Measuring epilepsy networks: combining simultaneous fMRI/EEG and functional connectivity.

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Introduction

Epilepsy is a disease that involves abnormal circuits of electrical activity that may disrupt normal cognitive function, as well as generating a variety of symptoms. The process by which the abnormal behaviour of a focal region can evolve to recruit the whole brain is poorly understood. Functional connectivity is a method that allows us to directly image extended brain networks with correlated signal behaviour. It thus promises to provide new insight into how brain networks differ in the epileptic brain. In the present study we wished to establish the method of functional connectivity as a tool to explore the network involved with a focal lesion, and distinguish this network from cognitive brain networks in the healthy brain.

Methods

11 patients with partial or generalised epilepsy were considered in this study. The cohort included patients with mixed symptoms, which made a clear clinical diagnosis difficult, and motivated extended fMRI analysis. The fMRI studies were performed with a 3 tesla GE Signa LX scanner (GE, Milwaukee, WI). 30-60 minutes of simultaneous EEG and fMRI were acquired in each case, using a purpose-built, in-house MR-compatible EEG system that includes suppression of gradient artefact in the EEG trace. Analysis was performed using SPM2 (www.fil.ion.ucl.ac.uk/spm) and iBrain (www.brain.org.au/iBrain). fMRI/EEG analysis involved treating interictal discharges as events of interest in an event related fMRI analysis. The focal regions identified in this way were then used as seed regions in a functional connectivity analysis, to detect the extent to which other brain regions were fluctuating in harmony with these seeds. Finally, this pattern was statistically compared to the patterns seen in a group of 34 healthy controls, in order to detect regions that were significantly more involved in the network in the patient than the healthy population.

Results

The utility of the proposed method is best demonstrated by considering a number of the patients.

Fig 1 considers the data of patient A. This subject was a 19-year-old female with evidence of focal discharges confounding the diagnosis of juvenile myoclonic epilepsy. Panels A and B show the patterns of activation associated with two of her interictal discharges, with A having a focal EEG pattern , and B a more generalised EEG pattern. Panels C, D and E show two distinct networks of activity. Panel C and D show a focal region of right frontal activation with surrounding deactivated tissue, together with involvement of the brainstem. In contrast, panel E shows a more generalised involvement of cortical regions, but no brainstem involvement.

Fig 2 considers the data of patient B. This subject was a 22-year-old female with a history of febrile convulsions, and EEG discharges consistent with a diagnosis of idiopathic generalised epilepsy. Panels A and B show the patterns of activation associated with two her two spike morphologies, with panel A being the result of 8 spikes, and B the result of 3 polyspike events. Panels C and D show that both of the focal regions appear to be part of a single network involving the caudate and widespread involvement of occipital cortex.

Discussion

In this study we have demonstrated that it is possible to use the results of fMRI/EEG analysis as seeds in a functional connectivity analysis, and thereby detect abnormal networks of activity in patients with epilepsy. We present a method for differentiating this network from normal variation in the healthy brain. Activation detected in this manner can represent both epilepsy networks that do not exist in the healthy brain, as well as significantly heightened activity within existing brain networks. Further, we have demonstrated how the network information detected in this manner can yield further insights into the disease characteristics of individual patients with epilepsy.

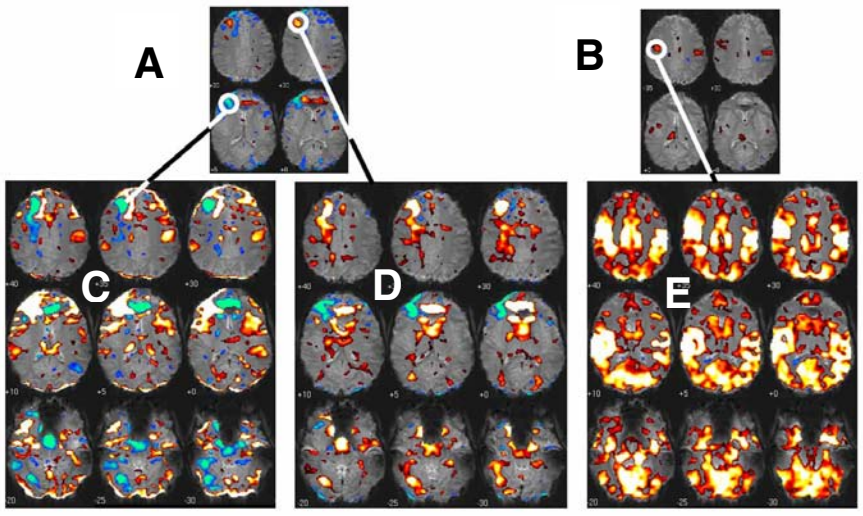

Figure 1. A,B: spike-related BOLD activity identifies different foci. C,D,E: A number of seeds identify two distinct epilepsy networks

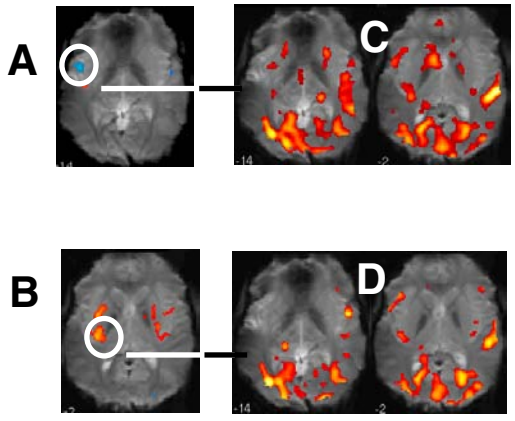

Figure 2. A,B: two forms of IED identify different foci. C,D: Seeds from these distinct foci identify a single, extended epilepsy network