Chapter

Awake Craniotomy and Brain Mapping for Brain Tumor Resection in Pediatric Patients

Roberto Garcia-Navarrete, Javier Terrazo-Lluch, Alfonso Marhx-Bracho, Ericka León Alvárez, Natael Olvera González, Beatriz Alvárez-Mora, Rosario Aguilar Silva, Cointa Arroyo, Vianey Maceda Morales, Luz María Cordero, Daniel Magos Rodríguez, Sandra Luz Lizarraga-Lopez, Ana Niembro Zúñiga and Juan Alberto Díaz Ponce Medrano

Abstract

Brain tumor resection in pediatric patients constitutes a real challenge. In order to improve survival and to preserve neurological function, we will further on describe our experience with awake craniotomy and functional mapping for brain tumor resection in pediatric patients. Although our experience with this technique was relatively short, we did not observe complications, and a gross total resection was successfully achieved in all cases. In the postoperative period we did not find any new deficiency in our patients. We observed functional recovery - motor and sensitive aphasia, motor strength improvement in hemiplegic patients, and recovery of neurodevelopmental milestones during follow-up. In our experience, the use of awake craniotomy and brain mapping for brain tumor resection in pediatric patients is truly safe and reliable.

Keywords: Awake craniotomy, Brain mapping, Brain tumor, Cancer

1. Introduction

The last year, the *Instituto Nacional de Pediatría* at Mexico is commemorating the 50th anniversary of its foundation. Throughout the years, the Pediatric Neurosurgery Department has consolidated itself as an emblematic service in our hospital among the civilian population and has become the reference center in Mexico to treat brain tumors and complex neurosurgical diseases.

The *Centro Médico Naval* is the referral center for the treatment of complex neurosurgical diseases in the health services of the *Secretaría de Marina* of Mexico. We serve military personnel and their families, as well as civilian population under certain public health circumstances, as COVID-19 pandemic. The Neurosurgery Department is equipped with the ultimate technological devices for brain tumor treatment, such as neuronavigational systems (Brainlab and Medtronic Systems), intraoperative imaging devices (O-arm), neurophysiological equipment for brain mapping and subcortical stimulation.

This review describes our protocol in both centers for **Awake craniotomy and brain mapping for brain tumor resection in pediatric patients.**

In recent years, the collaborative work performed by an experienced group of neuroscientific specialties - Neuroanesthesiologist (LAE, NOG), Neuropsychologist (BAM, RAS, CA), Neurophysiologist (LMC/DMR), and a specialist from the Intensive care unit (SLL) and pediatric oncologist (AN); allows us to treat brain tumors located in eloquent areas in young brains.

2. Neuropsychological evaluation

Most neurological diseases have variable expressiveness; the severity of symptoms that define the disorder varies between individuals. The variability of symptom expression should be identified, and the expected effects of treatment defined. The neurological pathology is complex and comprises a set of unique conditions, therefore it is required a multidisciplinary team of professionals and specialists in pediatric neurosurgery and neuropsychology.

Neuropsychological pediatric evaluation faces certain peculiarities. The brain's functional systems are in development. Thus, certain functions are not able to be properly evaluated. The neuropsychological evaluation tries to obtain a capacity profile which contains weak and strong points. When certain neuropsychological abilities (behavioral and cognitive) are selectively impaired, they may be compatible with the neurological alteration detected. The purpose of an evaluation depends mainly on the reference reason, and this, in turn, depends on the patient's age, academic grade and cognitive development. Neuropsychological tests are essential for establishing a cognitive disorder; in a patient with a brain tumor, it is crucial to have several chronologically ordered evaluations. All improvements can also be monitored by repeating a series of tests, and changes in symptomatology can be detected early. Furthermore, the intervention's effectiveness can be documented, and neuropsychological rehabilitation interventions can be scheduled.

Concerning tumors, the tumor growth site does often relate to neuropsychological deficits (e.g., left hemisphere tumors often affect language). However, due to compression and displacement effects, more widespread damage and overall neuropsychological impairment may occur [1].

It is essential to mention that neuropsychological functions result from a complex functional system that cannot be located in restricted areas of the cerebral cortex or isolated cells. With the use of such specific MRI techniques as blood oxygenation level dependent imaging (BOLD), we know that those functions must be organized into systems of areas that work harmoniously, each of which plays its part within the complex functional system, being located in entirely different areas often very distant from each other in the brain.

Neuropsychological functioning is related to tumor malignancy and behavior; neuropsychological performance assessment may be more sensitive in predicting early tumor recurrence than imaging techniques [1].

In recent years, there has been an increase in the need for neuropsychological evaluations in people who have suffered from known organic diseases and psychiatric pathologies where brain dysfunction is suspected. Interestingly, in most western countries, there has been a crescent incorporation of neuropsychologists into hospital services.

The neuropsychological assessment's primary objective is to identify a possible alteration of functions which are regulated by the cerebral cortex and powerful neuropsychological interventions during sequelae early identification and treatment [2].

When someone faces the need to perform a neuropsychological evaluation, they deal with people who retain a very diverse set of skills depending on their personality characteristics, disease topography, brain edema. These conditions prevent the talk of a rigid evaluation protocol and a set of tests established in advance; they require, on the other hand, a certain level of knowledge to determine in each case the most appropriate evaluation tests [2].

The neuropsychological evaluation has been used during surgeries such as epilepsy and deep brain stimulation to identify adverse outcome risks. The results of this evaluation represent the starting point for neuropsychological treatment and rehabilitation [3].

In a pediatric patient with a brain tumor, the neuropsychological evaluation is performed to determine the patient's overall cognitive status, specifying the skills preserved in contrast with those affected by brain edema and destruction of tissue secondary to the tumor [4, 5].

To set up the overall cognitive status of the patient before surgery, it requires the application of specific instruments, including standardized batteries, or a set of tests which adapt to the specific problems and needs of each patient; allowing to establish:

a. Preserved and altered cognitive functions, i.e., a baseline against which to evaluate postoperative function.

b. The ability of patients to cooperate with transoperative and postoperative needs.

The role of the Neuropsychologist in CNS surgery is divided into different stages. The preoperative evaluation aims to locate, if possible, the focus by associating cognitive deficits in a particular brain region. Set a baseline for measuring changes. Predict cognitive risks after surgery and, in conjunction with the neurosurgeon and family members, assess the procedure's risks/benefits in their quality of life. It is useful as a guide to the neurosurgeon to decide which areas of the brain are at risk and adjust, from there, educational and cognitive rehabilitation programs. Finally, the evaluation can help diagnose psychiatric disorders and their potential impact on cooperation in the operating room. Several reports note that much of the success of awake patient surgery is due to the patient's active participation in the intraoperative process. During functional testing, patient cooperation allows the team to make real-time surgical decisions to achieve maximum tumor resection with minimal functional deterioration to ensure a better quality of life.

There is no protocolized structure for neuropsychological exploration and monitoring that these patients need; there is not enough information about candidates' psychological profiles and eligibility criteria. The transoperative evaluation is based on the literature on the Wada test's use, mainly evaluating language and memory in the dominant hemisphere.

The evaluation depends on the patient's cooperation and what can be applied; if possible, it should include the functions of speech and language:

- Verbal fluency
- Denomination
- Verbal understanding

- Repetition of sentences
- Oral reading (if possible)

Memory evaluation should include:

- Guidance
- Sequencing
- Image remembrance/recovery
- Repetition of digits
- Calculation

Already standardized test subtests measure these areas such as Wechsler Scales, Luria test, Woodkock test, a word list with a letter. These tests are appropriate for the child's age and the evaluation context.

Postoperative evaluation allows monitoring of its evolution, possible sequelae, and the creation of stimulation programs to achieve its full potential.

It has been estimated that there are transient changes in cognitive functioning within the first three months of post-surgical recovery, which are relatively permanent within the following six months after the intervention. However, the most significant changes can occur up to one year after the intervention.

3. Neuroanesthesiological evaluation

Several anesthetic considerations for awake craniotomy should be granted to avoid injuries in brain surgery. The primary goal is to carry out the lesion's resection with maximum preservation of neurological functions [6, 7]. This type of management in pediatric patients is limited by anxiety and insufficient understanding, limiting their cooperation during the procedure [8].

The awake craniotomy technique had been developing since the second half of the 19th century when local anesthetics (LA) became widely available. With proper local analgesia, Prof. Horace Horsley was able to perform a craniotomy in awake patients. The benefits were not recognized until 1951, when Prof. Wilder Penfield published LA value for craniotomy in patients with epilepsy to facilitate the resection of epileptogenic focuses [9].

Prof. Penfield argumented that patients with functional neurological pathology should be operated on awake modality and at the same time performing complex and motor activities.

It was initially designed for patients undergoing functional neurological surgery. It is currently offered in pathologies that involve eloquent or motor areas, where real-time monitoring of superior or motor functions is required during tumor resection [10].

The anesthesiologist should know the problems faced during the brain tumor resection in the awake patient, should be aware that at any time, surgery can be switched to a classic craniotomy under total endovenous anesthesia [11].

Scenarios that may be confronted during both phases, asleep or awake, are seizures or movements typical of the patient, result of the suboptimal neuromuscular blockage, or movements in the presence of anxiety or insufficient analgesia. These symptoms can result in severe damage, from lacerations to the scalp, skull fractures, including cervical spine injuries [9]. This technique aims to provide the neurosurgeon tools to perform the lesion's resection with maximum preservation of eloquent or motor anatomical areas, preserve the patient's integrity, minimize neurological damage and not to increase the deficit already installed [7, 8]. This technique involves inducing general anesthesia and maintaining airway control with a supraglottic device, it also includes invasive monitoring (catheter placement and urinary catheter), administration of scalp blockage, patient positioning, including fixing the skull to Mayfield's head clamp to opening the dura mater [9, 10].

The technique consists of awakening the patient, ousting the supraglottic device, and performing cortical mapping or delimitation of the lesion and resection. At the end of the resection, general anesthesia is again continued, the supraglottic device is reinserted, and the dura mater, skull, and skin are closed.

The main objective of anesthetic management is to ensure adequate patient cooperation, maintain comfort throughout the procedure concerning the chosen position for surgery, prevent and treat nausea, vomiting, seizures, and maintain systemic and neurological homeostasis to provide adequate ventilation, hemodynamic stability, and brain relaxation [11].

Optimal tumor resection is maximum mass removal without significant neurological deficits, such as damage to motor or language function. Therefore, it is now considered the treatment of choice for brain tumor surgery in eloquent areas. Compared to craniotomy under general anesthesia, an awake craniotomy may provide a higher degree of tumor removal without postoperative neurological deficits and better survival rates in these patients [12].

The pediatric patient represents a tremendous challenge for the awake craniotomy technique's success. The cognitive level and emotional maturity will determine their cooperation during the procedure. It is well known that the patient under the age of 16 does not yet have an adult's maturity, and therefore requires more significant psychological support. In the literature, few patients from 8 to 15 years of age have demonstrated this procedure's feasibility [11]. Patients under the age of 10, chosen for this procedure, must demonstrate a rigorous level of maturity and motivation, so the child's degree of development will determine the possibility of exercising this technique [10].

Multidisciplinary assessment (Pediatric neurosurgeon, Neuroanesthesiologist, Neuropsychologist, and Neurophysiologist) is indispensable to mitigate the patient's stress. Some authors prepare the patient psychologically using videos and teaching material to explain the procedure. The previous visit to the operating theater can be an excellent option to gain the child's trust and confidence [12, 13].

The Neuroanesthesiologist should know the surgical and neurophysiological needs required for this procedure. We have a wide variety of anesthetics that can be useful but should be individualized to each patient. Propofol, remifentanil, dexmedetomidine, and scalp nerve blockage provide the right conditions for intraoperative brain mapping. Proper patient selection, adequate perioperative psychological support, and correct anesthetic management at each stage of surgery are all crucial for the safety, satisfaction, and success of the procedure. All of them must allow analgesia and a required sedation level according to the surgical moment [10]. It should be emphasized that certain anesthetics may affect the neurophysiological evaluation [12].

The neuroanesthesiologist should describe the procedure to follow, including position, scalp nerve blockage, possible discomfort, motor, and language testing. It would help to relieve the patient's anxiety and discomfort and to ensure the surgery's success [13, 14].

There are different craniotomy techniques in an awake patient, but Sleep-Awake-Sleep (SAS) is the most convenient in pediatric patients for its cognitive characteristics. Regardless of the technique chosen, the Neuroanesthesiologist or the person designated for the case must always maintain visual and verbal communication throughout the procedure. The communication at each stage should be clear, and according to the patient's age, questions and tasks should be planned to consider, explain what the sensation may be, explain the noises of the room and maintain an adequate distraction of the patient to avoid anxiety. Heavy traffic within the room should also be avoided, limit staff access, and minimize room noises that confuse the patient which may cause anxiety. (4) Cooperation will depend on the total absence of pain, leading to an outstanding surgical experience; this is based on the anesthetics offered during the procedure, including efficient regional anesthesia with scalp blockage [15].

The premedication should be personalized according to each patient's needs; short-lived anxiolytics such as midazolam is preferred. It does not affect neurocognitive functions and limits confusion or delirium during the procedure. Minimum doses (100-200mcg/kg) are beneficial for controlling anxiety in young patients with normal preoperative neurological functions. However, in the case of mapping and resection of epileptogenic lesions, any suppressive medication of epileptiform and anticonvulsant activity, including benzodiazepines and barbiturates, should be avoided [16].

Analgesia during awake craniotomy is achieved by blocking nerves in the scalp with local anesthetics. Therefore, the patient's hemodynamic and physiological state may be more stable in awake craniotomy than in general anesthesia [13].

The first phase of surgery may be performed with total intravenous anesthesia and a supraglottic device. There are current reports of possible adverse effects of general anesthetic agents, including inhaled agents and opioids, on cancer prognosis, such as increased recurrence or metastasis after surgery [14].

Anesthesiologists should provide sufficient sedation and analgesia during the initial craniotomy; a combination of remifentanil and propofol has been considered the standard protocol for sedation of the first stage of awake craniotomy due to ease of use and reliability. The state of drowsiness but with a quick response, is considered the optimal level of sedation in awake craniotomy. Schneider's model is recommended for propofol's controlled infusion into awake craniotomy to maintain patients' spontaneous ventilation [17].

Dexmedetomidine, an alpha-2 agonist, is a propofol alternative for sedation in such procedures, minimally interferes with neurophysiological monitoring, and it also has a minimal respiratory depressant effect. Concomitant dexmedetomidine with scalp blockage provides sufficient conditions for performing awake craniotomy, compared to the propofol-remifentanil combination and the increased risk of respiratory depression [13].

Complications of awake craniotomy include seizures (3–30%), respiratory depression or airway obstruction (7–16%), hypertension (17–24%), nausea and vomiting (0–9%), cerebral edema (7–14%) [18, 19]. In expert hands, the failure of awake craniotomy occurs in less than 2% of cases, regardless of the proper anesthetic technique carried out [18, 20].

Monitored anesthesia care involves keeping the patient awake under spontaneous breathing with low doses of sedative to resection the lesion by avoiding an acute transition from sleep to wakefulness, leading to hypoactive or hyperactive delirium and decrease mapping reliability [19]. The team's skill and experience are required to achieve optimal sedation, maintaining spontaneous breathing with the patient drowsy but easily reactive [21, 22].

Advantages: Lower requirements for anesthetic agents, lower opioid use, better cooperation during intraoperative testing, shorter surgery duration, and shorter hospital stay.

Disadvantages: Oversedation leading to airway obstruction with respiratory depression, carbon dioxide (CO2) retention, and consequent cerebral edema; or sub-optimal sedation that leads to the patient's likelihood of anxiety and movements [21].

The SAS technique is preferred in cases of requiring more profound sedation during the craniotomy until before the resection of the tumor, and its objectives are to provide comfort for the patient and the surgical team during the pre-awakening phase, protection of painful sensations, to avoid ventilation distress, and to dismiss postoperative memories about the awake phase throughout the surgery [19].

Advantages: Provides the opportunity to control brain edema through hyper-ventilation, to avoid intraoperative movements of the patient, to lower frequency of seizures and agitation. Used during the implementation of this technique in new hospitals or during the surgical team's learning curve [8].

Disadvantages: In high-risk patients with comorbidities, difficult airway predictors, or a high risk of bleeding; the SAS technique is controversial [21].

3.1 Anesthetic depth monitoring in awake craniotomy

Researchers compared the Patient State Index, Masimo's PSi, an electroencephalogram (EEG) parameter obtained from SedLine's brain function monitoring system® with Medtronic's Bispectral Index (BIS™) for anesthetic depth monitoring, found that PSi 1.0 was less affected by monopolar Bovie device [23].

Both can be used to monitor anesthetic depth trends in the Sleep-Awake-Sleep phase, to achieve an early and gentle awakening of total intravenous anesthesia [24]. The use of processed electroencephalography indices improves anesthetic titration in the intraoperative period. Processed EEG monitors deliver raw stroke data, numerical anesthesia/sedation depth index, and 2D spectrogram. Deep sedation is associated with poor short- and long-term outcomes in critical patients; cognitive and psychological complications, increased hospital stay and mortality [25].

The use of processed EEG systems as an objective guide to sedative dosing, may decrease medical complications of excessive sedation, such as depressed cardiac contractility and hypotension. BIS's use provides a decrease in the use of sedation, analgesia, decreased agitation, and fewer failures in extubation.

Processed electroencephalogram can help optimize drug doses in individuals with different pharmacogenomics and sedative clearance; global knowledge of the technology and processed EEG traces is required to avoid misinterpretations, significantly when muscle activity interferes with the processing algorithm [26].

Some pathological states, such as seizures or altered EEG states (Suppression of iatrogenic bursts or seizure coma), may be revealed by processed EEG and thus a complete EEG may be requested [27].

PSi values can range from 0 to 100; higher values indicate a lower degree of sedation as follows: 0–24 outbreak suppression with varying degrees of suppression, 25–49 general anesthesia, and > 50 mild sedation [23]. The algorithm uses specific frequency band performance power combined with symmetry and synchronization changes in multiple cortical regions [24]. Without a doubt, processed EEG systems are an excellent tool to optimize sedation and plan proper awakening in awake craniotomy.

4. Electrocorticography and brain stimulation for brain tumor resection in the awake pediatric patient

Neurophysiological brain cortical mapping is a valuable tool for brain tumor resection by optimizing the extent of resection and minimizing or avoiding a neurological deficit. In the context of resection of supratentorial malignancies, the gross-total resection improves survival, and by the usage of brain mapping, the functional outcome and quality of life are safeguarded in the postoperative period [28].

4.1 Principles

Stimulation can be bipolar or monopolar. In bipolar stimulation, the cathode and anode are at the level of the selected tissue. It is made using a grid of electrodes, deep electrodes, or an intraoperative manual stimulator (**Figure 1**).

The electric field produced is confined to a small area, usually half the distance between the electrodes, having a low risk of distal activation. Stimulation does not occur unless the electrodes are set directly over the tract, activating the axon's initial part and its Ranvier nodes, where the most sodium channels are contained. Bipolar stimulation in cortical mapping and the technique described by Penfield and Ojemann, are the most commonly used [29, 30].

The standard stimulation paradigm for cortical stimulation described by Penfield, is based on applying a rectangular two-phase pulse with a frequency of 50 Hz on trains lasting 3 to 5 seconds. Pulse duration remains constant at 0.3 ms, starting with an intensity of 1 mA, which increases from 1 mA waiting for a response to stimulation, to a maximum of 15 mA. When using the depth electrodes, the pulse intensity is diminished to a range of 0.5–2.5 mA. In contrast, in monopolar stimulation, a single electrode administers the stimulus, and another reference electrode, usually inserted into the temporal muscle, receives it. The stimulus field is diffuse, and the volume of brain tissue is more significant, with the possibility of activating numerous axons in the motor pathways at a distance of 20 to 25 mm from the stimulation point. It is generally used for subcortical tracks and is known as the High-Frequency Train Technique or Taniguchi Technique [31].

This technique can be used for subcortical functional monitoring in patients under the effect of general anesthesia. A five-pulse monopolar train is typically administered at frequencies between 300 and 500 Hz, with a repetitive frequency

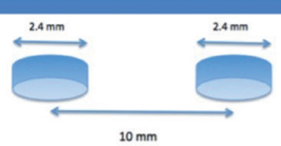
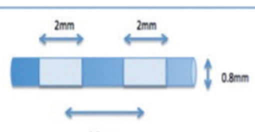
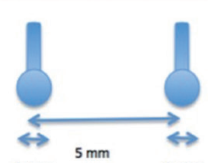
Electrode type	Geometry	Surface (mm²)	Current (mA)	Width pulse (ms)	Frequency pulse (Hz)	Train duration
Grid Ø 2.4 mm		4.5	1-15	0.3	50/60	3-10
Deep Ø 0.8 mm		5.0	0.5-2.5	1	50/60	3-5
Bipolar stimulator Ø 1.0 mm		1.6	1-10	1	%0/60	3-5

Figure 1.
Principal characteristics of electrodes for brain mapping and bipolar stimulation.

DOI: http://dx.doi.org/10.5772/intechopen.97101

of 1 to 3 Hz, including a pulse duration of 0.5 milliseconds and a range between stimuli of 2 to 4 milliseconds (**Figure 2**). This method is used to assess motor pathways and can also produce motor responses at lower intensities. It is not affected by the preoperative motor state, and the possibility of post-stimulation discharges is low.

The register is carried out through the potential evoked motor with electrodes placed in the contralateral limb muscles, such as the abductor pollicis brevis, the flexor, and forearm extender, which are usually good options for the upper extremity. In contrast, the abductor hallucis brevis is the best muscle in the case of the lower limb. For facial muscles, we have as options the orbicularis of the mouth and eyes, and the genius, which allow us to register the language articulation.

4.2 Indications

The intraoperative functional mapping in awake patients is directed to those with neoplastic or epileptogenic diseases located adjacent to the motor, visual, somatosensory, or language areas. We require patient cooperation to detect the change or deficit of their cognitive functions by stimulation during the procedure. Monitoring cortical and subcortical regions, allows us to resect brain tumors near eloquent cortical and white matter tracts, respectively, at the same surgical event. The limitation is that we have little time to perform the cognitive tasks necessary for transoperative assessment. It could represent an anesthesiological challenge because of the technical difficulty of performing a craniotomy in the awake patient and the high risk of transoperative seizures.

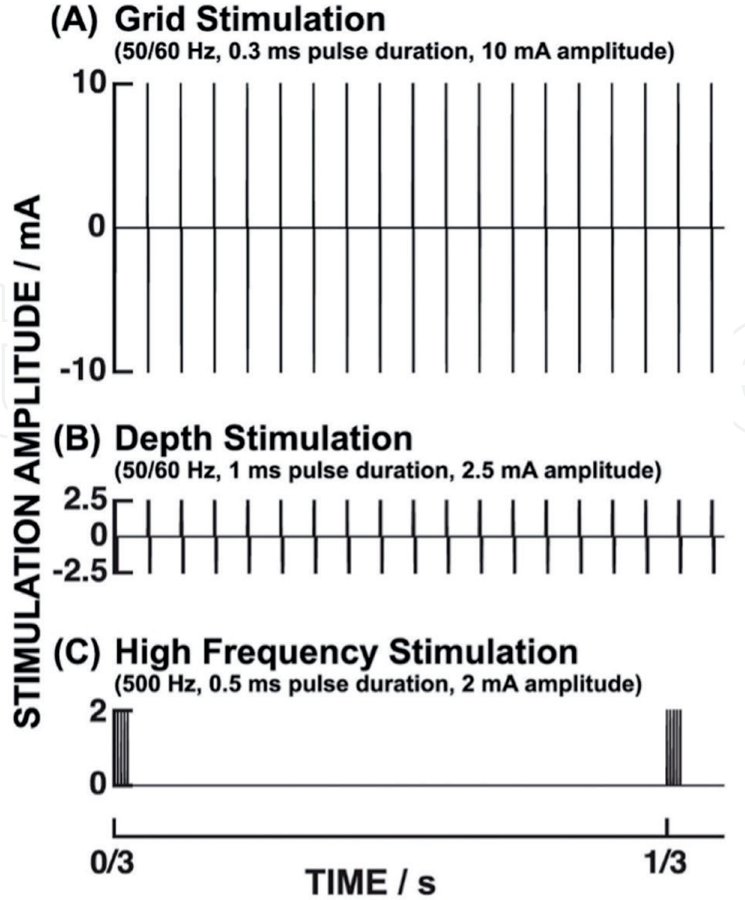


Figure 2.
Stimulation techniques.

4.3 Procedure

General Considerations. Patients are premedicated with midazolam. The surgeon performs local anesthesia with a mixture of 1:1 bupivacaine at 0.5% and lidocaine at 1%; 1:100000 epinephrine for infiltration upon placement of the Mayfield's head clamp. Sedation is performed by means of propofol (above 100 ug/kg/min) and remifentanil (0.05–2 ug/kg/min). Once the craniotomy is completed, the dura mater and the muscle are infiltrated with lidocaine, and no sedation is offered. At all times of the mapping, propofol and icy ringer solution should be ready to use to suppress post-stimulation discharges. Once the mapping is finished, sedation is carried out with dexmedetomidine (1 ug/kg/min) and remifentanil (0.05 ug/kg/min) [32].

In the case of monitoring asleep patients, the purpose of mapping is exclusively to monitor motor response, so that short-acting opioids, such as remifentanil, supplemented with propofol or dexmedetomidine, are used. Almost all agents inhaled at high doses suppress motor responses, so it is suggested to use at low doses (less than 0.25 MAC), with nitrous oxide being the least suppressive. Propofol, commonly used for mapping, can suppress the motor response between 30 and 60% at levels of 1 to 2 mg/ml, so it is suggested at 1ug/ml doses. Other agents, such as ketamine, opioids, benzodiazepines, have minimal effect on motor responses. The most commonly used scheme is a short-acting opioid with propofol or dexmedetomidine.

Other factors to consider in surgery include temperature, blood pressure, oxygen saturation, and CO_2. Hypothermia (less than 35 degrees) or hyperthermia (greater than 38 degrees) can increase the motor response latency, decrease amplitude or suppress it altogether. Hypercapnia (greater than 70 mmHg) and hypocapnia (13 to 30 mmHg) can alter mapping and promote cerebral edema.

Due to late myelinization, larger intensities of 15 mA and a longer stimulus duration of 500 ms are recommended in pediatric patients. It is suggested that the minimum age for evaluating language should be ten years old and for motor evaluation a minimum of 5 years. In case the patient does not cooperate and needs to remain under general anesthesia, the monopolar subcortical stimulation technique is recommended, where a stimulus is administered with a train of five monopolar pulses at frequencies typically between 300 and 500 Hz, with a repeat frequency of 1 to 3 Hz including a pulse duration of 0.5 milliseconds, and an interval of 2 to 4 milliseconds between stimuli.

4.4 Functional mapping

Once the craniotomy is performed and exposed to the cerebral cortex to map, the bipolar stimulation already described is carried out:

Pulse	Biphasic
Frequency	50 Hz
Pulse duration	0.2–03. ms
Stimulus duration	3–5 s
Language	5 s Negative almost 10 s
Current intensity	Increase 0.5–1 mA
Maximal current intensity	10–15 mA

Brain function	Anatomic stimulation	Clinical response
Motor	Primary motor cortex (Brodmann 4): precentral gyrus, 10 mm anterior to the central sulcus and posterior region of central sulcus.	Contralateral muscle contraction.
	Supplementary sensitive-motor area: dorsal region of the superior frontal gyrus.	Limb movements vocalization and contralateral cephalic movements.
	Silent primary motor cortex: inferior or medial frontal gyrus. Supplementary motor cortex: mesial surface of the superior frontal gyrus, paracentacral lobule and cingulum gyrus.	The negative response inhibits the motor response in the awake patient.
Sensitive	Sensitive primary cortex (Brodmann 3,1,2): poscentral gyrus.	Contralateral paresthesias o dysesthesias.
Language	Expressive language (Broca's area): posterior region of the inferior frontal gyrus in dominant hemishere. Posterior region of medial frontal gyrus, and anterior region of superior temporal gyrus in dominant hemisphere.	Negative response or language disturbances when the patient is asked to read, count numbers, or repeat sentences.
	Sensitive language (Wernicke's area): posterior temporoparietal area or temporal basal area of language (Inferior temporal gyrus, fusiform or hippocampal gyrus).	Negative response; alterations in understanding. Visual confrontation and nomination pictures.
Visual	Primary visual cortex (Brodmann 17): occipital cortex.	Contralateral phosphenes and disturbances in perception of shapes, colors, or lines.
	Secondary visual cortex (Broadmann 18) and secondary association cortex (Brodmman 19).	Visual illusions.
Hearing	Primary auditive cortex (Brodmann 22) Posterior peri-Syilvian region.	Hearing distortion. Complex listening experiences.

Table 1.
Cortical areas to stimulate during functional mapping.

The stimulus should be applied at least three times; it is considered positive when at least 2 out of three times an answer is found. Responses can be either positive (regional movements, dysesthesias, phosphenes) or negative (motor inhibition, language alteration, anomia) (**Table 1**).

Language tasks such as nomination, articulation, reading, counting, and comprehension are evaluated. It is stimulated with a pulse duration of 0.25 ms on trains from 4 to 60hz, usually used from 1.5 mA and increased to 6. The stimulation is applied from one to two seconds during the completion of the task. The point is stimulated at least three times. A positive point is considered when a 66% language error is observed, such as the absence of language, anomia, and paraphasia. Some authors [30, 33, 34] have established the 10–20 mm concept as a safe margin, i.e., the distance from the resection edge to the mapped language site, in order to determine the risk of language deficits during the postoperative period. Usually, if this distance is greater than 1, the risk of language deficit in the frontal lobe is low.

4.5 Functional mapping considerations

The limitation of the technique is associated with several factors:

a. **Patient's condition.** Previous deficit. These include a pre-existing deficit; usually the most accurate responses are obtained in patients with preserved motor and language functions. Any significant variation in sensation, motor paresis, or alterations of language or anomia, will not allow an appropriate check-in in those areas. Patient's age. Reduced myelination in pediatric patients, so motor responses are typically more challenging to activate than the standard parameters used in adults. Due to incomplete functional maturation, the motor and language areas can be identified with confidence after 5 and 10 years old, respectively. Some suggested strategies to improve motor monitoring include pulse duration as large as 500 microseconds and increasing load intensity (more than 25 mA); this has been observed in children between 5 and 7 years old, but as they grow and enter adolescence, they get thresholds similar to adulthood. One option for pediatric patients who cannot perform awake functional mapping, is to use other techniques such as primary motor cortex localization using the reserve phase technique, which indirectly allows us to locate the motor area (**Figure 3**).

b. **Effect of different types of brain injuries.** Pre-existing injuries, i.e., brain edema, hemorrhage, herniation syndromes, can increase stimulation thresholds. The restoration of local homeostasis improves the stimulation threshold. Moreover, modification in the functional expressiveness of cortical areas due to the mass effect secondary to neoplasms. In patients with cortical malformations such as dysplasia, an abnormal somatotopic organization is observed and induces several secondary mechanisms, leading to a compensatory reorganization known as neural plasticity [35].

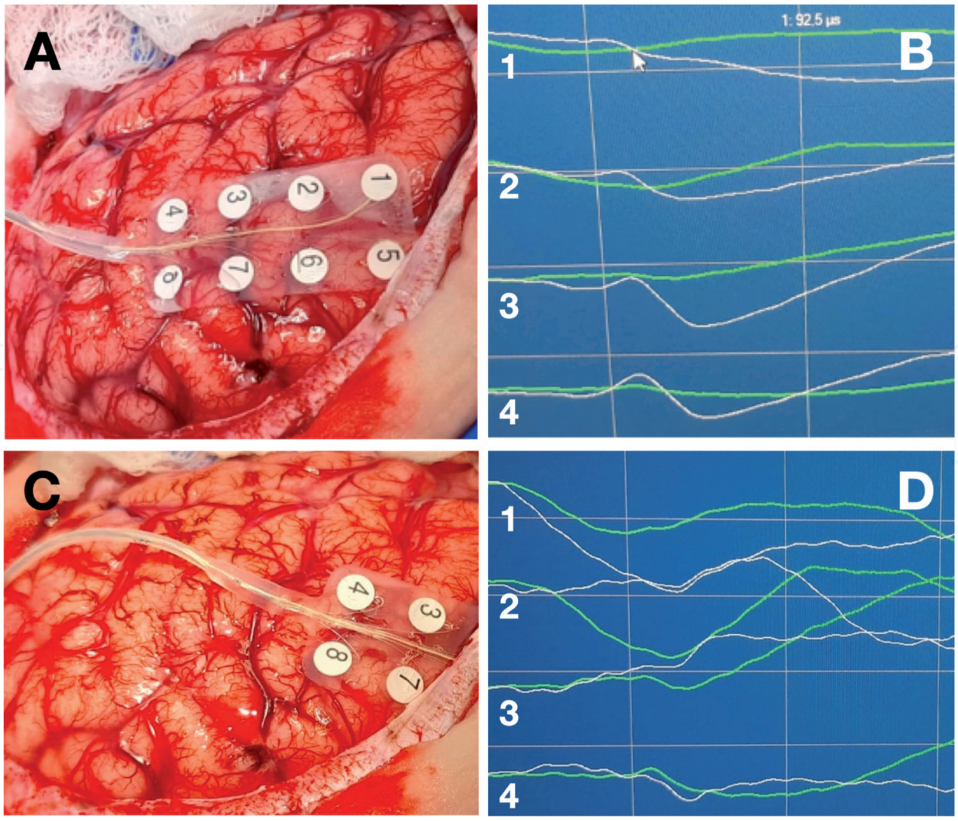


Figure 3.
Reverse-phase. An electrode grid is applied to identify the motor and somatosensory primary cortex. A) Parietal lobule exploration. B) Neurophysiological typical response for somatosensory cortex stimulation. C) Electrode-grid relocation to identify primary motor cortex. D) Reverse-phase demonstration.

4.6 Technical limitations

4.6.1 Lack of standardization

Negative mapping does not protect and creates a questionable problem concerning the reliability of the stimulation. There is a lack of consensus on stimulation paradigms and techniques. Significant variations were observed, not only in stimulation environments, but also in proven functions and protective margins preserved in resection. An example is deficit in language functions after functional mapping. In the survey, several centers where the functional mapping is practiced, only half responded that they regularly tested the four commonly checkable functions (speech production, comprehension, denomination, reading), creating the possibility of false-negative results related to unproven function. It may explain why 41% of centers reported persistent postoperative language deficiencies despite the preservation of language areas, and 56% of this group mentioned the failure to identify crucial language sites [28]. Variability in mapping thresholds has been observed not only at the population level but also in individual patients. One maneuver to facilitate the response in eloquent areas could be to increase the current at each cortical site, regardless of the adjacent post-estimate discharge threshold, instead of mapping the entire exposed cortex into a single current level. Besides, their findings highlighted the need for ECoG during electrocortical stimulation mapping, both to identify when post-stimulation discharges occur and to verify stimulation by recording stimulation artifacts [36].

4.6.2 Post-stimulation

Post-stimulation discharges can evolve into seizures during the surgical procedure, which is why the anesthesiologist should always be ready with propofol as well as the surgeon with an icy ringer solution. These stimuli thresholds are not significantly higher than those used to stimulate sensory, motor, or linguistic responses. However, post-stimulation discharges have been reported during awake craniotomy at 12% [37, 38].

4.6.3 Anesthesiologic challenge

From an anesthetic perspective, cortical functional mapping with an awake patient imposes essential demands on the anesthesiologist ability to facilitate sleep-awake-sleeping procedures and avoid inadequate or excessive sedation. Pain, emesis, and emotional intolerance to the technique are rarely observed, and, of course, seizures can occur. Failure of the functional cortical mapping technique leads to a lower macroscopic total resection incidence and increased postoperative morbidity.

4.7 Intraoperative electrocorticography

4.7.1 Objectives and limitations of intraoperative electrocorticography

Epilepsy surgery involves complete resection of the epileptogenic area (the alleged site generating epileptic seizures, removal or disconnection is necessary in order to prevent further seizures) with minimal postoperative deficits. Electrocorticography (ECoG) allows the epileptogenic zone to be delimited using flexible electrodes placed before and after resection, and to use the electrodes to stimulate and delimit the eloquent area. However, sampling is limited by reduced registration time during surgery [39].

So ECoG is not sufficient to define the epileptogenic zone; many preoperative studies are required, such as video-EEG, functional and structural MRI including PET, SPECT, and sometimes invasive recording with grid placement. The ECoG intraoperative utility as a single element for defining the epileptogenic zone in a reliable way, is based on the assumption that interictal discharges are trustworthy markers of the epileptogenic zone. This assumption has proven unreliable in many cases. One of the most significant transoperative electrocorticography limitations is that primary epileptiform discharges may not be identified from secondary ones by propagating to a distant area. More importantly, ECoG's in patients with refractory epilepsy to medical treatment has shown interictal multifocal activity, making focus identification a difficult task.

Interictal activity may be affected by anesthetic agents use, as some of those agents decrease activity while others increase them. It is said that the log is reliable when a pattern of awake interictal poly points is observed with a tip frequency exceeding one per minute. Some activation maneuvers, such as hyperventilation or some intravenous anesthetics such as methohexital, etomidate, propofol, and thiopental, have been used.

Unfortunately, the activation induced by these agents could be expanded to previously silent areas. Opioids, such as remifentanil and alfentanil, increase the activity in the epileptogenic zone. Remifentanil has been reported to suppress tips in the normal brain.

Other attempts have been made to locate the epileptogenic area using repetitive cortical electrical stimulation and evaluate its susceptibility to start a discharge and reproduce the patient's usual seizure. Although early researchers expected post-stimulation discharges originating in the epileptogenic area to have distinctive characteristics (lower post-discharge thresholds and longer durations), this is not true. The use of electrical stimulation to induce the patient's usual seizures has also shown not to be useful.

Three types of electrodes are used to register intraoperatively, often in combination:

The first type consists of silver wires insulated with a carbon ball or a distal silver ball/silver chloride located on the cortical surface. These electrodes are arranged in an electrode clamping device mounted on the skull at the edge of the craniotomy and attached to the recording device inputs. Although flexible and precise electrode placement, particularly along the resection cavities, is an excellent resource of this type of electrode; the exact distance between electrodes can be problematic, limiting the ability to engrave in a bipolar assembly. Therefore, recording in a reference montage is preferred. Also, electrode placement is limited only to the cortex areas, so it is impossible to register from the lower and medial surfaces. These electrodes can be sterilized and reused.

The second type of electrode is disposable and consists of silver stainless steel, or platinum disc electrodes embedded in silicone sheets. These blades are arranged in advance as strips containing 4 to 8 electrodes, with a separation of 10 to 15 mm, or larger grids containing 64 electrodes or more. These electrodes can be placed on the exposed cortical surface and allow the flexibility to slide under the craniotomy margins to cover the cortex uncovered surfaces. Because the distances between electrodes are standardized, it is possible to make recordings in both bipolar and referencing assemblies. However, due to the potential for cancelation of common-mode activity under two adjacent electrodes in a bipolar recording, referencing assembly remains preferred and universally accepted as being more reliable. Functional stimulation can also be performed through band and grid electrodes.

Finally, a four-contact depth electrode can also be used to be inserted into the brain's deeper structures. It is not uncommon for these various electrodes to be used simultaneously, with ball electrodes used to register over the lateral cortex or along the resection margins, while electrode strips are placed in the cortical areas. The recording electrodes can be referenced to several locations, including the mastoid, cervical, and bone flap region.

The ECoG can be registered using digital or analog instruments, although digital has become more used. As the activity recorded on the cortical surface is significantly higher than the one recorded on the skin surface, the recording parameters must be adjusted. Sensitivities between 10 and 50 mV/mm are the most commonly used. Other recommended recording parameters include a 0.5 Hz low-frequency filter and a 70 Hz high-frequency filter.

The usefulness of electrocorticography in anteromedial temporal lobectomy allows delimiting the degree of resection of the hippocampus. The most significant cause of seizure recurrence after temporal lobectomy is the incomplete resection of the affected hippocampus. Therefore, the resection of the hippocampus guided by electrocorticography has been the only procedure with a predictive value. Its usefulness has also been seen in patients with refractory epilepsy to extratemporary location medical treatment, where the need for all patients to require an invasive chronic record is controversial.

In patients with a high concordance between neuroimaging (MRI, PET, and SPECT) and the clinic of seizures, although EEG may not be conclusive in identifying the ictal area, it is indicated to perform the resection of the epileptogenic focus in a single surgical time guided by electrocorticography.

Electrocorticography is very useful in the resection of structural lesions that generate seizures, such as low-grade astrocytomas or malformations, and the surrounding epileptogenous cortex. Patients who had only the lesion resection, have a probability of being free of crisis by 50% and increasing to 87% when electrocorticography is offered.

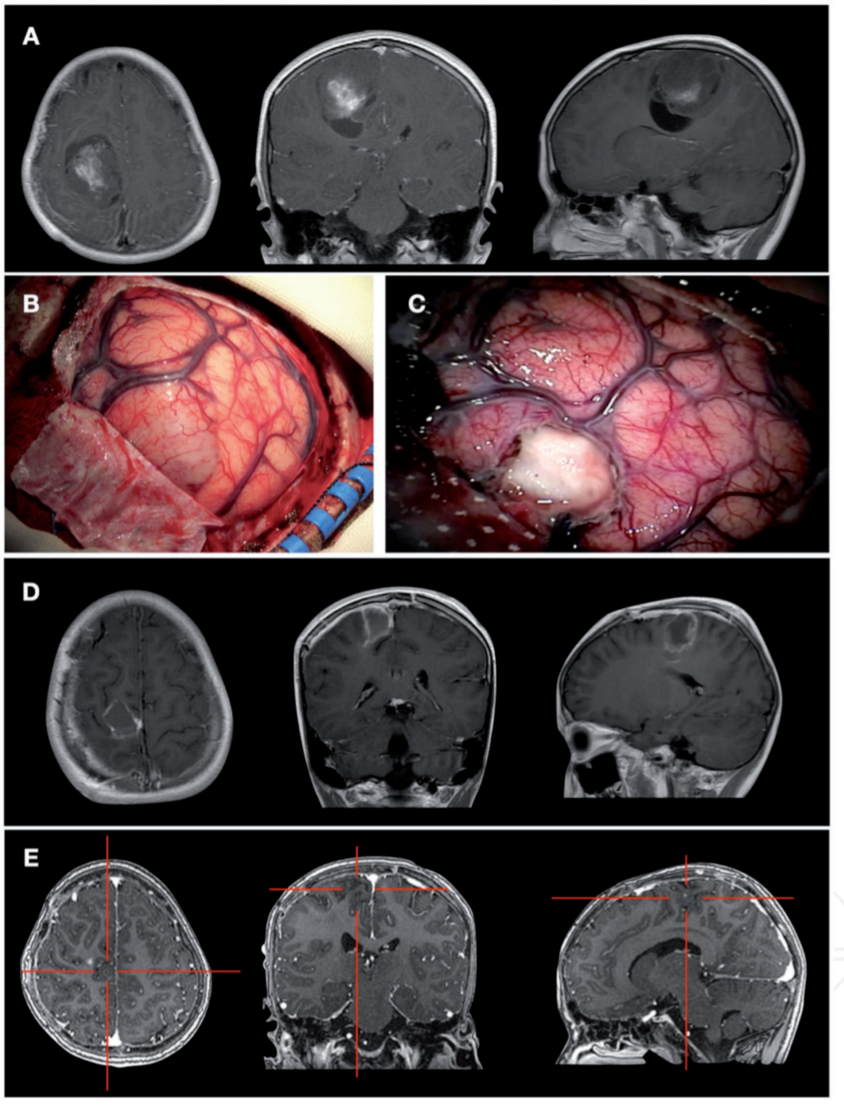
Electrocorticographography has been very useful in cortical dysplasia resection, where sometimes the image is not very clear, especially in type I cortical focal dysplasias, and where electrocorticography helps define the edges of the margins of the resection.

Finally, ECoG should be used during functional mapping to detect post-stimulus discharges that can occur over a wide threshold range (2 to 15 mA), usually lasting seconds, but some downloads last more than 90 seconds. Post-stimulus discharges have been present in 12% of patients undergoing cortical functional mapping; 65% of these discharges involve more than one electrode, and 10% become epileptic electrographic activity.

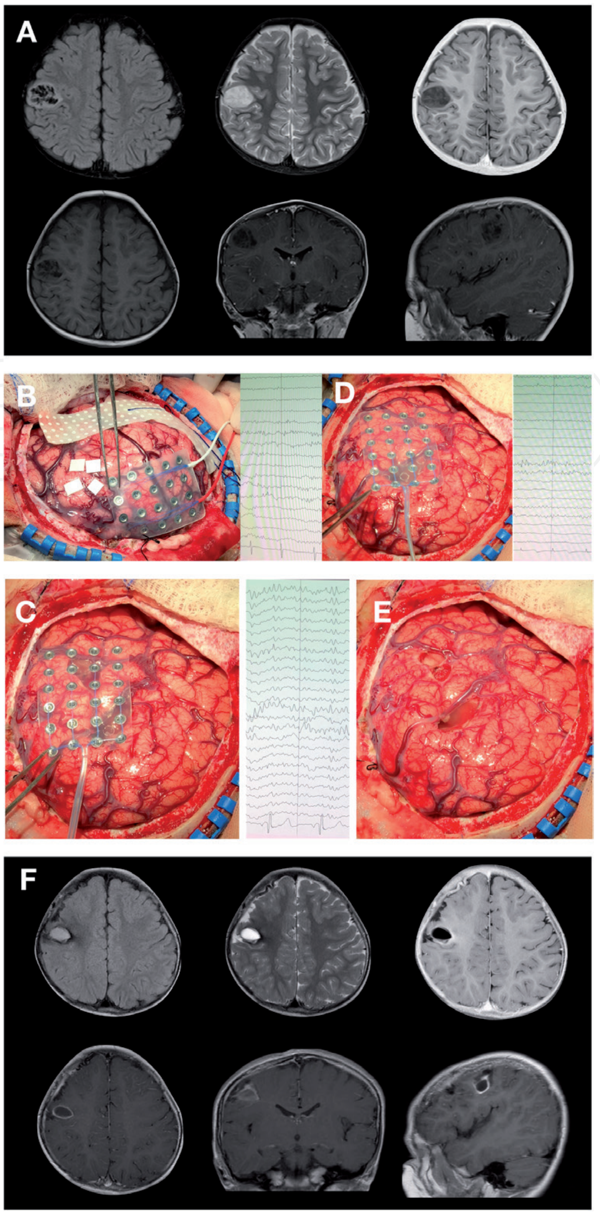
5. Clinical experience

Since 2017, we have performed awake craniotomies and brain mapping for brain tumor resection in 8 and 5 cases, respectively. The average age of patients was 12.2 years old with a range of 10–15 years old. No gender predominance was observed (Male/Female ratio 1). The neuropsychological evaluation was performed in all cases. A series of neuropsychological tests were applied to meet the maturity and neurological performance in all cases. Before considering each case as a candidate for an awake craniotomy, an assay was conducted by the neurosurgeon and the neuroanesthesiologist to gain the patient's confidence. In all cases, the technique was completed. In some cases, conversion to total-endovenous anesthesia was necessary. Intraoperative seizures were not observed during brain mapping or stimulation of eloquent areas in the neighborship of brain tumors.

In order of frequency, the most common histopathological diagnosis was diffuse glioma (n = 3), supratentorial glioblastoma multiforme (n = 2), dysembryoplastic tumor (n = 2), and Primitive Neuroectodermal Tumor (PNET) (n = 1). In all cases, gross total resection was achieved. In malignant gliomas, the overall survival was 32 months. In this group, all patients received adjuvant chemotherapy and radiotherapy. In the cases of diffuse glioma, we have not observed fatalities so far. Currently, the overall survival is 38 months. In the case of PNET, adjuvant therapy and radiotherapy with a linear accelerator were indicated. The free of disease period was 18 months, a new surgical treatment was indicated to improve survival, but in the postoperative period, the patient's family declined the second-line chemotherapy, and the patient died after 28 months— **Case 1** VIDEO.



In all cases, during follow-up, we observed a clinical improvement of neurological deficits. In the two cases of epilepsy secondary to brain tumor activity – dysembryoplastic tumor, the cortical mapping and brain stimulation in eloquent areas improved the seizure control and functional recovery in the postoperative period. In one of these cases, after the tumor's gross-total resection, a new ECoG helped us identify epileptic activity isolated from the brain tumor. Histopathological analysis revealed cortical dysplasia. After removing the epileptic foci by corticectomy, the new ECoG register showed regular electrocorticographic activity — **Case 2** Currently, the two patients with dysembryoplastic tumors are seizure-free (Engel's class Ia).



6. Conclusions

The SAS technique is a reproducible, safe, and probably the most convenient technique for awake craniotomy in pediatric patients with brain tumors. It is imperative to maintain good communication with the patient from pre-anesthetic assessment, explaining the most confident procedure. SAS will provide the most outstanding comfort before awakening and during neuropsychological and motor tests, recognizing that the neurological evaluation during and after the surgical procedure will be the best indicator of the patient's condition and success.

Cortical functional mapping allows us to delimit lesions that require resection, such as an epileptogenic zone or a tumor from eloquent regions. For this purpose, with a mature and cooperative patient, surgery may be performed with an awake patient. This technique is reserved for patients without severe neurological deficits in order to preserve the language, somatosensory, or motor functions. If the patient does not cooperate, as are pediatric patients below eight years old, the cortical functional mapping for motor functions could be performed with general anesthesia.

Electrocorticography is widely used in epilepsy and brain tumor surgery. Its usefulness has also been seen in patients undergoing temporary mesial lobectomy to determine the hippocampus degree of resection. Another utility is in resective surgery for structural lesions that cause seizures (tumors, cortical, vascular malformations), in order to delimit the surrounding epileptogenic zone and expand it.

Finally, electrocorticography must be accompanied by the mapping procedure to identify post-stimulation discharges.

7. Clinical cases

Case 1. An 8-year-old boy presented at the emergency department with a two-month history of headache, left-sided weakness (1/5), and generalized seizures. MRI study shows a premotor right brain tumor (A). An awake craniotomy was performed, and gross total resection was achieved. VIDEO. (https://bit.ly/3vXzr2S) (C). The pathology service reports a Primitive Neuroectodermic tumor. The patient receives chemotherapy (Iphosphamide - Carboplatine - Etoposide) and radiotherapy 54 Gy (Lineal-accelerator). During follow-up, a recurrence was suspected (D), and a new surgical treatment was performed (E).

Case 2. A 4-year-old female presented to the neurosurgery department with a history of symptomatic epilepsy since she was 3 years old. A few months later, autism disorder was detected. Partial motor seizures with hand-forearm-shoulder involving and secondary generalization were observed. An MRI study was performed, and a neoplastic lesion in the primary motor cortex was identified. A comprehensive case review was performed. Because of the history of autism disorder, the patient was dismissed as a candidate for awake craniotomy. However, she was considered a candidate for surgical treatment by total endovenous anesthesia. The primary motor cortex was identified with the reverse-phase technique in the operating room, and transoperative electrocorticography was performed. The gross-total resection was achieved for the brain tumor, and a subpial resection was completed after the identification of epileptic foci identified by a new ECoG. A) Preoperative MRI. B) ECoG to define the epileptic activity. C) ECoG after brain tumor resection. D) ECoG identifies epileptic activity in the rostral region of pars triangularis. E) After subpial resection of epileptic foci. F) Follow-up MRI.

Acknowledgements

We acknowledge the intense work, dedication, and commitment of Pediatry and Pediatric Specialties residents, to the great nurse's team and social workers at the Instituto Nacional de Pediatría and at the Centro Médico Naval of México.

This work is dedicated to respect and honor relatives and worldwide medical staff members who fell during the COVID-19 pandemic.

Conflict of interest

"The authors declare no conflict of interest."

Author details

Roberto Garcia-Navarrete[1,2,3]*, Javier Terrazo-Lluch[1,3], Alfonso Marhx-Bracho[1], Ericka León Alvárez[4], Natael Olvera González[5], Beatriz Alvárez-Mora[6], Rosario Aguilar Silva[7], Cointa Arroyo[7], Vianey Maceda Morales[6], Luz María Cordero[8], Daniel Magos Rodríguez[8], Sandra Luz Lizarraga-Lopez[9], Ana Niembro Zúñiga[10] and Juan Alberto Díaz Ponce Medrano[11]

1 Neurosurgery Department, Instituto Nacional de Pediatria, Mexico City, Mexico

2 Neurosurgery Department, Centro Medico Naval (Secretaria de Marina Armada de Mexico), Mexico City, Mexico

3 Neurosurgery Department, Centro Medico ABC, Mexico City, Mexico

4 Anesthesiology Department, Instituto Nacional de Pediatria, Mexico City, Mexico

5 Anesthesiology Department, Centro Medico Naval, Secretaria de Marina Armada de Mexico, Mexico City, Mexico

6 Psychology Department, Centro Medico Naval, Secretaria de Marina Armada de Mexico, Mexico City, Mexico

7 Mental Health Department, Instituto Nacional de Pediatria, Mexico City, Mexico

8 Neurophysiology Department, Instituto Nacional de Pediatria, Mexico City, Mexico

9 Intensive Care Unit, Instituto Nacional de Pediatria, Mexico City, Mexico

10 Oncology Department, Instituto Nacional de Pediatria, Mexico City, Mexico

11 Centro Medico Naval, Secretaria de Marina Armada de Mexico, Mexico City, Mexico

*Address all correspondence to: roberto.gns@gmail.com; rgarcianavarretes@pediatria.gob.mx

References

[1] Ownsworth T, Chambers S, Walker D.G., and Shum D. Neuropsychological Assessment of Individuals with Brain Tumor: Comparison of Approaches Used in the Classification of Impairment. Front Oncol. 2015; 5: 56.

[2] Rausch, R. Psychological evaluation. In: Surgical treatment of epilepsies. New York. Raven Press. 2001.

[3] Tröster A. Some Clinically Useful Information that Neuropsychology Provides Patients, Carepartners, Neurologists, and Neurosurgeons About Deep Brain Stimulation for Parkinson's Disease. Arch Clin Neuropsychol. 2017 Nov; 32(7): 810-828

[4] Kaplan, E. F., Goodglass, H., & Weintraub, S. The Boston naming test. Philadelphia: Lippincott Williams & Wilkins, 1983-2001

[5] Peña-Casanova J. Integrated neuropsychological exploration program-Barcelona test revised. Barcelona: Masson; 2005

[6] Luria, A.R. El cerebro en acción. Barcelona; Martinez Roca; 1984

[7] Everett LL, Van Rooyen IF, Warner MH, Shurtleff HA, Saneto RP, Ojemann JG. Use of dexmedetomidine in awake craniotomy in adolescents: Report of two cases. Paediatric Anaesthesia 2006; 16 (3): 338-342.

[8] Ramírez-Segura EH. Anestesia para craneotomía con el paciente despierto: Técnica dormido-despierto-dormido. Revista Mexicana de Anestesiología 2014; 37(1): 42-46.

[9] Chui J. Anestesia para craneotomía en el paciente despierto: una actualización. Revista Colombiana de Anestesiología 2015; 43: 22-28.

[10] McClain CD, Landrigan-Ossar M. Challenges in Pediatric Neuroanesthesia. Awake Craniotomy, Intraoperative Magnetic Resonance Imaging, and Interventional Neuroradiology. Anesthesiology Clinics 2014; 32(1): 83-100.

[11] Solera RI, Uña OR, Valero I, Laroche F. Awake craniotomy. Considerations in special situations. Revista Española de Anestesiología y Reanimación 2013; 60(7): 392-398.

[12] Meng L, McDonagh DL, Berger MS, Gelb AW. Anesthesia for awake craniotomy: a how-to guide for the occasional practi- tioner. Can J Anaesth 2017; 64: 517-529.

[13] Gerritsen JKW, Arends L, Klimek M, Dirven CMF, Vincent AJE. Impact of intraoperative stimulation mapping on high-grade glioma surgery outcome: a meta-analysis. Acta Neurochir (Wien) 2019; 161: 99-107.

[14] Richardson AM, McCarthy DJ, Sandhu J, Mayrand R, Guerrero C, Rosenberg C, et al. Predictors of successful discharge of pa- tients on postoperative day 1 after craniotomy for brain tumor. World Neurosurg 2019; 126: e869–e877.

[15] Delion M, Terminassian A, Lehousse T, Aubin G, Malka J, N'Guyen S, Menei P. Specificities of awake craniotomy and brain mapping in children for resection of supratentorial tumors in the language area. World Neurosurgery 2015; 84(6): 1645-1652.

[16] Zhang K, Gelb AW, Francisco FS. Awake craniotomy: indications, benefits, and techniques. Colombian Journal of Anesthesiology 2018; 46: 49-55.

[17] Soehle M, Wolf CF, Priston MJ, Neuloh G, Bien CG, Hoeft A, et al. Propofol pharmacodynamics and bispectral index during key moments of awake craniotomy. J Neurosurg Anesthesiol 2018; 30: 32-38.

[18] Spena G, Roca E, Guerrini F, Panciani PP, Stanzani L, Salmaggi A, et al. Risk factors for intraoperative stimulation-related sei- zures during awake surgery: an analysis of 109 consecutive pa- tients. J Neurooncol 2019; 145: 295-300.

[19] Eseonu CI, ReFaey K, Garcia O, et al. Awake craniotomy anesthesia: a comparison of the monitored anesthesia care and asleep-awake-asleep techniques. World Neurosurg 2017; 104:679-686.

[20] Flexman AM, Wang T, Meng L. Neuroanesthesia and outcomes: evidence, opinions, and speculations on clinically relevant topics. Curr Opin Anaesthesiol. 2019 Oct;32(5):539-545.

[21] Kulikov A, Lubnin A. Anesthesia for awake craniotomy. Current Opinion in Anaesthesiology 2018; 31(5): 506-510.

[22] Sewell D, Smith M. Awake craniotomy: Anesthetic considerations based on outcome evidence. Current Opinion in Anaesthesiology 2019; 32(5): 546-552.

[23] Bloom, J., Wyler, D., Torjman, M. C., Trinh, T., Li, L., Mehta, A., ... Romo, V. (2020). High Incidence of Burst Suppression during Propofol Sedation for Outpatient Colonoscopy: Lessons Learned from Neuromonitoring. Anesthesiology Research and Practice, 2020, 1-6.

[24] Castellanos Peñaranda, C., Casas Arroyave, F. D., Gómez, F. J., Pinzón Corredor, P. A., Fernández, J. M., Velez Botero, M., ... Marulanda Toro, C. (2020). Technical and clinical evaluation of a closed loop TIVA system with SEDLineTM spectral density monitoring: Multicentric prospective cohort study. Perioperative Medicine, 9(1). doi:10.1186/s13741-019-0130-2

[25] Wang ZH, Chen H, Yang YL, et al. Bispectral index can reliably detect deep sedation in mechanically ventilated patients: a prospective multicenter validation study. Anesth Analg. 2017;125:176-183

[26] Wang ZH, Chen H, Yang YL, et al. Bispectral index can reliably detect deep sedation in mechanically ventilated patients: a prospective multicenter validation study. Anesth Analg. 2017; 125:176-183.

[27] Devlin JW, Skrobik Y, Gélinas C, et al. Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU. Crit Care Med. 2018;46:e825–e827

[28] Ritaccio AL, Brunner P, Schalk G. Electrical stimulation maping of the brain: Basic Pinciples and emergin alternatives J Clin Neurophysiol, 2018 Marzo (2): 86-97.

[29] Penfield W, Boldrey E. Somatic Motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. Brain 1937; 60:389-443

[30] Ojemann G, Ojemann J, Lettich E, Berger M. Cortical language localization in left, dominant hemnisphere. An Electrical stimulation mapping investigation in 117 patiens. J Neurosurg 1989;71:316-326

[31] Taniguchi M, Cedzich C, Schramm J. Modification of cortical stimulation for motor evoked potentials under general anestesia: technical description. N ueursurgey, 1993, 91 379-385

[32] Wang DD, Rolston JD Berger M. Cortical stimulation and Mapping. Cataltepe O, Jallo GI. Pediatric Epilepsy Surgery. Thieme 2ª ed 2020, 277-283

[33] Haglund MM, Berger MS, Shamseldin M, Lettich E, Ojemann GA. Cortical localization of temporal lobe

language sites in patients with gliomas. Neurosurgery. 1994; 34:567-576. discussion 576.

[34] Berger MS, Kincaid J, Ojemann GA, Lettich E. Brain mapping techniques to maximize resection, safety, and seizure control in children with brain tumors. Neurosurgery. 1989; 25:786-792.

[35] Tuxhorn I, Extra- and Intraoperative electrocortical stimulation. Cataltepe O, Jallo GI. Pediatric Epilepsy Surgery. Thieme 2ª ed 2020,134-142

[36] Galletine WB, Mikati MA Intraoperative Electrocorticography and cortical stimulation in children. Journal of Clinical Neurophysiology 2009;26(2): 95-108

[37] Bank AM, Schevonb CA, Hamberger MJ. Characteristics and clinical impact of stimulation-evoked seizures during extraoperative cortical mapping. Epilepsy & Behavior. 2014; 34:6-8

[38] Nossek E, Matot I, Shahar T. Barzilia O, Rapopolrt Y, Gonene T, et al. Intraoperative seizures during awake craniotomy: incidence and consequiences: analisys of 4677 patients. Neurosurgery 2013; 73 135-140

[39] Pouratian N, Cannestra AF, Bookheimer SY, et al. Variability of intraoperative electrocortical stimulation mapping parameters across and within individuals. J Neurosurg. 2004;101: 458-466.