EDITORIAL

Passive language mapping

Jeffrey G. Ojemann, MD

Department of Neurological Surgery, University of Washington, Seattle Children's Hospital, Seattle, Washington

IN this issue of the journal, Tamura and colleagues¹⁵ report on 5 patients who underwent awake craniotomy for tumor resection in which the investigators generated, using a high-frequency electrocorticography (ECoG) signal, activation maps from listening and evoked responses without overt patient cooperation. The idea that eloquent language cortex can be determined without active patient cooperation has driven studies for years⁶ in the hope of augmenting or replacing the extensive experience with disrupting language processes by using electrocortical stimulation (ECS) during the task performance.¹⁰

Changes in the high-frequency component of the ECoG signal have been increasingly studied because they are spatially focal and are thought to represent the function of the underlying cortex.¹⁴ The ability to generate maps using ECoG has been known for some time;³ the use of passive tasks was described 5 years ago,¹⁶ and the application to intraoperative, real-time mapping was understood.¹¹ This approach has the additional benefit, which has been reported by many, of being feasible in pediatric populations.^{8,9} The methods described by the authors are nearly identical to those that are freely available to researchers in a toolkit developed by investigators at the Wadsworth Institute, and can be readily acquired if direct access to the ECoG signal is possible.¹³

Generating a map and generating a valid representation of language is not the same thing. Importantly, Tamura et al.¹⁵ make an effort to assess the specificity and sensitivity of their approach. This has been addressed in prior efforts,^{1,3,4,5,16} and the results have been mixed. In some reports the match is quite poor, in fact, perhaps mimicking functional MRI (fMRI) mapping in having a strong dependence on the specific task used for mapping.¹ One misleading aspect of sensitivity measures is that the placement of electrodes is already biased toward parts of the brain which, statistically, are likely to have language function.¹⁰ Thus, a small, biased sample of a new test can give misleadingly high statistics as to its accuracy. A more salient question is whether the approach would give a sur-

geon confidence and whether a small series is sufficient to address this issue with any confidence.

Cortico-cortical evoked potentials (CCEPs) are an intriguing approach to assessing critical areas passively, and a recent series¹² in 13 patients also showed promise that this method may identify some areas. Other approaches to assessing endogenous networks in the absence of a task have been explored⁷ and may even allow for mapping under certain levels of anesthesia, as has been reported for sensorimotor networks.²

Even ECS mapping fails to deal with the fact that language is not a unitary phenomenon. Mapping of one task may or may not prevent deficits in other domains. Even if the authors demonstrate an effective way of mapping auditory speech areas, this may not be sufficient (or may be overly proscriptive) to replace standard mapping regimens. The goal of finding a dynamic, state-independent correlate to essential language cortex is an interesting and important topic. A larger study, focusing on surgical decision making in the approach to this question is needed.

<http://thejns.org/doi/abs/10.3171/2015.6.JNS15927>

References

1. 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** 6:524–531, 2013
2. Breshears JD, Gaona CM, Roland JL, Sharma M, Bundy DT, Shimony JS, et al: Mapping sensorimotor cortex with slow cortical potential resting-state networks while awake and under anesthesia. **Neurosurgery** 71:305–316, 2012
3. Brunner P, Ritaccio AL, Lynch TM, Emrich JF, Wilson JA, Williams JC, et al: A practical procedure for real-time functional mapping of eloquent cortex using electrocorticographic signals in humans. **Epilepsy Behav** 15:278–286, 2009
4. Cervenka MC, Boatman-Reich DF, Ward J, Franaszczuk PJ, Crone NE: Language mapping in multilingual patients: electrocorticography and cortical stimulation during naming. **Front Hum Neurosci** 5:13, 2011
5. Genetti M, Tyrand R, Grouiller F, Lascano AM, Vulliemoz

- S, Spinelli L, et al: Comparison of high gamma electrocorticography and fMRI with electrocortical stimulation for localization of somatosensory and language cortex. **Clin Neurophysiol** 126:121–130, 2015
6. Goldring S, Harding GW, Gregorie EM: Distinctive electrophysiological characteristics of functionally discrete brain areas: a tenable approach to functional localization. **J Neurosurg** 80:701–709, 1994
 7. Ko AL, Weaver KE, Hakimian S, Ojemann JG: Identifying functional networks using endogenous connectivity in gamma band electrocorticography. **Brain Connect** 3:491–502, 2013
 8. Korostenskaja M, Chen PC, Salinas CM, Westerveld M, Brunner P, Schalk G, et al: Real-time functional mapping: potential tool for improving language outcome in pediatric epilepsy surgery. **J Neurosurg Pediatr** 14:287–295, 2014
 9. Miller KJ, Abel TJ, Hebb AO, Ojemann JG: Rapid online language mapping with electrocorticography. **J Neurosurg Pediatr** 7:482–490, 2011
 10. Ojemann G, Ojemann J, Lettich E, Berger M: Cortical language localization in left, dominant hemisphere. An electrical stimulation mapping investigation in 117 patients. **J Neurosurg** 71:316–326, 1989
 11. Roland J, Brunner P, Johnston J, Schalk G, Leuthardt EC: Passive real-time identification of speech and motor cortex during an awake craniotomy. **Epilepsy Behav** 18:123–128, 2010
 12. Saito T, Tamura M, Muragaki Y, Maruyama T, Kubota Y, Fukuchi S, et al: Intraoperative cortico-cortical evoked potentials for the evaluation of language function during brain tumor resection: initial experience with 13 cases. **J Neurosurg** 121:827–838, 2014
 13. Schalk G, Leuthardt EC, Ojemann JG, Gerhardt LA, Wolpaw JR: Real-time detection of event-related brain activity. **Neuroimage** 43:245–249, 2008
 14. Sinai A, Bowers CW, Crainiceanu CM, Boatman D, Gordon B, Lesser RP, et al: Electrocorticographic high gamma activity versus electrical cortical stimulation mapping of naming. **Brain** 128:1556–1570, 2005
 15. Tamura Y, Ogawa H, Kapeller C, Prueckl R, Takeuchi F, Anei R, et al: Passive language mapping combining real-time oscillation analysis with cortico-cortical evoked potentials for awake craniotomy. **J Neurosurgery** [epub ahead of print March 18, 2016. DOI: 10.3171/2015.4.JNS15193]
 16. Wu M, Wisneski K, Schalk G, Sharma M, Roland J, Bresshears J, et al: Electrocorticographic frequency alteration mapping for extraoperative localization of speech cortex. **Neurosurgery** 66:E407–E409, 2010

Disclosures

The author reports no conflict of interest.

Response

Yukie Tamura, MD,¹ Hiroshi Ogawa, MD,¹
 Christoph Kapeller, MSc,² Robert Prueckl, MSc,²
 Fumiya Takeuchi, PhD,³ Ryogo Anei, MD, PhD,¹
 Anthony Ritaccio, MD, PhD,⁴ Christoph Guger, PhD,² and
 Kyousuke Kamada, MD, PhD¹

¹Department of Neurosurgery and ³Center for Advanced Research and Education, School of Medicine, Asahikawa Medical University, Hokkaido, Japan; ²Guger Technologies OG, Graz, Austria; and ⁴Department of Neurology, Albany Medical Center, Albany, New York

In commenting on our article, Professor Ojemann summarized the clinical benefit and limitations of our study. Although the combination of different electrophysiological

monitoring techniques contains the practical potential to support a surgical decision-making approach, we understand that inconsistent findings of ECoG and ECS mapping still occurred in previous reports.^{1,2,7,10,11} We expected that we would not be able to reach 100% of concordance between ECS and ECoG mapping, because the basic mechanisms are totally different. In addition, previous methods and our ECoG techniques needed several seconds for rest and active periods, and used statistical analysis to make functional maps, which was similar to fMRI.^{10,11} This procedure sacrificed the time resolution of ECoG (i.e., it might not reflect real-time ECoG activity) and might subtract activity and affect the mapping results.

As Professor Ojemann pointed out in his previous work, each person has different distributions of language-related functions. Because we understand the individual variability, we are also eager to adapt new techniques such as ECoG and fMRI to obtain more (and more precise) functional information. On the other hand, neurosurgeons usually keep safe margins (5–10 mm) between eloquent cortices and lesions for safety reasons, despite accurate ECS mapping.⁸ Our concept of brain mapping was to quickly obtain rough functional maps by ECoG and switch to ECS mapping for validation.

On the basis of our experience, the language lateralization could be determined by functional imaging techniques in most cases. According to fMRI studies with language tasks, it has been sufficient to identify the language lateralization instead of using the Wada test for more than a decade.³ However, we still need to localize language function for lesion resection. Our previous study showed higher sensitivity and lower specificity of language-related fMRI results by comparing the findings with ECS mapping, and concluded that fMRI was not yet sufficient to localize the higher brain functions.⁵ Furthermore, a characteristic of fMRI activation was dominantly observed on the frontal language areas by common language tasks such as word reading and picture naming. By comparing fMRI and high gamma activity (HGA) dynamics, we found different HGA profiles on the frontal and posterior language areas with word reading tasks. The HGA of the frontal language area lasted much longer than that of the posterior language area.

The electrophysiological differences might explain variations in fMRI activation and HGA mapping in different brain regions.⁴ Because the various brain regions have different electrophysiological profiles, ECS, which interrupts the brain functions, might show different thresholds and findings in each brain region. We believe that it is important to use multiple language tasks not only for ECS, but also for HGA mapping to find appropriate conditions for the critical borders. From the ideal point of view of neuroscience, the concordance between them should reach approximately 100% accuracy. However, in the operating theater, neurosurgeons had little time for mapping and first needed rough functional localization after inspection of brain anatomy. We believe that values between 85% and 90% for sensitivity and specificity of HGA mapping were sufficient in practice to decide the critical borders for awake craniotomy.

We encountered one patient (not reported here) who

failed to perform any tasks during awake craniotomy. Despite mild dysarthria before the operation, he was not able to cooperate in either HGA or ECS mapping. This experience led us to consider a technical development for patients who had mapping problems with multiple factors. As a result, the noncooperation (i.e., passive) mapping technique occurred to us, and we applied this technique for the first case in our manuscript. The CCEP is a unique technique, which demonstrates huge responses on functionally connected areas by single-pulse stimulation without a patient's cooperation.⁶

Compared to previous reports about CCEP recording with awake craniotomy,^{9,12} our passive mapping delivered the linguistic sounds to patients and showed increased HGA in the posterior language area. We then recorded CCEPs in the frontal language area by stimulating the posterior language area. As a result, we were able to obtain the classic language areas without any patient's cooperation, and these results were ultimately validated by ECS.

To detect HGA in the posterior language area, we applied word-reading and picture-naming tasks and 1-KHz pure tone and linguistic sounds delivery. The first two tasks had shorter HGA periods,⁷ and the third showed little HGA accumulation. As a result, linguistic sounds, which consisted of various pitches and frequencies, succeeded in activating the posterior language area. By stimulating the identified area, we consistently observed CCEPs in the frontal language area and validated the areas by using ECS. After we submitted our work, we investigated more patients during awake craniotomy. All of them demonstrated higher sensitivity and specificity of the passive mapping than in our original article. Because the CCEP technique is not the only way to detect connectivity, we can apply resting-state ECoG or find HGA fluctuations over time to detect language networks. In our report, we would like to at least stress rapid (real-time) and passive mapping, especially for awake craniotomy. Since we stored all the ECoG data, we would like to check them again by offline data analysis and make another report according to Professor Ojemann's suggestions.

Nevertheless, ECS is still the gold standard, because of the wealth of accumulated knowledge and skills. By learning the ECS procedure, we intended to establish a real-time mapping technique, searching appropriate tasks and frequencies. Professor Ojemann's comments encouraged us to investigate more patients and analyze the data in detail to convince neurosurgeons to prove the reliability of our passive procedure.

References

1. 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** 6:524–531, 2013
2. Kamada K, Ogawa H, Saito M, Tamura Y, Anei R, Kapeller C, et al: Novel techniques of real-time blood flow and functional mapping: technical note. **Neurol Med Chir (Tokyo)** 54:775–785, 2014
3. Kamada K, Sawamura Y, Takeuchi F, Kuriki S, Kawai K, Morita A, et al: Expressive and receptive language areas determined by a non-invasive reliable method using functional magnetic resonance imaging and magnetoencephalography. **Neurosurgery** 60:296–306, 2007
4. Kunii N, Kamada K, Ota T, Greenblatt RE, Kawai K, Saito N: The dynamics of language-related high-gamma activity assessed on a spatially-normalized brain. **Clin Neurophysiol** 124:91–100, 2013
5. Kunii N, Kamada K, Ota T, Kawai K, Saito N: A detailed analysis of functional magnetic resonance imaging in the frontal language area: a comparative study with extraoperative electrocortical stimulation. **Neurosurgery** 69:590–597, 2011
6. Matsumoto R, Nair DR, LaPresto E, Najm I, Bingaman W, Shibasaki H, et al: Functional connectivity in the human language system: a cortico-cortical evoked potential study. **Brain** 127:2316–2330, 2004
7. Ogawa H, Kamada K, Kapeller C, Hiroshima S, Prueckl R, Guger C: Rapid and minimum invasive functional brain mapping by real-time visualization of high gamma activity during awake craniotomy. **World Neurosurg** 82:912.e1–912.e10, 2014
8. Ojemann G, Ojemann J, Lettich E, Berger M: Cortical language localization in left, dominant hemisphere. An electrical stimulation mapping investigation in 117 patients. **J Neurosurg** 71:316–326, 1989
9. Saito T, Tamura M, Muragaki Y, Maruyama T, Kubota Y, Fukuchi S, et al: Intraoperative cortico-cortical evoked potentials for the evaluation of language function during brain tumor resection: initial experience with 13 cases. **J Neurosurg** 121:827–838, 2014
10. Sinai A, Bowers CW, Crainiceanu CM, Boatman D, Gordon B, Lesser RP, et al: Electrocorticographic high gamma activity versus electrical cortical stimulation mapping of naming. **Brain** 128:1556–1570, 2005
11. Wu M, Wisneski K, Schalk G, Sharma M, Roland J, Bresshears J, et al: Electrocorticographic frequency alteration mapping for extraoperative localization of speech cortex. **Neurosurgery** 66:E407–E409, 2010
12. Yamao Y, Matsumoto R, Kunieda T, Arakawa Y, Kobayashi K, Usami K, et al: Intraoperative dorsal language network mapping by using single-pulse electrical stimulation. **Hum Brain Mapp** 35:4345–4361, 2014