Preservation of Higher Cortical Functions in Brain Tumor Surgery: Past, Present and Future

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Editorial

Surgery of brain tumors is intended to remove injuries resulting in functional deficits as well as save the lives of affected persons. This is particularly the case for malignant tumors, in which life expectancy must necessarily be correlated to a discreet quality. What it means: the neurosurgeon must preserve so-called eloquent areas, especially in the case of frontal and temporal brain tumors. It is known that the frontal lobe of the left cerebral hemisphere contains the center of the motor language, the Broca’s area, located in the superior frontal gyrus and the neurons responsible for the motility, while the anteriorfrontal cortex, the prefrontal cortex, houses important cognitive functions for relationship life, like behavior [1]. The same applies to brain tumors of the temporal lobe, in which there is the center of sensory language, Wernicke’s area, as well as functions such as memory and behavior. In short, they are eloquent cortical areas, fundamental to the individual and inter-individual social life, which need to be spared in brain surgery. For this reason surgery of brain tumors located in eloquent areas is often contraindicated and the neurosurgeon is posed in front of a huge problem to solve. Historical steps: since the beginning of the ’30s, Wilder Graves Penfield (January 26, 1891- April 5, 1976) a Canadianneurosurgeon, expanded brain surgery’s methods and techniques, including mapping the functions of various regions of the brain such as the cortical homunculus, introduced the use of Electrical Stimulation Mapping (ESM) of cerebral cortex, to localize sensorimotor and language sites in patients [1,2]. Penfieldinvented the Montreal procedure in which he treated patients with severe epilepsy by destroying neuron pools where the seizures originated. Before operating, he stimulated the brain with electrical probes while the patients were conscious under only local anesthesia, and observed their responses. In this way he could more accurately target the areas of the brain responsible, reducing the side-effects of the surgery. This technique also allowed him to create maps of the sensory and motor cortices of the brain, showing their connections to the various limbs and organs of the body. These maps are still used today, practically unaltered. With Herbert Jasper, he published this work in 1951 (2nd ed., 1954) as the landmark Epilepsy and the Functional Anatomy of the Human Brain [2]. This work contributed a great endeavour to understanding the localization of brain function. Penfield’s maps showed considerable overlap between regions (i.e. the motor region controlling muscles in the hand sometimes also controlled muscles in the upper arm and shoulder) a feature which he put down to individual variation in brain size and localisation: it has since been established that this is due to the fractured somatotropy of the motor cortex. From these results he developed his cortical homunculus map, which is how the brain sees the body from an inside perspective.

Penfield also reported that stimulation of the temporal lobes could lead to vivid recall of memories. Then American neurosurgeon George Ojemann focused his reseach on the neurobiology of human cognition, particularly cortical organization for language and memory, which he investigates in the context of awake neurosurgery under local anesthesia. In order to study these aspects of cognition, Ojemann utilizes techniques ranging from electrical stimulation mapping to recording of activity of single neurons, which have resulted in methods for reducing the risk of cortical resections for epilepsy and tumors demonstrating the individual variability of location of language function while founding that location of motor and sensory cortex was less variable [3]. The ESM therefore presupposed a surgery in an awake patient. About the technique used, stimulation was applied randomly to the cortex near or overlying the lesion, to the brain parenchyma infiltrated by the tumor and to the cortical sites likely to be involved in sensorimotor or language function, avoiding to stimulate consecutively cortical sites distant less than 2 cm, delivering a low current about 1 mA. Different
types of tests, employed to evaluate both the syntactic-morphological and the semantic-lexical functions. In order to test denomination patients were asked to name different drawn objects, excluding the ones they did not name exactly during preoperative testing. All stimulated cortical sites were spotted by sterile etiquettes and colored or marked differently to ascertain the different effects, resulting from deficits or errors in the answers, as speech arrest and anomia, and with regard to motor functions, sudden difficulty in moving a limb. ESM is still practiced today, and there are numerous studies in literature, such as extensive research carried out in a thorough case study by Italian and French researchers [4]. This study, carried out on malignant brain tumors, shows not only the indications, but also the ESM's limits. However, the various studies so far have shown that ESM in brain tumors is a method which has the advantage of saving eloquent cortical areas with remarkable precision while the limits are predominantly represented by infantile age, psychiatric disorders and fear which catches the patient awake. As for ESM risks, these, cerebral infections and haemorrhages are not superior to those developed during traditional neurosurgical interventions [4,5].

For some years now a new technique is being established, the Diffusion Tensor Imaging (DTI), a magnetic resonance tool through which three-dimensional, biomedical images can be constructed. Fiber Tractography (FT) is a 3D reconstruction technique to access neural tracts using data collected by DTI. This technique has the ability to study and analyze the nerve fibers of the white matter. Some of the clinical applications of DTI are in the trait-specific localization of lesions of the white matters various types of trauma and in determining the severity of the traumatic brain injury diffused [6,7]. The localization of the tumor in relation to the white matter due to infiltration was one of the most important initial applications. In the planning of surgical procedures for certain types of brain tumor, neurosurgery is assisted by the knowledge of proximity and relative position of the corticospinal tract with respect to the tumor. In short, DTI tractography is a novel approach for defining alterations in WM pathways induced by brain lesions. The advantage of this technique is the ability to relate the anatomy of the white matter to the neurological symptoms and signs. In particular, the presence of intact fascicles in the white matter may be predictive of a better surgical outcome, because these conditions show a higher probability of total resection than did subtotal and partial resection. Instead, the presence of infiltrated or displaced or infiltrated fascicles may predict a lower probability of total resection, especially for tumors with preoperative volume <100cm³. DTI tractography can thus be considered to be a promising tool for estimating preoperatively the degree of radicality to be reached by surgical resection. This information will aid clinicians in identifying patients who will mostly benefit from surgery. Tractography has been employed successfully in patients with tumors in language areas, preoperatively, demonstrating the relationships between the tumors to resect and the language fascicles to preserve from lesion. With the use of the tractography-integrated navigation system and intraoperative DTI, language functions were preserved in all patients. The mean volumetric resection was 93.0 ± 10.4% of the preoperative tumour volume, with a gross total resection in 60% of patients. So, the intraoperative combination of DTI tractography contributed to maximum safe resection of gliomas located in language areas. Diffusion Tensor Imaging (DTI) tractography can visualize the course of white matter tracts inside or around a tumor, and it provides the surgeon with important information in resection planning. Preoperative DTI tractography turns out useful in predicting the extent of the resection achievable in surgical removal of brain tumors. DTI tractography is the only noninvasive method, allowing detection of the trajectories of main WM fascicles, and it can provide information whether a tract is displaced, infiltrated/edematous, or interrupted by a tumor. Seems the accuracy of DTI tractography for detecting motor and speech pathways has been validated with ESM, with 82% to 97% concordance across studies [5]. The introduction of DTI changed the way neuroscientists look at WM. In time, DTI has developed into a sophisticated and complex MR multidisciplinary field with the contribution of physicists, biomedical engineers, mathematicians, cognitive neurologists, neuroradiologists, and neurosurgeons. With the development of DTI tractography, the trajectories of multiple WM fascicles can be identified in the individual subject, and their relationship with a focal lesion can be illustrated and used for presurgical brain mapping [6,7]. It is now recognized that a detailed understanding of the geometric WM changes induced by a tumor is valuable in order to maximize lesion resection while avoiding permanent postoperative morbidity. This is particularly true in cases of infiltrating tumors located within eloquent regions of the brain.

Tractography today has gained a certain reputation for explaining WM architecture. Mapping of WM pathways may improve presurgical planning and surgical targeting with neuronavigational devices, and it may important in reducing intraoperative time. Clinical use of DTI tractography is growing in importance, and exams in patients are being increasingly requested by neurosurgeons worldwide.

Although advanced diffusion imaging methods are currently available in most MRI scanners, DTI is not yet considered “standard of care”. The processes that lead to establishing clinical practice are also complex, especially at a time when emphasis on economic difficulties affects health-care decisions. DTI is an extremely useful method that can contribute to improve clinical outcome and to reduce complication rates. Personally, I believe that scientific research has made tremendous progress over time: brain cortical electrical stimulation with mapping has shown how to perform neurosurgical intervention in brain tumors, saving eloquent areas, language and motility. This was a fundamental step, followed by DTI tractography in today’s time, which has made it clear that by examining the state of the white matter fibers, it is possible to remove a brain tumor with some precision, without damaging the healthy tissue. Ultimately, this is the way to go, until new methods are born.

References
