Factors related to the magnitude of T2* MR signal changes during functional imaging

Abstract Our aim was to determine whether age, sex, the degree of weakness, anticonvulsants, the histology of the underlying lesion(s), the presence of oedema or the distance of the lesion from the motor region have an impact on the blood oxygenation level-dependent (BOLD) signal strength and therefore on the validity of functional MRI (fMRI). We studied 98 patients with masses near the central region imaged for surgical planning at 1.5 tesla, employing a BOLD sequence during a motor task. We calculated percentage signal change in the primary motor cortex between rest and activation and carried out multiple linear regression to examine the impact of the above factors on signal strength. Using a stepwise analysis strategy, the distance of the lesion from the motor region had the strongest influence ($r = 0.653$, $P < 0.001$). The factor with largest uncorrelated additional impact on signal change was the presence of oedema. Both predictors together formed a highly significant multiple $r = 0.739$ ($P < 0.001$). No other predictive factor was identified (all $P > 0.20$). Disturbances of cerebral blood flow and metabolism induced by the tumour were presumed to be the causes of a decrease in signal in the adjacent cortex.

Keywords Functional magnetic resonance imaging · Surgical planning · Motor cortex
Introduction

A major problem of functional MRI (fMRI) employing the blood oxygenation level-dependent (BOLD) technique is the low signal-to-noise ratio (SNR). Change in signal from small vessels within the brain following motor activation is typically about 2.5% [1]. The problem of a low SNR in the parenchymal vessels becomes especially important when one considers that larger veins with an uncertain spatial relationship to the activated brain tissue have a higher signal change and therefore more significant “activation” than vessels in the parenchyma [2]. In surgical planning, for which some groups use fMRI, this might lead to misinterpretation of the position of cortical areas involved in a specific task. We therefore tried to evaluate what factors affect magnitude of signal change in routine preoperative planning. A few reports describe low signal in patients with masses close to the central region [3, 4, 5], but were based on small series. No study has systematically investigated which factors are related to the magnitude of signal change, possibly because the groups of patients were too small to yield statistically significant results.

We have employed fMRI for surgical planning for tumours close to the central motor region for 3 years, and have examined 110 patients in this way. We retrospectively analysed this group of patients and looked at whether demographic data such as age or sex, the degree of weakness, the medication (anticonvulsants), the histology of the lesion, the presence of oedema or the distance from the motor region had an impact on the BOLD signal strength and therefore potentially on the validity of the fMRI. Our aim was to determine which of these factors were related to imaging failure due to low signal and thereby to examine the limits of fMRI for surgical planning. This might help us decide in which patients functional mapping modalities other than fMRI (e.g. magnetoencephalography, positron-emission tomography or transcranial magnetic stimulation) should be employed for valid localisation.

Materials and methods

We investigated 110 patients, 49 male, 61 female, mean age 48 years, range 9–79 years, with masses affecting the central region. Consent was obtained prior to each functional examination. The lesions were frontal in 55 patients, parietal in 39 and frontoparietal in 16; the right hemisphere was affected in 45, the left in 66 patients (one had a large falxine meningioma affecting both central regions).

MRI was performed on a clinical 1.5 tesla imager with echo-planar imaging (EPI). Head movements were minimised by immobilisation with foam pads and Velcro straps. All images were acquired using a standard head coil. Field homogeneity was optimised for each subject before each scan using an automatic shimming sequence. After localising images, we obtained 15 contiguous 7 mm axial T1-weighted EPI inversion recovery slices for anatomical reference, parallel to the intercommissural line, which typically covered the whole brain including the cerebellum. Imaging parameters were TR 2000 TE 22 TI 400 ms, field of view (FOV) 220×220 mm, matrix 256×256. After the functional imaging the anatomical sequence was repeated with contrast enhancement. BOLD imaging was performed using a multishot T2*-weighted gradient echo EPI sequence: TR 4000 TE 40 ms, flip angle 40°, matrix 64×564, FOV 250×250 mm, slice thickness 7 mm, no interslice gap, 15 slices), at the same level and with the same orientation as the anatomical slices. During a total imaging time of 4.24 min we generated 66 images (4 s/image). Each task paradigm consisted of six 44 s blocks alternating between rest and motor activation.

Statistical analysis of task-related haemodynamic change was performed on a voxel-by-voxel basis using the non-parametric Kolmogorov-Smirnov test, creating statistical maps which were overlaid on the anatomical T1-weighted images. This method was chosen to take account of the non-normal distribution of the T2* signal, which is presumably due to rhythmic fluctuations related to the cardiac and respiratory cycles. Transition times (i.e., 2 time-points=8 s after a signal was given) were not included in the statistical analysis, to compensate for the delayed haemodynamic response. Activation maps were colour-coded on a thermal scale according to the degree of statistical significance of the difference between the rest and activation states and overlaid on the anatomical and the contrast-enhanced images for anatomical reference and detection of veins. Percentage signal change was calculated from the time course of the signal in the voxel within the parenchyma of the presumed primary motor area, which did not overlay a visible vein on the contrast-enhanced anatomic studies and gave the highest statistical significance (smallest P value) on Kolmogorov-Smirnov analysis. To minimise partial-volume effects, only this single voxel was analysed further. The mean MR signal intensities for each rest and activation period of a single functional examination were computed separately. We calculated the percentage change from the signal at rest to that in the activated state. The average signal change was then determined as the mean of the three pairs of rest and activation states. We analysed dependency between signal change and age, sex, treatment with anticonvulsants, the presence of oedema, the distance between the lesion and the site of activation, the degree of weakness and tumour histology.

The shortest distance between the lesion (including any cerebral oedema) and the activated parenchyma was measured on the high-resolution contrast-enhanced T1-weighted images. The degree of weakness was rated on a scale of 0–5 according to the memran-dum of the Medical Research Council [6]. Patients were grouped according to their degree of weakness: group a: none (5/5); group b: slight (4/5); and group c: marked weakness (<4/5). The lesions were allocated to five groups: 1: meningiomas; 2: slow-growing infiltrating tumours: low-grade gliomas (astrocytoma II, oligoastrocytoma II, oligodendroglioma II); 3: WHO grade III gliomas (astrocytoma III, oligoastrocytoma III, oligodendroglioma III); 4: WHO grade IV gliomas (glioblastoma multiforme, gliosarcoma); and 5: metastases, irrespective of the primary tumour.

Results

We obtained activation within the primary motor area in 94 of the 110 patients. In 12, no functional information was obtained due to excessive and uncorrectable head-movement artefacts, and in four the percentage signal change in the presumed primary motor area was too low to yield statistically significant results. Patients with excessive movement artefacts were not included in any further analysis, but those who had a too low a signal