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Original article

Technical principles of direct bipolar electrostimulation for cortical and subcortical mapping in awake craniotomy

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ABSTRACT

Introduction. – Intraoperative application of electrical current to the brain is a standard technique during brain surgery for inferring the function of the underlying brain. The purpose of intraoperative functional mapping is to reliably identify cortical areas and subcortical pathways involved in eloquent functions, especially motor, sensory, language and cognitive functions.
Material and methods. – The aim of this article is to review the rationale and the electrophysiological principles of the use of direct bipolar electrostimulation for cortical and subcortical mapping under awake conditions.
Results. – Direct electrical stimulation is a window into the whole functional network that sustains a particular function. It is an accurate (spatial resolution of about 5 mm) and a reproducible technique particularly adapted to clinical practice for brain resection in eloquent areas. If the procedure is rigorously applied, the sensitivity of direct electrical stimulation for the detection of cortical and subcortical eloquent areas is nearly 100%. The main disadvantage of this technique is its suboptimal specificity. Another limitation is the identification of eloquent areas during surgery, which, however, could have been functionally compensated postoperatively if removed surgically.
Conclusion. – Direct electrical stimulation is an easy, accurate, reliable and safe invasive technique for the intraoperative detection of both cortical and subcortical functional brain connectivity for clinical purpose. In our opinion, it is the optimal technique for minimizing the risk of neurological sequelae when resecting in eloquent brain areas.

1. Introduction

The aim of glioma surgery is to maximize the extent of the resection, while minimizing the risk of neurological deficit, in order to maintain both quality of life and survival [1]. An individually tailored approach is mandated because: the frequent location of the glioma in eloquent areas; major interindividual anatomico-functional variability in cortical and subcortical organization; and the potential for postoperative plasticity [2,3]. The purpose of the intraoperative functional mapping is to reliably identify cortical areas and subcortical pathways involved in motor, sensory, language and cognitive function. Intraoperative application of electrical current to the brain has become a standard technique during brain surgery for understanding cortical functions in humans. Although there are similarities, the application of mapping at different centers involves a diversity of approaches [4]. The aim of this article is to review the rationale and the electrophysiological principles of the use of direct bipolar electrostimulation for cortical and subcortical mapping in awake craniotomy within the field of surgical neuro-oncology in adults. For an overview of the other electrical stimulation techniques, see Szelenyi et al., Berger and Hadjipanayis. [4,5].

2. Historical perspective

The intraoperative application of direct electric current onto the human cortex for the localisation of functions started in the late

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19th century. The first description is attributed to Robert Bartholow et al. in 1874 [6]. The first application for neurosurgical purposes is attributed to Victor Horsley and David Ferrier in 1884 followed by William Keen in 1888, Leonard Bidwell and Charles Sherrington in May 1893, and Fedor Krause in November 1893 [7]. The modern methods and principles were pioneered in the early 20th century by Fedor Krause who described the first map of the human motor cortex, which was then refined by Harvey Cushing, Otfrid Foerster and Wilder Penfield [5]. The use of direct electrical stimulation to intraoperatively map eloquent brain areas was established as a reliable, routine procedure in epilepsy surgery by Wilder Penfield [4–9]. The technique was further refined by Georges Ojemann in the seventies, by introducing a biphasic current, with constant pulse and by optimizing the intraoperative testing tasks [10]. In the nineties, Mitchel Berger applied the direct electrical stimulation method for mapping eloquent cortical areas for oncological neurosurgery purposes [11,12] and first described its application to the localization of subcortical motor and sensory pathways [5,13,14]. Then, Hugues Duffau extended and codified the indication of direct electrical stimulation at cortical and subcortical levels to investigate intraoperatively the individual functional connectivity of the brain [2,15,16]. In the last decade, popularized by the reported successes [8,17–20], the technique has spread all over the world.

3. Rationale of intraoperative cortical and subcortical mapping during brain resection

Functional neuroimaging has shown considerable advances. Functional MRI estimates the location of the eloquent cortical areas, informs on language lateralization, and helps in the selection of the best surgical approach. The reliability of functional MRI is suboptimal in glioma patients (sensitivity ranging from 82 to 100% for sensorimotor cortical sites, but less than 66% for language cortical sites) [2,8,21,22]. Blood-oxygen-level dependent imaging, which is the standard technique used to generate fMRI images, is altered in the vicinity of gliomas, due to neurovascular decoupling which in turn depends on tumor grade, brain and glioma perfusion changes, distance to tumor, patient age, intracranial pressure, antiepileptic drugs and neurological deficits [2,9,21]. Functional MRI and diffusion tensor imaging are useful adjuncts for intraoperative direct stimulation mapping [8].

In addition, the nature [23–25] of infiltrative gliomas is such that tumor cells permeate the perilesional brain parenchyma [26,27] that are still functional regarding language in 46% of cortical sites and in 35% of subcortical structures [22]. These results illustrate the importance of performing brain mapping in glioma surgery in order to delineate and then avoid individual anatomico-functional relevant areas of a particular patient's brain with a view to performing a functionally-based maximal resection which should ensure the best oncological outcome [20].

Consequently, these observations mandate the use of invasive electrophysiology to maximize resection, preserving function and to ensure a satisfying neurological outcome after surgery for cerebral gliomas within or close to eloquent brain structures [2,4,8,17–19,28].

Invasive electrophysiological investigations include surface recordings and direct electrical stimulation. Somatosensory evoked potentials were extensively used for tumor resection around the central sulcus with an overall sensitivity and negative predictive value of central sulcus localization of 79 and 96%, respectively. Motor evoked potentials only control the monitored muscles and do not allow detecting and avoiding motor deficits in non-monitored muscles. In addition, intraoperative evoked potentials cannot currently be used to quickly and reliably map language, memory, or other higher functions [2]. Extraoperative electrophysiological recording and stimulation have also been performed using implanted subdural grids. The 1 cm-spaced electrodes have a restricted spatial definition and do not enable mapping of subcortical structures, whereas gliomas have a predisposition to migrate along these white matter tracts [2]. Surface electrocorticographic recordings can be taken intraoperatively using a grid made of 1 cm-spaced electrodes separated to augment direct bipolar electrical stimulations [29]. It has been shown that this type of combination could be useful to detect remote afterdischarges and to adjust stimulation parameters, thus improving sensitivity and specificity of the direct electrical stimulations [29,30].

Consequently, considering the advantages and the limitations of these different mapping techniques, we consider the use of direct bipolar intraoperative electrical stimulation as the gold standard for the monitoring of cortical and subcortical functional areas during brain resection [31].

4. Effectiveness of intraoperative functional mapping for cerebral resection

Whatever the grade of malignancy, glioma survivals are linked to the extent of resection and to the functional status of the patient. One could argue that the extent of resection and the postoperative functional status of the patient are also directly linked; supporting the view that intraoperative functional mapping should be universally adopted in glioma surgery. Daily practice has demonstrated the functional and survival benefit of intraoperative electrostimulation functional mapping for glioma resection. A large and recent meta-analysis incorporating more than 8000 patients who had resective surgery for supratentorial infiltrative glioma with or without use of intraoperative electrostimulation functional mapping illustrated that glioma resections with the use of intraoperative mapping were associated with fewer late severe neurological deficits (3.4% vs. 8.2%) and more extensive resection (75% vs. 58%) [19]. This study indicated in addition that early and reversible loss of function of critical brain structures was more frequent after resective surgery for supratentorial infiltrative glioma with use of intraoperative electrostimulation functional mapping, but irreversible neurologic damage was more effectively avoided, in comparison with resective surgery without use of intraoperative electrostimulation functional mapping. Similarly, a cohort study of supratentorial infiltrative glioma patients who had resective surgery with or without use of intraoperative electrostimulation in the same institution demonstrated that glioma resections with functional mapping were associated with fewer late severe neurological deficits (6.5% vs. 17%) and more extensive resection (76% vs. 44%) and they involved eloquent locations more frequently (62% vs. 35%) [32].

5. Indications for intraoperative functional mapping for cerebral resection

In neuro-oncology, the use of intraoperative cortical and subcortical electrostimulation mapping is currently mandatory to remove infiltrative lesions, such as cerebral gliomas, located within or close to eloquent areas. In addition, it can be used to map and preserve brain networks around a well-circumscribed lesion – such as a metastasis – and to guide the removal of perilesional brain tissue that may contain isolated tumor cells or epileptogenic foci. Lastly, it can be used to map and preserve brain networks to functionally tailor a transcortical approach as an alternative to the classical transulcal approach to reach a deep-seated lesion [33]. Invasive electrophysiological stimulation is currently considered the "gold standard" clinical tool for brain mapping during cerebral resection in neuro-oncology [9].