Editorial

Functional neurooncology

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Brain tumors, especially gliomas, do not respect functional borders and often involve both cortex and subcortical white matter. Surgical planning thus becomes essential, especially when these lesions are located adjacent to functional anatomy. Different methods, including diffusion tensor MRI and subcortical electrostimulation, have been developed to further delineate important tracts and avoid them intraoperatively. These have been combined with neuronavigation to improve functional outcomes. Other methods, including using diffusion-weighted images combined with T1-weighted postcontrast images, have been used to identify and thus avoid optic radiations.

Substantial emphasis has been placed on sensorimotor mapping with little attention directed toward the visual system. Functional boundaries involving language and motor function—especially when these lesions are located adjacent to functional anatomy—have been better defined with neuronavigation to improve functional outcomes. Other methods, including using diffusion-weighted images combined with T1-weighted postcontrast images, have been used to identify and thus avoid optic radiations.

Gras-Combe and colleagues present a new target to further define functional boundaries during awake surgeries for glioma resections involving the visual pathways. Previously, efforts have been made to better define functional boundaries involving language and motor function with little emphasis on preservation of visual functions. In their article “Intraoperative subcortical electrical mapping of optic radiations in awake surgery for glioma involving visual pathways,” Gras-Combe et al. report on a series of 14 patients who underwent intraoperative mapping of optic radiations with subcortical electrical stimulation during resection of low-grade gliomas involving the optic radiations. The mean age of the patients was 38 years, and the group included more males (10) than females. All patients presented with seizures. The majority of lesions were located at the temporooccipitoparietal junction. Preoperatively, no visual field deficits were identified. Each patient underwent surgery in the lateral position under local anesthesia. Electrical stimulation was performed utilizing a bipolar electrode with 5-mm spaced tips delivering a biphasic current for 1 msec from 2 to 4 mA. Cortical mapping of sensory, motor, and language pathways (if applicable) was performed first. A second surgical stage was performed with alternating resection and subcortical stimulation. During mapping of the visual pathways, patients were exposed to 2 pictures placed diagonally on a screen situated in the quadrant to be saved and another in the opposite quadrant. This allowed testing of both language and visual function. While unaware of subcortical stimulation, the patients reported transient visual disturbances (blurred vision, phosphenes, shadow) within the contralateral visual hemifield. The visual disturbances were attributable to subcortical stimulation because they lasted the duration of the stimulation and stopped after cessation of the stimulation. All resections were limited based on functional boundaries especially relating to visual pathways. Ophthalmological examinations were performed between 1 to 6 months postoperatively, using perimetry, and MRI studies were performed immediately and at the 3-month follow-up examination. Six patients had speech disturbances that resolved within 3 months with rehabilitation. One patient suffered a homonymous hemianopia, and 10 others suffered an expected quadrantopia. Complete resection was obtained in 3 cases, subtotal (residual tumor volume < 10 cm³) in 8, and partial resection (residual tumor volume > 10 cm³) in 3. One patient had postoperative aphasia, which resolved with rehabilitation.

This innovative study does have some limitations. First, the authors acknowledged that evaluation of visual disturbances was subjective, with multiple variations, making it possible that the reported disturbances were not a result of subcortical stimulation of the visual system. The most clearly defined disturbance was that of blurred vision; phosphenes and shadows were less clearly described. The goal of the subcortical mapping of the visual pathways was to prevent homonymous hemianopia. Viegas et al. found that patients with a homonymous hemianopia following occipital glioma resection resumed normal social and professional lives with Karnofsky Performance Status scores of 90. This suggests that this visual loss is well tolerated and individuals are able to return to their lives. This brings into question whether, in fact, a homonymous hemianopia prevents someone from having a good quality of life. Is sparing the subcortical visual pathways important enough even to risk leaving gross tumor behind? Clearly, the study was not designed to answer this question. Quality of life was not assessed by means of objective measure before or after the surgery. Furthermore, from an oncological standpoint, follow-up was limited to 3 months, which leaves the question of long-term outcome, in light of there being only 3 patients who had complete resections and 11 who had subtotal resections. The authors did point out that their average extent of resection was 93.6%, but several studies now suggest that the more extensive the resection of low-grade gliomas, the better the long-term survival. In addition, the study group was a homogeneous population of younger individuals (mean age 38 years) who primar-
ily had WHO Grade I or II oligodendroglialomas. This brings into question whether the findings can be generalized to individuals with other types of astrocytomas or high-grade gliomas. Further investigation comparing neuronavigation and subcortical stimulation would also be beneficial, as neuronavigation with diffusion tensor tractography has been shown to maintain a high rate of functional preservation. Following recommendations in regard to effect on duration of surgery, blood loss, hospital stay, and cost-effectiveness may also limit the utility of subcortical electrical stimulation for visual mapping.

Regardless, the authors should be commended for developing a technique for intraoperative electrical mapping of the visual pathways. Preservation of all visual function may be very important to some patients and this study provides an additional tool for the neurosurgeon to try and accomplish this, if needed. Utilizing functional boundaries to limit resection not only limits postoperative deficits but ultimately leads to an improved quality of life. In this case series, homonymous hemianopia was avoided in all but one of the patients and permanent language and motor deficits were avoided in all. Insightfully, the authors acknowledged the future implications of visual pathway mapping and its ability to be generalized beyond glioma surgery. Further study is needed to determine its utility in epilepsy surgery and beyond.

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Disclosure

The authors report no conflict of interest.

References


Response

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Of course, we acknowledge that our study has some limitations, especially due to the fact that visual disturbances were subjective, with multiple variations. This is the reason why, in comparison with our first case report based only on the subjectivity of the patient, we have here proposed a new protocol in which 2 pictures were placed diagonally on a screen situated in the quadrant to be saved and another in the opposite quadrant. This task enabled us to map simultaneously and to differentiate both language and visual processing, and allowed more objective assessment, as supported by a 93% rate of favorable outcomes with no homonymous hemianopia. In addition, since we have generated postoperative permanent quadrantanopia in 12 patients (of 14), in essence, it means that we were in contact with the optic radiations at the end of the resection. Taken together, these findings confirm that transient visual disturbances during surgery were actually a result of subcortical stimulation of the visual system—even though this visual system is likely composed of distinct subpathways underlying different processes (perception and higher-level visual integration), which explains the induction of multiple visual disorders (including blurred vision, phosphenes, shadow).

We also confirm that avoiding homonymous hemianopia is crucial to preserving a normal quality of life, especially allowing patients to drive. We previously reported that intentional induction of a permanent homonymous hemianopia might be considered, but only in cases of occipital glioma. Indeed, when glial tumors involve both the visual cortex and the optic radiations, total or subtotal resection cannot be achieved without generating homonymous hemianopia. Therefore, due to the significant impact of maximal resection of gliomas on the natural history of the disease, the “onco-functional” balance argues in favor of a complete occipital lobectomy.
in patients with occipital glioma despite homonymous hemianopia—which can be well tolerated but prevents the patient from driving. Fortunately, occipital gliomas are rare.\textsuperscript{3} In the present article, the rationale was totally different, because the challenge was to achieve a complete or at least a subtotal resection while avoiding homonymous hemianopia in the frequent cases of lesions located at the temporoooccipitoparietal junction. In other words, in this location, we claim that it is possible to optimize the benefit-to-risk ratio of surgery by improving both the oncological results (mean extent of resection in our series: 93.6\%) as well as the functional outcomes (all patients are able to drive, including the patient with homonymous hemianopia, because the visual field defect was not complete). Therefore, we suggest that the surgical strategy should be adapted to the individual patient—that is, that neurosurgeons should evolve towards a personalized “functional neurooncology.”\textsuperscript{1}

Furthermore, regarding the residual tumor, which will continue to grow in the 11 subtotal resections, all of our patients know that they may require additional surgery in several years. Indeed, the first goal in low-grade glioma is to delay malignant transformation by maximizing the extent of resection, but not to cure the patient, even in cases of “supratotal” removal.\textsuperscript{4} In this state of mind, our group recently proposed the use of a new tool for low-grade glioma studies—plotting cumulative time with good quality of life versus time to malignant transformation. Applying this concept to nonoccipital gliomas involving the optic radiations may lead us to propose a first subtotal resection, which will allow for significant decrease in the risk of anaplastic transformation while preserving optimal quality of life (including driving). Then, once the glioma has regrown several years later, the goal is to perform a more extensive resection with removal of the part of the tumor invading the optic radiations, by accepting, in this second surgery, the generation of homonymous hemianopia, since it can be well tolerated despite the associated decline in quality of life.\textsuperscript{3} Because we explain the advantages of such a dynamic approach at the time of diagnosis, the patients in this series have accepted the principle of this multistage surgery.

Finally, we confirm that subcortical stimulation of optic radiations can be generalized to individuals with high-grade gliomas: indeed, we have successfully incorporated 2 patients with a Grade III astrocytoma in the present series. We also suggest the use of awake visual mapping in epilepsy surgery, because deficit of the visual field remains frequently reported in the literature, despite the integration of results from presurgical diffusion tensor imaging tractography in neuronavigation. Indeed, it is worth noting that diffusion tensor imaging is able to provide only anatomical information, but no functional data.

In summary, visual functions should be more extensively studied in brain surgery.

References

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