REVIEW ARTICLE doi: 10.2176/nmc.ra.2014-0395

Neurol Med Chir (Tokyo) 55, 367–373, 2015 Online April 28, 2015

Evaluation of Language Function under Awake Craniotomy

Aya KANNO[1] and Nobuhiro MIKUNI[1]

[1]*Department of Neurosurgery, Sapporo Medical University School of Medicine, Sapporo, Hokkaido*

Abstract

Awake craniotomy is the only established way to assess patients' language functions intraoperatively and to contribute to their preservation, if necessary. Recent guidelines have enabled the approach to be used widely, effectively, and safely. Non-invasive brain functional imaging techniques, including functional magnetic resonance imaging and diffusion tensor imaging, have been used preoperatively to identify brain functional regions corresponding to language, and their accuracy has increased year by year. In addition, the use of neuronavigation that incorporates this preoperative information has made it possible to identify the positional relationships between the lesion and functional regions involved in language, conduct functional brain mapping in the awake state with electrical stimulation, and intraoperatively assess nerve function in real time when resecting the lesion. This article outlines the history of awake craniotomy, the current state of pre- and intraoperative evaluation of language function, and the clinical usefulness of such functional evaluation. When evaluating patients' language functions during awake craniotomy, given the various intraoperative stresses involved, it is necessary to carefully select the tasks to be undertaken, quickly perform all examinations, and promptly evaluate the results. As language functions involve both input and output, they are strongly affected by patients' preoperative cognitive function, degree of intraoperative wakefulness and fatigue, the ability to produce verbal articulations and utterances, as well as perform synergic movement. Therefore, it is essential to appropriately assess the reproducibility of language function evaluation using awake craniotomy techniques.

Key words: awake surgery, language, electric stimulation, mapping, monitoring

Introduction

Awake craniotomy is a neurosurgical technique used to safely and extensively remove cerebral lesions such as gliomas and epileptic foci that are located close to the functional regions. Both glioma and epilepsy are diseases whose prognosis is affected by the extent of resection. Broca and Wernicke identified the areas involved in language function in the 1860s, and other cerebral functions were later localized. In 1886, Sir Victor Horsley conducted awake craniotomy using cortical electrical stimulation to identify an epileptic focus, and subsequently several studies utilized the technique for epilepsy treatment. However, in the 1950s, after it became possible to precisely regulate patients' awake state during general anesthesia by using sedatives such as codeine together with analgesics, Penfield et al. performed electrical stimulation during epilepsy surgery and published a detailed report on the cerebral areas that control the movement of each body part. Such localization is closely related to the Brodmann's areas that are based on the cytoarchitecture of the cerebral cortex, and it is still widely utilized. In the 1960s, the neurolept anesthesia (NLA) was introduced in anesthesiology, making it possible to conduct awake craniotomy without tracheal intubation. Since then, mainstream epilepsy surgery has concentrated on removing the focus under general anesthesia, after first identifying the focus location and mapping brain function by placing subdural electrodes during a patient's hospital stay.[1)]

Awake craniotomy began to be commonly performed worldwide in 1990, after the introduction of intravenous anesthesia using propofol. With advances in surgical support technology such as brain functional imaging devices and neuronavigation systems, studies over the last dozen years have reported the safety and clinical usefulness of functional brain mapping with electrical stimulation under an awake state, and

Received November 19, 2014; Accepted January 5, 2015

evaluation of nerve function during lesion resection.[2] Awake craniotomy is the only established way to intraoperatively verify the preservation of language function. The European Federation of Neurological Societies-European Association for Neuro-Oncology (EFNS-EANO) guidelines for low-grade glioma issued in 2010 in Europe identified brain mapping during awake craniotomy as a method to obtain Class II evidence. Furthermore, it is employed as a method to obtain Class III evidence for identifying the cortical or subcortical structures underlying language function.[3] In Japan in 2012, the Japan Society for Awake Surgery issued guidelines for awake craniotomy with the aim of promoting and standardizing this technique.[4]

Preoperative Assessment Methods

I. Functional magnetic resonance imaging (fMRI)

fMRI is used to identify which areas of the brain are active during particular mental processes, by comparing the proportion of oxyhemoglobin to reduced-type hemoglobin in different regions when patients are at rest or performing tasks. Commonly used language-related tasks include *Shiritori* (a Japanese word game: say a word starting with the last syllable of the previous one), word retrieval tasks, and reading tasks. Although the *Shiritori* is simple and does not require any preparation, it largely relies on the patient's volition, so in some cases the relevant brain regions are not sufficiently activated. When conducting reading tasks, a projector is set in the MRI room and a mirror is placed at the head of the subject so the material can be read. Regular external stimulation prevents the patient from falling asleep during the examination and thus permits effective activation. A weakness of reading tasks is that they cannot be conducted in patients with serious visual impairment.

In addition to language tasks, it is also necessary to conduct tasks in which the patient moves their lips so that the primary motor areas related to lip and tongue movement can be identified. Such an approach is required because the presenting symptoms of language disorders may be problems with articulation or utterance.

It has been reported that in 90% of cases, the dominant hemisphere can be identified by using fMRI to assess language function using simple word retrieval tasks and reading of words. Regarding the localization of language function in the brain, the sensitivity of fMRI in identifying active brain regions was reported to be 90%, and its specificity was reported to be 20–60%.[5] These results were obtained by electrically stimulating the cerebral cortex. Merits of this method include its non-invasiveness and the fact that it can be conducted repeatedly. However, it is less than ideal in terms of temporal resolution as well as threshold setting.

II. Diffusion tensor imaging (DTI) and tractography

DTI is based on the fact that the dispersion of water molecules in the cerebral parenchyma is limited by white matter fibers. DTI images of the brain, which are made using tensor analysis based on multiple diffusion-weighted images, can identify white matter fibers that travel as bundles or tracts (tractography).

Subcortical mapping is useful for resecting nerve fibers near the cortex that are identified as a functional region. In addition, preoperative tractography is useful for localizing the areas to be mapped via electric stimulation.[6] By combining fiber tracking with DTI and subcortical electrical stimulation during awake craniotomy, subcortical nerve fibers can be identified with high accuracy. It is expected that such combinations of techniques will result in improved postoperative prognoses, including successful resection, by shortening surgical time, reducing patients' fatigue, and suppressing intraoperative spasms.[7] Weaknesses of these approaches are that the fibers cannot be described clearly when crossing fibers are present within a voxel or compressive or edematous changes have occurred due to tumorous lesions, and the described fibers have some arbitrariness due to settings of regions of interest.

III. Wada test

The Wada test was developed by Jun Wada in 1948, and since then it has been the gold standard for identifying the dominant hemisphere for language. By temporarily inactivating the function of one cerebral hemisphere, the test assesses the lateralization of language and memory functions. While amobarbital used to be employed as a hypnotic sedative, currently propofol is used, which in some cases requires caution in order to reduce the frequency of adverse effects.[8] Although the Wada test can compare the on and off states of each hemisphere, as well as the right and left hemispheres' functions, the dominant hemisphere sometimes cannot be localized in cases where the blood flows through the anterior or posterior communicating artery. With improvements in the accuracy of non-invasive neuroimaging tests, the application range of the Wada test is narrowing.[9]

IV. Cognitive function test

The Standard Language Test of Aphasia (SLTA) and the Western Aphasia Battery (WAB) aphasia test are frequently employed for more detailed evaluation of language function, which cannot be assessed during awake craniotomy. For patients with cognitive dysfunction, in addition to screening using the revised Hasegawa's Dementia Scale (HDS-R) and the Mini-Mental State Examination (MMSE), the Wechsler Adult Intelligence Scale III (WAIS-III) Intelligence Scale, and the Wechsler Memory Scale-Revised (WMS-R) are conducted as needed. To prevent the patient from remembering the contents of previous tests, the interval between each test is set at around 3 months. These tests are necessary to precisely assess the preoperative symptoms and the effects of surgery related to the language functions.

Methods of Intraoperatively Evaluating Language Function

I. Intraoperative evaluation of language function

Verbal components include utterance, naming, plural naming, reading words, voluntary speech, word retrieval, *Shiritori*, repetition, auditory comprehension, sentence processing, reading figures, and color naming. Each of these functions is localized to a different brain area. In order to precisely identify each functional region within a limited period of time while minimizing the patient's fatigue, the guidelines for awake craniotomy advise the use of tasks such as number counting, visual naming, and auditory comprehension.[4] The function of utterance can be evaluated using number counting (from the viewpoint of motion), visual naming (viewpoint of expression), and auditory comprehension (viewpoint of both perceiving and expression).

Traditionally, the function of language areas has been estimated based on aphasic symptoms due to apoplexy and other conditions. Although it has been understood that visual and auditory information are recognized as "vocabulary," words are integrated through comprehension of "meaning," and this then leads to "utterance and speech." These processes involve a complex series of both long and short neural paths.[10] Therefore, stimuli affecting some of these paths do not always induce disorders, and damage to paths do not always result in permanent disorders.

II. Navigation system

Intraoperative navigation systems are now indispensable devices. These load MRI and computed tomography (CT) images obtained preoperatively and use an intraoperative system similar to Global Positioning System (GPS) navigation in automobiles to show the positional relationship between the lesion and normal tissues. Based on information derived using the aforementioned intraoperative fMRI or tractography, they can display the positional information of functional regions involved in language during the surgery in real time.

III. Electric stimulation of cortex and deep white matter

The most common technique for intraoperative functional brain mapping is currently electrical stimulation of the brain. It provides two types of responses: the "positive response" in which brain function is induced by electric stimulation and the "negative response" that is suppressed by the stimulation.

Phenomena such as delay or suspension of utterances observed when stimulating the language areas, and the Gerstmann syndrome that is induced by stimulating the inferior parietal lobule in the dominant hemisphere are categorized as negative responses. However, when evaluating such observations, close attention is required because the suspension of utterances is caused not only by electrical stimulation of language areas but also by the positive motor response that results in the contraction of the muscles related to articulation and utterance and the (primary) negative motor response that suppresses the synergic movement. The positive motor response corresponds to the primary motor areas related to the face, pharynx, larynx, and vocal cords in the inferior part of the precentral gyrus. To identify this response, it is necessary to confirm the presence or absence of vocal cord paralysis when the patient is asked to utter a single sound and to observe the muscle contractions around the oral cavity. The region corresponding to the negative motor response exists in the precentral gyrus, which induces motor apraxia of the tongue or fingers when stimulated. Hence, it should be distinguished from the tongue primary motor area and the frontal language area by adding a stimulus while the patient is moving their tongue and elevating both upper extremities. Just after resecting the negative motor area, a transient deficit in skilled motor activities occurs. It is considered that the parietal lobe is responsible for this function.[11]

For language-related cortex electrical stimulation, high frequency stimuli (e.g., 50–60 Hz) are commonly used. In contrast to the case with low frequencies, this results in significant facilitation effects, even if the stimulus intensity is relatively low. It is suitable for evaluating higher brain functions during patient behavior that is elicited by cortex stimulation (aphasia or suspension of motion). The intensity of stimuli is increased up to 15 mA by increments of about 1 mA, until some nerve response or afterdischarge is observed. Considering the safety of the cerebral cortex, the standard stimulus parameters have been established as 0.3 msec square-wave pulses of alternating polarity for up to 5 sec. Localization of cortical white matter in the primary motor cortex and the corticospinal tract using electric stimulation during awake craniotomy can performed with almost 100% success, but in language areas and their nerve fibers, the identification success rates are 58% and 59%, respectively.[12,13]

There are several general precautions for electrical stimulation. First, in some cases false-negative results occur because convulsive seizures are induced by the stimulation, and thus the stimulus intensities cannot be increased to sufficient levels. Second, there is considerable inter-individual variability in cortical excitability, so in some cases false negatives occur because stimulation at 15 mA is not strong enough to induce a positive reaction; in particular, children show minimal responses to electrical stimulation due to low levels of myelination in the language areas. Third, depending on the conditions used (frequency, intensity, duration) the stimulation depth and facilitation effects may vary.

IV. Cortico-cortical evoked potentials (CCEPs)

This method investigates inter-cortex functional linkage by recording short-latency evoked potentials in the cortex (CCEPs) from neighboring or remote cortex using single-pulse electric stimulation from subdural electrodes, which are placed at the surface of the cortex during surgery.[14] It was recently reported that by identifying CCEPs in both the anterior and posterior language areas, the inter-region connections through the arcuate fasciculus can be identified electrophysiologically.[15]

Surgery with Awake Evaluation of Language Function

In terms of glioma surgery, Sanai et al. reported that cerebral tumors could be resected safely by conducting negative mapping, which identifies the cortical regions where language disorders are not induced by electrical stimulation.[12] These authors successfully identified the language areas in 145 (58%) of 250 patients with gliomas by conducting language mapping of the frontal and temporal lobes using three tasks: number counting, naming, and reading out loud. They then resected these patients, and reading outs, leaving a margin of 1 cm around the identified language areas. They resected their cerebral tumors unless they showed no deficits in language tasks during electrical stimulation. Temporary language deficits were observed in 22% of cases, while permanent language deficits occurred in merely 1.6%. In addition, Bello et al. reported that nerve fibers related to language could be identified by subcortical electrical stimulation at a rate of 59%. While 67.3% of all cases in their study showed temporary language deficits, permanent language deficits occurred in only 2.3%.[13] Chang et al. found that although tumors close to functional areas were associated with increased recurrence rates and decreased survival times, resecting these lesions as extensively as possible using intraoperative mapping technique should result in longer survival.[16] In a meta-analysis of 8,091 patients, only 3.4% of the group undergoing surgery with intraoperative stimulation mapping developed serious delayed postoperative complications. On the other hand, 8.3% of those undergoing surgeries without simulation mapping developed such issues. Furthermore, mapping allowed for more extensive resection to be achieved.[17] Similarly, for epilepsy, it was reported that in 9 of 10 cases, seizures were abolished after surgery with intraoperative mapping, and function was preserved in all but 1 case in which the focus and eloquent cortex existed at the same location.[18] In 55 cases with non-lesional epilepsy undergoing chronic placement of subdural electrodes and awake focal resection, seizures were abolished in 49.1% of patients, 16.4% experienced decreased seizure frequency of three times or less per year, and 25.5% experienced a 90% decrease in seizure frequency. Although the symptoms were quite mild, 12.7% experienced postoperative neurological deficits.[19] It was suggested that by conducting awake focal resection with intraoperative brain mapping, foci of non-lesional epilepsy involving eloquent areas can be resected effectively and safely.[19]

About the factor of postoperative neurological deficits, Nossek et al. reported that failures of awake craniotomy were associated with postoperative morbidity.[20] Kumabe et al. summarized 59 awake craniotomies for language mapping, they also experienced high incidence of severe deficits, 3 as early and 2 as late of 8 cases, were identified with failed awake surgery.[21] They mentioned about correlations between the results of intraoperative mapping and neurological outcome, negative language mapping cases did not suffer severe deficits. Positive cortical mapping is controversial, but it seems that neither positive mapping nor intraoperative neurological changes has a significant impact on the overall extent of resection.

Our case presentation is a 52-year-old male with anaplastic oligodendroglioma in the left frontal lobe (Fig. 1a), which was diagnosed by seizure onset. He had no preoperative neurological deficits. fMRI imaging showed that the activated areas within the posterior middle frontal gyrus made contact with the tumor

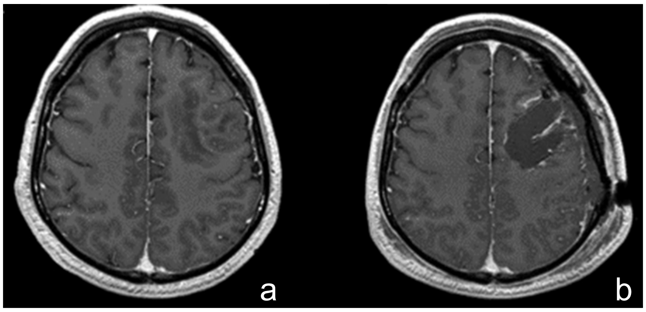

Fig. 1 Pre- (a) and postoperative (b) gadolinium-enhanced magnetic resonance images in a patient with anaplastic oligodendroglioma located in the left frontal lobe.

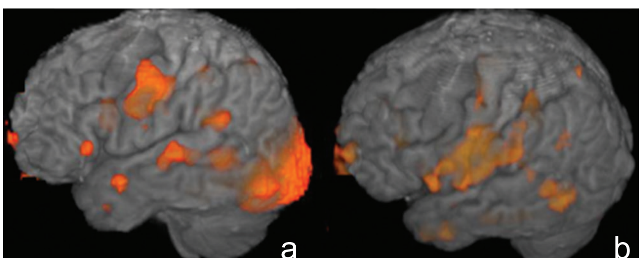

Fig. 2 Preoperative functional magnetic resonance imaging (fMRI) during reading (a), mouth motion (b), and right hand motion (c).

(Fig. 2a). On intraoperative examination during awake craniotomy, a comprehension deficit and perseveration were observed when resecting the posterior deep part of the tumor. Using an intraoperative navigation system and cerebral cortex electrical stimulation, we identified the frontal language area and identified the connections between the cortical functions of the frontal and posterior language areas (Fig. 3a, b). Then we resected the tumor while preserving the language areas. Cortical stimulation consisted of 0.3 msec alternating polarity square wave pulses delivered from a constant current stimulator in 5-sec trains at 50 Hz across 5-mm bipolar electrodes. The current raised from 3 mA to 8 mA, did not evoke any afterdischarges. Apraxia of speech occurred on cortical stimulation of the posterior part of the inferior frontal gyrus (pars triangularis), as well as on stimulation of the deep white matter through a cavity produced after lesion resection in the frontal segment of the middle frontal gyrus. The patient has not experienced any postoperative permanent nerve symptoms or reoccurrence of the tumor.

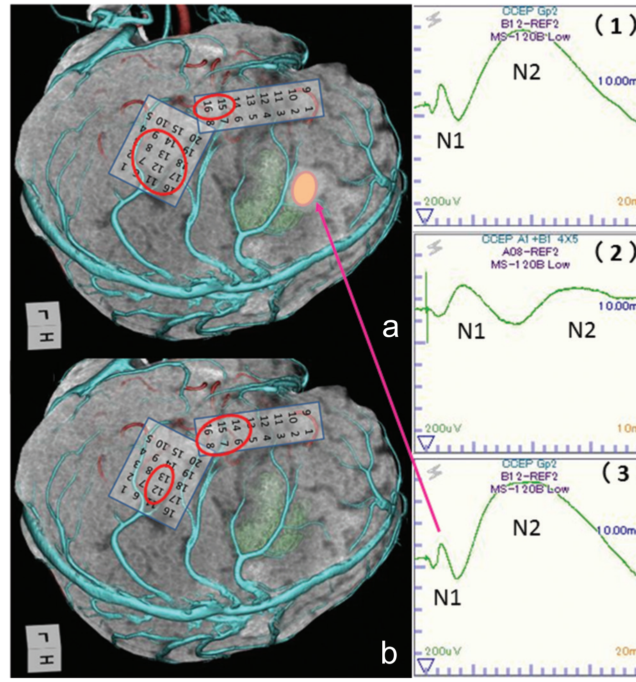

Fig. 3 Intraoperative evaluation of language function by electrical stimulation. a and b: A 4 × 5-electrode plate was placed on the temporo-parietal lobe and a 2 × 8-electrode plate was placed on the frontal lobe to identify the language cortex. The small *red circle* represents the area of stimulation and the *large circle* indicates the area in which cortico-cortical evoked potentials (CCEPs) were recorded. (1–3): CCEPs during operation. (1) CCEPs recorded from the temporoparietal lobe (the posterior language area: 4 × 5-electrode Nos. 7, 8, 9, 11, 12, 13, 16, 17) in response to bipolar stimulation of the frontal lobe (the anterior language area: 2 × 8-electrode Nos. 15–16). (2) CCEPs also recorded from the anterior opercular region (the anterior language area: 2 × 8-electrode Nos. 7, 8, 14, 15, 16) in response to bipolar stimulation of the inferior parietal lobule (the posterior language area: 4 × 5-electrode Nos. 12–13), the area where the maximum reaction was recorded in the previous stimulation (1). The electrophysiological connection between these two areas appeared to be bidirectorial. (3) Monitoring of CCEPs from the posterior language area (4 × 5-electrode) by stimulating Nos. 15–16 of the 2 × 8-electrode plate intraoperatively. The N1 peak was slightly reduced compared with the control amplitude shown in (1) during awake resection of the anterior base of the tumor (*orange circle*), when impaired auditory comprehension and visual naming were observed.

Challenges

In this article, we discuss the challenges of evaluating language function during awake craniotomy. One is the issue of brain shift. During craniotomy, brain shift occurs, resulting in spatial gaps between the preoperatively obtained brain functional cortex and nerve fibers displayed on the navigation system during surgery. Furthermore, the degree of brain shift is affected by degree of head rotation, individual differences, gravity, and leakage of cerebrospinal fluid; therefore, in cases of space-occupying lesions such as meningioma and glioma, the brain shift may be as significant as 1–2 cm. Efforts are being made to correct for brain shift using intraoperative MRI and a CT-based shift model.[22] When resecting lesions close to functional regions, it is essential to carefully assess the results of brain electrical stimulation under an awake state.

Next, the limitations of awake craniotomy should be considered. During this procedure, patients usually can be kept awake for up to 2 hours. During this limited period, it is important to implement all tasks and assess results in a well-focused manner. Patients must have sufficient language function to understand the intraoperative tasks. Additionally, they need to have adequate cognitive function and emotional maturity to perform tasks in the demanding environment of the craniotomy. These factors reduce the number of potential subjects to some extent. Taking these requirements into consideration, the aforementioned Japan Society for Awake Surgery guidelines limit the target patient population to 15–65 years old. In addition, since during the surgery the patient's head is fixed and covered with cloth, depending on the patient's posture the evaluation of the face and mouth may be difficult.

Furthermore, if the operator misunderstands the evaluation, severe neurological deficit may be remained. In order to share the information by all members of surgical team, intraoperative examination monitor for awake surgery (IEMAS), which can display plural intraoperative information (images of neuronavigation system and surgical layer of microscope, provided task and the face of the patient etc.) in one screen, was developed.[23]

Finally, it is necessary to address the challenges associated with the evaluation of language function during awake craniotomy. The functions related to the primary motor cortex, such as visual perception and motor function, have been clarified in terms of their anatomic localization, and the associated test methods have been established with high specificity. However, regarding language function, the localization of functions varies greatly among individuals and different pathological conditions. In addition, even with the aforementioned multiple preoperative test methods, the identification of the dominant hemisphere or the functional regions remains difficult in some cases. Furthermore, evaluation of these functions is difficult due to complex inter-fiber connections and the complexity of language functions, which consist of input and output, for instance "comprehension" and "cognition" (input) and "articulation" and "utterance" (output). The expression of language functions is not only affected by the aforementioned issues of articulation, but also influenced greatly by the degree of the patient's wakefulness and fatigue; therefore, when evaluating the test results, close attention is required.

Conclusion

This article outlines the current state of language function evaluation during awake craniotomy, based on the literature and our case presentation. There is currently no single established examination method to preserve patients' language functions. When determining which method to use, it is essential to comprehensively consider the preoperative evaluation, the awake intraoperative symptoms, and the response to cortical stimulation. In addition, caution should be taken when deciding whether to apply awake craniotomy as a way to assess language function in combination with other functional brain mapping or monitoring techniques.

Conflicts of Interest Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings reported in this article.

References

1) Luders HO, Awad IA: Conceptual considerations. *Epilepsy Surgery* 7: 51–62, 1991
2) Duffau H: Contribution of cortical and subcortical electrostimulation in brain glioma surgery: methodological and functional considerations. *Neurophysiol Clin* 37: 373–382, 2007
3) Soffietti R, Baumert BG, Bello L, von Deimling A, Duffau H, Frénay M, Grisold W, Grant R, Graus F, Hoang-Xuan K, Klein M, Melin B, Rees J, Siegal T, Smits A, Stupp R, Wick W; European Federation of Neurological Societies: Guidelines on management of low-grade gliomas: report of an EFNS-EANO Task Force. *Eur J Neurol* 17: 1124–1133, 2010
4) Kayama T; Guidelines Committee of the Japan Awake Surgery Conference: The guidelines for awake craniotomy guidelines committee of the Japan awake surgery conference. *Neurol Med Chir* (*Tokyo*) 52: 119–141, 2012
5) Trinh VT, Fahim DK, Maldaun MV, Shah K, McCutcheon IE, Rao G, Lang F, Weinberg J, Sawaya R, Suki D, Prabhu SS: Impact of preoperative functional magnetic resonance imaging during awake craniotomy

procedures for intraoperative guidance and complication avoidance. *Stereotact Funct Neurosurg* 92: 315–322, 2014
6) Duffau H: The anatomo-functional connectivity of language revisited. New insights provided by electrostimulation and tractography. *Neuropsychologia* 46: 927–934, 2008
7) Bello L, Gambini A, Castellano A, Carrabba G, Acerbi F, Fava E, Giussani C, Cadioli M, Blasi V, Casarotti A, Papagno C, Gupta AK, Gaini S, Scotti G, Falini A: Motor and language DTI Fiber Tracking combined with intraoperative subcortical mapping for surgical removal of gliomas. *Neuroimage* 39: 369–382, 2008
8) Mikuni N, Yokoyama Y, Matsumoto A, Kikuchi T, Yamada S, Hashimoto N, Miyamoto S: Intravenous methylprednisolone reduces the risk of propofol-induced adverse effects during Wada testing. *Neurol Med Chir (Tokyo)* 50: 622–626, 2010
9) Papanicolaou AC, Rezaie R, Narayana S, Choudhri AF, Wheless JW, Castillo EM, Baumgartner JE, Boop FA: Is it time to replace the Wada test and put awake craniotomy to sleep? *Epilepsia* 55: 629–632, 2014
10) Hamberger MJ: Cortical language mapping in epilepsy: a critical review. *Neuropsychol Rev* 17: 477–489, 2007
11) Mikuni N, Ohara S, Ikeda A, Hayashi N, Nishida N, Taki J, Enatsu R, Matsumoto R, Shibasaki H, Hashimoto N: Evidence for a wide distribution of negative motor areas in the perirolandic cortex. *Clin Neurophysiol* 117: 33–40, 2006
12) Sanai N, Mirzadeh Z, Berger MS: Functional outcome after language mapping for glioma resection. *N Engl J Med* 358: 18–27, 2008
13) Bello L, Gallucci M, Fava M, Carrabba G, Giussani C, Acerbi F, Baratta P, Songa V, Conte V, Branca V, Stocchetti N, Papagno C, Gaini SM: Intraoperative subcortical language tract mapping guides surgical removal of gliomas involving speech areas. *Neurosurgery* 60: 67–80; discussion 80–82, 2007
14) Matsumoto R, Nair DR, LaPresto E, Najm I, Bingaman W, Shibasaki H, Lüders HO: Functional connectivity in the human language system: a cortico-cortical evoked potential study. *Brain* 127: 2316–2330, 2004
15) Yamao Y, Matsumoto R, Kunieda T, Arakawa Y, Kobayashi K, Usami K, Shibata S, Kikuchi T, Sawamoto N, Mikuni N, Ikeda A, Fukuyama H, Miyamoto S: Intraoperative dorsal language network mapping by using single-pulse electrical stimulation. *Hum Brain Mapp* 35: 4345–4361, 2014
16) Chang EF, Clark A, Smith JS, Polley MY, Chang SM, Barbaro NM, Parsa AT, McDermott MW, Berger MS: Functional mapping-guided resection of low-grade gliomas in eloquent areas of the brain: improvement of long-term survival. Clinical article. *J Neurosurg* 114: 566–573, 2011
17) De Witt Hamer PC, Robles SG, Zwinderman AH, Duffau H, Berger MS: Impact of intraoperative stimulation brain mapping on glioma surgery outcome: a meta-analysis. *J Clin Oncol* 30: 2559–2565, 2012
18) Yang TF, Chen HH, Liang ML, Chen C, Chiu JW, Wang JC, Lai CJ, Liao KK, Chan RC: Intraoperative brain mapping to identify corticospinal projections during resective epilepsy surgery in children with congenital hemiparesis. *Childs Nerv Syst* 30: 1559–1564, 2014
19) Kim YH, Kim CH, Kim JS, Lee SK, Chung CK: Resection frequency map after awake resective surgery for non-lesional neocortical epilepsy involving eloquent areas. *Acta Neurochir (Wien)* 153: 1739–1749, 2011
20) Nossek E, Matot I, Shahar T, Barzilai O, Rapoport Y, Gonen T, Sela G, Korn A, Hayat D, Ram Z: Failed awake craniotomy: a retrospective analysis in 424 patients undergoing craniotomy for brain tumor. *J Neurosurg* 118: 243–249, 2013
21) Kumabe T, Sato K, Iwasaki M, Shibahara I, Kawaguchi T, Saito R, Kanamori M, Yamashita Y, Sonoda Y, Iizuka O, Suzuki K, Nagamatsu K, Seki S, Nakasato N, Tominaga T: Summary of 15 years experience of awake surgeries for neuroepithelial tumors in tohoku university. *Neurol Med Chir (Tokyo)* 53: 455–466, 2013
22) Suzuki K, Akiyama Y, Sugino T, Mikami T, Wanibuchi M, Inagaki T, Irie S, Saito K, Mikuni N: A new brain-shift model for neurosurgery with fronto-temporal craniotomy. *JSM Neurosurg Spine* 2: 1040, 2014
23) Yoshimitsu K, Maruyama T, Muragaki Y, Suzuki T, Saito T, Nitta M, Tanaka M, Chernov M, Tamura M, Ikuta S, Okamoto J, Okada Y, Iseki H: Wireless modification of the intraoperative examination monitor for awake surgery. *Neurol Med Chir (Tokyo)* 51: 472–476, 2011

Address reprint requests to: Nobuhiro Mikuni, MD, PhD, 291, S1 W17, Chuo-ku, Sapporo, Hokkaido 060-8543, Japan.
e-mail: mikunin@sapmed.ac.jp