Identification of eloquent cortical areas using resting state fMRI: A validation with in vivo direct cortical electrical stimulation in humans

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Introduction

Questions
• How accurately do different methods for deriving functional networks from resting state fMRI (rsfMRI) identify functionally distinct cortical areas as defined by direct cortical electrical stimulation (DCES)?
• How does the accuracy of these rsfMRI methods compare to task-based fMRI mapping?

Background

When evaluating a patient for neurosurgery it is critical to identify “eloquent cortex” necessary for core cognitive functions such as language and motor control that must be preserved. The clinical “gold standard” for identifying functional areas is DCES. DCES is effective but is an invasive, time consuming procedure that increases patient risk and cannot always be fully completed due to patient exhaustion or epileptogenic DCES effects. An alternative method for defining eloquent cortex is rsfMRI. It is well established that functionally related brain areas have similar patterns of rsfMRI which allows them to be segregated from one another and identified via tools like independent component analysis (ICA) and cluster analysis. However, it is not clear if rsfMRI can resolve eloquent cortex with sufficient precision to make it clinically useful. Previous work has shown that hand sensorimotor regions identified by rsfMRI are similar to those defined by a finger tapping paradigm in neurosurgical candidates, but it is not clear how well these results correspond with DCES.

Our Study

Here we evaluate the ability of rsfMRI to define hand sensorimotor, tongue sensorimotor, and expressive language areas as defined by DCES in patients undergoing evaluation for neurosurgical treatment of epilepsy. We use three methods of rsfMRI analysis to identify these areas: ICA, cluster analysis, and logistic regression. In addition, we compare the accuracy of these rsfMRI results to more conventional task-based fMRI estimates of these regions.

Methods

Participants

• 20 volunteers, all functionally intact apheresis undergoing evaluation for epilepsy surgery.
• Individuals were included in each analysis only if the DCES procedure identified areas involved in the function of concern.

DCES Procedure

• Conducted preoperatively according to standard clinical protocol using grids and strips of tinfoil electrodes (Medtronic), or directly applied to the cortex via a needle for receptor mapping.
• Parts of nonimplanted electrodes (minimum 360uA per patient using a Grass S-12 stimulator, stimulation current limited to 0.5mA, maximum current limited to 30mA, standard safety protocols applied). No additional current was delivered via any intraoperative or postoperative means.
• Motor-evoked responses were identified as movement or sensation in the fingers, palm, or wrist.
• Phonogenic and speech evoked responses were identified as movement or sensation in the tongue or face.
• Electrical stimulation was delivered via a needle placed at the site of maximum isoelectric potential.
• Parts of electrodes whose stimulation produced post, seizure, or antagonistic responses were removed from the analysis. Pairs of fMRI produced expression and receptive speech calculus were included as expressive speech.

MRI/IMRI Procedure

Before electrosurgery, functional and structural MRIs were acquired on a General Electric Signa HDx 3T scanner.

Resting State

• Data was acquired over a 20-minute period with eyes closed for five minutes.
• fMRI data were acquired using an EPI protocol with 35 axial slices and 22 oblique slices (TR=2,000ms, TE=30ms, Flip angle=90, FOV=24cm, matrix=64x64, slice thickness=3mm).
• fMRI data were corrected for 6 head motion parameters, signals derived from the ventricles, white matter, and (as the global signal).

Finger Tapping Task

• Participants were instructed to rest with their eyes closed for five minutes.
• Sensitivity to electrical stimulation was assessed using a 2x2 factorial design, in which the intensity ( 0, 0.5, or 1.0 mA) and site of stimulation (sensorimotor, tongue sensorimotor, expressive language, and non-hand sensorimotor) were varied.

Covert Picture Naming Task

• Participants were instructed to rest with their eyes closed for five minutes.
• Sensitivity to electrical stimulation was assessed using a 2x2 factorial design, in which the intensity ( 0, 0.5, or 1.0 mA) and site of stimulation (sensorimotor, tongue sensorimotor, expressive language, and non-hand sensorimotor) were varied.

Task-Based Analyses

• Functional connectivity maps were created for each participant using individualized connectivity analysis with fMRI data acquired on a General Electric Signa HDx 3T scanner.
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• 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 (as the global signal).

ICA

• Data were preprocessed and band-pass filtered (0.009-0.1Hz), and then downsampled to 0.01Hz.
• Data were smoothed (6mm Full Width at Half Maximum Gaussian blur) and back-transformed to the native space.
• ICs were categorized based on functional connectivity to the eloquent cortex as defined by DCES.
• Each component was used to train a logistic regression model which was then used to estimate the probability that each voxel contributed to an IC.

Cluster Analysis

• Voxels were categorized into clusters of functionally related areas using a researcher blind to DCES results. AUC was estimated from these.
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Expressive Speech Classifier

• Voxels were categorized into clusters of functionally related areas using a researcher blind to DCES results. AUC was estimated from these.

Conclusions

• ICA and cluster analysis of resting state fMRI can identify eloquent cortical areas about as well as task-based fMRI.
• Logistic regression of resting state fMRI using a subset of DCES results can identify eloquent cortical areas better than task-based fMRI.
• These results validate the use of these techniques for defining some functional networks, though clearly some improvement is needed (especially for language networks for which task-based fMRI is also poor).