# Predicting the success of epilepsy surgery using resting state fMRI

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## Introduction

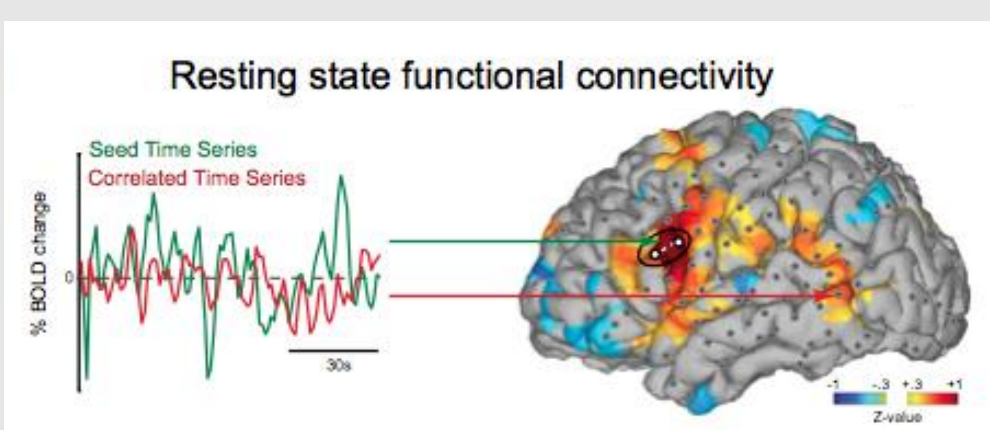
### Question

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

### Background

For the most severe cases of epilepsy, current pharmacological therapy may be ineffective in as many as 33-80% of cases[12]. 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 neuroimaging 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, a signal that quantifies 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 neurally-active 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.




source: Keller et al 2011[3]

It is now well established in the scientific literature that disruptions of intrinsic signalling (measured as the resting state BOLD signal) abound in the epileptic brain[4]. More specifically, it has been proposed that the EZ shows an abnormally high BOLD correlation with itself[5]. Several studies have investigated the clinical use of rsfMRI in both presurgical testing[5] for epileptic patients and postsurgical analysis[4] of resections. At this time only one study known to the authors of this presentation has linked BOLD correlation within the EZ to surgical outcome[6]. 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.

### Our Study

In this study we evaluate the ability of rsfMRI to predict the outcome of epilepsy surgery. We use an anatomically-derived region of interest in a seed region-based fMRI analysis[4]. The ROI for each subject corresponded to the area of the brain that was resected during surgery (which we term the "resected zone"). We then compare the BOLD signal correlation with areas outside the resected zone in patients with varying degrees of surgical success, with the goal of being able to predict a patient's surgical outcome based solely on the BOLD correlation within and outside a planned resection.

## Methods

### Participants

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

### MRI/fMRI Acquisition

Before electrode implantation functional and structural MRIs were acquired on a General Electric Signa HDx 3T scanner. Postresection structural MRIs were acquired using the same scanner when possible, but on some occasions only a 1.5T scanner was available.

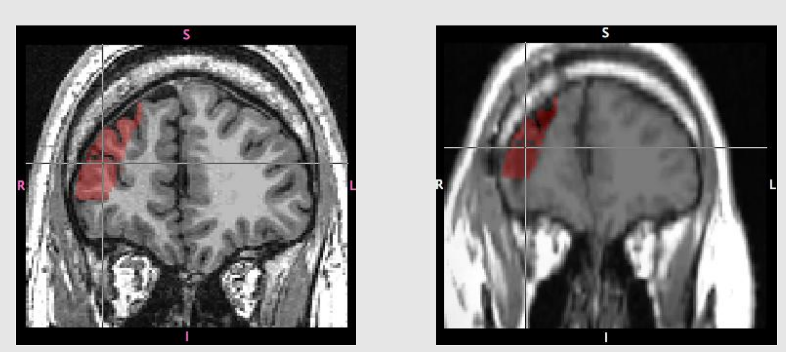
#### Resting State

•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 4x3.5x3.5 (3.4mm3), matrix 642, TR=2000 ms, TE=30, FOV=220 (240mm), flip angle=50 (77), axial acquisition plane, 150 contiguous volumes.
•Slice timing correction for interleaved slice acquisition, motion correction, despiking, spatial smoothing (6mm full-width at half-maximum Gaussian blur), band-pass filtering (0.009-0.1Hz), and linear and quadratic detrending
•Global signal regression was performed by regressing each patient's preprocessed time series on 9 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 area
•Coregistration of post- to preoperative MRI 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 coregister the postoperative MRI to the preoperative MRI. The coregistration for Subject 4 was performed using a nonlinear coregistration due to inadequacy of the affine transform function to account for significant postresection brain shift.



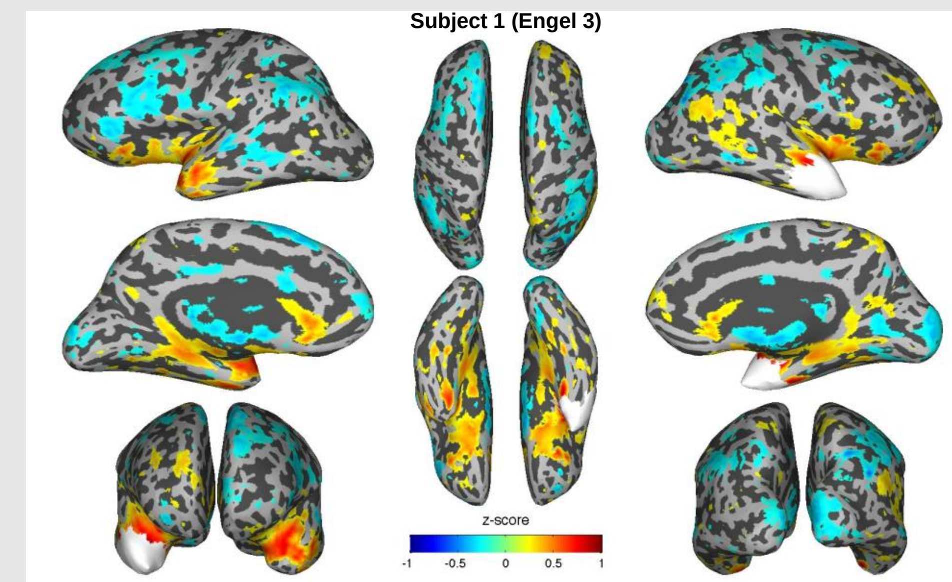
#### Functional Data

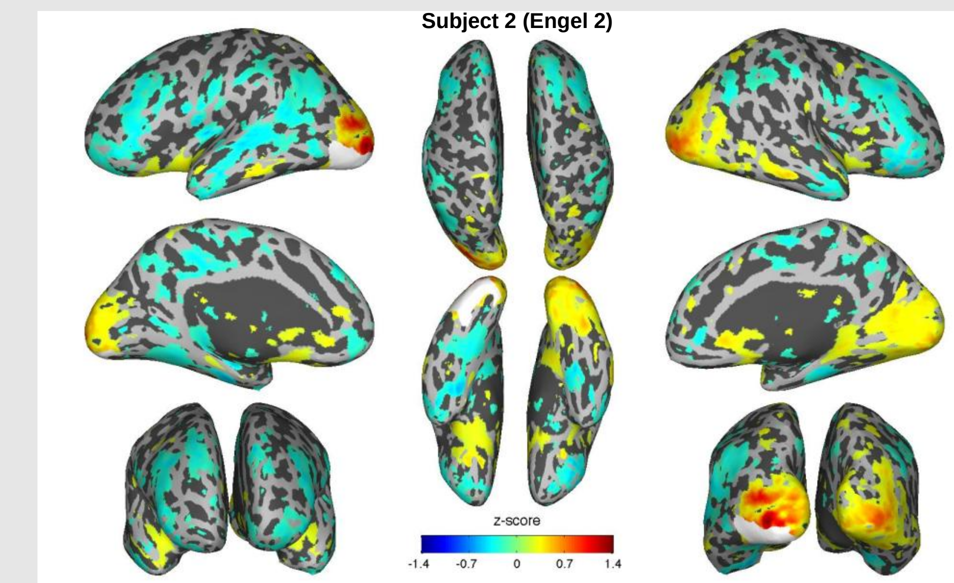
•Mean BOLD time series of voxels within the resection was computed. Voxels partially within resection were included, weighted for the percentage of the voxel located within the resection.
•Correlation (Pearson's r) with mean BOLD time series from the resection was computed for all voxels in neocortex, amygdala, and hippocampus. The correlation was z-transformed using Fisher's r-to-z transform to make the correlations more normally distributed.

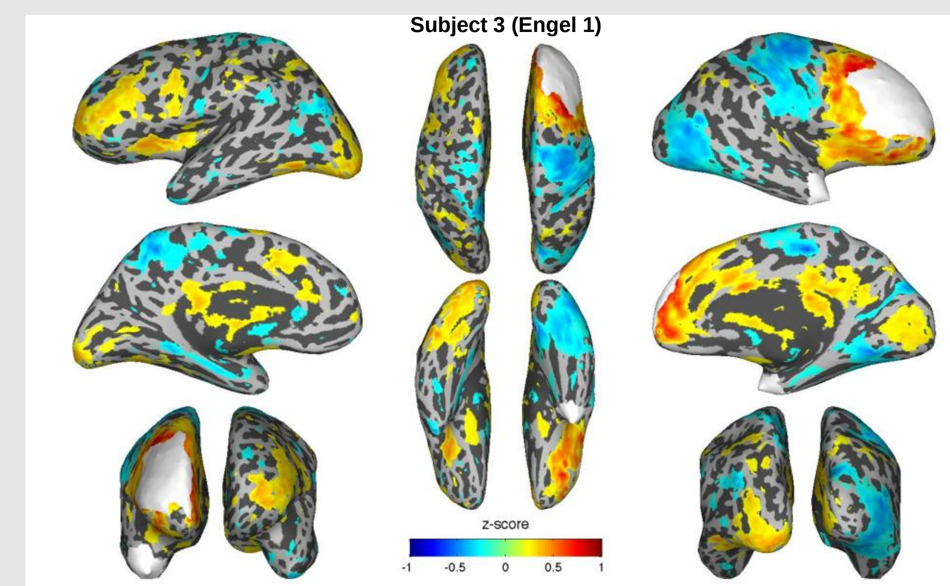
### Outcome Criteria

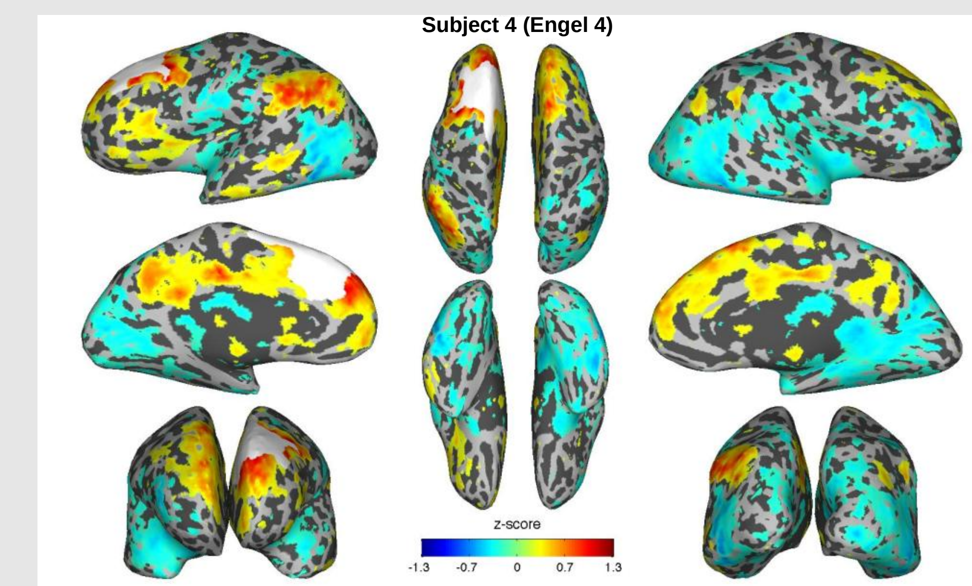
We used the Engel classification system* for the success of epilepsy surgery, which recognizes four classes of surgical outcome:
•Class I: free of disabling seizures
•Class II: rare disabling seizures
•Class III: worthwhile improvement
•Class IV: no worthwhile improvement

## Results



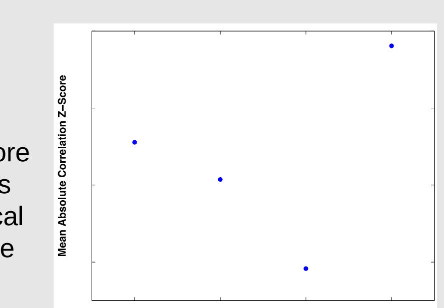




### Qualitative Data

Inflated cortical surfaces of both hemispheres are shown for all subjects (light gray is gyrus, dark gray is sulcus). Uncolored cortical surface is that which showed z-score < .2. The heat map shows regions of positive and negative BOLD signal correlation with the mean BOLD time series of the resected area, which has been masked in white. Regions of strong positive correlation outside the resected area suggest functional connectivity with the resected zone, the proposed epileptogenic zone.

### Statistical Analysis

The Engel classification did not show conclusive correlation with the mean absolute correlation z-score outside the resection 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 is observed as a focus of high BOLD correlation outside the resected zone in both subjects with Engel 3-4 outcomes.
- Accurate statistical analysis of resting state BOLD signal correlation requires much more data.
- Most voxels correlated with the resected zone are only weakly correlated, so removing these from the analysis might reveal a stronger pattern than the mean correlation value. This could be accomplished by analyzing BOLD correlation at different correlation value thresholds, a viable next step in this investigation.

## References

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