Neuroelectric detection in fMRI data of frequent interictal activity in patients with epilepsy

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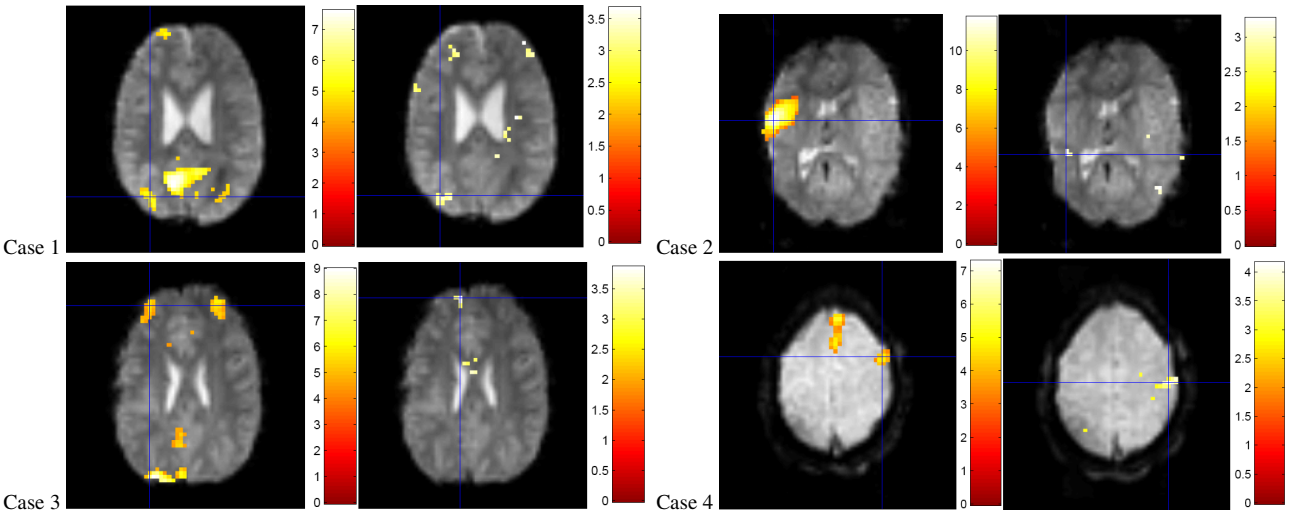
Introduction: Previous theoretical and experimental studies have suggested that the direct detection of neuronal-electrical (neuroelectric) activity using MRI may be possible [1,2] with some recent in-vivo imaging studies providing a degree of support [3,4]. The weakness of the induced magnetic field due to the small neuronal currents makes it necessary to have a considerable amount of neuronal events in order to stand a chance of detection. Timing of the acquisition in relation to the neuronal event is also crucial and therefore frequent periodic stimuli would seem to be ideal, although the results using this approach have been mixed. On the other hand, large neuronal currents may help detection and therefore epileptiform activity may provide a good experimental model. In this case, however, the occurrence of the activity is unpredictable therefore precluding synchronized MRI acquisition. Here we perform neuroelectric analysis of EEG-fMRI data acquired in cases with periods of extremely frequent focal interictal activity in which we took great care to include BOLD and motion-related effects in addition to any signal changes related fast (possibly neuroelectric) activity.

Materials and Methods: Three children (age range: 6-9; cases # 1-3) and one adult (case #4) with focal epilepsy were selected for this study according to the following criteria: (1) correspondence between localisation of at least one of epileptic foci based on electro-clinical information and BOLD result of spike-related analysis of the fMRI data [5]; (2) number of interictal events (IE) exceeding 500 per 20-minute EPI acquisition session; (3) written informed consent. Cases 1-3: MRI was obtained using a 3T Philips Achieva scanner with an eight-channel SENSE head coil. An fMRI time-series was obtained using gradient echo EPI and the following parameters: TR=2262 ms, TE=45 ms, 30 slices, 64×64 matrix, slice thickness=3.5 mm, FOV=200 mm, flip angle=90°, 540 scans per 20 min. An additional T1-weighted structural scan was obtained:,1 mm slice thickness, 208×208 matrix, 150 slices, FOV=208 mm, TE=3.6 ms, TR=7.8 ms, flip angle=8°, NSA=2. Case 4: MRI data was obtained using a 3T GE Signa Excite scanner and a standard head coil: fMRI time-series was obtained using gradient echo EPI and the following parameters: TE/TR=40/3000 ms, interleaved acquisition 43x5 mm slices; field of view=24×24 cm2; 64×64 matrix); An additional T1-weighted structural scan was acquired: FSPGR TE/TR/TI=3.1/8.2/450 ms; 170x1.1 mm slices; 256x256 matrix. For all cases, EEG was recorded simultaneously during fMRI has been acquired using BrainAmp 32-channel system (BrainProducts, Germany). The number of IE identified by a trained neurophysiologist were: case 1: 1493, case 2: 555, case 3: 1686, case 4: 1147.
fMRI time series data were realigned and smoothed using an isotropic Gaussian kernel of 8 mm in SPM2 (http://www.fil.ion.ucl.ac.uk/spm). Using masks for three consecutive slices, three separate, slice-specific voxel-based statistical analyses were performed for each case. The slices were chosen so that the central slice bisected the cluster resulting from previous modeling of the BOLD response and which were concordant with the electro-clinical information. In this new analysis, a separate slice-specific GLM was built with EEG derived event onsets corrected for slice acquisition time to model neuroelectric and BOLD effects. Neuroelectric activity was modeled using a FIR model containing 6 regressors with the n-th (n=0,..., N-1) containing a delta function or finite impulse response (FIR) occurring at a fixed time $n\Delta t$ after each event with a duration Δt [3]. BOLD regressors were modeled by convolution of interictal events (IE) labeled at their peaks with hemodynamic response function and its temporal derivative. Additional regressors were used to remove confounding effects of motion as described in [5]. F statistics and T statistics were formed to test for fast changes represented by all 6 FIR regressors and for the BOLD response correspondingly. SPM{T} for the HRF were thresholded at P<.00001 (uncorrected); SPM{F} for the FIR were thresholded at P<.01 (uncorrected).

Results: Clusters of BOLD and neuroelectric changes were revealed in all slices analysed in all cases. Figure 1. shows the results for the slice showing the best degree of visual correspondence between the neuroelectric and BOLD patterns (indicated by crosshair). SPMs for BOLD (left on the figure) and neuroelectric (right on the figure) responses are given for each case with z score. For case 4, the main neuroelectric cluster was significant at the conventional threshold level



Discussion: All cases demonstrated some activation putatively related to a fast neuroelectric response at a very low threshold of significance. We used a low significance threshold for the neuroelectric effect in an attempt to reveal suspected weak effects in regions identified based on strong prior knowledge (BOLD effect and electro-clinical data). In cases 1 and 3 co-localised BOLD and 'neuroelectric' activation were seen. The results for case 4 are quite discordant. The discrepancy between results of those two types of analysis could be partially explained by the fact the neuronal activity and BOLD response can come from slightly different locations [6]. Another possible explanation for discrepancy is the propagation of neuronal activity which is common for epileptic activity. We conclude that despite very high levels of intense neuronal activity the neuroelectric effect is extremely weak at best. Further possible steps to increase level of confidence in correspondence of the neuroelectric analysis to electro-clinical information are (1) acquiring multi-channel EEG in order to perform 3D source reconstruction and (2) the improvement of the MRI data acquisition specifically for neuroelectric detection, either by a reduced slice, short TR EPI acquisition or through novel approaches such as MEG-like MRI [7].

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