Predicting the success of epilepsy surgery using resting state fMRI

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Background

For the most severe cases of epilepsy, current pharmacological therapy may be ineffective in as many as 33-60% of cases1. For these patients, the only hope for seizure remission is surgical excision of the epileptogenic zone (EZ), the region of the brain whence the seizures originate. In order to do this, however, the EZ must first be identified, an invasive and time-consuming process that currently involves the surgical placement of intracranial EEG electrodes. Further, the success of surgical resection in the treatment of epilepsy is highly variable, some patients becoming seizure-free after surgery and others with little to no benefit whatsoever. These considerations as well as others have motivated epileptologists, neurosurgeons, and neuromaging experts to search for improvements in the methodology for determining the EZ.

Functional Magnetic Resonance Imaging (fMRI) is an imaging technique used to noninvasively study brain activity. fMRI measures the blood-oxygenation level dependent (BOLD) response, i.e., it measures the oxygenation of blood in the small vessels of the brain over time. The BOLD signal is used as a correlate of brain activity, as more actively engaged brain regions are also more metabolically active and thus require greater oxygen delivery. Recently, resting state fMRI has emerged as a method for determining the degree of functional connectivity between two brain areas. rsfMRI relies on small fluctuations in the BOLD signal that occur when the brain is at rest; correlation of these fluctuations in two distinct brain areas provides evidence that they are functionally connected.

Introduction

Question

• Can rsfMRI analysis of a resected zone be used to predict the likely outcome of surgical resection of an epileptogenic brain area?

Methods

Participants

Subjects scheduled for surgical treatment of pharmacologically-tractable epilepsy were recruited for use in data in various research projects. Four of these subjects who experienced varying degrees of seizure remission following surgery were used in this analysis.

fMRI/MRI Acquisition

Before electrode implantation functional and structural MRIs were acquired on a General Electric Sigma HD T scanner. Postresection structural MRIs were acquired using the same scanner when possible, but on some occasions only a 1.5T scanner was available.

Resting State

• Participants were instructed to rest with their eyes closed for five minutes.
• fMRI data were acquired using one of two EPI gradient echo sequences: voxel size 4x4x3.5 (2.4mm3), matrix 64x64, TR=2000ms, TE=30, FOV=220 (240mm), flip angle=50 (77), total acquisition plane, 150 contiguous volumes.
• Slice timing correction for interleaved slice acquisition, motion correction, despiking, spatial smoothing (5mm full-width at half-maximum Gaussian blur), band-pass filtering (0.009-0.1 Hz), and linear and quadratic detrending.
• Global signal regression was performed by regressing each subject’s preprocessed time series on nuisance covariates (6 head motion parameters, signals derived from the ventricles, white matter, and the global signal).

Analysis

Defining the Resection Area

• Postoperative structural MRI was compared to preoperative structural MRI to anatomically determine the resected zone.
• Correlation of post- to preoperative fMRI and identification of resected area were carried out using FSL (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSL).
• For Subjects 1, 2, and 3, an affine transformation was used to compute the postoperative MRI to the preoperative MRI. The coregistration for Subject 4 was performed using a nonlinear coregistration due to inadequacy of the affine transformation.

Results

Resting state functional connectivity

It is now well established in the scientific literature that disruptions of intrinsic neural signaling (measured as the resting state BOLD signal) abound in the epileptic brain2. More specifically, it has been proposed that the EZ shows an abnormally high BOLD correlation with Brodmann area 46. Several studies have investigated the clinical use of rsfMRI in both presurgical planning3 for epilepsy patients and postsurgical analysis4. The current study is known to the authors of this presentation has linked BOLD correlation within the EZ to surgical outcome5. This little-investigated use of rsfMRI has the potential to help the neurosurgeon predict the success of a proposed resection in the treatment of epilepsy before the surgeon takes knife to brain.

Statistical Analysis

The Engel classification did not show conclusive correlation with the mean absolute correlation r-score outside the resected area (right). Rho (Spearman’s rank correlation coefficient) is a measure of statistical dependence between two variables. The results are ambiguous given the small sample size (n=4).

Conclusions

• Qualitative analysis of resting state BOLD signal correlation suggests a possible difference between patients with varying degrees of surgical success.
• This was observed as a focus of high BOLD correlation outside the resected zone in both subjects with Engel Class III-IV outcomes.

References