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Language mapping using high gamma electrocorticography, fMRI, and TMS versus electrocortical stimulation

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HIGHLIGHTS

- There is considerable concordance between CSM, high gamma ECoG (hgECoG), fMRI, and TMS.
- TMS, hgECoG, and fMRI are valuable tools for presurgical language mapping.
- A multimodal language mapping approach can overcome the limitations of CSM.

ABSTRACT

Objective: The aim of the present study was to compare localization of the language cortex using cortical stimulation mapping (CSM), high gamma electrocorticography (hgECoG), functional magnetic resonance imaging (fMRI), and transcranial magnetic stimulation (TMS).
Methods: Language mapping using CSM, hgECoG, fMRI, and TMS were compared in nine patients with epilepsy. Considering CSM as reference, we compared language mapping approaches based on hgECoG, fMRI, and TMS using their sensitivity, specificity, and the results of receiver operating characteristic (ROC) analyses.
Results: Our results show that areas involved in language processing can be identified by hgECoG, fMRI, and TMS. The average sensitivity/specificity of hgECoG, fMRI, and TMS across all patients was 100%/85%, 50%/80%, and 67%/66%, respectively. The average area under the ROC curve of hgECoG, fMRI, and TMS across CSM-positive patients was 0.98, 0.76, and 0.68, respectively.
Conclusions: There is considerable concordance between CSM, hgECoG, fMRI, and TMS language mapping. Our results reveal that hgECoG, fMRI, and TMS are valuable tools for presurgical language mapping.
Significance: Language mapping on the basis of hgECoG, fMRI, and TMS can provide important additional information, therefore, these methods can be used in conjunction with CSM or as an alternative, when the latter is deemed impractical.

1. Introduction

One of the goals in neurosurgery is to resect pathological brain tissue, while minimizing postsurgical functional impairments. In view of inter-individual variability in functional anatomy, especially for language (Ojemann, 2003), it becomes necessary to perform presurgical functional mapping and assess the risk of

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neurological impairments following surgery on an individual basis. Cortical stimulation mapping (CSM) is the conventional clinical standard-of-care for functional mapping (Ojemann et al., 1989), though it has several limitations (Papanicolaou et al., 2014). For example, CSM can produce after-discharges and electrically-induced seizures that put the patient at risk and make additional immediate testing problematic or even impossible (Lesser et al., 1984; Blume et al., 2004). Furthermore, CSM is time-consuming and requires patient cooperation that makes functional mapping in young, uncooperative, and developmentally delayed patients quite challenging (Schevon et al., 2007; Kojima et al., 2012).

Given the limitations of CSM, other functional mapping approaches have been developed, including high gamma electrocorticography (hgECoG), functional magnetic resonance imaging (fMRI), and transcranial magnetic stimulation (TMS) (Crone et al., 2006; Swanson et al., 2007; Picht et al., 2013). A multi-modality language mapping approach using fMRI, hgECoG, and TMS can complement, or in some cases even replace, CSM given the complementary nature of these modalities and their ability to assess different aspects of neurophysiological task-specific activation (Papanicolaou et al., 2014). That is, fMRI records local task-specific hemodynamic changes, hgECoG measures local task-specific changes in power of high gamma oscillations, and TMS generates reversible lesions.

Often, patients with intractable epilepsy being considered for surgery undergo invasive electrophysiological monitoring involving electrocorticographic (ECoG) recordings from subdural electrodes. Besides aiding localization of the ictal onset zone, subdural electrodes also facilitate extraoperative functional mapping. Enhancement of the power of ECoG recordings in the high gamma (>50 Hz) frequency range has been shown to be a reliable marker of local task-related cortical activation and has provided promising results for functional mapping (Crone et al., 1998; Cervenka et al., 2013). Functional mapping through ECoG has several advantages over CSM, most notably the elimination of the risk of producing seizures during passive ECoG recordings and a reduction of the time required for functional mapping. Several investigators have utilized hgECoG changes during language tasks to localize eloquent cortex and have reported good concordance between hgECoG and CSM (Sinai et al., 2005; Kojima et al., 2012; Babajani-Feremi et al., 2014). However, there are discrepancies across these studies in the reported sensitivity and specificity of hgECoG.

Of the non-invasive brain mapping methods, fMRI has recently become a routine procedure in presurgical evaluation in a large number of clinical centers. Several studies have shown the utility of fMRI in presurgical planning, particularly for mapping language functions (Binder et al., 1997; Bookheimer, 2007; Swanson et al., 2007). Presurgical language mapping using fMRI has been compared against CSM mapping and a fair concordance between these two methods has been reported. However, as with hgECoG, there is inconsistency across different studies with regard to the sensitivity and specificity of fMRI for language mapping (FitzGerald et al., 1997; Kunii et al., 2011; Genetti et al., 2015).

More recently, another non-invasive functional mapping method that is being increasingly utilized is TMS. Similar to CSM but unlike fMRI and hgECoG, stimulation of essential language areas using TMS causes speech disruption. However, the utility of TMS as a non-invasive alternative to CSM in presurgical language mapping has yet to be fully explored. To date, few studies have compared language mapping using TMS with that of using intraoperative CSM (Picht et al., 2013; Picht et al., 2013; Tarapore et al., 2013; Ille et al., 2015). Direct comparisons of presurgical language mapping using CSM and TMS demonstrated good concordance between the two methods and a sensitivity of 90% for TMS was reported (Picht et al., 2013; Tarapore et al., 2013). However, these studies reported high numbers of false positive findings, and varying degrees of specificity. Moreover, these TMS studies examined only patients who had a brain tumor in the vicinity of the language cortex and were based on intra-, rather than extra-, operative CSM. Consequently, additional studies that compare TMS language mapping against other functional mapping methods are necessary to assess the reliability of TMS language mapping.

Thus far, language mapping using CSM has been compared to that using either fMRI, hgECoG, or TMS (e.g., FitzGerald et al., 1997; Sinai et al., 2005; Picht et al., 2013), or to that using fMRI and hgECoG (Genetti et al., 2015). The aim of the present study was to compare presurgical language mapping using CSM, fMRI, hgECoG, and TMS. To the best of our knowledge, this is the first study that compares the efficiency of language mapping using all three modalities against that of CSM. In addition, given the lack of consistency in the reported sensitivity and specificity of fMRI, hgECoG, and TMS, we also sought to clarify the accuracy and the reliability of these methods. Furthermore, evaluation of the performance of TMS in the present study is desirable since there are very few (and inconsistent) studies that directly address it. Moreover, in contrast to the previous TMS studies, the present study is based on the patients with epilepsy who had no MRI-positive pathology in the vicinity of their language cortex and it involves extraoperative CSM which does not have the drawbacks of the intraoperative CSM used in previous TMS studies (Picht et al., 2013; Tarapore et al., 2013).

2. Methods

2.1. Patients

Nine patients (5 males; aged 15–37 years, 23 ± 8 (mean ± SD) years) who underwent a Phase II epilepsy surgery evaluation at the Le Bonheur Children's Hospital were retrospectively selected for this study (Table 1). The study was approved by the Institutional Review Board of the University of Tennessee Health Science Center. Informed consent was obtained from all participants in accordance with the Declaration of Helsinki. A comprehensive neuropsychological evaluation was performed on all patients and all patients but Patient 5 performed at an average or above average level. Results of the neuropsychological evaluation on Patient 5 suggested overall low average cognitive abilities (General Conceptual Ability standard score = 87, i.e., 19th percentile).

All patients had a diagnosis of medically intractable epilepsy and were native English speakers. The patients were selected on the basis of the following inclusion criteria: (i) left language dominance; (ii) no history of frontal lobe pathology that could affect cortical representation of language; (iii) had undergone all four presurgical language mapping methods (CSM, fMRI, TMS, and hgECoG). Eight patients were right-handed and one patient (Patient 3) was left-handed. We did not exclude the left-handed patient from this study since he was left language dominant based on the results of his WADA test. Six patients underwent the Wada test, prior to electrode implantation. Four patients (1, 3, 5, and 6) were deemed to be left hemisphere dominant for language, and two patients (4 and 8) had bilateral language representation, with a preponderance of left hemisphere involvement. Patients 2, 7, and 9 who did not undergo the Wada test, were right-handed and considered left language dominant on the basis of the presurgical mapping using fMRI, magnetoencephalography (MEG), and TMS.

The CSM did not result in speech arrest (or speech disruption) and receptive language errors in Patients 3, 8, and 9 despite extensive stimulation of the subdural electrodes and complete cooperation of the patient. As other authors have done (e.g., Genetti et al., 2015), we did not exclude these patients from our study because the CSM-negative sites in these patients were used to verify the false-positive sites identified by fMRI, TMS, or hgECoG.