(Non-) invasive mapping of cortical language areas

The precise localization of eloquent cortex is crucial for planning the extent and exact location of cortical resection in neurosurgical settings. While all brain areas are of functional importance, the term "eloquent" brain region refers to structures where damage can result in severe neurological symptoms that significantly affect the patient's functional outcome and quality of life. Presurgical functional mapping has become an essential tool to avoid neurological impairment after surgical resection in patients with focal epilepsy or resectable tumors. Nowadays, cortical stimulation mapping (CSM) represents the gold standard for intraoperative mapping of brain functions (Giussani et al., 2010). Well in advance of CSM, electrocorticography (EcoG), can be directly recorded from the exposed areas of the cortex affording a very good temporal and spatial resolution of the signal. However, both CSM and EcoG have several drawbacks, including the invasiveness of the procedure, the relatively long time required for mapping and the prerequisite of the patient's cooperation. Consequently, non-invasive alternatives such as functional MRI, magnetoencephalography, transcranial magnetic stimulation (TMS) or electroencephalography are increasingly being applied in clinical settings to map motor or language functions and assist preoperative planning (Picht, 2014; Picht et al., 2015). While these techniques cannot replace intraoperative CSM, some of them might reduce the number of invasive diagnostic measures prior to treatment and help to better stratify patients for intraoperative cortical mapping (Binder et al., 1996; Roux et al., 2003).

Among these methods, fMRI and TMS are relatively well established for presurgical mapping of motor functions (e.g. (Krieg et al., 2012; Picht et al., 2015)), while their reliability and accuracy for language mapping remains unclear (Tarapore et al., 2013; Krieg et al., 2014; Picht, 2014). Since language is a complex process that involves different networks for various sub-functions (e.g., phonological, semantic and syntactic processes), robust identification of critical areas might require the application of various paradigms that cover different linguistic aspects (e.g., verb generation, picture naming, sentence processing) (Rutten et al., 2002). Moreover, reliable localization of core language regions is complicated by the fact that there are no reliable morphological landmarks for cortical language areas. Consequently, future studies with large patient cohorts and comparable designs are required. In this context, TMS might be more comparable to CSM than fMRI as the former techniques share similar mechanisms. TMS has previously been used to assess causality of structure–function relationships by transiently disrupting task-related activity in the healthy language system (Devlin and Watkins, 2007; Hartwigsen, 2015). A small number of studies also used TMS-based language mapping in tumor patients or epileptic surgery candidates (see Picht, 2014 for review). However, optimal stimulation parameters still remain to be determined (i.e., timing of the onset of the TMS pulses, frequency and duration of TMS bursts as well as stimulation intensity) (Tarapore et al., 2013; Krieg et al., 2014). Hence, chronometric approaches in healthy subjects might guide future preoperative applications with respect to TMS mapping over different areas at various time points during linguistic tasks.

Electrocorticography has the potential to be an important invasive tool to longitudinally increase the temporal window of the mapping procedure. With its help, region- and task-specific changes in electrophysiological activity can be recorded and analyzed in and optimal temporal and frequency domain. An increase of power in a specific frequency domain can for instance be considered as a read-out parameter during a task for functional mapping (Crone et al., 2006; Bauer et al., 2013). Further methods to analyze ECoG signals are time frequency analyses (Mitra and Pesaran, 1999) and spatial activation maps interpolated on individual MRI (Taimouri et al., 2014). Other functional modalities with a similar temporal and frequency resolution like EEG and MEG necessitate complex inverse solutions to deliver a good spatial mapping of the identified sources during a particular task and have not been widely implemented in preoperative testing (Muthuraman et al., 2012, 2014).

A way forward for an optimal mapping procedure would be the integration of multimodal information that can be applied to improve the accuracy of preoperative planning and facilitate decision making during surgical resections. Since different mapping techniques provide complementary information (e.g., fMRI: spatial resolution in millimeter range; TMS and EcoG: temporal resolution in milliseconds range), an integrative approach will be mostly useful in the context of preoperative planning.

In this issue of Clinical Neurophysiology, Babajani-Feremi and colleagues publish a work describing the use of CSM, ECoG, fMRI, and TMS for language mapping in a multi-modal approach, testing the sensitivity and specificity of each tool (Babajani-Feremi et al., 2016). The same battery of tools was applied in each patient, providing optimal within-subject comparability of the effects. The authors adapted the environment of either an object-naming task and/or a sentence-completion task and used the receiver operating characteristic (ROC) analysis to evaluate the effect of variation of the threshold of significance level between the modalities, finally calculating the Euclidean distance to test the methods quantitatively in the spatial domain. It is an important work on the evaluation of the modalities for presurgical language mapping in epilepsy patients, adapting the comparability of the modalities in all three domains of comparison, namely temporal, frequency and spatial. This work closes an important gap for language mapping between different modalities by the application of a multimodal testing battery and reveals the complementary strengths of each, as well as establishing a solid framework for clinical assessments. In future studies, however, it will be important to determine whether similar outcomes are also observed for tests assessing different linguistic aspects (verb generation, picture naming, sentence processing). Further effort will also be required to improve the sensitivity/specificity of the non-invasive mapping techniques. The time of Wada tests has definitely ended; however, we stress the necessity to improve the precision of these techniques, which can only be achieved through multimodality.

Acknowledgements

This work was supported by the German Research Council (SFB CRC-TR 128). The funding does not have any involvement in the study design, in the collection, analysis and interpretation of data, in the writing of the manuscript, and in the decision to submit the article for publication.

Conflict of interest: None of the authors have potential conflicts of interest to be disclosed.

References

Bauer PR, Vansteensel MJ, Bleichner MG, Hermes D, Ferrier CH, Aarnoutse EJ, et al. Mismatch between electrocortical stimulation and electrocorticography frequency mapping of language. Brain Stimul 2013;6:524–31.

Babajani-Feremi A, Narayana S, Rezaie R, Choudhri AF, Fulton SP, Boop FA, et al. Language mapping using high gamma electrocorticography, fMRI, and TMS versus electrocortical stimulation. Clin Neurophysiol 2016;127:1822–36.

Binder JR, Swanson SJ, Hammeke TA, Morris GL, Mueller WM, Fischer M, et al. Determination of language dominance using functional MRI: a comparison with the Wada test. Neurology 1996;46:978–84.

Crone NE, Sinai A, Korzeniewska A. High-frequency gamma oscillations and human brain mapping with electrocorticography. Prog Brain Res 2006;159:275–95.

Devlin JT, Watkins KE. Stimulating language: insights from TMS. Brain 2007;130:610–22.

Giussani C, Roux FE, Ojemann J, Sganzerla EP, Pirillo D, Papagno C. Is preoperative functional magnetic resonance imaging reliable for language areas mapping in brain tumor surgery? Review of language functional magnetic resonance imaging and direct cortical stimulation correlation studies. Neurosurgery 2010;66:113–20.

Hartwigsen G. The neurophysiology of language: Insights from non-invasive brain stimulation in the healthy human brain. Brain Lang 2015;148:81–94.

Krieg SM, Shiban E, Buchmann N, Gempt J, Foerschler A, Meyer B, et al. Utility of presurgical navigated transcranial magnetic brain stimulation for the resection of tumors in eloquent motor areas. J Neurosurg 2012;116:994–1001.

Krieg SM, Tarapore PE, Picht T, Tanigawa N, Houde J, Sollmann N, et al. Optimal timing of pulse onset for language mapping with navigated repetitive transcranial magnetic stimulation. Neuroimage 2014;100:219–36.

Mitra PP, Pesaran B. Analysis of dynamic brain imaging data. Biophys J 1999;76:691–708.

Muthuraman M, Hellriegel H, Hoogenboom N, Anwar AR, Mideksa KG, Krause H, et al. Beamformer source analysis and connectivity on concurrent EEG and MEG data during voluntary movements. PLoS One 2014;9:e91441.

Muthuraman M, Heute U, Arning K, Anwar AR, Elble R, Deuschl G, et al. Oscillating central motor networks in pathological tremors and voluntary movements. What makes the difference? Neuroimage 2012;60:1331–9.

Picht T. Current and potential utility of transcranial magnetic stimulation in the diagnostics before brain tumor surgery. CNS Oncol 2014;3:299–310.

Picht T, Frey D, Thieme S, Kliesch S, Vajkoczy P. Presurgical navigated TMS motor cortex mapping improves outcome in glioblastoma surgery: a controlled observational study. J Neurooncol 2015. http://dx.doi.org/10.1007/s11060-015-1993-9.

Roux FE, Boulanouar K, Lotterie JA, Mejdoubi M, LeSage JP, Berry I. Language functional magnetic resonance imaging in preoperative assessment of language areas: correlation with direct cortical stimulation. Neurosurgery 2003;52:1335–45 [discussion 45–7].

Rutten GJ, Ramsey NF, van Rijen PC, Noordmans HJ, van Veelen CW. Development of a functional magnetic resonance imaging protocol for intraoperative localization of critical temporoparietal language areas. Ann Neurol 2002;51:350–60.

Taimouri V, Akhondi-Asl A, Tomas-Fernandez X, Peters JM, Prabhu SP, Poduri A, et al. Electrode localization for planning surgical resection of the epileptogenic zone in pediatric epilepsy. Int J Comput Assist Radiol Surg 2014;9:91–105.

Tarapore PE, Findlay AM, Honma SM, Mizuiri D, Houde JF, Berger MS, et al. Language mapping with navigated repetitive TMS: proof of technique and validation. Neuroimage 2013;82:260–72.

Muthuraman Muthuraman *

Department of Neurology, Mainz, Germany

* *Address: Movement Disorders and Neurostimulation, Department of Neurology, Focus Program Translational Neuroscience (FTN), Johannes-Gutenberg-University Hospital, Langenbeckstr. 1, 55131 Mainz, Germany. Tel.: +49 6131 17 8236; fax: +49 6131 17 6495.*

E-mail address: Muthuraman.Muthuraman@unimedizin-mainz.de

Gesa Hartwigsen

Department of Neuropsychology, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

Sergiu Groppa

Department of Neurology, Mainz, Germany