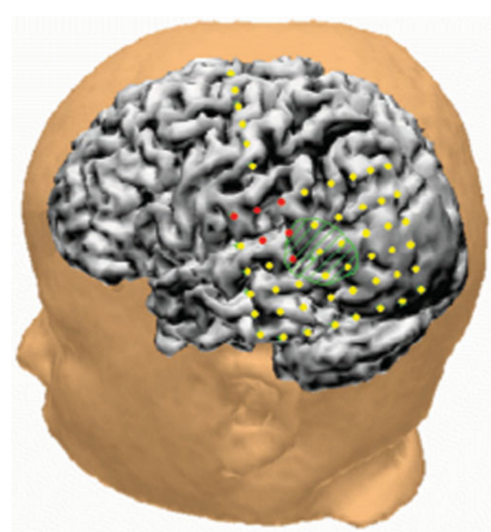

Figure 3. Results of intracranial monitoring and stimulation of the left hemisphere in case 6. The lesion is located within the green hatched area. Speech interference was seen on stimulated electrodes highlighted in red, consistent with fMRI language activation results in that region (Fig. 2d). Reprinted from Cross JH. Functional neuroimaging of malformations of cortical development. Epileptic Disord 2003;5(Suppl):S73-S80, with permission from John Libbey Eurotext.

zures began to occur in clusters lasting 20–120 minutes. Medication involving six anticonvulsants tried consecutively and in various combinations led to little benefit. Video EEG results suggested a left frontal seizure onset, and MRI revealed a lesion suggestive of a focal cortical dysplasia in the left inferiolateral frontal lobe.

Given the location of the lesion, i.e., in the region of the classic "Broca's area" (classically defined as the pars opercularis and triangularis of the inferior frontal gyrus), fMRI was used to identify possible reorganization of language functions. Of particular interest was the question as to whether language functions had remained within the left hemisphere despite the developmental abnormality seen. The results indeed revealed an area of brain activation dorsal to the lesion, in the left middle frontal gyrus (see patient 7 in Ref. 6, and Fig. 2a). Because fMRI identified putative functional language-related cortex in the vicinity of the lesion, she subsequently underwent invasive subdural EEG monitoring. Electrocortical stimulation in the region identified by fMRI induced speech arrest, and thus provided converging evidence that this region had to be spared during surgery. On the basis of this finding and seizure onset, she underwent a focal resection that spared functional language cortex. No speech or cognitive deterioration was observed postoperatively, and she became seizure-free without medication.

Case 4

Case 4, a girl, presented at the age of 17 years for presurgical evaluation. She was delivered at normal term, but early concern had arisen at 18 months in view of developmental delay and right hemiplegia. She subsequently made good progress developmentally. When she was 11 years old she experienced her first seizure, during which she fell off a chair and lost consciousness for about one minute. This was followed by several similar episodes, and antiepileptic medication was initiated. Despite treatment with five anticonvulsant drugs, she continued to have frequent seizures that involved a warning, loss of awareness, automatisms with ultimate stiffening, and twitching of the right side. At other times intermittent jerking of the right arm was noted. Ictal EEG revealed slow waves over the left hemisphere in association with frequent jerks of the right side. MRI showed left hemiatrophy with perisylvian polymicrogyria, while the right hemisphere looked normal. Neuropsychological assessment showed overall intelligence within the low range, with literacy and numeracy skills in line with that, but no discrepancy between verbal and nonverbal intellectual abilities. In view of the wide area of hemispheric abnormality on MRI, it was thought that, if justifiable, a hemidisconnection procedure would be the surgery of choice.

fMRI was used to identify whether language functions were left-lateralized or had reorganized to the right hemisphere. Results indicated inferior frontal activation in the right hemisphere (see patient 10 in Ref. 6), but also in the left hemisphere within the area of polymicrogyria (see Fig. 2b).

Although the epilepsy is quite disruptive to her independence, it was decided after discussion that she had much to lose in the way of function from hemispherectomy with regard to hand function, visual fields, and language. She therefore did not proceed to surgery.

Case 5

Case 5, a girl, presented for evaluation at the age of 10 years. She was known to have an arteriovenous malformation involving the left perisylvian and parietal regions, and had undergone two embolization procedures at the age of 8 years. Her first seizure occurred at the age of four years, which involved right-limb jerking and associated vomiting for 10–15 minutes. There was a further seizure the following day, and she then remained seizure-free for one year. Regular episodes of behavioral arrest and right-limb jerking began to occur. Ultimately they occurred in recurrent clusters despite treatment with four anticonvulsant medications. She had no neurological deficit. Seizures recorded on video EEG showed frontal sharp and slow waves maximal over the left hemisphere, and MRI showed an extensive arteriovenous malformation extending medially almost to the basal ganglia and anteriorly to Broca's area. Her full-scale IQ was within the low range and showed progress with time despite frequent absences from school. Previous embolization had led to improvement in her epilepsy.

She was referred for fMRI to identify whether language functions had developed within the damaged left hemisphere or had reorganized to the right hemisphere. Results revealed predominantly left-sided activation, with frontal, parietal, and superior temporal regions of activation located adjacent to or within the area of arteriovenous malformation (see patient 3 in Ref. 6, and Fig. 2c). It was believed that a surgical resection would pose too much risk to function, and she therefore was referred for embolization of the lesion, which was believed to present less risk of cortical damage peripheral to the lesion. No deterioration of cognitive functions was observed one year post embolization.

Case 6

Case 6, a boy, presented for evaluation at the age of 15 years. After an uneventful early history, he experienced his first seizure (a generalized tonic clonic seizure of 30 minutes duration) at 7 years. Since the age of 8 years he had experienced recurrent focal seizures involving behavioral arrest, unresponsiveness, and oromotor automatisms at a frequency of up to five per day. This was despite treatment with six anticonvulsant medications. Video EEG telemetry documented one clinical event that suggested seizure onset over the left hemisphere, although localization was more difficult. MRI showed a left posterior temporal lesion with changes suggestive of a dysembryoplastic epithelial tumor. fMRI for language showed that functional cortex possibly lay in close proximity to the posterior margin of the lesion (see Fig. 2d). In view of this, he underwent invasive EEG recording and stimulation, which revealed seizure onset from the lesion but receptive language function at the posterior margin of the lesion (Fig. 3) as suggested by fMRI. A limited resection sparing the functional language-related area was therefore performed. Post-resection language fMRI confirmed activation at the posterior margin of resection. Although he was initially troubled by seizures, he now remains seizure-free on medication, and there was no postoperative deterioration in language function.

Case 7

Case 7, a boy, presented for evaluation at the age of 9 years. He was born at term by emergency section for fetal distress. He experienced a neonatal seizure at 24 hours and required treatment with phenobarbitone. Subsequently he was noted to be developmentally delayed with right hemiplegia. Seizures continued over the first year and responded poorly to anticonvulsant medication. Seizures were recorded that involved him staring and stiffening, with posturing of the right arm followed by generalized jerking. Interictal EEG showed persistent left parietal sharp and slow wave complexes; ictally these arose from the left frontal and centrotemporal regions. MRI showed a full-thickness middle cerebral artery territory infarct that had led to porencephalic cyst formation.

Neuropsychological evaluation showed a marked discrepancy between verbal and nonverbal intellectual abilities, which were within the average and exceptionally low ranges, respectively. A left-ear preference on dichotic listening suggested possible right-hemisphere dominance for language functions. fMRI revealed a right-sided pattern of activation (see Fig. 2e). In view of the right hemiplegia already present and language lateralization to the right hemisphere, he underwent a left hemispherectomy.

One year after hemispherectomy, he was seizure-free off medication. Verbal and performance IQ remained stable, with a discrepancy similar to that observed preoperatively. No language deterioration was observed, and all expressive and receptive language functions were within the low average to average range. He remains seizure-free with no increased neurological deficit three years after surgery.

DISCUSSION

The above-described investigations illustrate the role that fMRI can play in the presurgical evaluation of children with epilepsy. By identifying regions of eloquent cortex, the technique can help in a number of ways to guide the neurosurgical decision-making process.

In some cases (case 2 for motor function, and cases 3 and 6 for language functions), fMRI results helped to localize areas of eloquent cortex, and in turn to identify where the subdural grid should be placed for further invasive functional mapping (cortical stimulation). In those three cases, results from cortical stimulation provided converging evidence that circumscribed resection would minimize any loss of function. In cases 2 and 3, it is possible that if fMRI had shown reorganization of function to the intact hemisphere, invasive cortical stimulation would not have been considered necessary. In case 1, fMRI findings also located a region of eloquent cortex, but this region was in the depth of the sulcus and could not have been identified through cortical stimulation via subdural grids placed on the surface of the cortex. In all cases there was a successful postsurgical outcome in terms of the quality-of-life balance between seizure reduction and maintenance of function. Our experience with such studies is that in addition to guiding the extent of resection for cases in which eloquent cortex can be spared, fMRI results can be useful for counseling parents and children when surgical resection of functional cortex may be considered.

Cases 4 and 5 illustrate the role for fMRI studies of language lateralization when the need for surgery is evaluated. In these cases, if there had been no fMRI results, reorganization of function to the right hemisphere might have been suspected, given that the pathology was congenital. In numerous studies, fMRI has helped investigators develop the idea that lateralization of language function cannot be predicted on the basis of onset, location, or size of lesion (6), and that abnormal cortex can be functional (as in case 4). More systematic use of fMRI, which is well tolerated by children over seven years of age, with a wide range of cognitive abilities, has therefore greatly reduced the need for invasive investigation. Our cases have demonstrated why we rarely, if ever, are now required to perform a Wada (sodium amytal) test when history, neuropsychology, and fMRI are considered together. This is an important development given the invasiveness and potential morbidity associated with Wada testing, which involves anesthetizing each hemisphere while the patient is awake and is asked to perform several tasks (e.g., counting aloud, moving fingers). This procedure can be particularly distressing for young patients. By demonstrating noninvasively that functions may be subserved by developmentally abnormal tissue, and therefore that presumptions cannot be made that such cortex can be removed safely, fMRI results such as those seen in cases 4 and 5 may contribute to the decision that surgical resection is not the best option.

For some patients, fMRI results show that reorganization of function to the intact hemisphere has already occurred (e.g., case 7). This helps the physician decide whether extensive surgery (such as hemispherectomy or lobectomy) is unlikely to result in dramatic loss of function, and might therefore be the best option for both quality of life and control of epilepsy.

In all of these cases we have seen that fMRI investigations can contribute to postoperative prognosis. In this respect, the use of fMRI in a pediatric institution is not too dissimilar to that in an adult setting (16). However, there is a potentially important difference, which is that brain functional plasticity may differ between adults and children. The great potential for reorganization of function in the developing brain can be counteracted by the disruptive effect of epilepsy. This makes it very difficult to predict whether reorganization of function has occurred, and may complicate the decision-making process. Finally, in addition to contributing to this process, fMRI has the advantage of being noninvasive and can even be repeated if necessary. In our experience, young people who are candidates for epilepsy surgery are very familiar with the MRI environment and do not consider fMRI investigations to be unpleasant.

In conclusion, we emphasize again that fMRI should be used in the context of a strongly multidisciplinary evaluation program, and that neurosurgical actions should be taken on the basis of the overall picture that is built up by many contributing tests, which include EEG and neuropsychological evaluation. It is therefore not very meaningful to try to measure in a quantitative way the specific contribution that fMRI makes to the surgical decision-making process. It suffices to say that it is now an important and relatively routine component of our epilepsy surgery program, and that the cases reported here illustrate the additive role that fMRI plays in the overall decision-making process.

ACKNOWLEDGMENT

We thank our many colleagues on the Great Ormond Street Hospital for Children epilepsy surgery team.

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