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Case report

Intraoperative awake language mapping correlates to preoperative connectomics imaging: An instructive case

Harshal A. Shah [a], Faina Ablyazova [a], Annabelle Alrez [a], A. Gabriella Wernicke [e], Morana Vojnic [d], Justin W. Silverstein [b,c], Beril Yaffe [a], Randy S. D'Amico [a,*]

[a] Department of Neurological Surgery, Lenox Hill Hospital, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, New York, NY, USA
[b] Department of Neurology, Lenox Hill Hospital, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, New York, NY, USA
[c] Neuro Protective Solutions, New York, NY, USA
[d] Department of Hematology and Oncology, Lenox Hill Hospital, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, New York, NY, USA
[e] Department of Radiation Medicine, Lenox Hill Hospital, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, New York, NY, USA

A R T I C L E I N F O

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A B S T R A C T

Connectomics enables the study of structural-functional relationships in the brain, and machine learning technologies have enabled connectome maps to be developed for individual brain tumor patients. We report our experience using connectomics to plan and guide an awake craniotomy for a tumor impinging on the language area. Preoperative connectomics imaging demonstrated proximity of the tumor to parcellations of the language area. Intraoperative awake language mapping was performed, revealing speech arrest and paraphasic errors at areas of the tumor boundary correlating to functional regions that explained these findings. This instructive case highlights the potential benefits of implementing connectomics into neurosurgical planning.

1. Introduction

Aggressive cytoreductive surgery remains one of few modifiable prognostic factors for high grade gliomas (HGG). However, the survival benefits of achieving gross total resection (GTR) must be weighed against the risks of iatrogenic surgical injury, especially in tumors arising in peri-eloquent locations, as postoperative functional deficits worsen outcomes. [1].

Existing imaging tools including T1 and T2 magnetic resonance imaging (MRI) sequences, as well as diffusion tensor imaging (DTI) are limited in their ability to identify and assist in protection of functional networks which may be displaced or re-organized by tumors. Newer methods of imaging the connectome can be incorporated into conventional neuronavigation systems to be used intraoperatively and may offer a better understanding of the interplay of networks involved in neurocognitive functions. [2] While functional connectome networks have been validated, to date clinical studies describing their identification and preservation in planning neurosurgical procedures, and understanding the changes in these networks and their influence on post-operative outcomes, are sparse. [3] Here we describe an illustrative case highlighting the potential utility of connectomics in neurosurgical planning and decision making.

2. Case report

A 31-year-old Swedish-English bilingual woman with no relevant past medical history presented after multiple seizures. Computed tomography (CT) and contrast-enhanced MRI was performed and a connectome scan was generated using the Quicktome connectomics software (Omniscient Neurotechnology, Sydney, Australia). Imaging demonstrated a lesion concerning for a primary glial neoplasm (Fig. 1). Given its location, associated symptoms and imaging characteristics, the decision was made to proceed with an awake craniotomy for safe, maximal resection.

A comprehensive neuropsychological battery was administered in English (her most used language) to assess general intellectual functioning, attention, executive functions, language, visuospatial ability, and memory, revealing weaknesses in executive functioning, attention, and processing speed. Language (in Swedish), visuospatial functions, and verbal and nonverbal memory were spared. Baseline language

* Correspondence to: Department of Neurosurgery, Lenox Hill Hospital, 100 E 77th St, New York, NY 10075, USA.
E-mail addresses: hshah5@northwell.edu (H.A. Shah), fablyazova@northwell.edu (F. Ablyazova), gwernicke@northwell.edu (A.G. Wernicke), mvojnic@northwell.edu (M. Vojnic), jsilverst2@northwell.edu (J.W. Silverstein), byaffe2@northwell.edu (B. Yaffe), rdamico8@northwell.edu (R.S. D'Amico).

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testing in English determined items to be utilized during intraoperative mapping.

Preoperative connectome imaging demonstrated proximity to language areas, specifically the left parabelt complex (PBelt), left parahippocampal temporal (PHT) area, left superior temporal sulcus dorsal posterior (STSdp) area, and left parietal area F, part M (PFm) (Fig. 2). These images were used to plan a craniotomy to avoid functional networks and to guide intraoperative neuronavigation and mapping.

The patient underwent a left temporo-parietal craniotomy for tumor resection with awake language mapping. Intraoperatively, once the brain was exposed the patient was woken from conscious sedation for participation. A 1 × 8 strip electrode was placed anteriorly in the subdural space to identify the motor and sensory cortices via the phase reversal technique from median nerve stimulation. The motor cortex was found to be distant to the resection site and not at risk during the procedure. The patient then underwent language testing using open conversation in English and Swedish and standardized testing including auditory comprehension and naming to assess language function. Electrical mapping was performed with a cortical stimulator using the Penfield method of stimulation with a bipolar probe (low frequency, 60 Hz, 5-second trains starting at 2 mA and increasing incrementally to 6 mA).

Speech arrest was noted and resection was stopped in the gyrus and within the sulcus immediately anterior to the tumor entry point. This correlated on navigation to the left PBelt, PHT, and STSdp on connectome imaging (Fig. 3). For speech preservation, internal debulking was performed and then the peri-eloquent margins were dissected using the bipolar stimulation probe to retract the leading edge of the tumor with dynamic continuous stimulation at 5 mA for cortical and subcortical language tract activation. The anterior resection was stopped when speech arrest was encountered with stimulation. At the posterior superior boundary of the tumor, manipulation and stimulation resulted in many paraphasic errors in English and Swedish. This correlated to regions of the left PFm on the connectome imaging. Again, the tumor was debulked using an inside out approach at this margin until paraphasic errors were consistently generated at 5 mA of stimulation. Once sufficient function-preserving resection was completed, the margins were checked and the operation was finished. The patient awoke from surgery with an intact sensory-motor exam and with clinically preserved language and visual functioning.

Surgical pathology confirmed an IDH-mutated, MGMT promotor methylation negative WHO grade III astrocytoma. Postoperatively she continued on 1000 mg levetiracetam twice daily for seizure prophylaxis and underwent adjuvant radiotherapy to the resection cavity and residual disease to 60 Gy in 2 Gy per fraction with concurrent temozolomide. Of interest, she had no problems with Swedish but had occasional word finding difficulties in English.

Neuropsychological evaluation performed 2 months postoperatively demonstrated improvements in attention, working memory, and processing speed, though some of these scores are still believed to be somewhat below expectations given her high baseline, suggestive of mild frontal-subcortical dysfunction. A decline was noted in confrontation naming, which overlaps with her subjective word finding difficulties, though this was noted to be retrieval-based, rather than suggesting a semantic network dysfunction. MRI demonstrated disease progression.

3. Discussion

Prior to surgery, functional connectivity imaging revealed proximity of the tumor to the left PBelt, PHT, STSdp, and PFm areas. Speech arrest was identified within the gyrus immediately anterior to the planned corticectomy site, correlating to the PBelt, PHT, and STSdp areas. The PBelt is a parcellation of the auditory cortex functionally involved in auditory story, motor cue, and arithmetic tasks. [4] The PHT is a task-positive area found at the anterior subcentral gyrus, structurally connected to the AF and superior longitudinal fasciculus (SLF). Functionally, it is involved in retrieval of conceptual knowledge and notably, speech production. [5,6] Involvement of parcellations of the PHT in this patient's lesion, resection, or disease recurrence may explain intraoperative speech arrest and weaknesses with verbal initiation observed at follow-up. Notably, the left PHT is highly functionally connected to areas in the frontal lobe, insula, parietal lobe, and occipital lobe. The STSdp is located at the posterolateral superior temporal gyrus. The

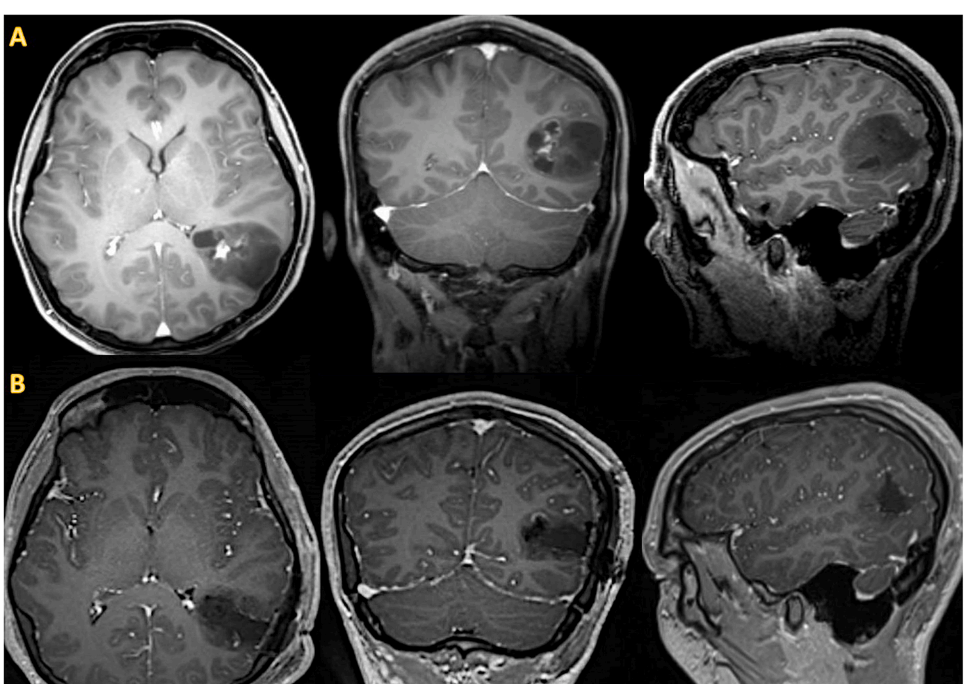

Fig. 1. A) Preoperative axial, coronal, and sagittal MRI showing tumor in the left inferolateral parietal lobe and posterior temporal lobe junction. B) Postoperative MRI showing reduction of tumor volume, and residual tumor in areas correlating to intraoperative speech arrest and paraphasic errors.

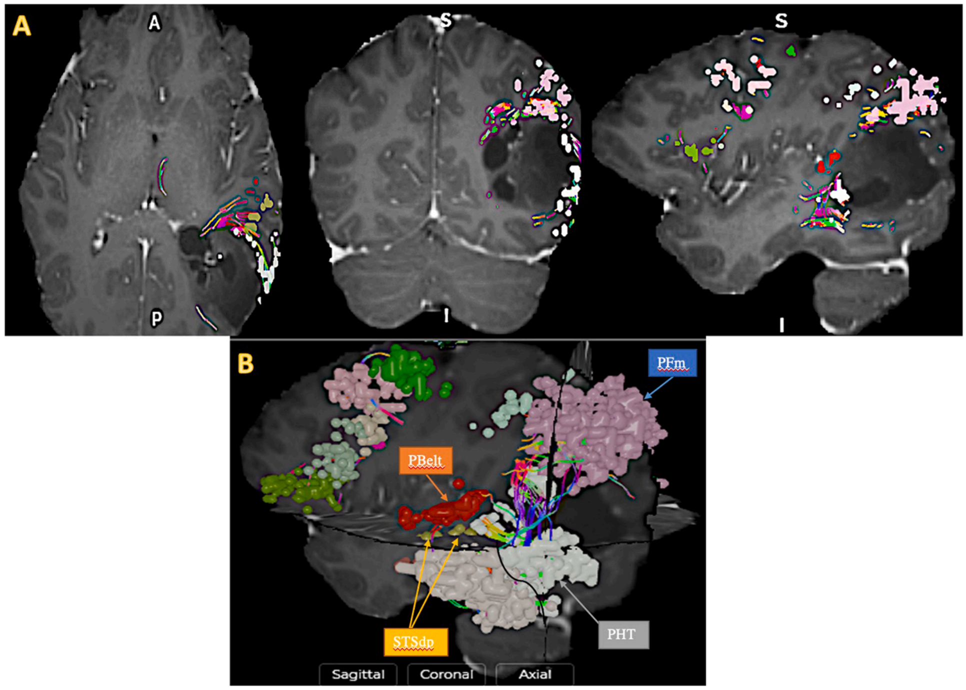

Fig. 2. A) Preoperative axial, coronal, and sagittal connectome imaging showing language network parcellations and tracts displaced by tumor growth. B) Language areas in proximity to the anterior tumor boundary (PBelt, PHT, STSdp) and superior-posterior boundary (PFm).

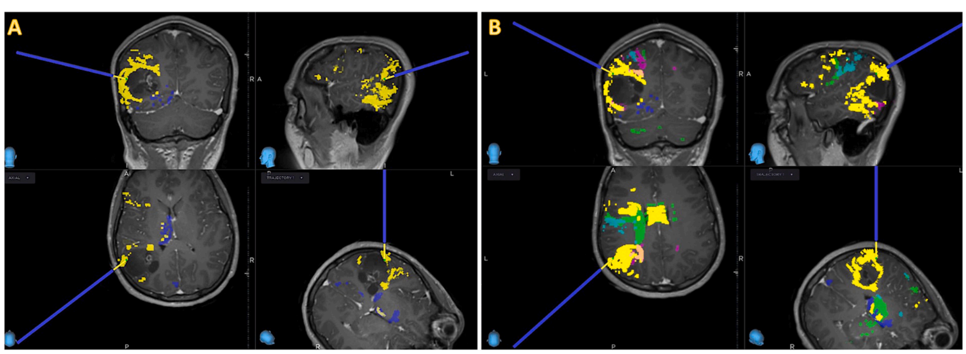

Fig. 3. A) Intraoperative location of speech arrest correlating to the PBelt, STSdp, and PHT areas demonstrated on navigated connectomics imaging. B) Intraoperative connectome neuronavigation correlating to the location of paraphasic errors (area PFm). Colors are not coordinated to connectome imaging (Fig. 2) due to limitations of the navigation software to import color schema.

posterior aspect of the STSdp, which was more anatomically involved in the presented case, is functionally involved in primary language tasks and language comprehension. [5,7].

The preoperative connectome scan demonstrated a superior displacement of the left PFm by the tumor. At the posterior superior tumor boundary, near the left PFm on preoperative connectome imaging, paraphasic errors were noted. Area PFm is involved in decision making when switching choices, attentional processing, working memory, motor cue, and risk-related tasks and has white matter connections to the AF and SLF. [6] The AF and SLF are traditionally implicated in conduction aphasias, characterized by frequent phonemic paraphasic errors as observed during intraoperative stimulation in this patient. Additionally, the AF and SLF are associated with phonemic fluency and postoperative changes regarding area PFm may explain this patient's weaknesses with phonemic fluency at postoperative follow up. [6].

Importantly, this case study demonstrates how implementing connectomes in surgical planning and decision making confers several advantages to traditional preoperative imaging modalities which are critically limited in cases of more complex brain networks such as the language network. This report highlights how connectomics may be utilized by neurosurgeons for preoperative surgical planning, counseling patients regarding possible postoperative neurologic deficits, optimizing awake mapping by preoperatively determining regions to focus mapping, and, when possible, planning a connectome-sparing resection. Our report corroborates that preoperative connectomics imaging can be used to identify networks intraoperatively based on language errors correlating to the functions of these networks.

There are several limitations to this study that should be considered. This report highlights our experience utilizing a novel technique in the case of a tumor affecting the language network, but further exploration is warranted with more systematically designed investigation to improve generalizability to other types of lesions affecting other brain regions and networks. Additionally, although connectome changes correlated to findings on postoperative neuropsychology testing, the individual effects of surgical resection, radiation, medical therapy, or disease progression on connectome changes are unclear. The technology implemented is also limited and does not account for intraoperative factors such as brain shift, and additionally processes language assuming the use of Western languages and left-hemisphere dominance.

4. Conclusions

Preoperative connectome imaging reveals functional regions at risk of damage during resection, and correlates to intraoperative language mapping findings. Connectomics can be helpful in assessing risk of functional deficits, guiding surgical planning in craniotomies for peri-eloquent tumor resection, directing intraoperative mapping stimulation, and prognosticating postoperative function.

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