Intra-operative mapping and language protection in glioma

Shi-Meng Weng[1], Sheng-Yu Fang[1], Lian-Wang Li[1], Xing Fan[1], Yin-Yan Wang[1,2], Tao Jiang[1,2,3]

[1]Beijing Neurosurgical Institute, Capital Medical University, Beijing 100070, China;
[2]Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, Beijing 100070, China;
[3]Research Unit of Accurate Diagnosis, Treatment, and Translational Medicine of Brain Tumors, Chinese Academy of Medical Sciences, Beijing 100070, China.

Abstract

The demand for acquiring different languages has increased with increasing globalization. However, knowledge of the modification of the new language in the neural language network remains insufficient. Although many details of language function have been detected based on the awake intra-operative mapping results, the language neural network of the bilingual or multilingual remains unclear, which raises difficulties in clinical practice to preserve patients' full language ability in neurosurgery. In this review, we present a summary of the current findings regarding the structure of the language network and its evolution as the number of acquired languages increased in glioma patients. We then discuss a new insight into the awake intra-operative mapping protocol to reduce surgical risks during the preservation of language function in multilingual patients with glioma.

Keywords: Glioma; Intra-operative mapping; Language function; Language protection

Introduction

Language is one of the most important abstract inventions in human history. To date, little is known about the biological mechanisms underlying the language functions. Various neurosurgical diseases can affect language functions, and the protection and recovery of language functions have always been a focus of neurosurgeons. In this review, we introduce the current understanding of language networks and consider glioma as an example, while expounding on the influence of cerebral-occupying lesions on language networks. Moreover, we discuss the existing modalities for locating language-related brain areas and propose a monitoring strategy to protect language functions for patients who are proficient in over three languages.

Traditional language regions

In the late 19th century, two major language-related cortical regions were identified and named after scholars, namely the Broca and Wernicke areas. Broca area, which is located at the posterior inferior frontal gyrus (IFG), is mainly responsible for the language expression, whereas the Wernicke area, which is located in the middle to posterior portion of the superior temporal gyrus (STG), mainly contributes to decoding the semantic meaning of auditory information. To date, vast linguistic studies have been conducted on these two areas and the distribution of language functions in the cerebral cortex has been previously studied in detail.[1-3] Recent findings have shed new light on their anatomical definition and functional responsibilities. Broca area has been considered as the reference for the entire IFG and whether it is more involved in phonological or semantic processing remains controversial. The anatomical definition of Wernicke area has evolved over time and most researchers have reached a consensus that it should cover the angular gyrus, superior marginal gyrus, STG, middle temporal gyrus, and posterior parts of the inferior temporal gyrus (ITG).[4] Mesulam *et al*[5] found that the neural substrates of word and sentence comprehension are dissociable, and Wernicke area is not a center but a part of the entire language processing system. Other cortical areas, including Broca area and the dorsal premotor cortex, are also important for the process of language comprehension.

Specific language regions

With the deepening of relevant research, the study of language networks is not limited to the two traditional regions and some specific language regions have been identified. For instance, a recent study showed that the right fusiform gyrus is activated for the analysis of characters when processing information in pictographs (Chinese).[6] Another study showed that compared with Indo-European languages, spoken word recognition in Chinese can lead to greater activation in the right

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Correspondence to: Dr. Tao Jiang, Beijing Neurosurgical Institute, Capital medical University, 119, The Western Road of the Southern 4th Ring Road, Beijing 100070, China
E-Mail: taojiang1964@163.com

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temporoparietal region.[7] Moreover, the right anterior temporal lobe is equally as important as its left homolog for tone language comprehension.[8] The anterior supplementary motor area, anterior cingulate cortex, middle frontal gyrus, and left caudate nucleus play special roles in language switching tasks.[9-11] The IFG is activated only when the amount of information increases and the language network needs more regions to process.[12] Similarly, a study identified that as the word combination task becomes longer and more complex, the right IFG and medial frontal gyrus are activated to process semantic comprehension and expression.[13] Hence, the entire language network is not always involved in every task. Some language regions are stimulated only by specific tasks and difficulty levels. To explore the entire network of language processing, language tasks should be diversified and paired with different difficulty levels.

Fiber tracts

Subcortical fibers participate in linguistic processing by connecting different language-related cortices and building language networks. Hence, damage to the fiber tracts can also cause linguistic deficits. The ventral and dorsal streams are the two primary pathways in the language network, also known as the dual-stream model.[14-16] In the ventral stream, the extreme fiber capsule system contains the inferior longitudinal fasciculus, inferior fronto-occipital fasciculus, uncinate fasciculus, and middle longitudinal fasciculus, which connects the middle temporal lobe to the ventral lateral prefrontal cortex.[14,17,18] The ventral stream assists people in matching sounds and objects to semantic meaning by transmitting linguistic information contained in sounds and visuals to accomplish semantic comprehension.[14,18] Damage to this stream can cause impairment of target recognition or expression and amnesia symptoms.[19,20] In the dorsal stream, the arcuate fasciculus (AF) and superior longitudinal fasciculus (SLF) are the two main tracts that are responsible for integrating hearing and perception, which deliver comprehended information to the receptive region in the integration of a corresponding expressive response.[14,19,21] The AF connects the frontal cortex to the occipital and parietal cortices and is primarily responsible for the expressive function. Damage to the AF can also cause speech impairments, such as failure to present oneself with logic.[19,21] The SLF has three parts (I, II, and III) and connects the occipital, parietal, and temporal lobes to the frontal cortex. It mainly conveys linguistic information, attention, memory, and emotion.[19,21] Damage to the SLF can cause different degrees of aphasic symptoms because of conceptual impairment.[16,22,23] The components of the dual-stream model complement each other, so the language network can accurately integrate and respond with auditory, visual, and cognitive information as references.[14]

Adaptability of Original Language Network

The results of the studies presented above show that different language structures and uses would activate different functional areas at the cortical level. However, the mechanism of the language network was mostly understood from a monolingual perspective. As an increasing number of people acquire multiple languages, how would the original language network mediate the adoption of the function to process the acquired languages? The original language network was established to process the native language.[6,24] Therefore, when processing a second language, the brain tends to translate the contents into the native language before comprehending the meaning.[25,26] After completing meaning comprehension and response in the native language, the brain translates the response back to the second language to express.[26,27] While translating back and expressing with the second language, the brain also needs to use cognitive control and executive function to suppress the urge to express directly in the native language and to select the translated second language for output.[26,27] In this whole second language processing, apart from thinking in the native language, the dual translation, suppression, and execution are extra steps that monolinguals do not need to execute. This process of language transformation also applies to multilingual patients, who may require additional steps to duplicate the transformation between the second and third languages. Therefore, it is logical to consider that bilinguals or multilinguals would activate a wider range of functional regions than monolinguals.[28] In addition to different mechanisms and involved brain regions, Duffau *et al*[29] and Bello *et al*[30] also found that different languages activate different white matter fiber tracts. Thus, in terms of subcortical layers, simultaneous acquisition of more than one language entails different cortical and subcortical organizations.

Moreover, the onset of acquisition and proficiency was found to have a significant impact on the distribution of multilingual networks.[31] The age of 7 years has been used as a criterion to distinguish between early and late acquisition.[31,32] Almost all functional magnetic resonance imaging (fMRI) results suggest that early acquired languages have a significant overlap with the distribution of language networks in the native language.[25,33-36] In contrast, late acquired languages are more widely distributed, as observed by direct cortical evidence.[24,30,37-39] In addition, fMRI findings indicate that the proficiency level of late acquired languages is positively correlated with overlapping range with the native language.[6,40] Thus, a certain proficiency level can compensate for differences in activation areas arising from differences in the onset of the acquisition. However, we do not know much about the required proficiency level and the compensation process. The direct electrical stimulation results, acting as a clinical "gold standard," indicate that there are differences in the distribution of language sites across patients and languages, and the statistical power is not sufficient for researchers to draw an applicable rule for the distribution of multilingual networks.[24,29,30,37-39] Hence, the changes that the acquired languages stimulate to the original language network are unpredictable.

The effect of glioma on language function

Gliomas are the most common intracranial primary growths and often invade language-related cerebral structures.[41] Different types of language dysfunction are induced by gliomas based on the infiltration of different locations. However, not all patients with gliomas located in language-related regions suffer from language deficits. Gliomas not only induce language impairment but also induce language plasticity.[42] Previous studies have shown that the plasticity of cortices is far stronger than that of subcortical fibers.[1,2] However, subcortical fibers also have plasticity. Moreover, in the same fiber, different fiber locations also have different plasticities. Herbet *et al*[43] found that the anterior SLF/AF had stronger plasticity than the other parts of the SLF/AF. This may be because the limited cortices were connected by the anterior SLF/AF.[44] Hence, regarding these fibers with low plasticity, we should concentrate on subcortical mapping and protection.

Measurements in language-related eloquent identifying among glioma patients

Regarding language-related cortices, conventional measurement uses task fMRI with cooperating language tasks, such as picture naming, reading, and so on.[45-47] However, unlike sensorimotor functions involving limited cortices, language functions are associated with many cortices and it was difficult to identify language-related eloquent areas relying on one language task. Additionally, patients were unable to perform many tasks at one time.[48,49] Moreover, neurovascular uncoupling is an inevitable effect that leads to a decrease in the accuracy of the fMRI location.[50,51] Consequently, solely using fMRI to identify language-related cortices and guide glioma resection is not recommended. Hence, fMRI normally serves as the primary source for guidance for language mapping with direct cortical stimulation (DCS) during the clinical practice.

Language mapping with DCS during awake craniotomy was prevalent and this measurement was highly accurate for mapping cortices.[52-57] For mapping subcortical fibers, the validity was affected by the angle of stimulation and density.[58-61] Hence, post-operative language deficits were not completely avoided by DCS. Unfortunately, we were unable to use a monopolar stimulator to monitor the distance from the stimulating point to the fibers, such as when mapping the cortico-spinal tracts. Further investigation on how to improve the effects of language mapping using DCS is recommended. Another technique named stereo-electroencephalography (SEEG) may improve brain mapping. SEEG is known to identify the cortical function in epilepsy surgery, but its reliability in other clinical situations is rarely documented.[62,63] It also has some limitations in terms of spatial resolution and lability.[64] Although DCS has some limitations, it should still be recommended for the delineation of the distribution of cortical functions in glioma treatments.

Fatigue is another reason for the decline in DCS accuracy.[61] With the increasing number of patients who are bilingual or multilingual, the adequate protection of each language function has become an important challenge in neurosurgery. The conventional language mapping protocol recommends mapping each language. However, the time of language mapping is significantly increased and the cooperation of patients worsens with increasing time.[61] Hence, simplifying the protocol of language mapping of multilingualism under the premise of protecting each type of language function is a key point to explore.

Compared with adults in Western countries,[39] it is rare for the Chinese adults nowadays to acquire a second language in the early stage (before 7 years old). Previous studies have shown that the distribution of functional cortical structures related to the second language varies with the period in which the second language was obtained.[65] Based on fMRI, the results showed that in people acquiring a second language in the early stage, the activated cortices of the second language were similar to those of the native language. This means that the activation area of the second language and the native language had a high degree of coincidence for those people. Nevertheless, those who learned a second language after 7 years of age showed a wider range of activated cortices when they processed the same non-native language tasks.[31,66-68] Subsequently, several studies have verified this theory at the electrophysiological level (direct evidence) by using intra-operative language mapping.[22,38,39,69] Consequently, mapping only the native language was recommended for patients with fatigue and those who were unable to cooperate in identifying multilingual cortices.[39] However, these findings are not entirely consistent with the Chinese adults, since most Chinese adults acquire a second language after 7 years of age. Hence, for Chinese patients who are bilingual, we should locate both native and non-native languages to ensure adequate protection of their language functions. Moreover, previous fMRI studies have shown that there is an optimization process in the language network. After acquiring a kind of language, when the completion of a task in this language is required, the activated cortices gradually shrink and finally form an optimized network.[35,70] This finding suggested that early exposure and acquisition of a language required a small range of cortices for language tasks, while more extensive cortices are required for the recruitment of recently acquired languages or those that the person is unskilled at.[71] Thus, regarding Chinese patients who acquired more than three languages (especially any non-native languages acquired in the late stage), we recommend that intra-operative mapping of only the cortical distribution of the native language and the least proficient acquired language is sufficient to protect all language functions. For other acquired languages, selective mapping is recommended based on the degree of fatigue in patients.

Conclusion

In this study, we reviewed language-relevant areas that gliomas commonly invade and the detailed language impairments induced by glioma. Moreover, based on a previous study and our clinical experience of contemporary Chinese patients, we propose a new protocol for language mapping using direct cortical stimulation.

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Conflicts of interest

None.

References

1. Tate MC, Herbet G, Moritz-Gasser S, Tate JE, Duffau H. Probabilistic map of critical functional regions of the human cerebral cortex: Broca's area revisited. Brain 2014;137:2773–2782. doi: 10.1093/brain/awu168.
2. Tate MC, Herbet G, Moritz-Gasser S, Tate JE, Duffau H. Reply: Probabilistic map of language regions: challenge and implication. Brain 2015;138:e338. doi: 10.1093/brain/awu253.
3. Wu J, Lu J, Zhang H, Zhang J, Mao Y, Zhou L. Probabilistic map of language regions: challenge and implication. Brain 2015;138:e337. doi: 10.1093/brain/awu247.
4. Binder JR. The Wernicke area: modern evidence and a reinterpretation. Neurology 2015;85:2170–2175. doi: 10.1212/WNL.0000000000002219.
5. Mesulam MM, Thompson CK, Weintraub S, Rogalski EJ. The Wernicke conundrum and the anatomy of language comprehension in primary progressive aphasia. Brain 2015;138:2423–2437. doi: 10.1093/brain/awv154.
6. Wang RM, Ke SS, Zhang Q, Zhou K, Li P, Yang J. Functional and structural neuroplasticity associated with second language proficiency: an MRI study of Chinese–English bilinguals. J Neurolinguist 2020;56:100940. doi: 10.1016/j.jneuroling.2020.100940.
7. Valaki CE, Maestu F, Simos PG, Zhang W, Fernandez A, Amo CM, *et al*. Cortical organization for receptive language functions in Chinese, English, and Spanish: a cross-linguistic MEG study, English. Neuropsychologia 2004;42:967–979. doi: 10.1016/j.neuropsychologia.2003.11.019.
8. Ge J, Peng G, Lyu B, Wang Y, Zhuo Y, Niu Z, *et al*. Cross-language differences in the brain network subserving intelligible speech. Proc Natl Acad Sci USA 2015;112:2972–2977. doi: 10.1073/pnas.1416000112.
9. Abutalebi J, Della Rosa PA, Ding G, Weekes B, Costa A, Green DW. Language proficiency modulates the engagement of cognitive control areas in multilinguals. Cortex 2013;49:905–911. doi: 10.1016/j.cortex.2012.08.018.
10. Wang X, Wang YY, Jiang T, Wang YZ, Wu CX. Direct evidence of the left caudates role in bilingual control: an intra-operative electrical stimulation study. Neurocase 2013;19:462–469. doi: 10.1080/13554794.2012.701635.
11. Sierpowska J, Fernandez-Coello A, Gomez-Andres A, Camins À, Castañer S, Juncadella M, *et al*. Involvement of the middle frontal gyrus in language switching as revealed by electrical stimulation mapping and functional magnetic resonance imaging in bilingual brain tumor patients. Cortex 2018;99:78–92. doi: 10.1016/j.cortex.2017.10.017.
12. Van Ettinger-Veenstra H, McAllister A, Lundberg P, Karlsson T, Engström M. Higher language ability is related to angular gyrus activation increase during semantic processing, independent of sentence incongruency. Front Hum Neurosci 2016;10:110. doi: 10.3389/fnhum.2016.00110.
13. Kim SY, Liu L, Cao F. How does first language (L1) influence second language (L2) reading in the brain? Evidence from Korean-English and Chinese-English bilinguals. Brain Lang 2017;171:1–13. doi: 10.1016/j.bandl.2017.04.003.
14. Friederici AD. The brain basis of language processing: from structure to function. Physiol Rev 2011;91:1357–1392. doi: 10.1152/physrev.00006.2011.
15. López-Barroso D, de Diego-Balaguer R. Language learning variability within the dorsal and ventral streams as a cue for compensatory mechanisms in aphasia recovery. Front Hum Neurosci 2017;11:476. doi: 10.3389/fnhum.2017.00476.
16. Saur D, Kreher BW, Schnell S, Kümmerer D, Kellmeyer P, Vry MS, *et al*. Ventral and dorsal pathways for language. Proc Natl Acad Sci USA 2008;105:18035–18040. doi: 10.1073/pnas.0805234105.
17. Mancini M, Vos SB, Vakharia VN, O'Keeffe AG, Trimmel K, Barkhof F, *et al*. Automated fiber tract reconstruction for surgery planning: extensive validation in language-related white matter tracts. Neuroimage Clin 2019;23:101883. doi: 10.1016/j.nicl.2019.101883.
18. Catani M, Dawson MS. Conn PM. Chapter 31. Language processing, development and evolution. Conn's Translational Neuroscience San Diego: Academic Press; 2017;679–692.
19. Ramos-Fresnedo A, Segura-Duran I, Chaichana KL, Pillai JJ. Chapter 2. Supratentorial white matter tracts. In: Chaichana K, Quiñones-Hinojosa A, eds. Comprehensive overview of modern surgical approaches to intrinsic brain tumors. US and UK: imprint of Elsevier; 2019: 23–35.
20. Papagno C, Miracapillo C, Casarotti A, Romero Lauro LJ, Castellano A, Falini A, *et al*. What is the role of the uncinate fasciculus? Surgical removal and proper name retrieval. Brain 2011;134:405–414. doi: 10.1093/brain/awq283.
21. Ocklenburg S, Güntürkün O. Ocklenburg S, Güntürkün O. Chapter 4. Language and the left hemisphere. The Lateralized Brain San Diego: Academic Press; 2018;87–121.
22. Yagmurlu K, Middlebrooks EH, Tanriover N, Rhoton AL Jr. Fiber tracts of the dorsal language stream in the human brain. J Neurosurg 2016;124:1396–1405. doi: 10.3171/2015.5.JNS15455.
23. Dick AS, Bernal B, Tremblay P. The language connectome: new pathways, new concepts. Neuroscientist 2014;20:453–467. doi: 10.1177/1073858413513502.
24. Giussani C, Roux FE, Lubrano V, Gaini SM, Bello L. Review of language organisation in bilingual patients: what can we learn from direct brain mapping? Acta Neurochir (Wien) 2007;149:1109–1116. doi: 10.1007/s00701-007-1266-2.
25. Fabbro F. The bilingual brain: cerebral representation of languages. Brain Lang 2001;79:211–222. doi: 10.1006/brln.2001.2481.
26. Briellmann RS, Saling MM, Connell AB, Waites AB, Abbott DF, Jackson GD. A high-field functional MRI study of quadri-lingual subjects. Brain Lang 2004;89:531–542. doi: 10.1016/j.bandl.2004.01.008.
27. Abutalebi J, Weekes BS. The cognitive neurology of bilingualism in the age of globalization. Behav Neurol 2014;2014:536727. doi: 10.1155/2014/536727.
28. ReFaey K, Tripathi S, Bhargav AG, Grewal SS, Middlebrooks EH, Sabsevitz DS, *et al*. Potential differences between monolingual and bilingual patients in approach and outcome after awake brain surgery. J Neurooncol 2020;148:587–598. doi: 10.1007/s11060-020-03554-0.
29. Duffau H, Capelle L, Sichez N, Denvil D, Lopes M, Sichez JP, *et al*. Intraoperative mapping of the subcortical language pathways using direct stimulations. An anatomo-functional study. Brain 2002;125:199–214. doi: 10.1093/brain/awf016.
30. Bello L, Acerbi F, Giussani C, Baratta P, Taccone P, Songa V, *et al*. Intraoperative language localization in multilingual patients with gliomas. Neurosurgery 2006;59:115–125. doi: 10.1227/01.NEU.0000219241.92246.FB.
31. Perani D, Abutalebi J, Paulesu E, Brambati S, Scifo P, Cappa SF, *et al*. The role of age of acquisition and language usage in early, high-proficient bilinguals: an fMRI study during verbal fluency. Hum Brain Mapp 2003;19:170–182. doi: 10.1002/hbm.10110.
32. Frenck-Mestre C, Anton JL, Roth M, Vaid J, Viallet F. Articulation in early and late bilinguals' two languages: evidence from functional magnetic resonance imaging. Neuroreport 2005;16:761–765. doi: 10.1097/00001756-200505120-00021.
33. Pouratian N, Bookheimer SY, O'Farrell AM, Sicotte NL, Cannestra AF, Becker D, *et al*. Optical imaging of bilingual cortical representations. Case report. J Neurosurg 2000;93:676–681. doi: 10.3171/jns.2000.93.4.0676.
34. Cao F, Young Kim S, Liu Y, Liu L. Similarities and differences in brain activation and functional connectivity in first and second language reading: evidence from Chinese learners of English. Neuropsychologia 2014;63:275–284. doi: 10.1016/j.neuropsychologia.2014.09.001.
35. Liu X, Tu L, Wang J, Jiang B, Gao W, Pan X, *et al*. Onset age of L2 acquisition influences language network in early and late Cantonese-Mandarin bilinguals. Brain Lang 2017;174:16–28. doi: 10.1016/j.bandl.2017.07.003.
36. Middlebrooks EH, Yagmurlu K, Szaflarski JP, Rahman M, Bozkurt B. A contemporary framework of language processing in the human brain in the context of preoperative and intraoperative language

mapping. Neuroradiology 2017;59:69–87. doi: 10.1007/s00234-016-1772-0.
37. Roux FE, Trémoulet M. Organization of language areas in bilingual patients: a cortical stimulation study. J Neurosurg 2002;97:857–864. doi: 10.3171/jns.2002.97.4.0857.
38. Walker JA, Quiñones-Hinojosa A, Berger MS. Intraoperative speech mapping in 17 bilingual patients undergoing resection of a mass lesion. Neurosurgery 2004;54:113–117. doi: 10.1227/01.neu.0000097270.95721.3b.
39. Fernández-Coello A, Havas V, Juncadella M, Sierpowska J, Rodríguez-Fornells A, Gabarrós A. Age of language acquisition and cortical language organization in multilingual patients undergoing awake brain mapping. J Neurosurg 2017;126:1912–1923. doi: 10.3171/2016.5.JNS152791.
40. Van de Putte E, De Baene W, Brass M, Duyck W. Neural overlap of L1 and L2 semantic representations in speech: a decoding approach. Neuroimage 2017;162:106–116. doi: 10.1016/j.neuroimage.2017.08.082.
41. Jiang T, Nam DH, Ram Z, Poon WS, Wang J, Boldbaatar D, *et al.* Clinical practice guidelines for the management of adult diffuse gliomas. Cancer Lett 2021;499:60–72. doi: 10.1016/j.canlet.2020.10.050.
42. Ille S, Engel L, Albers L, Schroeder A, Kelm A, Meyer B, *et al.* Functional reorganization of cortical language function in glioma patients - a preliminary study. Front Oncol 2019;9:446. doi: 10.3389/fonc.2019.00446.
43. Herbet G, Maheu M, Costi E, Lafargue G, Duffau H. Mapping neuroplastic potential in brain-damaged patients. Brain 2016;139: 829–844. doi: 10.1093/brain/awv394.
44. van Geemen K, Herbet G, Moritz-Gasser S, Duffau H. Limited plastic potential of the left ventral premotor cortex in speech articulation: evidence from intraoperative awake mapping in glioma patients. Hum Brain Mapp 2014;35:1587–1596. doi: 10.1002/hbm.22275.
45. Hermann BP, Wyler AR, Somes G. Language function following anterior temporal lobectomy. J Neurosurg 1991;74:560–566. doi: 10.3171/jns.1991.74.4.0560.
46. Berger MS. Functional mapping-guided resection of low-grade gliomas. Clin Neurosurg 1995;42:437–452.
47. Ulmer JL, Krouwer HG, Mueller WM, Ugurel MS, Kocak M, Mark LP. Pseudo-reorganization of language cortical function at fMR imaging: a consequence of tumor-induced neurovascular uncoupling. AJNR Am J Neuroradiol 2003;24:213–217.
48. Zhang D, Johnston JM, Fox MD, Leuthardt EC, Grubb RL, Chicoine MR, *et al.* Preoperative sensorimotor mapping in brain tumor patients using spontaneous fluctuations in neuronal activity imaged with functional magnetic resonance imaging: initial experience. Neurosurgery 2009;65:226–236. doi: 10.1227/01.NEU.0000350868.95634.CA.
49. Shang HB, Zhao WG, Zhang WF. Preoperative assessment using multimodal functional magnetic resonance imaging techniques in patients with brain gliomas. Turk Neurosurg 2012;22:558–565. doi: 10.5137/1019-5149.JTN.5332-11.1.
50. Fang S, Liang J, Qian T, Wang Y, Liu X, Fan X, *et al.* Anatomic location of tumor predicts the accuracy of motor function localization in diffuse lower-grade gliomas involving the hand knob area. AJNR Am J Neuroradiol 2017;38:1990–1997. doi: 10.3174/ajnr.A5342.
51. Fang S, Bai HX, Fan X, Li S, Zhang Z, Jiang T, *et al.* A novel sequence: ZOOMit-blood oxygen level-dependent for motor-cortex localization. Neurosurgery 2020;86:E124–E132. doi: 10.1093/neuros/nyz441.
52. Zelitzki R, Korn A, Arial E, Ben-Harosh C, Ram Z, Grossman R. Comparison of motor outcome in patients undergoing awake vs general anesthesia surgery for brain tumors located within or adjacent to the motor pathways. Neurosurgery 2019;85:E470–E476. doi: 10.1093/neuros/nyz007.
53. Tuominen J, Yrjänä S, Ukkonen A, Koivukangas J. Awake craniotomy may further improve neurological outcome of intraoperative MRI-guided brain tumor surgery. Acta Neurochir (Wien) 2013;155:1805–1812. doi: 10.1007/s00701-013-1837-3.
54. Peraud A, Ilmberger J, Reulen HJ. Surgical resection of gliomas WHO grade II and III located in the opercular region. Acta Neurochir (Wien) 2004;146:9–17. doi: 10.1007/s00701-003-0165-4.
55. Martino J, Gomez E, Bilbao JL, Dueñas JC, Vázquez-Barquero A. Cost-utility of maximal safe resection of WHO grade II gliomas within eloquent areas. Acta Neurochir (Wien) 2013;155:41–50. doi: 10.1007/s00701-012-1541-8.
56. Gupta DK, Chandra PS, Ojha BK, Sharma BS, Mahapatra AK, Mehta VS. Awake craniotomy versus surgery under general anesthesia for resection of intrinsic lesions of eloquent cortex – a prospective randomised study. Clin Neurol Neurosurg 2007; 109:335–343. doi: 10.1016/j.clineuro.2007.01.008.
57. Duffau H, Lopes M, Arthuis F, Bitar A, Sichez JP, Van Effenterre R, *et al.* Contribution of intraoperative electrical stimulations in surgery of low grade gliomas: a comparative study between two series without (1985-96) and with (1996-2003) functional mapping in the same institution. J Neurol Neurosurg Psychiatry 2005;76:845–851. doi: 10.1136/jnnp.2004.048520.
58. Carrabba G, Fava E, Giussani C, Acerbi F, Portaluri F, Songa V, *et al.* Cortical and subcortical motor mapping in rolandic and perirolandic glioma surgery: impact on postoperative morbidity and extent of resection. J Neurosurg Sci 2007;51:45–51.
59. Young JS, Lee AT, Chang EF. A review of cortical and subcortical stimulation mapping for language. Neurosurgery 2021;nyaa436. doi: 10.1093/neuros/nyaa436.
60. Kinoshita M, Miyashita K, Tsutsui T, Furuta T, Nakada M. Critical neural networks in awake surgery for gliomas. Neurol Med Chir (Tokyo) 2016;56:674–686. doi: 10.2176/nmc.ra.2016-0069.
61. Kanno A, Mikuni N. Evaluation of language function under awake craniotomy. Neurol Med Chir (Tokyo) 2015;55:367–373. doi: 10.2176/nmc.ra.2014-0395.
62. Drane DL, Pedersen NP, Sabsevitz DS, Block C, Dickey AS, Alwaki A, *et al.* Cognitive and emotional mapping with SEEG. Front Neurol 2021;12:627981. doi: 10.3389/fneur.2021.627981.
63. Ritaccio AL, Brunner P, Schalk G. Electrical stimulation mapping of the brain: basic principles and emerging alternatives. J Clin Neurophysiol 2018;35:86–97. doi: 10.1097/WNP.0000000000000440.
64. George DD, Ojemann SG, Drees C, Thompson JA. Stimulation mapping using stereoelectroencephalography: current and future directions. Front Neurol 2020;11:320. doi: 10.3389/fneur.2020.00320.
65. Tham WW, Rickard Liow SJ, Rajapakse JC, Choong Leong T, Ng SE, Lim WE, *et al.* Phonological processing in Chinese–English bilingual biscriptals: an fMRI study. Neuroimage 2005;28:579–587. doi: 10.1016/j.neuroimage.2005.06.057.
66. Legault J, Grant A, Fang SY, Li P. A longitudinal investigation of structural brain changes during second language learning. Brain Lang 2019;197:104661. doi: 10.1016/j.bandl.2019.104661.
67. Hämäläinen S, Sairanen V, Leminen A, Lehtonen M. Bilingualism modulates the white matter structure of language-related pathways. Neuroimage 2017;152:249–257. doi: 10.1016/j.neuroimage.2017.02.081.
68. Berken JA, Chai X, Chen JK, Gracco VL, Klein D. Effects of early and late bilingualism on resting-state functional connectivity. J Neurosci 2016;36:1165–1172. doi: 10.1523/JNEUROSCI.1960-15.2016.
69. Lucas TH 2nd, McKhann GM 2nd, Ojemann GA. Functional separation of languages in the bilingual brain: a comparison of electrical stimulation language mapping in 25 bilingual patients and 117 monolingual control patients. J Neurosurg 2004;101:449–457. doi: 10.3171/jns.2004.101.3.0449.
70. Li Y, Yang Y, Tang AC, Liu N, Wang X, Du Y, *et al.* English spoken word segmentation activates the prefrontal cortex and temporo-parietal junction in Chinese ESL learners: a functional near-infrared spectroscopy (fNIRS) study. Brain Res 2020;1733:146693. doi: 10.1016/j.brainres.2020.146693.
71. Thieba C, Long X, Dewey D, Lebel C. Young children in different linguistic environments: a multimodal neuroimaging study of the inferior frontal gyrus. Brain Cogn 2019;134:71–79. doi: 10.1016/j.bandc.2018.05.009.

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