Clinical commentary

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Focal seizure propagation illustrated by fMRI

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ABSTRACT – We report the pattern of seizure propagation as detected by functional MRI (fMRI) in a 24-year-old man with frequent recurrent electrographic seizures. The EEG seizure onset was left occipital with later spread to the left hemisphere and, to a lesser extent, the right hemisphere. The fMRI showed initial increase in blood oxygen level-dependent (BOLD) signal in the left occipital pole. The increased signal then propagated to the right occipital-posterotemporal region, and subsequently, the right and left mesial temporal regions. fMRI can be an effective tool to study seizure onset localization and seizure propagation in patients with frequent recurrent seizures.

Key words: ictal, fMRI, seizure propagation, seizure localization, partial epilepsy, occipital

Functional MRI (fMRI) has been used extensively to study activation during tasks such as sensory, motor, language and other cognitive tasks. Visualization of activated areas is based on increase in blood oxygen level-dependent (BOLD) signal associated with increased perfusion of activated areas. Focal seizures are also associated with a focal increase in blood flow in involved regions which evolves with seizure propagation. While fMRI has a major advantage over EEG for excellent spatial resolution, it cannot generally be used to evaluate seizures for practical reasons since seizures may not usually be anticipated during scanning. However, when seizures recur frequently, they may be amenable to evaluation using fMRI.

We report a patient with frequent recurrent focal electrographic seizures originating from the left occipital region, clearly documented on continuous EEG recording. An fMRI study delineated a precise localization of seizure onset and propagation.

Case study

Our patient was a 24-year-old Asian Indian man with intractable lesional localization-related partial epilepsy since age 12. At that time he had a

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secondarily generalised tonic-clonic seizure. MRI suggested a left occipital tumour which was resected. The pathology was interpreted as oligodendroglioma and he underwent radiation therapy. Recognized clinical seizures were controlled with antiepileptic drugs, but he developed progressive cortical blindness with fluctuating severity. An EEG study revealed very frequent recurrent partial-onset seizures originating from the left occipital region, every 8-10 minutes, without clear clinical change, apart from occasional reports that he could see "red". In addition, he was amnestic to memory items given during the ictal discharge. The EEG suggested onset in the left occipital region with subsequent propagation in the left hemisphere and to a lesser extent the right hemisphere *(figure 1)*. Each ictal discharge lasted two to three minutes. After informed consent, he underwent an fMRI study using a Philips Achieva 3T MRI scanner (Philips Healthcare, Inc., Best, Netherlands). Scanning included a three-dimensional high-resolution

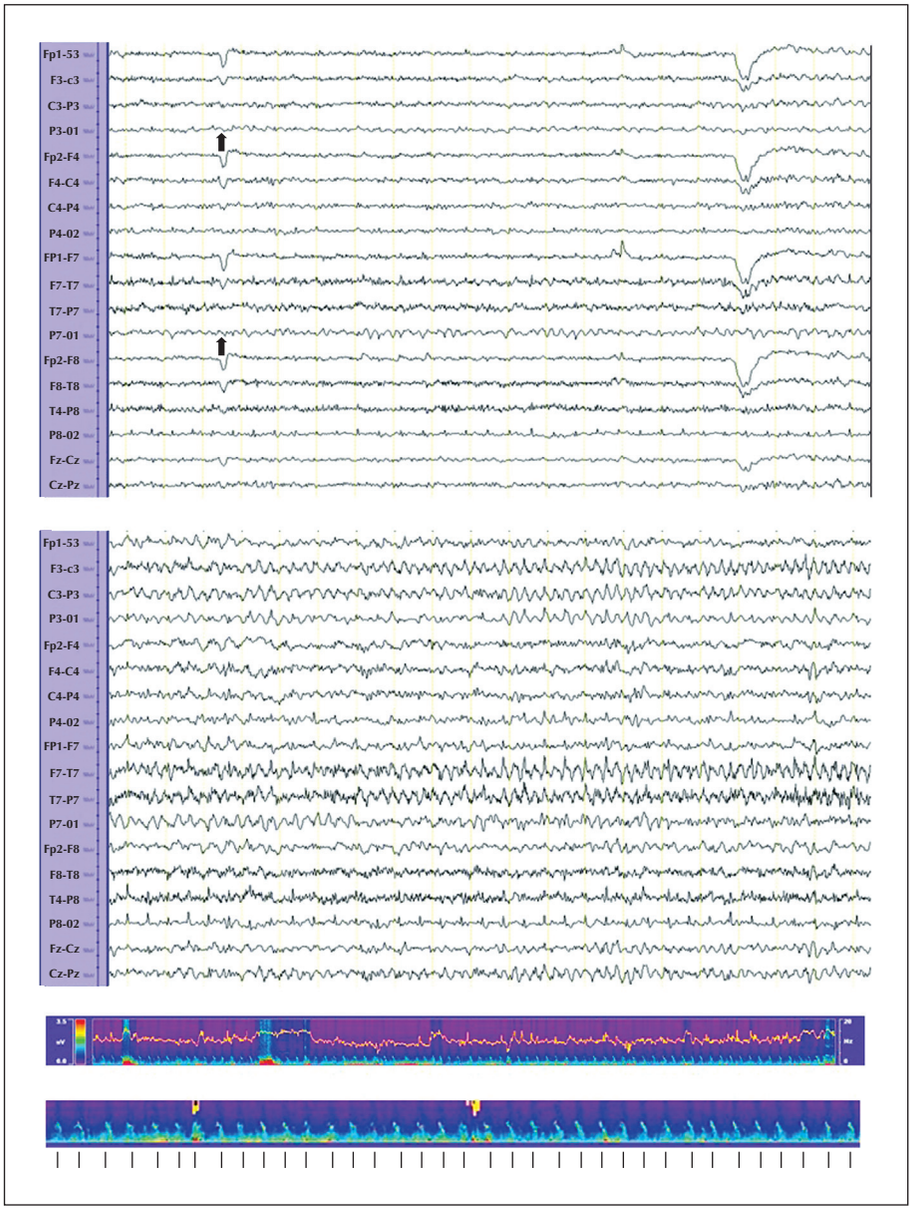

Figure 1. Seizure onset and propagation on EEG. The top figure shows the onset in the left occipital region. The middle figure shows propagation in the left hemisphere 20 seconds after onset. The lower two panels show the density spectral array (DSA) demonstrating recurrent seizures every 8-10 minutes. The bottom panel is a zoom of a DSA segment showing each seizure marked with a vertical line.

T1-weighted volume (1 mm × 1 mm × 1 mm) and a two-dimensional, T1-weighted high-resolution image covering the whole brain. Functional MRI scanning was performed using T2*-weighted gradient-echo, echo planar BOLD fMRI scans with the subject instructed to keep still with eyes closed (64 × 64, 3.75 mm × 3.75 mm, FOV = 240 mm, 4.5 mm thick/0.5 mm gap, TE = 35 ms, TR = 2 sec, 200 volumes per series). The fMRI scan was repeated for a total of four scans; the first of which is presented here *(figure 2)*.

The images were analyzed using the following procedure with SPM5 image analysis software (http://www.fil.ion.ucl.ac.uk/spm/software/spm5/). The fMRI image set was corrected for slice timing effects and motion corrected. Translation was less than 0.6 mm and rotation through time was less than 0.4 degrees. These images were spatially smoothed using a 7 mm FWHM kernel and each time series was temporally smoothed using a three-point moving average. An algorithm was written to search voxel-by-voxel for an average 3% signal change across a given time window in relation to a given baseline time window. The first four time points were discarded to allow for signal equilibrium. The baseline was determined by starting at the fifth time point in blocks of 10 seconds (five time points). For example, time points 11-15

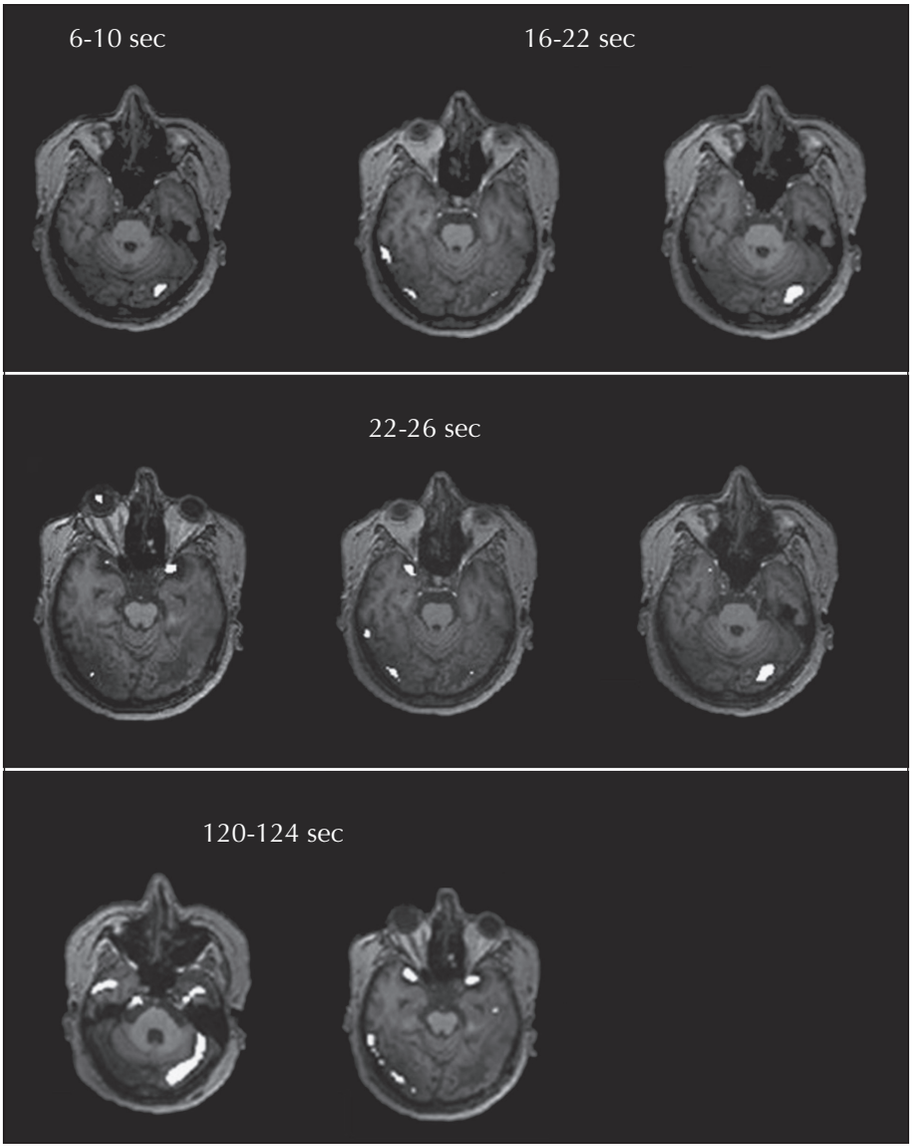

Figure 2. BOLD signal changes with time. Top panel: left occipital activation at 6-10 seconds then right occipital-posterior temporal activation at 16-22 seconds; middle panel: bilateral mesial temporal activation at 22-26 seconds; bottom panel: bilateral temporal activation was still present at 120-124 seconds, wider left occipital activation was also seen.

were compared to 5-10 (baseline). No voxels with 3% signal increase were determined. Next, time points 16-20 were compared to time points 5-15 (baseline). Again, no voxels with 3% signal increase were determined. This was continued until a change was found between time points 31-35 and 5-30 (baseline). This corresponded to a baseline of 10-60 seconds. Further signal increases were compared through time to this baseline and are shown in *figure 2*; the times listed are in relation to the baseline.

The fMRI analysis showed an initial BOLD activation focally in the left occipital region, with subsequent local spread and propagation to the right occipital-posterotemporal region, then right and left mesial temporal regions *(figure 2)*.

Discussion

We have demonstrated seizure propagation with fMRI in a patient with frequent recurrent electrographic seizures. The fMRI demonstrated propagation to the right occipital region, explaining cortical blindness, and to both mesial temporal regions, explaining ictal amnesia. While we recognize the limitations of our fMRI technique, for example averaging over five seconds, the fMRI was clearly superior to the EEG in explaining the clinical symptomatology. This and other published cases demonstrate that fMRI can be an effective localizing tool for focal seizures if started before the ictal onset (Detre *et al*., 1995; Jackson *et al*., 1994; Donaire *et al*., 2009). Ictal fMRI is usually a fortuitous event which requires seizures to start during MRI acquisition, without motion artefact. Three previous studies have reported active focal seizures detected by fMRI. Jackson *et al*. (1994) described fMRI changes with right face focal motor seizures in a four-year-old with extremely frequent seizures. They demonstrated consistent sequential activation in appropriate cortical regions during five clinical and one subclinical seizure. Detre *et al*. (1995) described subclinical fMRI changes in a 25-year-old with frequent right face focal motor seizures. The fMRI seizure onset localization seemed more precise than EEG based on subdural grid electrodes, ictal SPECT, PET and scalp EEG. Donaire *at al*. (2009) described ictal fMRI changes in five patients and concluded that this method could be potentially used for noninvasive localization of seizure foci. One remarkable finding was that all but one seizure onset zone, detected by fMRI, correlated with the localization of subtraction ictal single-photon emission computed tomography (SISCOM) and invasive EEG. In the one patient where fMRI suggested different seizure onset localization, fMRI seemed to be more precise. The fMRI suggested localization to the right insular cortex with immediate spread to the right mesial temporal cortex, while SISCOM and invasive EEG pointed to the right mesial temporal lobe as the seizure onset zone. This patient underwent an anterior temporal lobectomy involving the mesial temporal lobe structures, but he continued to have the same type of seizures at nearly the same frequency as before epilepsy surgery.

The main advantage of fMRI over EEG is an excellent spatial resolution which is equally high for superficial and deep structures. Standard EEG has a relatively poor spatial resolution and is useful only for superficial cortical activity. Successful ictal fMRI acquisition may also allow identification of the propagation networks, which may vary according to the seizure focus localization. If focal resection is not possible, disruption of propagation networks may be useful to control seizure spread and generalisation.

Functional MRI is a promising localizing noninvasive imaging modality in select patients with very frequent seizures or with seizures that can be provoked, provided there is no head movement artefact associated with seizure onset. If these patients are considered for epilepsy surgery, fMRI may potentially become an important component of their presurgical work up. □

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