Using EEG/fMRI and connectivity analysis to define epileptogenic 'circuits'

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Objective:

Recording of brain generated electrical potentials (EEG) inside the MRI has enabled the BOLD signal associated with epileptogenic 'events' to be analysed. This has given insight into the brain regions that may be involved in the generation of these abnormal events. One problem with this type of analysis is that these events may be sparse as they are spontaneously generated and often infrequent. A second problem is that spikes may have a different spatial distribution (or dipole). The first purpose of the current study was to analyse spikes that appeared different on the EEG to determine if the underlying brain activation was different. The second aim was to use connectivity analysis, seeded by the activated area detected in the spike study, to determine areas functionally connected with the seizure focus, which could represent an epileptic circuit that underlies this abnormal brain activity.

Methods:

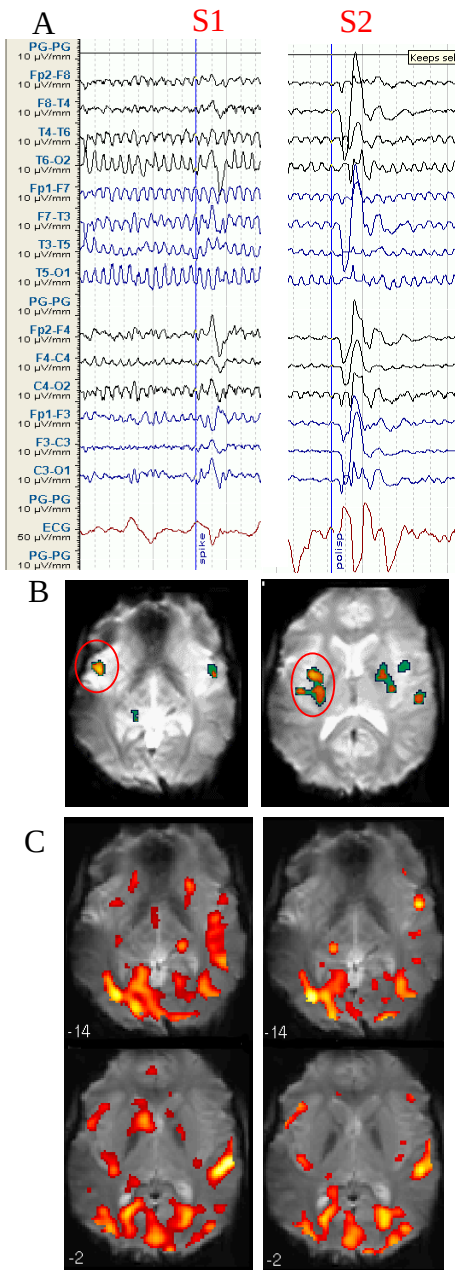
The fMRI studies were performed with a 3 tesla GE Signa LX scanner (GE, Milwaukee, WI). Structural imaging included T1-weighted 2D spin-echo images, acquired with the same geometric orientation and slice thickness as the subsequent functional images. Functional images were acquired as a series of gradient-recalled echo planar imaging (GR-EPI) volumes (TR/TE=3600/40ms, flip angle=60 degrees, 25 oblique slices 4mm thick+1mm gap, 24cm FOV, 128x128 matrix), over a period of one hour (1200 volumes).

Simultaneous fMRI/EEG was analysed using SPM99 (Wellcome Department of Cognitive Neurology, http://www.fil.ion.ucl.ac.uk/spm). Spike "events" were assigned independently by two trained neurologists, and two types of events, called S1 and S2 were identified (Fig A left, right). Each spike type was treated as an "event" in an event-related analysis, to obtain two maps of involved brain voxels. The points of maximum statistic from each map were then used as seeds in a functional connectivity analysis. The timecourse of each region (filtered to remove high frequency noise >0.08Hz) was correlated against all brain voxel time-courses to obtain a connectivity map for each seed. The patient connectivity maps were then contrasted statistically against the maps obtained seeding these regions in a group of four healthy control datasets.

Results:

We present results obtained in one individual with idiopathic generalised epilepsy of childhood onset (childhood absence epilepsy, CAE). Panel B shows the BOLD activation from the EEG/fMRI study. The first spike type (S1) is shown in the left panel, warm colors represent deactivation , and the second type (S2) is shown in the right panel where warm colors show significant activation. The S1 spikes showed primarily deactivation in the insular cortex. The S2 spikes showed a quite different pattern of activation with increased BOLD signal in subcortical nuclei, primarily the basal ganglia.

Panel C shows the increased connectivity above normal (control) levels measured statistically, based on the seed areas circled in panel B. Note that the areas involved in the connectivity pattern are virtually identical for each spike type, despite the seed point and the BOLD activation pattern being very different.



Conclusions:

Epileptic spikes in the interictal record may vary, both in the EEG appearance and in the underlying activation. Despite this, the activated and deactivated areas appear to be part of a widespread connectivity network that is not present in normal individuals. These data support the idea that interictal epileptiform events are an expression of activity in an epileptogenic network and the different expression of these events merely reflect peak activity in different parts of this network. This may help explain why interictal spikes may not always correlate with seizure onset area and suggests caution in the interpretation of interictal studies in terms of localisation. Connectivity analysis may give new insights into the biology that underlies seizure generation and may allow the definition of 'seizure circuits' as part of epilepsy pathophysiology.

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