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ORIGINAL ARTICLE

CME

Blood Oxygen Level–Dependent Functional Magnetic Resonance Imaging in Preoperative Brain Mapping and Making Surgical Decisions

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ABSTRACT

Objective: *To evaluate the efficacy of blood oxygen level–dependent functional magnetic resonance imaging in the preoperative mapping of sensorimotor cortices and language areas, and its impact on surgical decisions.*

Methods: *Fourteen patients with tumours or vascular malformations underwent functional magnetic resonance imaging (in the course of motor, sensory, and language tasks) and had structural magnetic resonance imaging scans in a 1.5T scanner. The functional magnetic resonance imaging findings were then correlated with their operative and clinical outcomes. Seven patients had a craniotomy with general anaesthesia, three had awake craniotomy with intraoperative mapping, two had radiosurgery, and two had no surgery.*

Results: *The technical success rate of functional magnetic resonance imaging signal activation in identifying eloquent cortices was 100% for all tasks except Chinese reading, for which the success rate was 83%. Functional magnetic resonance imaging mapping accuracy was determined by correlation with intraoperative cortical stimulation or somatosensory-evoked potentials phase reversal. Surgical decision making was influenced by functional magnetic resonance imaging in 75% of the patients, using a more aggressive approach in two patients and a safer approach in two others (due to lesion proximity of <2 cm from eloquent centres). More conventional craniotomies were performed in five patients due to larger margins (>2 cm) or contralateral location of the language centre. In one patient, there were conflicting results between Wada test and functional magnetic resonance imaging with respect to speech lateralisation; intraoperative cortical stimulation found that functional magnetic resonance imaging correctly predicted the side of speech dominance.*

Conclusion: *Blood oxygen level–dependent functional magnetic resonance imaging had a high technical success rate and was very accurate in mapping eloquent cortical areas preoperatively. Its role in preoperative surgical assessment is pivotal, and is recommended for most, if not all, resective brain surgery.*

Key Words: *Brain mapping; Magnetic resonance imaging; Neurosurgery*

中文摘要

血氧水平依賴腦功能磁共振成像對於 術前研究腦功能區活動的效用及對手術方式的影響

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目的：評估血氧水平依賴腦功能磁共振成像對於術前研究感應運動腦皮質區及語言區活動的效用，以及對手術方式採用決定的影響。

方法：14名患有腫瘤或血管畸形的病人接受功能磁共振成像（通過運動、感覺及語言任務）及1.5T的結構磁共振成像。並探討功能磁共振成像的結果與術中及臨床結果的相關性。最終共有7名病人接受全身麻醉的顱骨切開術、3人接受喚醒麻醉的顱骨切開術及術中成像、2人接受放射外科手術、2人未有接受手術。

結果：使用功能磁共振成像的信號強度辨認語言功能區的技術性成功率為100%，但閱讀中文方面則只有83%。腦功能磁共振成像的準確度的驗證取决於術中皮層電刺激或皮層體感誘發電位逆轉。有75%病人因功能磁共振成像的結果而影響其做手術方式的決定，其中2人採用更進取的方法，另2人因病灶距離語言功能區只有不足2 cm，所以採用較安全的方法。另5人由於距離大（超過2 cm）或語言區在對側位置，遂進行傳統的顱骨切開術。另1人的瓦達測試（Wada test）與功能磁共振成像在語言側化方面的結果矛盾，後進行術中皮層電刺激測試確定功能磁共振成像正確預測語言區優勢的一邊。

結論：血氧水平依賴腦功能磁共振成像有較高技術成功率，在術前辨認語言功能區方面相當準確。此技術對於術前評估起了關鍵作用，可推薦作大部分腦腫瘤切開術用作術前評估。

INTRODUCTION

As a non-invasive radiological tool, functional magnetic resonance imaging (fMRI) is used to localise eloquent brain regions, such as motor function, sensation and language, based on the change in ratio of oxyhaemoglobin to deoxyhaemoglobin, known as the blood oxygenation level–dependent (BOLD) effect. Notably, fMRI combines anatomical with functional information and has therefore been widely used for preoperative planning.[1] Surgeons can use this information preoperatively to determine the feasibility of a resection or the functional consequences of a planned resection. In addition, it may provide additional information pertinent to the surgical approach and selection of patients for invasive functional mapping.[2]

The aims of this study were to evaluate the efficacy of BOLD fMRI in preoperative mapping of sensorimotor cortices (BA 1-3, 4), language centres such as Broca's (BA 44, 45) and Wernicke's (BA 22, 39, 40) areas, and its effect on surgical decision-making.

METHODS

Patients

Fourteen Chinese patients with tumours (n = 8) and vascular malformations (n = 6) were studied. All the patients were referred from a university neurosurgical unit for preoperative brain mapping of eloquent cortical areas. The study received ethical approval by the local Institutional Review Board and each patient gave written informed consent prior to participation. There were seven male and seven female patients, with a mean age of 33 (range, 13-62) years. Seven patients had

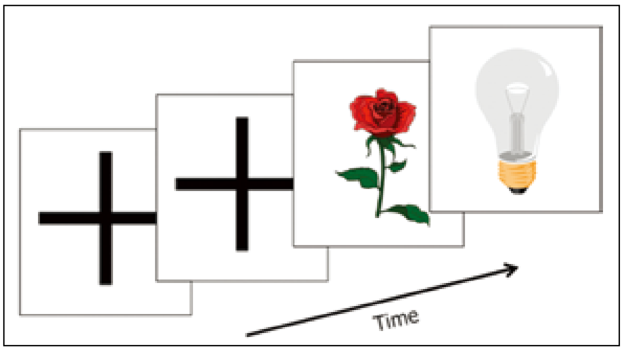

Figure 1. Paradigm for picture-naming task: subjects were asked to fixate on the cross and then silently name the pictures that appeared on the screen.

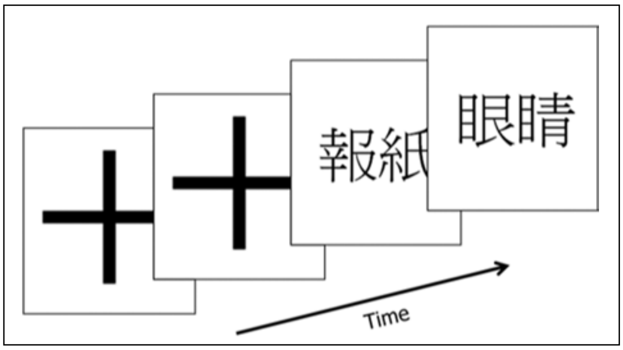

Figure 2. Paradigm for silent-reading task: subjects were asked to fixate on the cross and then silently read the Chinese words or proverbs shown on the screen.

a craniotomy with general anaesthesia, three had awake craniotomy with intraoperative mapping, two underwent radiosurgery, and two had no surgery.

Imaging

All magnetic resonance (MR) images were obtained using a 1.5T whole-body scanner (Intera-NT; Philips Medical Systems, Best, The Netherlands) equipped with echo-planar imaging (EPI) capabilities. Structural MRI scans included SE T1-weighted sequences for anatomical correlation. Imaging parameters of T1-weighted images were as follows: TR/TE = 1680 ms/11 ms, field of view = 175 mm × 220 mm, 5-mm section thickness, 1.5-mm intersection gaps, 256 × 256 matrix, and 24 sections acquired to cover the whole brain.

Functional Tasks

All patients undertook fMRI tasks (motor, sensory, and language in addition if deemed necessary). All paradigms were performed on a Windows XP platform, which could provide real-time video stimulus presentations, behavioural response monitoring, and accurate synchronisation with the MR imager. For sensorimotor tasks, patients were asked to squeeze a tennis ball with their hand, extend or flex the foot plantar, and were brushed on the dorsum of the hand. For language tasks, patients were shown pictures (targeting Broca's area) or Chinese proverbs or words (targeting Wernicke's area), and were asked to silently name or read (as shown in Figures 1 and 2). All patients were trained in verbal and motor tasks 10 minutes prior to examination by a dedicated physicist, radiologist, or experienced radiographer. Stimuli were projected onto a translucent screen positioned alongside the MR imager, and were viewed by way of a mirror mounted on the head coil.

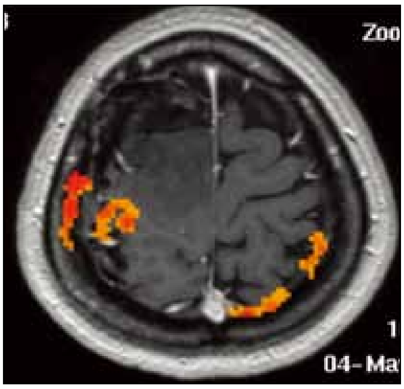

Figure 3. A patient with an oligodendroglioma: left hand motor task showing expected location of motor cortex in right precentral gyrus and grade III signal.

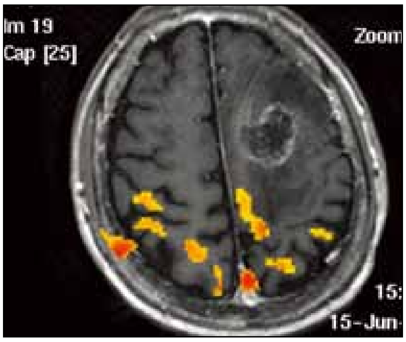

Figure 4. Preoperative magnetic resonance imaging in a patient with a glioblastoma multiforme. Right foot sensory task — grade II/III activation in left paracentral lobule, corresponding to the expected location of right foot homologue.

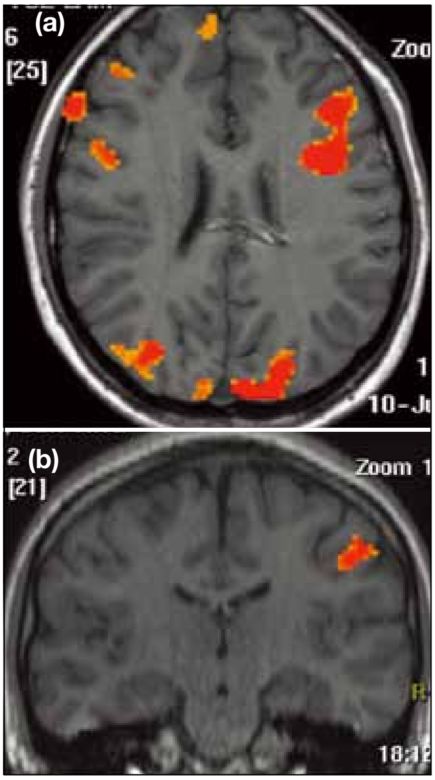

Figure 5. Picture-naming paradigms in two different patients for localisation of Broca's areas. (a) Grade III activation in the left inferior frontal gyrus and grade II signal in the right inferior frontal gyrus, indicating left dominance; and (b) left inferior frontal gyrus grade II activation.

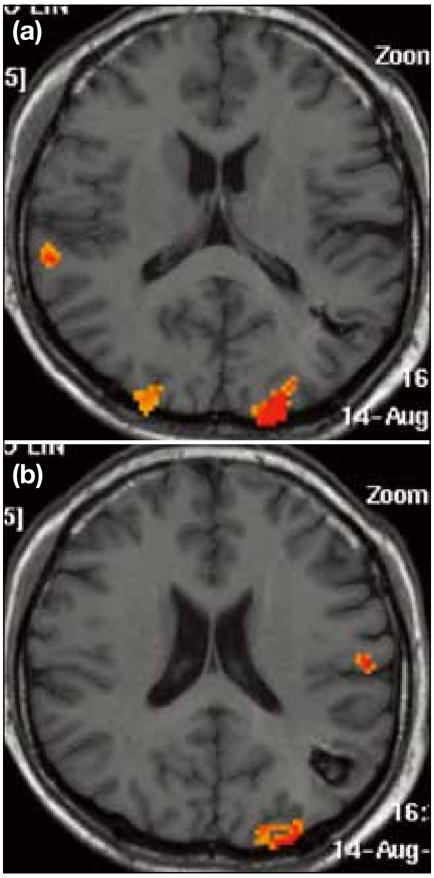

Figure 6. Chinese-reading task in the same patient with a vascular malformation: bilateral grade II activation in superior temporal gyri (Wernicke's area).

The BOLD images were obtained with a gradient EPI pulse sequence (TE = 40 ms; TR = 2000 ms). Each task lasted 2 minutes and 16 seconds (64 dynamics: 4 dummy, 10 rest, 10 active, 10 rest, 10 active, 10 rest, 10 active), with whole brain coverage at 5-mm slice thickness, 128 x 128 matrix size.

Two blinded readers (one neuroradiologist and one neurosurgeon) retrospectively interpreted the T1-weighted images, with thresholded activation maps as a colour-coded overlay, together and reached a consensus reading based on three aspects as described below.

Technical Success

According to the criteria of Håberg et al,[3] activation of eloquent cortical areas were graded as I, II, and III:

- Grade I/unsuccessful — no reliable activated signal was detected in the bilateral hemispheres, or activation was clearly demonstrated in one side of the hemisphere.
- Grade II/fair — location of the central sulcus was revealed. However, the activated voxels were decreased and / or more randomly scattered. Alternately, activity was well-delineated but the result was degraded due to motion artefacts.
- Grade III/very good — the BOLD signal unequivocally delineated the functional central sulcus areas. The functional activity on the affected side might show displacement, compared to the intact side.

Activated areas comparing with expected anatomical location (Figures 3 to 6) showed examples of different paradigms. The grading of activated signals and preservation of expected anatomical locations were demonstrated. Figures 7 and 8 show examples of

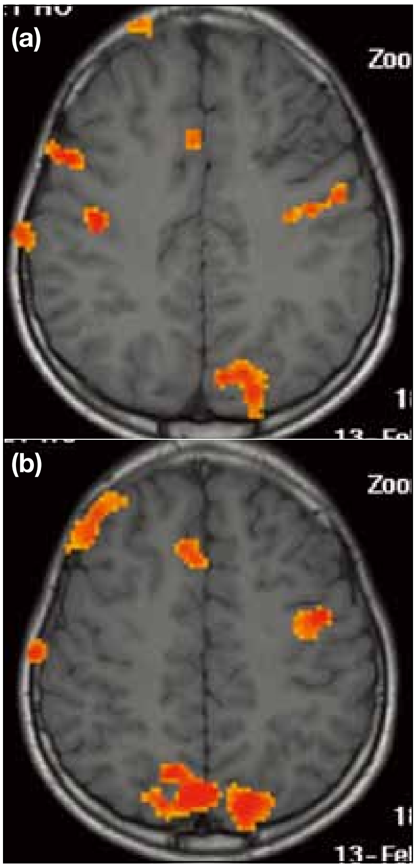

Figure 7. Preoperative functional magnetic resonance imaging in a patient with a left frontal vascular malformation. Picture-naming task: the Broca's area activation is displaced slightly posteriorly from its expected location in the left inferior frontal gyrus.

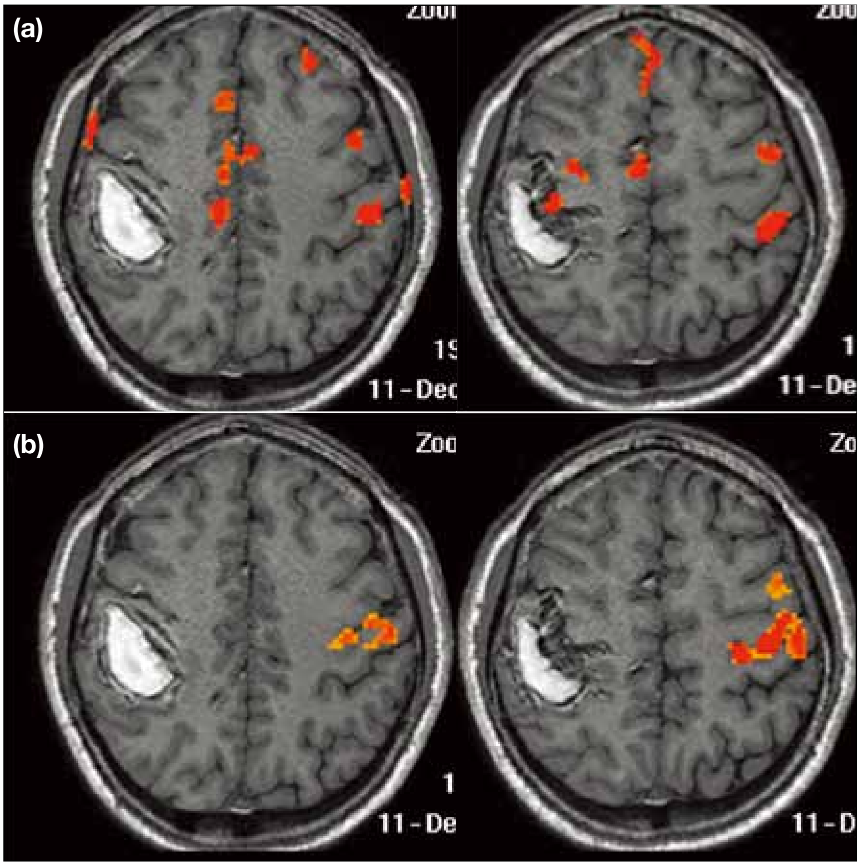

Figure 8. Left hand motor task in a patient with right parietal vascular malformation. (a) Left hand motor task revealed grade II/III left motor cortex and grade II right motor cortex activation, indicating plasticity, and (b) right hand motor task showed grade III left motor cortex activation.

Table 1. Evaluation of technical success — surgical regions of interest.
Note: Sensorimotor evaluation was performed on 14 subjects with a total of 16 tasks since 2 subjects performed both hand and leg paradigms. For picture-naming tasks, 2 subjects underwent the same paradigm twice, one each in the axial and coronal planes.*

Task	Central sulcus (N = 14)		Broca's area (N = 8)	Wernicke's area (N = 6)
	Sensory cortex	Motor cortex		
Sensory (n = 3)	3/3 (100%)	-	-	-
Motor (n = 16)	-	16/16 (100%)	-	-
Picture naming (n = 10)	-	-	9/10 (90%)	-
Chinese reading (n = 6)	-	-	-	5/6 (83%)
Composite sensitivity	14/14 (100%)		8/8 (100%)	5/6 (83%)

Abbreviations: N = total number of patients; n = total number of tasks.

Table 2. Comparison of functional magnetic resonance imaging (fMRI) with intraoperative mapping (5 patients).

Intraoperative (using CS or SSEP)	fMRI (≥2 cm from lesion)	fMRI (<2 cm from lesion)
Eloquent centre proven close (≤1 gyrus)	0	2
Eloquent centre proven far (>1 gyrus)	3	0

Abbreviations: CS = intraoperative cortical stimulation; SSEP = somatosensory evoked potential.

Table 3. Distance of lesion from eloquent centres.

Distance from eloquent centres	No risk (≥2 cm)	Close proximity	Within lesion
Sensorimotor area (14*)	9	5	0
Language (8†)	6	2	0

* Total number of preoperative patients with successful sensorimotor mapping.

† Total number of preoperative patients with successful language mapping.

displaced eloquent and motor areas, respectively, in the presence of pathology.

Accuracy of Functional Magnetic Resonance Imaging in Mapping Eloquent Cortical Areas

This was determined in a subgroup of five patients through correlation with intraoperative cortical mapping or somatosensory-evoked potential phase reversal for the central sulcus, which served as a gold standard.

Effect on Surgical Plan

The effect on the surgical plan was rated based on proximity of lesions to eloquent areas.

RESULTS

Pathological Results and Management

Surgery was performed on 10 patients with the following pathological findings: arteriovenous malformation or AVM (n = 2), cavernoma (1), glioblastoma multiforme or GBM (2), oligodendroglioma (2), oligoastrocytoma (2), meningioma (1). Radiosurgery was performed on two patients with AVMs, and two (one each with a cavernoma, and a calcified tumour) received conservative therapy.

Technical Success

The technical success rate of fMRI signal activation in identifying sensorimotor cortices, Broca's area, and Wernicke's area using anatomical locations on MR scans (as a reference) are shown in Table 1. There was a 100% success rate for sensorimotor function and >80% for speech functions.

Accuracy of Functional Magnetic Resonance Imaging in Mapping Eloquent Cortical Areas

The accuracy of fMRI mapping (5 patients) was determined by correlation with intraoperative cortical stimulation (three patients with awake craniotomy) or somatosensory-evoked potential phase reversal for the central sulcus (performed under general anaesthesia in patients) and was found to be 100% (Table 2).

Effect on Surgical Plan (12 patients)

An assessment of the proximity of brain lesions in relation to the eloquent centres is presented in Table 3. Surgical decision making was influenced by fMRI in 75% of the patients (9 out of 12, excluding 2 who had no surgery). Based on the fMRI findings, for lesions less than 2 cm from eloquent centres, the surgeons either adopted a more aggressive approach (awake craniotomy with intraoperative cortical stimulation[4]) in two (17%) patients or a safer approach (radiosurgery instead of surgical resection) in two (17%) AVM patients. A conventional craniotomy under general anaesthesia was performed in five (42%) patients since their eloquent centres had a 2 cm or larger margin (sensorimotor or language), or were located on the contralateral side (for language).

Of these 12 patients, surgical decision was contrary to fMRI mapping in three patients. A more aggressive approach was decided upon for one patient with a right-sided tumour because the Wada test found right lateralisation for speech dominance, whereas the fMRI found left dominance. However, intraoperative cortical stimulation found negative speech mapping on the right side and fMRI correctly predicted the side of speech dominance. In two patients (one with GBM and the other with an oligodendroglioma), a more conventional approach (using general anaesthesia) was decided based on clinical grounds, although fMRI found eloquent centres close to the lesions.

All patients except one showed no functional deficits postoperatively. The exception, who had only motor but no speech fMRI mapping, developed aphasia postoperatively, which gradually improved to 80% of the preoperative status within months.

DISCUSSION

As a relatively new brain mapping technique, fMRI was first described by Belliveau et al.[5] BOLD fMRI constructs functional images by exploiting the susceptibility produced by the paramagnetic nature of deoxyhaemoglobin.[5-7] Neuronal activation corresponding to specific functional tasks increases local blood flow to the eloquent cortices, which reduces deoxyhaemoglobin concentration and susceptibility, and thus increases signal intensity in a susceptibility-sensitive image.[8] This signal intensity change is referred to as the BOLD effect. Thus, BOLD fMRI has been widely used in research environment into clinical practice.[9,10]

Our study showed that BOLD fMRI had a high technical success rate (83-100%) using anatomical locations on MR scans as reference. On the other hand, intraoperative direct electrostimulation under awake anaesthesia has been used as a gold standard to locate the real site of critical eloquent domains as well as to distinguish functional areas from non-functional areas.[11,12] The results of preoperative BOLD fMRI mapping were compared with those of intraoperative direct electrostimulation in the study. The accuracy of fMRI mapping was determined by correlation with intraoperative cortical stimulation or somatosensory-evoked potential phase reversal for the central sulcus and found to be 100%. Comparison between studies in the literature of preoperative BOLD fMRI and those of intraoperative electrostimulation in this study revealed a general consistency.[13-15]

Notably, fMRI also correctly predicted the side of speech dominance. In one patient, the Wada test finding was contrary to that of fMRI in locating speech dominance; however, intraoperative cortical stimulation found the latter correctly predicted the side of speech dominance. The Wada test was traditionally the gold standard for determination of memory and language dominance, but it is an invasive technique with an incidence of stroke in the region of 0.6%. In the study by Petrella et al,[16] the Wada test that was initially planned for a few patients was cancelled after use of fMRI to localise the language centre. There is a growing volume of literature suggesting that fMRI is a valid alternative to the Wada test for assessing language dominance.[17] Based on its high technical success rate and accuracy, fMRI can be widely used in clinical practice.

The primary goal of neurosurgical treatment of brain lesions is maximal excision with minimal permanent injury to the surrounding normal brain tissue and no resultant neurological deficit. A new deficit may be caused by damage to the cortical areas surrounding a lesion or the brain tissue involved in the surgical approach. Central to minimally morbid surgery is to understand the anatomical and physiological relationship of a lesion to surrounding eloquent brain tissue. It is certainly difficult for neurosurgeons to decide on eloquent areas during an operation. Because of the plasticity of the cortex,[18] the eloquent areas may be displaced or deformed by the mass effects of brain lesions. Moreover, there is no definitive margin to eloquent areas such as Broca's or Wernicke's area, partly because of individual variability.[19] As the gold standard to locate the real site of critical eloquent domains, intraoperative direct electrostimulation technique is invasive, enlarges the operating field, prolongs surgical time, and thus increases the risk of the operation. Functional brain imaging such as fMRI provides information on the anatomic localisation of a variety of brain functions, while diffusion-tensor imaging assesses white matter tracts connecting critical areas. Together with conventional imaging methods used to localise the lesion, functional imaging can be helpful in defining the relationship of the lesion to critical brain structures. They can therefore be used to determine an optimal approach with a smaller craniotomy.

The results of our study indicate that fMRI has a significant effect (75%) on therapeutic planning. Due to proximity of lesions to eloquent centres revealed by fMRI, surgeons adopt either more aggressive or safer approaches. Conventional craniotomies were performed when eloquent centres were located far from the lesions. The effect of fMRI on therapeutic planning has been previously documented; the studies of Wilkinson et al[20] and Jack et al[21] showed no postoperative neurological deficits presented in patients who had undergone the procedure and suggested that it should be performed during therapy planning. The study of Wilkinson et al[20] also showed that fMRI data could be incorporated into neuronavigation-guided surgical approaches, which facilitated safe tumour resection in anatomical areas previously thought to be critical (without intraoperative cortical mapping). In a retrospective study, Lee et al[2] demonstrated that fMRI was complementary to invasive functional mapping. Petrella et al[16] showed that fMRI seemed to increase confidence of neurosurgeons in deciding to proceed with the planned treatment approach in the patients whose treatment plans were not altered. They also found that such surgery confirmed fMRI predictions, even in patients not originally planned to have surgery. The role of fMRI in preoperative surgical assessment is therefore pivotal.

Although there is increasing clinical acceptance of fMRI, its limitations should not be ignored. First, due to the intrinsic mechanism of the BOLD effect, the activation site is related to vessel effects (mainly draining veins), and not directly to neuronal activity. The pathological features of tissues may change the blood flow around the lesions to alter signal intensity on fMRI.[22,23] However, no neurovascular uncoupling was found in our cases with abnormal vasculature, but due caution should be exercised in their interpretation. Second, fMRI reveals the same brain areas that take part in the execution of a task. fMRI cannot differentiate between activation in brain areas that are simply correlated with a particular function and activation in brain areas that are truly essential for performing that function. Moreover, the signal alterations that are detected by the BOLD sequence are in fact very small compared with background noise, so the signal-to-noise (S/N) ratio is low. Sometimes, this low S/N could be improved by repeating experiments and averaging at the expense of time required to scan the patient. This limitation might be overcome with the advent of 3T MRI into clinical practice and a future study on its efficacy is awaited. Third, the paradigms for receptive and expressive speech can be refined. Picture naming and Chinese reading should involve both receptive and expressive speech centres, but the extents of such involvement are different. Empirically, picture naming is a reproducible task for Broca's area while Chinese reading is more variable for localisation of both areas. The current trend of preoperative fMRI tasks include picture naming, sentence completion and verb generation for Broca's area, and text listening for Wernicke's area. We have changed our paradigm for local Chinese to include generation of antonyms and sentence completion for expressive speech. Receptive speech is more accurately depicted by a text-listening task, which has replaced Chinese reading.

In conclusion, BOLD fMRI had a high technical success rate and was very accurate in mapping eloquent cortical areas preoperatively. Its role in preoperative surgical assessment is pivotal. Functional MRI has a significant effect on therapeutic planning in patients and we suggest fMRI be performed for most, if not all, patients undergoing resective brain surgery.

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