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Case Report

Eloquent glioma resection assisted by brain connectomics: A new tool for awake neurosurgery

José Luis Navarro-Olvera[1], Noé Pérez-Carrillo[1], José Damián Carrillo-Ruiz[1,2], Jesús Quetzalcóatl Beltrán Mendoza[1], Francisco de Jesús García-Mendoza[3], Gustavo Aguado-Carrillo[1], José de Jesús Martínez Manrique[1]

[1]Neurosurgical Service, General Hospital of Mexico "Dr Eduardo Liceaga", Mexico City, [2]Neuroscience Coordination, Faculty of Psychology, Anáhuac University Mexico, [3]Central Research Laboratory, Faculty of Medicine, Benemérita Universidad Autónoma de Puebla, Puebla, Mexico.

E-mail: José Luis Navarro-Olvera - luiginavarro97@hotmail.com; *Noé Pérez-Carrillo - noeperezcarrillo@outlook.com; José Damián Carrillo-Ruiz - josecarrilloruiz@yahoo.com; Jesús Quetzalcóatl Beltrán Mendoza - jqbm80@gmail.com; Francisco de Jesús García-Mendoza - franjegame@gmail.com; Gustavo Aguado-Carrillo - gustavoaguado@me.com; José de Jesús Martínez Manrique - jesus.martinez@neurocirugia-innn.com

***Corresponding author:**
Noé Pérez-Carrillo,
Neurosurgical Service,
General Hospital of Mexico "Dr Eduardo Liceaga", Mexico City, Mexico.

noeperezcarrillo@outlook.com

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ABSTRACT

Background: Awake craniotomy with intraoperative mapping remains the gold standard for resection of gliomas in eloquent brain regions, enabling functional preservation while maximizing tumor removal. Recent advances in brain connectomics provide a connectivity-based approach, complementing traditional localization strategies by visualizing patient-specific structural and functional networks. We report the first Latin American case of diffuse glioma resection in the motor cortex using connectome-guided neuronavigation combined with awake functional monitoring.

Case Description: A 43-year-old male presented with focal motor seizures affecting the left upper limb. Preoperative magnetic resonance imaging revealed a motor-eloquent lesion. Patient-specific connectome parcellation identified intratumoral motor parcels, guiding surgical approach planning. During awake craniotomy, intraoperative mapping confirmed motor activation sites, enabling selective resection. Surgery was halted upon detecting transient monoparesis (3/5, Daniels scale) to preserve function. Postoperative recovery was complete within 2 weeks. Pathology confirmed the World Health Organization grade 2 diffuse astrocytoma.

Conclusion: This case illustrates the synergistic potential of connectome-guided neuronavigation and awake surgery in achieving a balance between oncologic and functional goals. Connectomics enhances preoperative planning by delineating individualized cortical-subcortical networks, even in anatomically distorted brains. Awake mapping provides real-time functional verification, mitigating limitations such as brain shift and resolution constraints inherent to navigation alone. While evidence is still limited to small series, this integrated approach offers a promising avenue for safe maximal resection in eloquent gliomas. Further studies are needed to validate its impact on long-term functional and oncologic outcomes.

Keywords: Awake patient, Brain connectome, Neuronavigation

INTRODUCTION

Neurosurgeons have long sought different tools in oncologic surgery to guide maximum tumor resection with safe functional outcomes, each of which is a fundamental determinant of quality of life, overall survival, and progression-free survival.[22] Awake surgery with intraoperative electrocortical mapping has long been considered the standard for real-time intraoperative identification of safe functional boundaries, as the aggressiveness of surgical resection has conventionally been guided by the classic subdivision of "eloquent" or "noneloquent" brain areas, hoping to preserve the fragile balance between risk and benefit and oncologic and functional needs, with little consideration of the complete neuronal circuitry.[10] Neuronavigation, on the other hand, is an indispensable tool that allows for preoperative strategic planning of the best surgical approach according to anatomical landmarks, which can even be done in conjunction with other technologies.[21]

New technologies applied to neurosurgery allow us to obtain images of the brain's structural and functional connectivity, in essence, the "connectome." These tools allow us to visualize maps of each patient's specific connectivity.[23] This is because clinical tractography emerged at the beginning of this century with the discovery that noninvasive diffusion magnetic resonance imaging (MRI) can approximate human neuronal pathways *in vivo*. The use of connectome parcellation has been proposed as an adjunct for identifying critical networks during neuronavigation, but the combination of connectome-guided neuronavigation and simultaneous intraoperative mapping of awake surgery for tumor resection represents a novel approach for eloquent lesions. However, neurosurgeons currently lack a standardized method for using reconstructed estimates of white matter tracts in glioma surgery, given the heterogeneity of user-dependent features, the difficulty in validating image-function correlation, and the confusing variety of diffusion tensor imaging (DTI) and post-DTI algorithms available at some academic centers.[18]

We report the first case of connectome-guided neuronavigation using connectome-guided neuronavigation software during the surgical resection of a diffuse glioma in the motor cortex in Latin America. We present our experience using connectomics for surgical planning and intraoperative neuronavigation in awake patients.

CASE PRESENTATION

A 43-year-old male presented with no significant history of sleep-onset focal motor seizures with clonic movements in the left arm without impairment of alertness and no clinical focalization data on examination. A preoperative magnetic resonance imaging study was performed [Figure 1], identifying a tumor lesion in an eloquent area with motor function, so individual parceling was performed with a focus on the motor paradigm [Figure 2], identifying intratumoral parcels with motor functionality, so a neuropsychological evaluation was requested for scheduling resection in the patient awake.

Using the brain connectome, the approach and resection were planned using intraoperative neuronavigation with awake functional monitoring [Figure 3]. The analysis of the language network was performed as part of our research protocol on patients with brain tumors, since connectome-guided neuronavigation was originally validated in healthy brains rather than in subjects with tumor pathology. This allowed the identification of intratumoral motor activation areas, which, together with awake functional monitoring, allowed for a selective resection while preserving motor function to the extent possible [Figure 4]. Transurgical examination revealed monoparesis of the left upper extremity, 3/5 on the Daniels scale, so it was decided to limit the resection to avoid

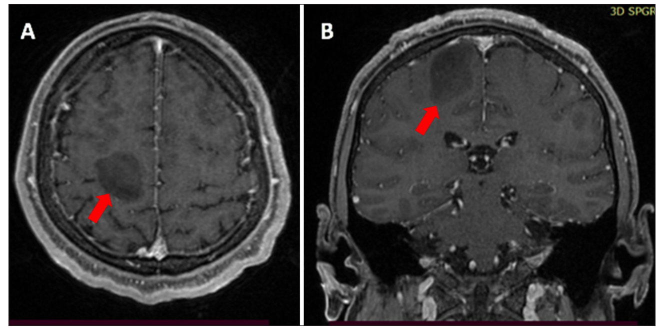

Figure 1: (A) Axial and (B) coronal contrast-enhanced T1-weighted magnetic resonance imaging (MRI) of the head show a hypointense lesion with poorly defined and diffuse borders in the right frontoparietal region indicated by a red arrow.

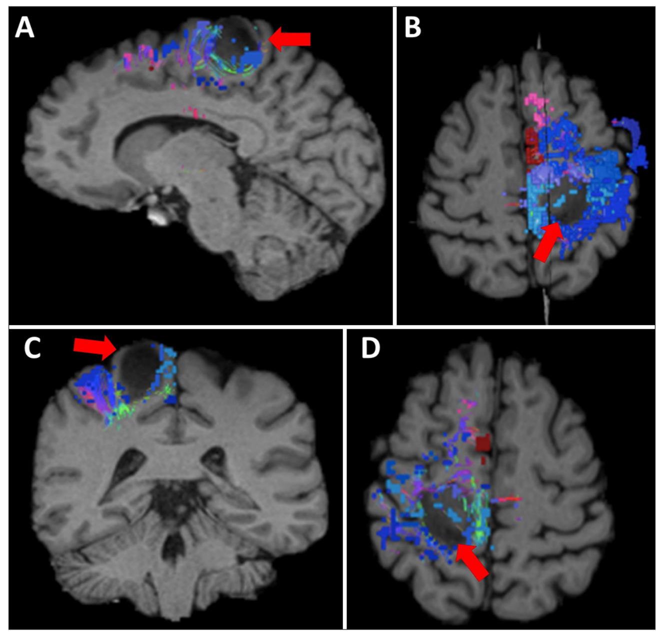

Figure 2: Preoperative planning of the sensorimotor network using connectome-guided neuronavigation, demonstrating functional areas within the lesion. (A) Sagittal MRI view obtained using connectome-guided neuronavigation, with the tumor indicated by a red arrow; (B) axial view highlighting that the software reverses left–right orientation during image reconstruction, with the tumor indicated by a red arrow; (C) coronal view intentionally inverted to normalize laterality, with the tumor indicated by a red arrow; and (D) axial view, with the tumor indicated by a red arrow.

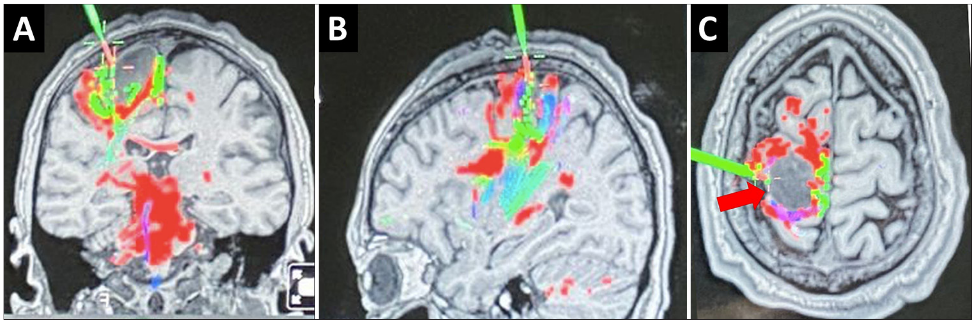

Figure 3: Brain connectomics in relation to a right frontoparietal tumor lesion, showing activation of intratumoral motor activity areas (green). (A) Coronal view; (B) sagittal view; and (C) axial view with the tumor indicated by a red arrow.

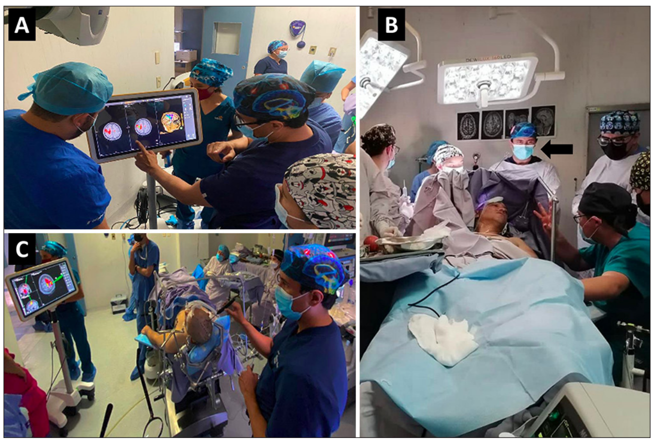

Figure 4: (A) Resection planning using connectome-guided neuronavigation. (B) Intraoperative monitoring of motor function in an awake patient, supported by the neuropsychology team. (C) Real-time delimitation of the surgical approach according to the lesion boundaries. The neurosurgeon's position, indicated by a black arrow, allows simultaneous visualization of both the connectome-guided navigation system and the surgical field.

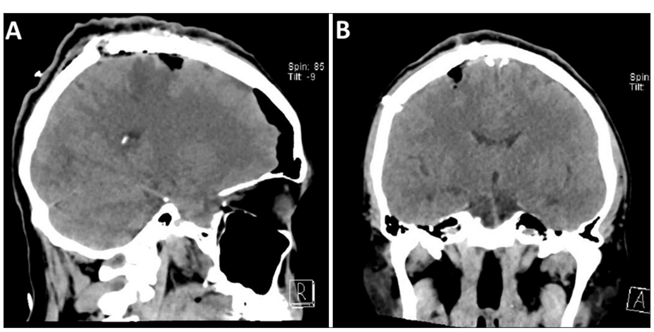

Figure 5: Immediate postoperative tomographic control, (A) sagittal and (B) coronal reconstructions with the presence of postsurgical changes and evidence of the resection site.

compromising function. The patient recovered to 5/5 after 2 weeks with the help of physical therapy and anti-edema measures [Figure 5]. The definitive pathology report was a diffuse astrocytoma, grade 2 according to the World Health Organization.

DISCUSSION

Surgical resection is an invaluable therapeutic approach for brain tumors. However, unlike oncologic surgery in other parts of the body, in neurosurgeries involving the parenchyma, maximum resection is not always possible without significantly affecting the patient's functional outcomes,[14] so a balance between the two is necessary. Identifying the boundaries of normal tissue, however, can be challenging, prompting the use of ancillary methods and technology. This represents a difficult decision-making process for neurosurgeons, which is why combining several of these methods has been recommended as a safer option that reduces the risk of damaging patients' neurological integrity.

Determining safe zones for surgical access is a complex task for the surgical team. Current understanding of the distribution of brain functions within cortical and subcortical topography has shifted from localizationism (localizing one cortical area to one function and vice versa) to a connectivity-based perspective, where a function spans a large network amongst several cortical and subcortical nodes, rather than being limited to finite cortical regions.[12] These connections are unique and different among people; inter-individual variability is intrinsic to neural connectivity, and thus, representation of these areas is not standardized and must thus be determined *de novo* in each patient. Connectomics, a branch of neuroscience that specializes in identifying these wide networks, has various methods for pinpointing these tracts, two of which are awake surgery mapping and atlas-based parcellation.[23]

Awake surgery for brain tumors is a unique modality where intraoperative mapping reveals whole-network dynamics by direct electrical stimulation of a small cortical area and visualization of the patient's performance of the task.[7] By simulating a "virtual transient lesion," mapping of the patient's unique brain connectivity is revealed with direct real-time proof of the functional area being localized. It is currently considered the standard of care for glioma surgery,[7,12] allowing for resection according to functional and not anatomical boundaries.[12]

Most supratentorial tumors can be resected in this manner, with relatively few contraindications. Several studies have observed high resection rates with a low range of permanent deficits or associated complications.[4] A 2021 meta-analysis revealed a nonsignificant higher rate of gross total resection and shorter length of stay, as well as a nonsignificant trend toward a smaller rate of late motor deficits with intraoperative awake mapping when compared to resection under general anesthesia.[2] It is possible that the impact of these findings is diminished due to high heterogeneity between studies. Proposed explanations of these findings include the fact that standard imaging mapping techniques used under general anesthesia cannot categorically exclude function, besides current limitations in representing spatial resolution, which is not yet as precise as direct stimulation.

Connectomics-based parcellation is a groundbreaking imaging software modality that identifies major networks (involving both cortical and subcortical elements) by simultaneously integrating multiple neurobiological properties from a single patient, such as cytoarchitecture, myeloarchitecture, and resting-state/task-based regional functional activation.[15,16] Machine-learning then processes this information by comparing it to atlases generated from large studies of hundreds of healthy subjects where statistically relevant averaged parcels corresponding to functional regions of interest were determined.[13,25] This parcellation scheme is applied to the new patient's data obtained by MRI, revealing the patient's unique functional network anatomical disposition, even when severe distortion is present, due to tumor mass effect, or major edema, etc.[15,24]

Parcellation comes close to precisely depicting major intracerebral networks in extreme detail and has been used in recent years for guiding surgical resection with promising results.[9,18] Although information is limited to small series or case reports, preoperative surgical planning and intraoperative navigation based on multi-modal networks come closer to accurately estimating functional areas than standard uni-modal imaging techniques, even accounting for small inter-individual variances in eloquent regions.[6,8,19]

Recent series have confirmed that awake craniotomy with intraoperative mapping is associated with a high extent of resection and low rates of permanent deficits, even in eloquent regions. Some contemporary meta-analyses, however, suggest that the superiority over surgery under general anesthesia does not always reach statistical significance, depending on the cohort and outcomes assessed.[3,20] In parallel, approaches without explicit connectomics, based on DTI/tractography combined with neuronavigation and neurophysiological monitoring, have demonstrated feasibility for more than a decade, with reasonable functional outcomes but inherent limitations such as user-dependent bias, spatial resolution constraints, and vulnerability to intraoperative brain shift.[1,5,26]

Multimodal connectomics provides an additional level of personalization by integrating structural and functional connectivity to delineate networks rather than discrete areas, offering guidance even in distorted brains. Early case reports and small series suggest that connectomics may optimize preoperative planning and complement awake mapping intraoperatively, although the evidence remains preliminary and lacks robust comparative trials.[23,27] In language-dominant regions, case series using connectomic analysis have demonstrated its value in identifying idiosyncratic functional parcels and predicting the risk of postoperative aphasia; moreover, preoperative connectome-based analyses have shown correlation with surgery-related language deficits.[11,23,27]

Overall, our findings align with this synergistic perspective: connectome-guided neuronavigation provides individualized strategic planning, while awake functional mapping validates these networks in real time, mitigating the shortcomings of navigation alone. In contrast, series performed without connectomic guidance, relying on DTI and intraoperative monitoring, have proven useful but remain more susceptible to tract modeling errors and interindividual variability.[5,26] Moreover, limitations include resolution during navigation and cost.

As seen above, both intraoperative mapping during awake surgery and multi-modal parcellation are comprehensive attempts to understand the anatomical disposition of complex brain connectomics. Each has great potential for oncological surgery, as well as important limitations. It would appear, however, that incorporating each with the other yields theoretical advantages. Major neuronavigation limitations, for example, include cost, limited resolution, as well as intraoperative brain-shift; awake surgery, on the other hand, has great resolution and readily available real-time functional mapping that can be repeated at any time during the surgery. Awake surgery is not without faults: one cannot plan with precision the approach until mapping is begun intraoperatively, there is a risk of intraoperative seizures during direct electrical stimulation, and finally, the accuracy of task testing relies on both the test, the tester, and the tested; all of which can be at fault or limited by progressive patient fatigue and cooperation.[17,27]

CONCLUSION

Neuronavigation with brain connectomics allows for the spatial identification of functional activation areas of specific functions that may be compromised by the tumor lesion. In addition, functional monitoring of the awake patient allows for safe resection of the lesion while preserving function to the extent possible, an important consideration given the scenario of a low-grade lesion.

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