Pediatr Radiol (2007) 37:964–974
DOI 10.1007/s00247-007-0556-4

ORIGINAL ARTICLE

Real-time functional MR imaging (fMRI) for presurgical evaluation of paediatric epilepsy

Chandrasekharan Kesavadas · Bejoy Thomas · Sreedharan Sujesh · Radhakrishnan Ashalata · Mathew Abraham · Arun Kumar Gupta · Kurupath Radhakrishnan

Received: 31 January 2007 / Revised: 25 April 2007 / Accepted: 13 May 2007 / Published online: 1 August 2007

Abstract
Background The role of fMRI in the presurgical evaluation of children with intractable epilepsy is being increasingly recognized. Real-time fMRI allows the clinician to visualize functional brain activation in real time. Since there is no off-line data analysis as in conventional fMRI, the overall time for the procedure is reduced, making it clinically feasible in a busy clinical sitting.
Objective (1) To study the accuracy of real-time fMRI in comparison to conventional fMRI with off-line processing; (2) to determine its effectiveness in mapping the eloquent cortex and language lateralization in comparison to invasive procedures such as intraoperative cortical stimulation and Wada testing; and (3) to evaluate the role of fMRI in presurgical decision making in children with epilepsy.
Materials and methods A total of 23 patients (age range 6–18 years) underwent fMRI with sensorimotor, visual and language paradigms. Data processing was done in real time using in-line BOLD.
Results The results of real-time fMRI matched those of off-line processing done using the well-accepted standard technique of statistical parametric mapping (SPM) in all the initial ten patients in whom the two techniques were compared. Coregistration of the fMRI data on a 3-D FLAIR sequence rather than a T1-weighted image gave better information regarding the relationship of the lesion to the area of activation. The results of intraoperative cortical stimulation and fMRI matched in six out of six patients, while the Wada test and fMRI had similar results in four out of five patients in whom these techniques were performed. In the majority of patients in this series the technique influenced patient management.
Conclusion Real-time fMRI is an easily performed and reliable technique in the presurgical workup of children with epilepsy.

Keywords Functional MRI (fMRI) · Epilepsy · Surgery · Children

C. Kesavadas (✉) · B. Thomas · A. K. Gupta
Department of Imaging Sciences and Interventional Radiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology,
Trivandrum 695011, India
e-mail: chandkesav@yahoo.com

S. Sujesh
Biomedical Technology Wing, Sree Chitra Tirunal Institute for Medical Sciences and Technology,
Trivandrum, India

R. Ashalata · K. Radhakrishnan
Department of Neurology, Sree Chitra Tirunal Institute for Medical Sciences and Technology,
Trivandrum, India

M. Abraham
Department of Neurosurgery, Sree Chitra Tirunal Institute for Medical Sciences and Technology,
Trivandrum, India

Introduction

The presurgical evaluation of candidates for epilepsy surgery is a multidisciplinary process involving clinical assessment, video EEG monitoring, MR imaging, neuropsychological assessment, and neuropsychiatric evaluation. In a patient with seizures due to a lesion sitting in the eloquent cortex there may be a need to map the eloquent cortex so as to minimize deficits after surgery. Traditionally, mapping of eloquent areas is achieved by methods such as intraoperative cortical stimulation in the awake patient, implantation of a subdural grid with extraoperative stimulation, or intraoperative recording of sensory-evoked potentials [1, 2]. These methods are accurate, but are invasive. fMRI can obtain these data preoperatively and completely noninvasively. fMRI has the potential to predict the possible deficits in language, and in visual, motor and sensory functions that would arise from the surgical intervention. This helps the treating physician or the surgeon to explain the relative risk of intervention and nonintervention so that a decision about treatment options can be made after considering their costs and benefits. In many cases the decision making requires a judgment to be made regarding the quality-of-life balance between reduction of seizures and maintenance of function.

Conventional fMRI for clinical studies requires time-consuming off-line processing using software such as statistical parametric mapping (SPM). This is free software working on Matlab developed by the Wellcome Institute of Neurology, London (http://www.fil.ion.ucl.ac.uk/spm/). In real-time fMRI, data from fMRI scans can be reconstructed, analysed, and displayed as it is acquired from the scanner with a latency of only a few seconds. This technique can be useful for a variety of purposes, including immediate confirmation of experimental results from simple block designs, real-time monitoring of "resting-state" activity, and tracking subject head movement. It can also make functional mapping more interactive by allowing ongoing paradigms to be adjusted if the need arises, making fMRI a more flexible tool for neurological investigations. Fully real-time fMRI analysis can also provide immediate feedback of the subject's "ongoing" brain activity, enabling clinicians to investigate the dynamic nature of the human brain [3–6]. It should, however, be noted that most real-time processing software uses only the simple Student's *t*-test for statistical analysis and the more elaborate general linear modelling (used in SPM) is avoided. Advances in real-time processing tools with more reliable data processing are expected soon. Secondly, event-related and complex block design paradigms are not usually processed by real-time fMRI.

Brain functional plasticity may differ between adults and children. Children with focal brain injury or a focal brain lesion, such as cortical dysplasia in the left hemisphere, rarely show pronounced speech and language impairment. 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. 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. Numerous factors contribute to this plasticity processes, including the size and site of the lesion, aetiology, and age at onset of habitual seizures [7]. Intracarotid amobarbital testing (IAT, the Wada test) has been the gold standard for identifying lateralization of language and memory functions preoperatively, but it is invasive and, therefore, carries risk [8]. fMRI offers a promising noninvasive alternative approach and can contribute to the decision-making process [9, 10]. Reorganization of sensorimotor functions may, likewise, be unpredictable following brain injury or in a congenital disease. Many factors other than aetiology and age at injury may influence the degree of residual sensorimotor function and cerebral reorganization [11–15]. Also, it is interesting to note that pathological cortex can be functionally active, especially in the case of developmental pathologies. Hence it would be advisable to do fMRI investigations in the course of neurosurgical planning.

Our study had three aims: (1) to study the accuracy of fMRI using real-time fMRI in comparison to offline processing using SPM; (2) to study the effectiveness of real-time fMRI for mapping the eloquent cortex in comparison to intraoperative cortical stimulation during awake craniotomy and/or postsurgical neurological assessment and the effectiveness of fMRI in comparison to IAT in identifying lateralization of language; and (3) to evaluate the role of fMRI in decision making during the presurgical evaluation of children with epilepsy.

Materials and methods

Patients

From February 2005 to December 2006, 23 children with epilepsy were evaluated with fMRI. The mean age of the children who underwent fMRI evaluation was 12.5 years (range 6–18 years). The decision to perform fMRI was taken at a combined meeting of neurophysicians, neurosurgeons and neuroradiologists.

In 11 children the language area was mapped, in 18 children the sensorimotor area was mapped, and in 2 children the visual area was mapped (Table 1). Language fMRI was performed either for cortical mapping of language regions when the lesion was near the classic language areas, or to provide evidence for assessing lateralization of language functions in candidates for temporal lobectomy or focal resection. Motor and/or sensory fMRI was performed in children in whom the lesion appeared to be near the primary or secondary sensorimotor region. Of the two children in whom the visual area was mapped, one complained of aura of blindness and one had a lesion lying close to the visual areas.

All patients were alert and able to follow instructions well. Children below 10 years of age were trained by the

Table 1 Patient details (*DNET* dysembryoplastic neuroepithelial tumour, *FCD* focal cortical dysplasia, *ICM* intraoperative cortical mapping)

Patient no.	Age (years)	Sex	MRI findings	fMRI findings	Decision	Surgery	Pathology
1	16	M	Right parietal mass lesion	Left hand motor activation; lesion separated by a gyrus	Surgery with ICM	Lesionectomy	DNET
2	6	M	Left frontal FCD	Language on right side; motor cortex located well away	Surgery	Lesionectomy	FCD
3	16	M	Right superior frontal FCD	Left hand motor activation 1 cm behind the FCD	Planned for surgery with ICM	–	–
4	12	F	Right frontoparietal gliosis	Left hand motor activation close to lesion	Planned for surgery with ICM	–	–
5	18	F	Left parietal FCD	Right hand motor activation anterior to FCD	Conservative management	–	–
6	17	F	Right frontal FCD	Left hand motor activation seen on the lesion	Conservative management	–	–
7	10	M	Right frontal FCD	Hand motor activation seen 1 cm behind FCD	Conservative management	–	–
8	9	M	Right frontal mass lesion, ?DNET	Left hand motor activation close to lesion	Conservative management	–	–
9	12	M	Left hemisphere atrophy with gliosis	Language on right side; right hand activation close to lesion	Surgery with ICM	Multilobar resection	Gliosis
10	16	F	Partially excised right parietal DNET	Motor activation seen at margin of excised area	Surgery after explaining risk	–	–
11	14	F	Right parietooccipital FCD	Visual activation more than 2 cm away from lesion; right motor cortex close to lesion	Surgery with ICM	Lesionectomy	FCD
12	12	M	Left parietooccipital mass lesion	Language on left side with angular gyrus activation close to lesion; visual activation away from lesion	Surgery with ICM	Lesionectomy	Oligodendroglioma
13	13	F	Left temporoopercular mass	Language on right side	Surgery	Lesionectomy	Left temporal DNET
14	17	M	Left posterior frontal mass lesion	Activation of leg area close to lesion	Surgery after explaining risk	Lesionectomy	Low-grade glioma
15	7	F	Right superior frontal gyrus mass lesion	Hand and leg motor activation within lesion	Surgery after explaining risk	Decompression	Astrocytoma
16	15	M	Left temporoparietal lobe encephalomalacia and gliosis	Language on right side; left motor strip close to lesion	Surgery	Left hemispherectomy	Gliosis
17	15	M	Right frontal gliosis	Language more on right side; right motor speech activation close to gliotic lesion	Surgery with ICM	Lesionectomy	Gliosis
18	17	M	Right frontal polymicrogyria with right mesial temporal sclerosis	Language on left side; motor activation well anterior to lesion	Waiting for invasive monitoring	–	–
19	18	M	Left frontal cortical dysplasia	Language on left side close to lesion; motor activation away from lesion	Surgery preserving language area	Lesionectomy	FCD
20	13	F	Gliosis left inferior frontal and superior temporal gyrus	Language on right side; hand motor activation well away from lesion	Waiting for invasive monitoring	–	–
21	9	M	Encephalomalacia with gliosis left inferior frontal gyrus	Language on right side; hand and leg activation away from lesion	No seizure after drug optimization	–	–
22	6	F	Left frontal FCD	Motor activation well away from lesion; language on left side	Conservative management	–	–
23	10	M	Right superior frontal FCD	Supplementary motor area activation on lesion	Surgery with ICM	Lesionectomy	FCD

neuroradiologists (C.K. and B.T.) on the performance of the task before they performed it within the machine. The inclusion of patients in this study was based on the following criteria: history of seizures, consideration for surgical treatment, and need for defining eloquent brain areas or language lateralization. Patients with an IQ less than 70 were excluded from the study. The IQ was assessed by a neuropsychologist using Malin's intelligence scale for Indian children (MISIC) for children below 15 years and the Indian adaptation of the Wechsler intelligence scale for children between 15 and 18 years. A presurgical workup for each child before the fMRI included studying the seizure semiology and a detailed clinical examination that included handedness, suggesting the underlying aetiology, studying the video electroencephalography and MR imaging findings.

Five patients in whom language lateralization was to be studied underwent the Wada test in addition to fMRI. Six patients in whom the lesion was close to the eloquent cortex underwent intraoperative cortical stimulation. Of the 23 patients who underwent fMRI, 12 had a detailed postsur-

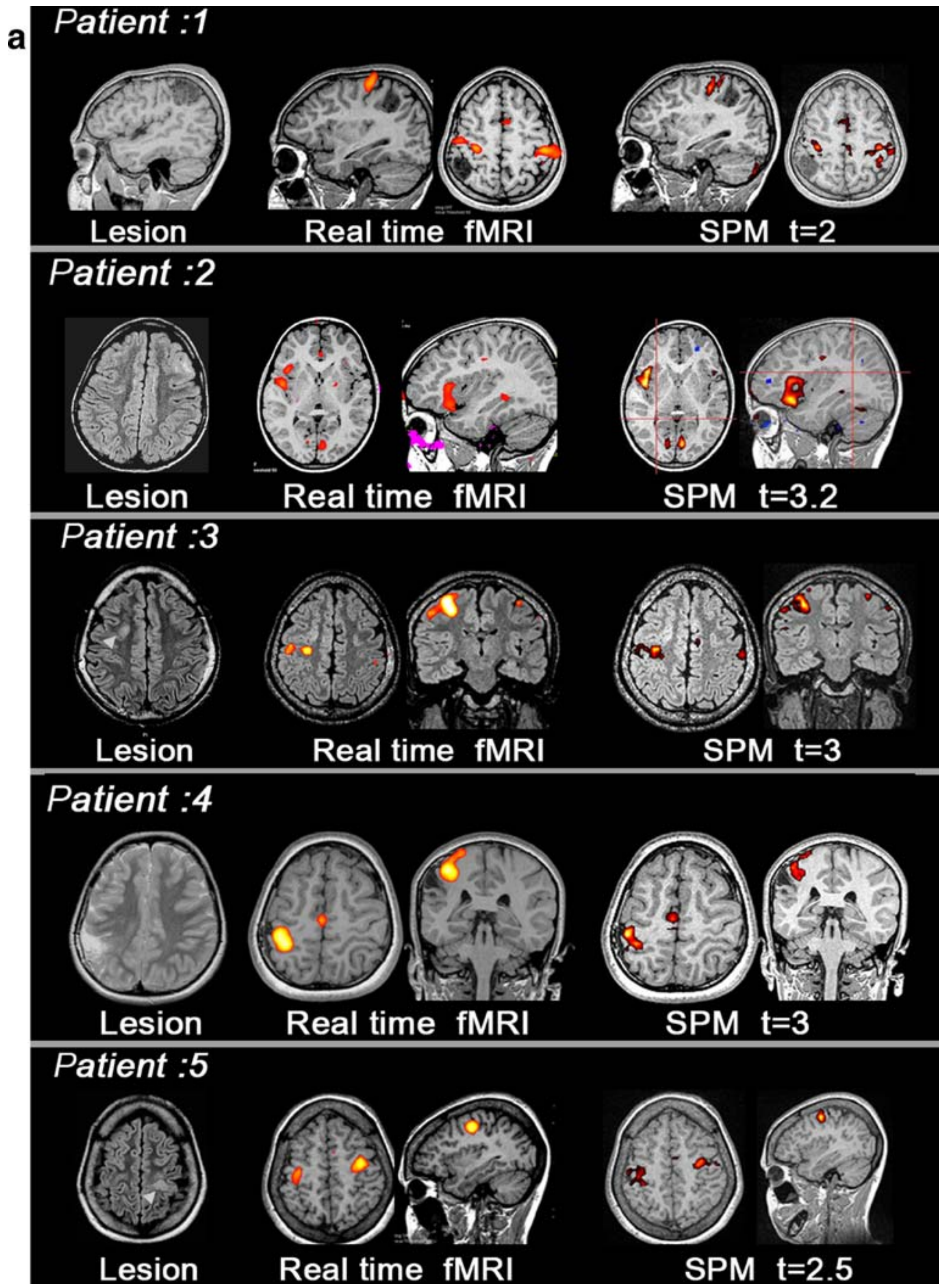

Fig. 1 Comparison of real-time fMRI and SPM in ten children (**a** patients 1–5, **b** patients 6–10). In each patient the first image shows the epileptogenic lesion. The second set of images shows the result of real-time processing, and the third set shows the result of SPM processing. The threshold used in the SPM processing is mentioned in each case. The threshold used in real-time fMRI (Student's *t*-test) in all patients was 4. In patients 3 and 5, the lesion (focal cortical dysplasia) is indicated by an *arrowhead*

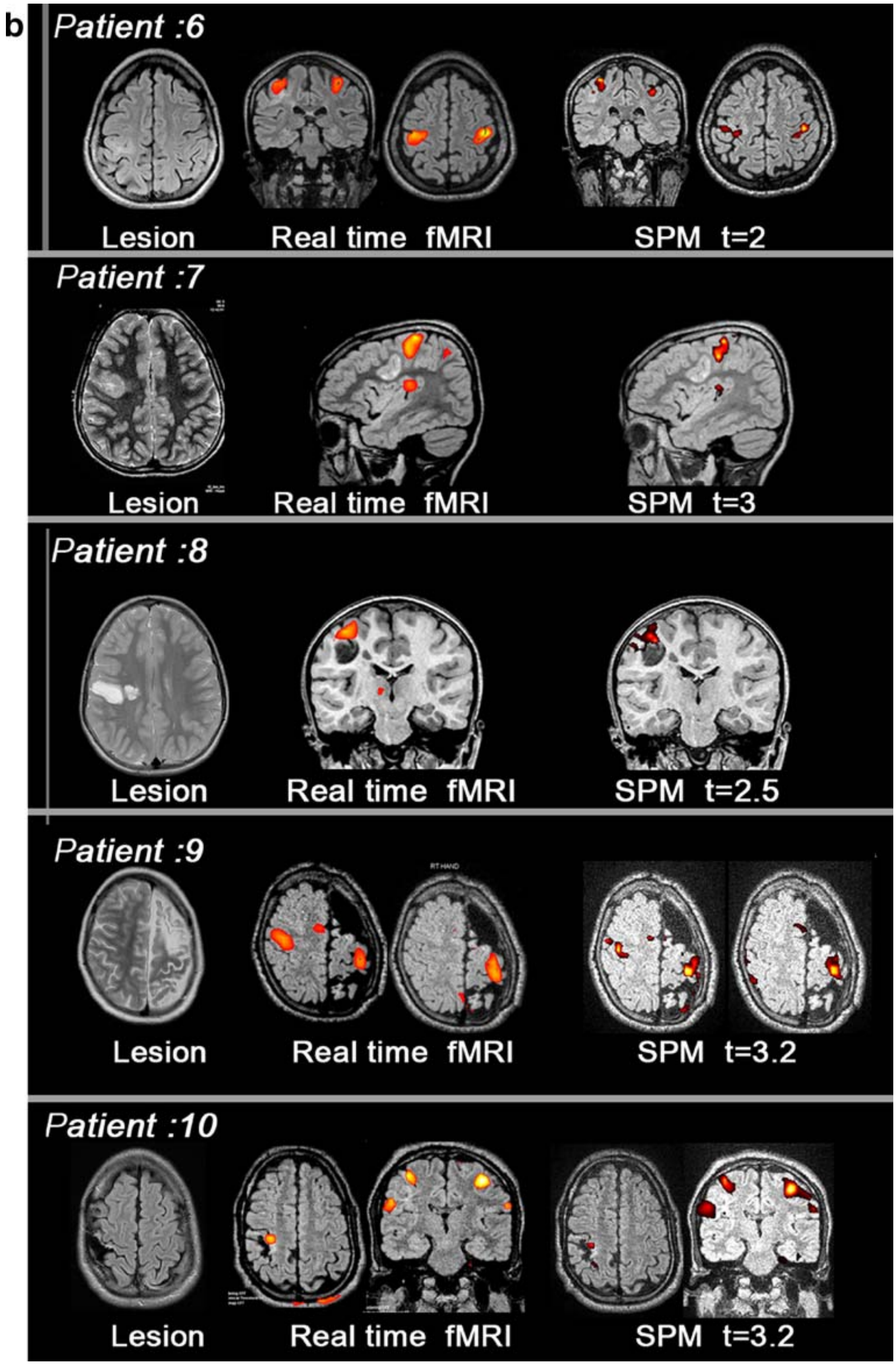

Fig. 1 (continued)

gical neurological assessment. Among these 12 patients, 4 showed cortical dysplasia on histopathology, 3 had gliosis, 2 had a dysembryoplastic neuroepithelial tumour (DNET), and 1 each had oligodendroglioma, low-grade glioma and astrocytoma.

Imaging

After the procedure was explained to the patient and parent or guardian, the patient was positioned in a 1.5-T MR imager (Avanto SQ engine, Siemens, Erlangen, Germany).

The auditory stimulus was delivered using MR imaging-compatible earphones. The visual paradigm was delivered through MR imaging-compatible goggles (Avotec, Stuart, Fl.) or in younger patients using a projector and screen connected to the computer.

Anatomical landmark images of the entire head were obtained with a 3-D spoiled gradient-recalled acquisition in the steady state sequence (3-D FLASH; TR/TE 11/4.94 ms, flip angle 15°, field of view 256 mm, slice thickness 1 mm, matrix 256×256). Following the availability of 3-D FLAIR (TR/TE/TI 5,000/405/1,800 ms, field of view 256 mm, slice thickness 1 mm, matrix 256×256) this additional sequence was used in ten patients. These sequences were used for final coregistration of the fMRI images to the anatomical images. The same sequence was used in both real-time and off-line processing for coregistration. The fMRI sequence (gradient-echo echoplanar 2-D PACE dynamic motion corrected) based on the blood oxygenation level-dependent (BOLD) effects (TR/TE 3,580/50 ms, flip angle 90°, field of view 250 mm, matrix 64×64) was applied after the gradient field mapping. By using the information from the gradient field map (map of the B0 field), it was possible to mask the image areas where there was distortion and local signal loss. A total of 36 transverse sections were obtained, each with a section thickness of 3 mm and an intersection gap of 0.8 mm. The total acquisition time for 100 measurements was 6.02 min.

Paradigms of eloquent areas were tailored according to the brain region of the suspected seizure focus. Motor, sensory and visual areas were explored when needed, according to the clinical particularities of each case. fMRI language paradigms included verbal fluency tasks and verb-generation tasks. In the task concerned with verbal fluency, the patient had to think of as many words as possible in each of five different categories (animals, vegetables, birds, cities and fruits). In the verb-generation task, the patient had to silently generate one or more verbs related to a list of nouns that were orally or visually presented. In children below 8 years of age who found silent verb generation difficult, overt verb generation was allowed. During the off epoch (baseline), the patient was given meaningless words or words in a language the patient could not understand.

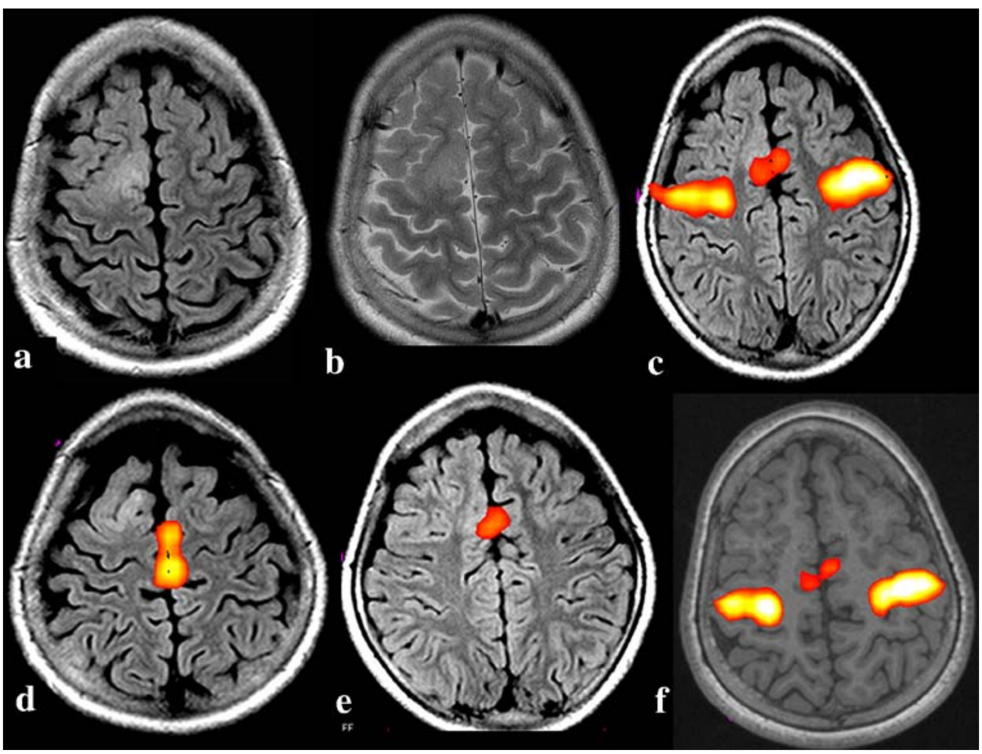

Fig. 2 Patient 23. Right superior frontal focal cortical dysplasia in a 10-year-old boy. **a**, **b** Axial (**a**) FLAIR and (**b**) T2-W images show thickening and hyperintensity on the medial aspect of the right superior frontal cortex. There is poor grey–white matter differentiation at the boundaries of the lesion. **c** Real-time fMRI coregistered on 3-D FLAIR obtained after bilateral finger tapping vs. rest shows that the activation of the supplementary motor area (SMA) lies on the lesion. The primary hand motor area is located about 1 cm away from the lesion. **d**, **e** Real-time fMRI coregistered on 3-D FLAIR obtained after bilateral toe movement vs. rest shows the closeness of the right foot motor area to the lesion. Again the SMA activation is seen lying on the lesion. **f** Real-time fMRI coregistered on 3-D FLASH. The lesion is poorly visualized in the 3-D FLASH sequence and hence the activation of the SMA within the lesion is hardly appreciated on the coregistered image. If the surgery is limited to the SMA the chance of developing postsurgical neurological deficits is minimal. However if the resection extends to the primary motor areas the chance of developing deficits is high. The primary motor areas were preserved during surgical resection with no postoperative deficits

The parents of patients below 10 years of age were requested to teach the child the commonly used nouns and their corresponding verbs before performance of the task. Motor paradigms included finger tapping contrasted with rest for the hand, and toe movement contrasted with rest for the leg. Movement of both hands/legs was studied together and individually. The visual paradigm included observing flashing lights during the on epoch and observing a blank screen during the off epoch. Each paradigm consisted of five off and five on blocks each lasting for 30 s. For the visual paradigm only three on and off blocks were used since good real-time activation was noted. The patient was briefly trained and tested with similar exercises before the procedure to ensure comprehension and good performance of the tasks. Subsequent image data were analysed using the vendor-supplied inline BOLD software (real-time fMRI). The inline BOLD data were coregistered on the 3-D FLASH and/or 3-D FLAIR sequences to get the final fMRI images.

Study analysis

Real-time fMRI using inline BOLD requires loading of the Neuro 3-D task card, which is used to examine results of functional imaging in their anatomical context. The anatomical data set is first loaded followed by the activation map, relevant BOLD volume and the field map. The functional visual property of the task card was then used to display the functional information. In the inline BOLD *t*-test (Student's *t*-test) activation maps were generated to reveal the degree to which variations in MR signal intensity corresponded to fluctuations in task stimulus and performance. These maps were thresholded to a *t* value of 4.

The fMRI data of the first ten patients were also analysed using SPM 2. SPM refers to the construction and assessment of a spatially extended statistical process used to test hypotheses about neuroimaging data from fMRI. The steps used in SPM processing were realignment for motion correction and

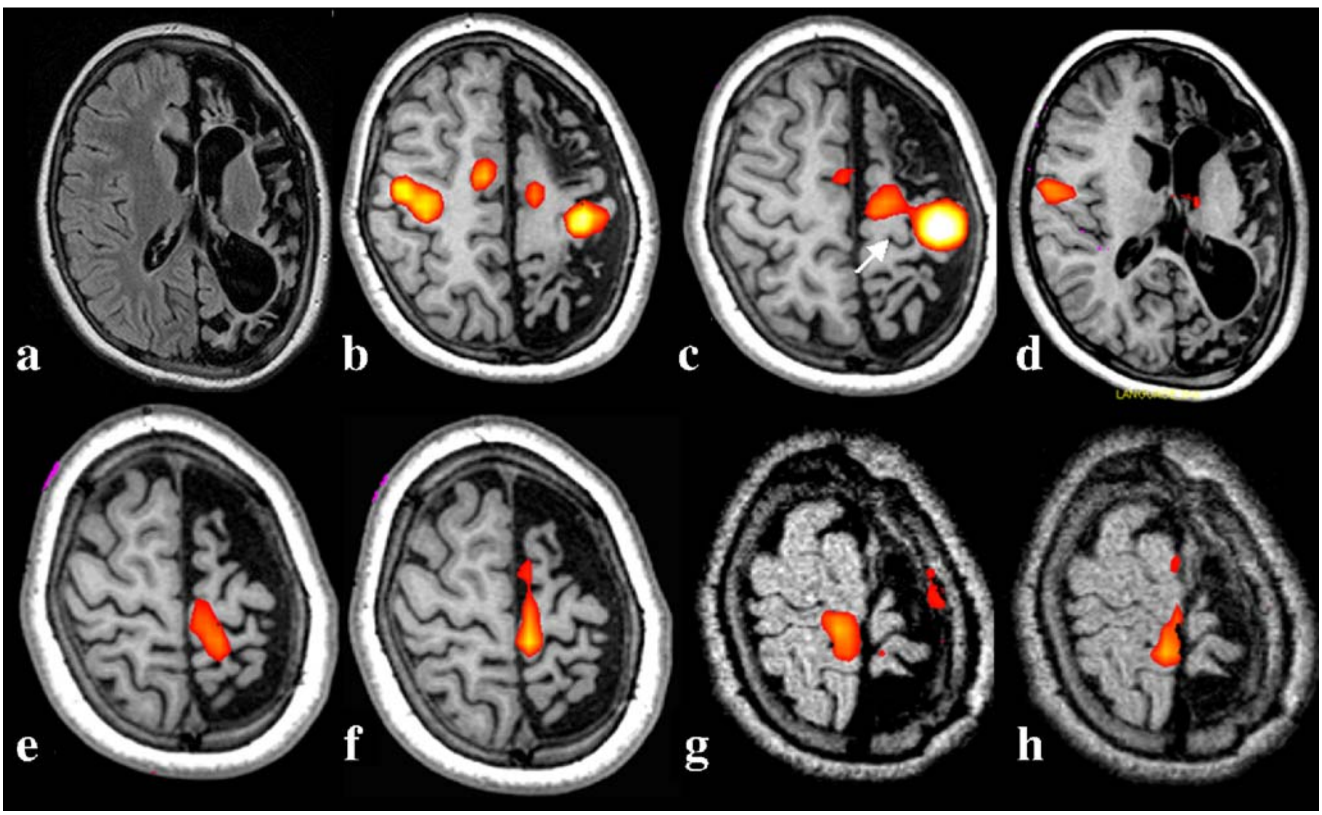

Fig. 3 Patient 9. A 13-year-old left-handed boy with left hemispheric atrophy following left frontal subdural haematoma possibly secondary to haemorrhagic disease of the newborn. **a** Axial FLAIR image shows marked gliosis and atrophy of the left hemisphere. **b**, **c** Real-time fMRI coregistered on 3D FLASH sequence: bilateral finger tapping vs. rest (**b**) and right finger tapping vs. rest (**c**) show that the left motor hand area subserves the function of the right hand. Note the relative shift of the motor activation more laterally from the anatomical hand area (*arrow*). **e**, **f** Bilateral leg movement vs. rest (**e**) and left leg movement vs. rest (**f**) show activation only from the left leg area. Interestingly there was no right leg area activation even on moving the left leg. **d** Verb-generation task vs. hearing meaningless words shows right lateralized language. During the Wada test, on injection of the left internal carotid artery there was right hemiplegia with paraparesis. A left hemispherotomy would result in seizure freedom, but would be complicated by right hemiplegia in this boy. Based on this information the left motor strip was spared during surgery with mild postoperative weakness of right upper and lower extremities. **g**, **h** Real-time fMRI coregistered on 3-D FLAIR sequence 1 year after hemispherotomy: bilateral leg movement vs. rest (**g**) and left leg movement vs. rest (**h**) shows shift of activation of leg movements to the right side

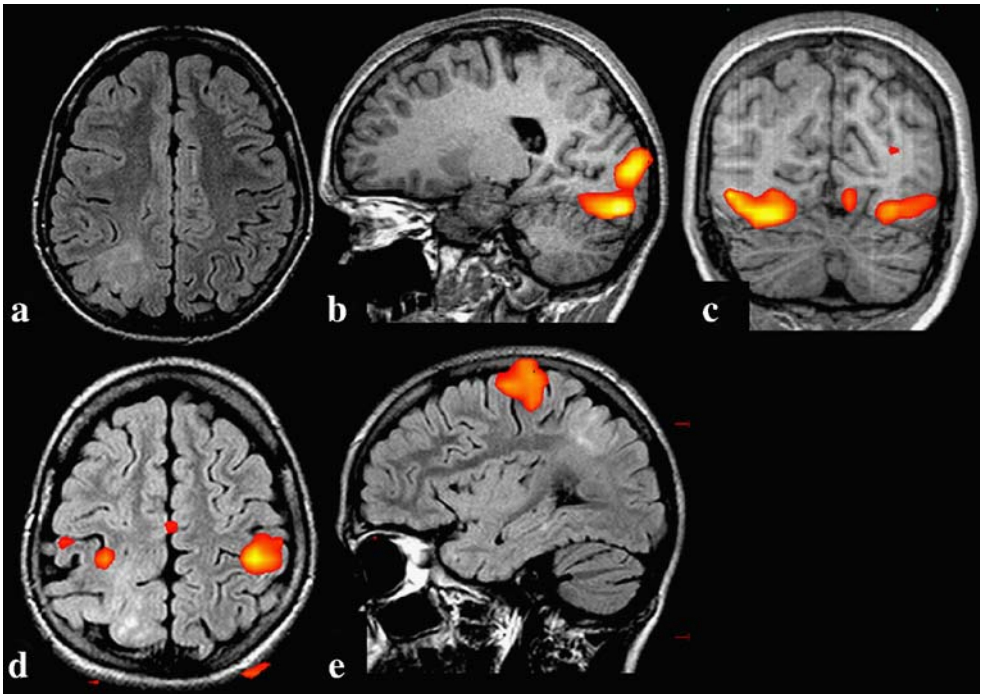

Fig. 4 Patient 11. A 14-year-old boy with right parietal focal cortical dysplasia. **a** Axial FLAIR image shows thickening with hyperintensity in the right parietal cortex and underlying white matter suggestive of cortical dysplasia. Since there was an aura of blindness, the epilepsy management team decided to perform an fMRI for mapping the visual areas. **b**, **c** Real-time fMRI coregistered on sagittal (**b**) and coronal (**c**) 3-D FLASH obtained after performing visual stimulation shows that the lesion is anterior and superior to the primary visual areas. The distance between the area of visual activation and the lesion is more than 2 cm. **d**, **e** Real-time fMRI coregistered on axial (**d**) and sagittal (**e**) 3-D FLAIR obtained after bilateral finger tapping vs. rest shows that the lesion is close to the right motor cortex. Since there was good clinical, electrographic and radiological concordance, he underwent lesionectomy with cortical mapping. The parents of the patients were warned about a possible lower limb weakness after surgery. Part of the lesion close to the leg area was not resected, thus avoiding postsurgical limb weakness

smoothing. Smoothing was done by convolving with a Gaussian kernel (FWHM of two voxels) and thresholded to a *t* value that varied from 2 to 3.2 depending on optimal localization of activation foci. The corresponding *P*-values varied from about 0.01 to 0.001. The coregistration of fMRI data into anatomical images (3-D FLASH/3-D FLAIR) was done using the software routinely available in SPM. MRIcro (http://www.sph.sc.edu/comd/rorden/mricro.html) was used to display the coregistered statistical images on the anatomical image. This program converts images to SPM-friendly Analyze format. It can also show images in many different formats, and export images in BMP, JPEG, PNG or TIF formats.

SPM processing of the data was done by an image processing specialist (S.S.). The fMRI images produced by real-time processing were then compared with SPM processed images by a neuroradiologist (C.K.). A visual comparison of the cortical areas of activation and amount of activation for the above-mentioned thresholds were done on the co-registered activation maps.

Results

In all the initial ten patients in whom a comparison of real-time fMRI and SPM processing was done (patients 1 to 10; Table 1), paradigms of sensorimotor, visual and language stimulation matched. There was significant concordance between the two techniques for the area of activation, amount of activation and the distance of the activated area from the lesion (Fig. 1). The threshold used in the SPM processing was indicated with each case. A lower threshold was used with SPM in comparison to real-time processing in all the patients. The result obtained was considered as a validation of the real-time fMRI processing, and this encouraged the epilepsy team to do away with the time-consuming off-line processing in the subsequent fMRI studies. Coregistration of the fMRI data on a 3-D FLAIR sequence gave better information about the relationship between the lesion and the area of activation (Fig. 2; patient 23). This was visually appreciated in all the patients in whom the coregistration of real-time fMRI was done on both the T1-weighted 3-D FLASH sequence and the 3-D FLAIR sequence. The site and extent of the lesion, especially focal cortical dysplasia, was seen with the FLAIR sequence, but was hardly seen with the FLASH sequence. The cortical dysplasia in patients 3, 5, 6 and 23 was hardly visualized in the 3-D T1-weighted FLASH sequence. Except for patient 5, the coregistration was also performed using 3-D FLAIR, which showed the distance between the lesion and the cortical activation.

In the small subgroup of five patients in whom we undertook fMRI and Wada testing (patients 9, 13, 16, 17 and 20) the results were similar in all except one patient (patient 17) in whom the Wada testing showed codominance for language and memory functions while there was strong right lateralized language on fMRI. In six patients, language lateralization was based solely on the fMRI results. The fMRI results of most of the patients in our study showed a strong language lateralization to one side. The fMRI results agreed with the results of intraoperative cortical stimulation in all six patients where both were performed (patients 1, 9, 11, 12, 17, and 23). The fMRI predicted the postsurgical neurological deficits in four patients (patients 9, 11, 15, 16) in whom the lesion was located extremely close to the eloquent cortex (Fig. 3; patient 9).

The results of fMRI altered patient management in a significant number of patients. Five patients in whom the lesions were located on or very close to the eloquent cortex and appeared to be benign/slow-growing on conventional MR imaging (focal cortical dysplasia, gliosis or DNET) were advised to continue with conservative management with regular follow-up until the seizures become more frequent and intractable. A further six patients who had very frequent seizures with a lesion lying close to or in the eloquent cortex underwent surgery with intraoperative cortical mapping. In many patients (patients 9, 11, 14, 19, 23) who underwent surgery, the extent of surgical resection was altered because eloquent areas were identified close to the seizure focus (Fig. 4; patient 11). As the seizure team gained more confidence in the fMRI results, invasive techniques such as the Wada test were avoided. Six patients, three of them below 10 years of age (patients 2, 21, 22), underwent only fMRI for language lateralization. In the majority of patients, the neurologists and neurosurgeon thought that the fMRI results altered patient and family counselling. The chances of developing a postsurgical neurological deficit could be better explained by showing the fMRI results and explaining the relationship of the functional activation to the lesion.

Discussion

The advent of real-time fMRI has made this imaging technique less time-consuming, easily performable and more clinically feasible. This technique is especially useful in children because studies can be monitored and stopped if the child is not cooperative during the procedure. It was, however, essential to confirm that the findings we obtained in real-time studies were true and hence we felt that validation of the results of on-line processing compared with those of well-known off-line processing techniques such as SPM was necessary. Since there was a high degree of concordance between real-time fMRI and SPM processing in all our initial group of ten patients, we believe that for routine clinical fMRI with simple block design paradigms, real-time fMRI using inline BOLD gives equally reliable results. The lower thresholds used in SPM processing are probably due to differences in the statistics used in the data processing between the two techniques. Schwindack et al. [6] reported that the activation produced by real-time fMRI for finger tapping and ankle movement was similar to that in SPM in a study of 11 patients with brain tumours.

In most of the earlier fMRI studies in which off-line processing of data was done, the coregistration was done on 3-D T1-weighted (3-D FLASH/SPGR) images. While this is adequate for an experimental set-up in volunteers, clinical fMRI in patients with brain lesions will be of much higher utility if coregistration is done on FLAIR or other T2-weighted sequences. This is because the lesion, especially a cortical dysplasia, and its extent are best appreciated with the FLAIR sequence and the distance between the lesion and the activation can be better appreciated. In our study, after the availability of a 3-D FLAIR sequence on our machine, we started coregistering the inline BOLD information to this sequence. The relationship between the activation and the lesion was easily appreciated once the coregistration was done on 3-D FLAIR.

Initially fMRI studies were primarily concerned with the feasibility and the validity of fMRI compared with corticography [16–18]. Most of the studies revealed good spatial correlation between the two methods. The findings were similar in our small subgroup of six patients. It was decided to perform intraoperative cortical mapping in these six patients because the fMRI had shown the nearness of the eloquent cortex to the lesion. Once a lesion has been localized to the eloquent area, it becomes important to assess the risk that a deficit may follow therapeutic intervention. Yetkin et al. [19] showed that when the distance between the representations of brain function (activated area) exceeds 2 cm, the patients show no postresection deficit and resection is safe. However, as the distance between the lesion and brain function decreased, the likelihood of postoperative deficits increased. When the lesion margin was 1–2 cm from the zone of activation, 33% of patients showed postoperative deficits. When the lesion margin was <1 cm from the zone of activation, 50% of patients experienced a postoperative deficit. This criterion is being used at our centre for counselling the patient and relatives regarding the relative risk of developing postsurgical neurological deficits.

An understanding of language lateralization is needed for presurgical planning of patients with a lesion close to the speech areas and in patients with intractable temporal lobe epilepsy (TLE). fMRI is able to spatially resolve functional activation within each hemisphere, and potentially guide tailored resections to spare the eloquent cortex. One of our patients (patient 2) had intractable seizures due to cortical dysplasia in the left hemisphere close to the motor speech area. Fortunately, the language lateralization was to the lesion-free right hemisphere and hence surgery was performed without the risk of producing a postsurgical language deficit. In another patient (patient 19) where the cortical dysplasia was placed close to the activated Broca's area, a tailored resection preserving the language area was performed. We have seen that the shift in language functions is difficult to predict in patients with malformations of cortical development. Knowledge of the distance between the angular gyrus subserving language and the cortical dysplasia in patient 12 permitted the surgeon to perform lesionectomy without producing a language deficit. Since several earlier studies have shown a good correlation between Wada testing and fMRI, our epileptologists have stopped doing the invasive Wada test for language lateralization. Also, in children below 10 years of age it is extremely difficult to perform Wada testing for language function. fMRI definitely serves as a noninvasive alternative, as was seen in three of our patients.

Several patients in this case series illustrate the role fMRI played in preoperative decision making by the epilepsy team. In five patients the expected postsurgical neurological deficits were weighed against conservative management with a trial of newer antiepileptic medication, and the decision was for conservative management. The decision to use intraoperative cortical mapping was made on the basis of the fMRI results. This helped the surgeon in surgical planning by deciding to preserve motor function close to the lesion. In a few of the subsequent cases the surgeon felt that he could rely on the findings of fMRI and avoid the invasive cortical mapping technique. In a retrospective study, Lee et al. [20] evaluated the therapeutic efficacy of fMRI and determined how often and in what ways fMRI studies influenced the management of individual patients. This study concluded that in epilepsy patients, fMRI results helped to assess the feasibility of resection in 70% of patients, to plan the surgical procedure in 43%, and to carry out invasive mapping in 52%.

Conclusion

The technique of real-time fMRI has made functional MRI an easily performable diagnostic tool for presurgical assessment of a paediatric patient with epilepsy. The results of this technique have been validated with the conventionally used off-line processing technique. Since the results of the fMRI technique correlated well with those of the Wada test, intraoperative cortical stimulation and postsurgical neurological assessment, the need for invasive interventions can be avoided or at least reduced. Finally, fMRI results influenced diagnostic and therapeutic decision making of the seizure team.

Acknowledgements The authors thank Mrs. Aley Alexander (neuropsychologist), Mrs. Annamma George (speech therapist), Ms. Haritha, and Mr. Sarin (project engineers) and the MR technologists for helping us perform the fMRI studies. The authors thank the Director of SCTIMST for permission to submit the paper for publication.

References

1. Berger MS, Cohen WA, Ojemann GA (1990) Correlation of motor cortex brain mapping data with magnetic resonance imaging. J Neurosurg 72:383–387
2. Gregorie EM, Goldring S (1984) Localization of function in the excision of lesions from the sensorimotor region. J Neurosurg 61:1047–1054
3. Bagarinao E, Nakai T, Tanaka Y (2006) Real time functional MRI: development and emerging applications. Magn Reson Med Sci 5:157–165
4. Cohen MS (2001) Real-time functional magnetic resonance imaging. Methods 25:201–220
5. Yoo SS, Guttmann CR, Zhao L et al (1999) Real adaptive functional MRI. Neuroimage 10:596–606
6. Schwindack C, Siminotto E, Meyer M et al (2005) Real time functional magnetic resonance imaging (rt-fMRI) in patients with brain tumours: preliminary findings using motor and language paradigms. Br J Neurosurg 19:25–32
7. Liegeois F, Connelly A, Cross JH et al (2004) Language reorganization in children with early onset lesions of the left hemisphere: an fMRI study. Brain 127:1229–1236
8. Wada J, Rasmussen T (1958) Intracarotid injection of sodium amytal for the lateralization of cerebral speech dominance. J Neurosurg 17:266–282
9. Binder JR, Swanson SJ, Hammeke TA et al (1996) Determination of language dominance using functional MRI: a comparison with Wada test. Neurology 46:978–984
10. Woermann FG, Jokeit H, Luerding R et al (2003) Language lateralization by Wada test and fMRI in 100 patients with epilepsy. Neurology 61:699–701
11. Cao Y, Vikingstad EM, Huttenlocher PR et al (1994) Functional magnetic resonance studies of the reorganization of the human hand sensorimotor area after unilateral brain injury in the perinatal period. Proc Natl Acad Sci USA 91:9612–9616
12. Cramer SC, Nelles G, Benson RR et al (1997) A functional MRI study of subjects recovered from hemiparetic stroke. Stroke 28:2518–2527
13. Alkadhi H, Kollias SS, Crelier GR et al (2000) Plasticity of the human motor cortex in patients with arteriovenous malformations. A functional MR imaging study. AJNR 21:1423–1433
14. Thulborn KR, Carpenter PA, Just MA (1999) Plasticity of language-related brain function during recovery from stroke. Stroke 30:749–754
15. Dettmers C, Liepert J, Adler T et al (1999) Abnormal motor cortex organization contralateral to early upper limb amputation in humans. Neurosci Lett 263:41–44
16. Jack CR Jr, Thompson RM, Butts RK et al (1994) Sensory motor cortex: correlation of presurgical mapping with functional MR imaging and invasive cortical mapping. Radiology 190:85–92
17. Lehericy S, Duffau H, Cornu P et al (2000) Correspondence between functional magnetic resonance imaging somatotopy and

individual brain anatomy of the central region: comparison with intraoperative stimulation in patients with brain tumors. J Neurosurg 92:589–598
18. Puce A, Constable RT, Luby ML et al (1995) Functional magnetic resonance imaging of sensory and motor cortex: comparison with electrophysiological localization. J Neurosurg 83:262–270
19. Yetkin FZ, Mueller WM, Morris GL et al (1997) Functional MR activation correlated with intraoperative cortical mapping. AJNR 18:1311–1315
20. Lee CC, Ward HA, Sharbrough FW et al (1999) Assessment of functional MR imaging in neurosurgical planning. AJNR 20:1511–1519