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Predicting postoperative language outcome using presurgical fMRI, MEG, TMS, and high gamma ECoG

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HIGHLIGHTS

- We predicted the postoperative language outcome using presurgical fMRI, MEG, TMS and high gamma ECoG.
- We compared performances of single modality and multimodality methods for prediction of the outcome.
- Developed multimodal method can be utilized prior to surgery for selecting an optimal surgical plan.

ABSTRACT

Objective: To predict the postoperative language outcome using the support vector regression (SVR) and results of multimodal presurgical language mapping.
Methods: Eleven patients with epilepsy received presurgical language mapping using functional MRI (fMRI), magnetoencephalography (MEG), transcranial magnetic stimulation (TMS), and high-gamma electrocorticography (hgECoG), as well as pre- and postoperative neuropsychological evaluation of language. We constructed 15 (2^4–1) SVR models by considering the extent of resected language areas identified by all subsets of four modalities as input feature vector and the postoperative language outcome as output. We trained and cross-validated SVR models, and compared the cross-validation (CV) errors of all models for prediction of language outcome.
Results: Seven patients had some level of postoperative language decline and two of them had significant postoperative decline in naming. Some parts of language areas identified by four modalities were resected in these patients. We found that an SVR model consisting of fMRI, MEG, and hgECoG provided minimum CV error, although an SVR model consisting of fMRI and MEG was the optimal model that facilitated the best trade-off between model complexity and prediction accuracy.
Conclusions: A multimodal SVR can be used to predict the language outcome.
Significance: The developed multimodal SVR models in this study can be utilized to calculate the language outcomes of different resection plans prior to surgery and select the optimal surgical plan.

1. Introduction

About 1% of people in the United States suffer from epilepsy, and one-fifth of epilepsy cases are pharmacologically intractable (Begley et al., 2000). Resection of the seizure onset zone is an effective treatment for intractable epilepsy but it carries the risk of postoperative impairment of essential brain functions, especially language. Presurgical language mapping is usually performed to minimize this risk. Cortical stimulation mapping (CSM) serves as the clinical gold standard for presurgical language mapping (Ojemann et al., 1989), though it has several limitations (Lesser et al., 1984; Blume et al., 2004; Brunner et al., 2009; Borchers et al., 2012; Wray et al., 2012; Desmurget et al., 2013;

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Papanicolaou et al., 2014). For example, CSM is invasive and can induce seizures (Lesser et al., 1984; Blume et al., 2004; Schevon et al., 2007; Kojima et al., 2012). Last but not least, surgical decision making based on CSM has been shown to lead to postoperative language deficits in 25–60% of patients with temporal lobe epilepsy (TLE) who underwent dominant hemisphere anterior temporal lobectomy (ATL) (Sabsevitz et al., 2003; Davies et al., 2005; Hamberger et al., 2005; Schevon et al., 2007; Binder et al., 2011; Sherman et al., 2011; Bonelli et al., 2012; Kojima et al., 2012, 2013; Cervenka et al., 2013; Genetti et al., 2015).

To date, several studies have shown the utility and reliability of language mapping using functional MRI (fMRI), magnetoencephalography (MEG), transcranial magnetic stimulation (TMS), and high gamma electrocorticographic (hgECoG) recordings (Binder et al., 1997; Simos et al., 1999; Crone et al., 2006; Picht et al., 2013; Babajani-Feremi et al., 2014). It has also been shown that presurgical language mapping using fMRI or hgECoG can predict the postoperative language outcome that was not predicted by CSM (Sabsevitz et al., 2003; Bonelli et al., 2012; Cervenka et al., 2013; Kojima et al., 2013; Genetti et al., 2015). Since fMRI, MEG, TMS, and hgECoG have complementary aspects, it is expected that a multimodal presurgical language mapping approach can provide an accurate and reliable prediction for postoperative language outcome. However, no study has yet investigated the predictive power of a multimodal approach for language outcome, and we addressed this deficit in the current study.

The underlying hypothesis of this study was that a multimodal presurgical language mapping approach, based on the extent of resected language areas identified by fMRI, MEG, TMS, and hgECoG, could predict the postoperative language outcome. This hypothesis had been supported by a few studies using a single modality approach (fMRI or hgECoG) (Sabsevitz et al., 2003; Bonelli et al., 2012; Cervenka et al., 2013; Kojima et al., 2013; Genetti et al., 2015). We proposed a multimodal approach to test this hypothesis by addressing the following challenges. First, the relationship between the extent of resected language area, identified by a given modality, and the degree of postoperative language deficit is unknown. This relationship is complex and may not be represented by a simple model such as linear regression. Another challenge is how to integrate modalities and benefit from their complementary aspects while minimizing possible redundancies. To address these challenges, we used the support vector regression (SVR). The data-driven approach in the support vector machine can model complicated and nonlinear relationships (Mourao-Miranda et al., 2005; Khazaee et al., 2015b, 2015a, 2016). The SVR can also identify an optimal model among all possible models when there is redundancy in inputs of the models.

2. Methods

2.1. Participants

A consecutive series of 26 patients with epilepsy who underwent resection for treatment of intractable epilepsy at the Le Bonheur Children's Hospital were prospectively selected for this study. The inclusion criteria were patients: (i) who were either left hemisphere dominant or bilateral for language according to the Wada test or results of presurgical language mapping using fMRI, MEG, and TMS; (ii) who had subdural electrodes implanted over the left temporal and extratemporal regions; (iii) underwent left hemisphere resection; (iv) and who performed post-operative neuropsychological language evaluation approximately six months after surgery. Of these 26 patients, 11 patients (7 males; aged 24 ± 9 (mean ± SD) years) met inclusion criteria (Tables 1 and 2). The study was approved by the Institutional Review Board of the University of Tennessee. Written informed consent was obtained from all participants.

2.2. Pre- and postoperative language assessment and presurgical language mapping

Patients received pre- and postoperative neuropsychological evaluation of language. Preoperative evaluation was performed within one month before surgery. Postoperative evaluation was performed approximately six months after surgery. Procedures for presurgical language mapping using fMRI, TMS, MEG, hgECoG, and CSM have been previously described in detail (Babajani-Feremi et al., 2014, 2016), and we employed the same procedures in this study. Briefly, these methods were conducted as follows.

2.2.1. fMRI presurgical language mapping

An object naming task or a sentence completion task was used covertly for language localization. We collected 5 min of fMRI data using a block design with 15 s alternations between task and rest. The blood oxygenation level-dependent (BOLD) fMRI data were collected using a 3-T MR scanner (GE, SIGNA) and a $T2^*$-weighted echoplanar imaging sequence (TR = 3000 ms; TE = 35 ms; flip angle = 90°; voxel size = $3.75 \times 3.75 \times 4$ mm; 33 slices). The SPM8 toolbox (www.fil.ion.ucl.ac.uk/spm/software/spm8) was used for processing of data. After pre-processing of fMRI data, a general linear model was used for each subject individually, and active voxles were identified based on $p < 0.05$ (corrected for multiple comparisons) (Fig. 1a).

2.2.2. MEG presurgical language mapping

A whole-head magnetometer containing 248 sensors (WH 3600, 4D Neuroimaging) was utilized for collecting MEG data. MEG data were recorded with a sampling rate of 1017.5 Hz. A Polhemus system was used for digitization of the fiducials and head shape. Three fiducials (nasion and left and right periauricular points) and two marker coils were digitized. Patient's head shape was also digitized in approximately 2500 points.

As a routine clinical procedure in our center, a word recognition task (WRT) was used for MEG presurgical language mapping. This task has been used for language localization and lateralization (Maestu et al., 2004; Papanicolaou et al., 2004; Babajani-Feremi et al., 2014). In the WRT, subjects listened to high-frequency words and were instructed to lift the index finger of the dominant hand if they heard five target words (Babajani-Feremi et al., 2014). One hundred-twenty words were presented followed by a random inter-stimulus interval (ISI) of 2–3 s. A native English speaker with a flat intonation produced the auditory stimuli (duration = 395–920 ms; mean = 587 ms; standard deviation = 85 ms). The auditory stimuli were delivered to the patients binaurally via plastic tubes terminating in ear inserts at the same intensity level in both ears.

The MEG data were processed using written MATLAB (The MathWorks, Inc., Natick, MA) scripts based on the Fieldtrip toolbox (Oostenveld et al., 2011). Noisy MEG sensors exhibiting high variance ratio or poor correlation to neighboring sensors were flagged and removed from further analysis (Winter et al., 2007). The physiological artifacts and noise, generated by electro-cardiogram and power supply bursting were identified using independent components analysis (ICA) and then removed from the MEG data (Mantini et al., 2011; Larson-Prior et al., 2013). It is noteworthy that subjects performed the WRT task in an eyes-closed condition and, thus, very rare eye blink and movement were observed in the MEG data. The time segments corresponding to the eye blink and movement were visually identified and excluded from analysis.

After pre-processing and removing artifacts, the clean MEG data were converted into epoch data and average event related fields (ERFs) were calculated. The dynamic statistical parametric maps