Brain networks detected with functional connectivity are disrupted in left temporal lobe epilepsy

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Introduction

Functional connectivity maps the distributed network of brain regions fluctuating synchronously during a continuous brain state. The ability of functional connectivity to focus on this distributed aspect of brain function may reveal new information about the healthy brain as well as reflecting new aspects of changes associated with brain disease.

Epilepsy is one of the most common serious neurological conditions. Focal seizures affect about 60% of patients with epilepsy. Epileptiform brain activity involves synchronized electrical activity, which may have a focal origin, but which may spread to involve multiple brain regions. Seizure generation is thought to involve a network of cortical and subcortical regions. Seizure spread may involve abnormal synaptic connections, as has been suggested in experimental models (2).

The present study seeks to apply the methods of functional connectivity to explore the language network in patients with focal, left temporal lobe epilepsy (TLE). We aimed to statistically compare the pattern of functional connectivity between patients and controls. We hypothesized that in contrast with controls, patients with left TLE would show a disturbance of the brain network detected with functional connectivity.

Methods

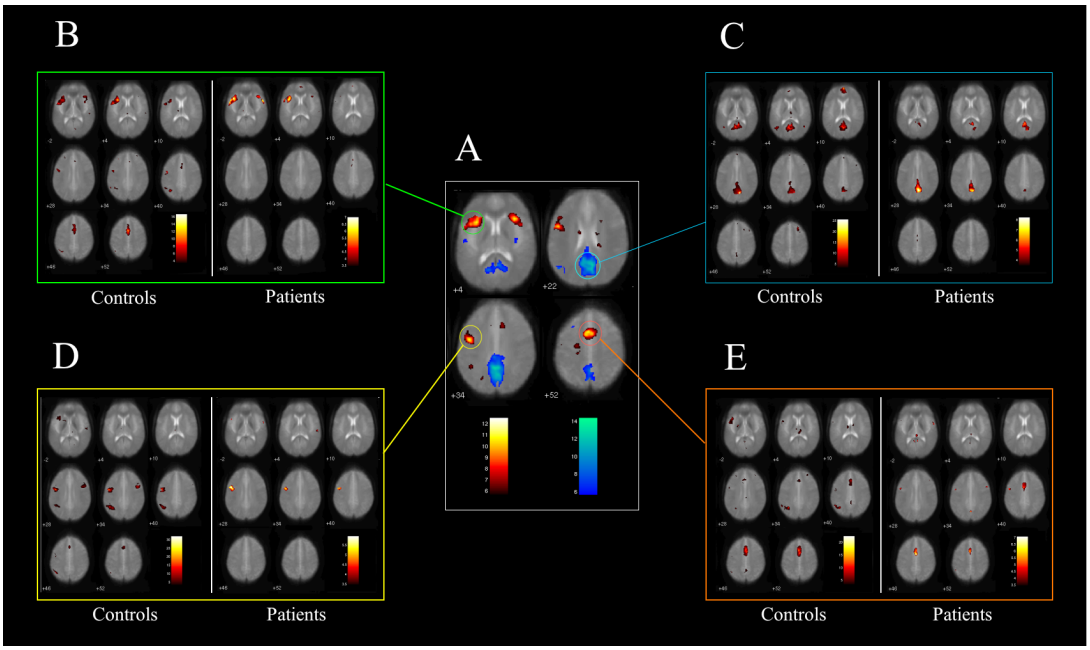
Eight healthy volunteers and 17 patients with left sided TLE were used in the connectivity analysis. A previous cohort of 30 controls performed the OLR task (see below) and their data was used to determine the seed regions. The fMRI studies were performed with a 3 tesla GE Signa LX scanner (GE, Milwaukee, WI). 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).

Data acquired included 90 volumes of resting state data and a block-design language task. During the language task, a visual fixation block was interleaved with a block of orthographic lexical retrieval (OLR), where the subject generated words beginning with a displayed letter. Standard block-design fMRI analysis of the OLR task was performed using SPM99 (www.fil.ion.ucl.ac.uk/spm). The time series for each subject was first pre-processed. This involved motion correction, transformation to standard space and smoothing by convolution with an 8mm isotropic Gaussian kernel. In the statistical analysis of the language activation data, motion correction parameters were included as covariates of no interest.

Seeds for the connectivity analysis were spheres of 5mm radius centred on the four voxels of highest t-score in the positive and negative OLR contrast for the group of 30 controls, namely left middle frontal gyrus (MFG), left inferior frontal gyrus (IFG), anterior cingulate cortex (ACC), and posterior cingulate cortex (PCC). Connectivity analysis was performed using SPM99 and iBrain® (www.brain.org.au/ibrain). Each dataset was low pass filtered (f<0.08Hz). Seed timecourses for each region and subject were then generated, then regressed against all brain voxel timecourses to obtain four connectivity maps for each subject. A second level analysis was used to generate results for patient and control groups. All results were thresholded at p<0.001 for the voxels, with a cluster threshold of p<0.05, corrected for multiple comparisons.

Results

Fig A shows the language activation of the 30 controls, together with the location of the 4 seeds. Figs. B-E show connectivity maps for the four regions for controls (left), and patients (right). Controls show widespread patterns of connectivity, involving a similar pattern to the activation result. The TLE group shows reduced extent in the maps, primarily showing the seed region in each map, together with the contralateral IFG in the IFG connectivity map.



Discussion

The reduction in the extent of patient connectivity suggests that patients suffer a disturbance of the physiological synchrony in neuronal activity during rest of the areas involved in language processing. This disturbance may be due to the frequent occurrence of highly synchronized pathological activity due to epileptic discharges, These discharges may disrupt normal network-level cognitive processing, as has been suggested in studies evaluating neuropsychological performance in relation to the frequency of epileptiform discharges (2). Alternatively, the alteration in functional connectivity may be due to an inhibition of neuronal processing associated with epilepsy-dependent alteration of excitability or due to general suppression of neuronal activity with antiepileptic medication.This indicates that functional connectivity is a method sensitive to changes in brain function in disease that are undetectable using fMRI activation.

References

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