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Department of Neurology and Neurosurgery, Universidade Federal de São Paulo, São Paulo- SP, Brazil *Introduction:* Surgery involving the brainstem is one of the most demanding procedures due to the abundance of neural structures and significantly increases the risk of postoperative neurologic deficits. Intraoperative Neurophysiological Monitoring has emerged as a tool, offering instantaneous feedback on the functional status of the neural structures located in the posterior fossa.

Material and methods: An extensive review of the literature relating to Intraoperative Neurophysiological Monitoring in Posterior Fossa Surgeries was performed. Mapping and monitoring techniques were detailed.

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Available at: http://www.archpedneurosurg.com.br/ *Conclusion:* The use of intraoperative neurophysiological monitoring has made the procedure safer, even with a distorted anatomy, allowing for greater resection and less chance of deficits.

Keywords: intraoperative monitoring, brainstem mapping, cranial nerves, brainstem surgery, evoked potential

INTRODUCTION

The surgical treatment of posterior fossa pathologies, especially brainstem tumors, is one of the most challenging procedures in neurosurgery. A high concentration of critical neural structures, including sensory and motor pathways, cranial nerve nuclei, and neuronal networks essential for the maintenance and control of vital functions increases surgical morbidity compared with other areas of the central nervous system [1].

Posterior fossa tumors are more prevalent in the pediatric population and in the past, pathologies in this region were called "no man's land" because of the high risk of postoperative neurological deficits [2]. Surgery was restricted to biopsy for a long time, but the surgical approach began to change when the functional anatomy of the brainstem was defined, and anatomical landmarks aimed to guide safe entry routes [3,4,5]. However, anatomy displaced and distorted by the tumor frequently makes it difficult to recognize these anatomical landmarks even under microscopic observation.

Advances in neuroimaging techniques [6,7], neuroanesthesia, and postoperative intensive care, associated with the development of intraoperative neurophysiological monitoring techniques, have provided surgeons with greater safety in posterior fossa surgeries. This increases the degree of lesions resection, maintains quality of life with little or no morbidity, and often modifies the prognosis of the disease [8].

Over the last 20 years, intraoperative neurophysiological monitoring has been established as a functional tool of great value in posterior fossa surgery [9]. It allows functional mapping of safe input zones in the brainstem and provides real-time information about the functional integrity of the neural pathways located in the posterior fossa. Most neurophysiological changes, when present, are gradual and progressive, if identified early, the surgical strategy can be changed on time to prevent injury and avoid or decrease postoperative neurologic deficits.

The aim of intraoperative neurophysiological monitoring is, to avoid surgery-induced neurological deficits and, predict functional outcomes.

MATERIALS AND METHODS

An extensive review of the literature relating to Intraoperative Neurophysiological Monitoring in Posterior Fossa Surgeries was performed with no date limit. MEDLINE database was accessed using PubMed Central at the U.S. National Institutes of Health's National Library of Medicine (NIH/NLM),(http://www.ncbi.nlm.nih.gov/pubmed/). The search was done with the following keywords and their



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Figure 1 - Multimodal neurophysiologic monitoring used in a brainstem tumor surgery.

associations: Neurophysiological monitoring; Intraoperative monitoring; Intraoperative neurophysiology monitoring; Intraoperative neuromonitoring; Intraoperative mapping; Evoked potential; Rhomboid fossa; Posterior fossa; Skull base surgery; Brain stem mapping; Safe entry zone; Surgical safe entry zone. A total of 34 articles were available for analysis.

RESULTS AND DISCUSSION

Mapping and monitoring

Intraoperative neurophysiological monitoring can be divided into two distinct functions: mapping and monitoring, both of which are essential for posterior fossa surgery.

Mapping techniques involve the identification of specific neural structures within the surgical field but are performed intermittently and do not provide information on functional status during two consecutive mappings. Mapping techniques used in posterior fossa surgery include brainstem mapping and triggered electromyography.

Monitoring techniques continuously analyze neural signals, testing them as frequently as possible, and providing a continuous and online assessment of the function of long pathways in the brainstem. Monitoring techniques used to assess the integrity of long pathways include motor-evoked, corticobulbar motor-evoked, somatosensory-evoked, and auditory brainstem-evoked potentials. The benefit of monitoring distinct long pathways is that they are in different locations in the brainstem. For example, corticospinal tract fibers are positioned in the most anterior region of the brainstem, whereas sensory (medial lemniscus) and auditory (lateral lemniscus) fibers have a more dorsal position in the brainstem. Free EMG is another monitoring technique used to assess irritation caused by mechanical manipulation of motor cranial nerves (Fig.1).

Mapping techniques

1. Trigged electromyography (T EMG)

T EMG is used to exclude the possibility that nerve fibers are involved in the lesion. It can also be used to verify a neural structure in the surgical field, whenever the anatomy is not sufficient for this. It can be performed with monopolar or concentric bipolar probes. The advantage of the bipolar stimulator is a limited spread of current, performing a more selective stimulation, and a lower risk of activating neighboring structures. The advantage of the monopolar stimulator is that the radial spread of current allows easier localization of nerve structures. Stimulation parameters are similar for both types of probes and typically use a rectangular pulse of 0.2ms duration, frequency of 1 to 3Hz, and intensity between 0.2 to 5mA where intensities above 2mA are used to obtain responses within the tumor tissue.

The recording is performed with needle electrodes positioned on the muscles innervated by the respective cranial nerves: inferior rectus (III), superior oblique (IV), masseter (V), lateral rectus (VI), orbicularis oculi (VII), orbicularis oris (VII), mentonian (VII), posterior pharyngeal wall (IX/X), vocal cord (X), trapezius (XI) and intrinsic muscle of the tongue (XII).

2. Brainstem mapping

When the surgeon approaches a lesion that protrudes into the brainstem surface, whether vascular or tumor, the lesion itself provides the route of entry into the brainstem. However, when lesions are intrinsic to the brainstem functionally safe regions must be identified. Anatomical landmarks are used but may not be visualized because of the mass effect of the lesions [10].

Brainstem mapping is a neurophysiological mapping technique used to localize cranial motor nuclei on the





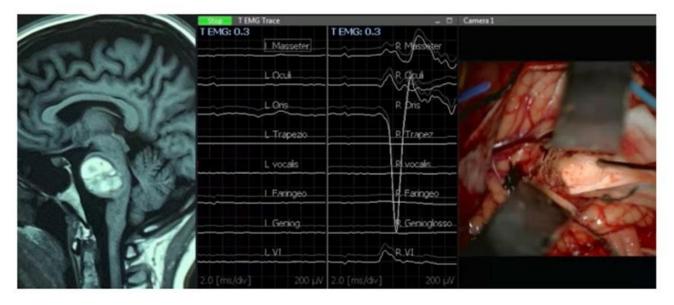


Figure 2 - Pre-operative MRI and neurophysiological mapping of the floor of the fourth ventricle

brainstem surface. Expansive lesions can displace the cranial nerve nuclei from their original positions, and these displacements often follow characteristic patterns [11]. In this case, direct stimulation of the brainstem surface is used to determine the safe entry zones.

When surgical access of a mesencephalic lesion occurs from the anterolateral region, it is important to avoid injury to the spinal cortical tract [12, 13]. The lateral mesencephalic vein can help with anatomical localization because the tract lies anteromedial to it. However, when the anatomy is distorted, tract identification is performed by intraoperative neurophysiological mapping. The anterolateral face of the midbrain is stimulated with a monopolar probe using trains of four to five stimuli, with a 0.5ms duration, and intensities from 0.5 to 2mA. When the motor response is recorded in one or more muscles in the contralateral limb, the probe is shifted in small increments of 1mm to determine the lowest response threshold and to better determine the functional location of the spinal cortical tract.

In the rhomboid fossa, at the level of the pons, the facial colliculus is an important intraoperative anatomical landmark. Damage to this area invariably causes paralysis of the facial and abducens nerves, in addition to conjugate gaze disturbances caused by dysfunction of the parapontine reticular formation. Mapping of the facial colliculus allows the determination of safe entry zones to the brainstem by identifying the supra- and infrafacial triangles. The stimulation parameters are similar to those used for motor cranial nerve stimulation.

In the medulla region, the hypoglossal and vagus triangles are mapped between the obex and the striae

medullaris. Some bulbar tumors may displace the IX, X and XII nuclei ventrally and these nuclei can often be localized only during lesion resection. The stimulus parameters are similar to those used in the pons and stimuli above 2mA are avoided because of cardiovascular changes.

Brainstem mapping is a very useful and valuable mapping technique. However, it is performed intermittently and is not a method for continuously monitoring cranial motor nerve integrity. Any damage that may occur during tumor resection should be continuously monitored using nuclear cortical motor-evoked potentials. Furthermore, the sensory parts of the motor cranial nerves and brainstem reflexes cannot be assessed using brainstem mapping (Fig.2).

Monitoring techniques

1. Brainstem auditory evoked potential (BAEP)

Short latency auditory evoked potentials, also called brainstem auditory evoked potentials (BAEP), are commonly used to monitor auditory pathways and provide information about the brainstem. These are the electrical responses recorded on the scalp following a click-type acoustic stimulus. The response is composed of five waves, named in roman numerals, and anatomically correlates with the auditory pathway and brainstem. They appear in less than 10ms and are resistant to anesthetic changes. The interpretation and alarm criteria are based on changes in the latency and amplitude of waves I, III, and V. and a 50% reduction in amplitude and/or 1ms prolongation in the absolute value of wave V or intervals I- III, III-V, and I-V are used [14].





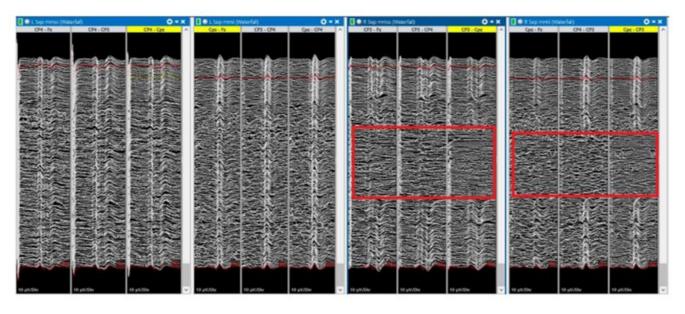


Figure 3 - The red box indicates the transient disappearance of the median and tibial SSEPs on the right side.

While approach intrinsic brainstem lesions, analysis of the BAEP wave decay pattern suggests the location of the affected area. The disappearance of wave I and consequently of the other components indicates cochlear ischemia secondary to the involvement of the internal auditory artery. If involvement occurs in the region of the cerebellar angle point, wave I is preserved, and changes occur in other components of the potential. Damage to the lower pons causes alterations in the I-III interval and damage to the midbrain region alters waves IV and V. An acute change suggests a wascular mechanism, whereas a gradual change suggests a mechanical cause [15].

Surgical maneuvers that may affect BAEP during posterior fossa surgery include compression or traction directly on the auditory nerve, thermal injury from electrical coagulation near the nerve, and vascular injury to the internal auditory artery or perforating branches of the brainstem. The auditory pathway crosses the midline at various levels. These decussations and commissures occur between the cochlear nuclei and the inferior colliculus: thus, waves III, IV, and V generally represent bilateral auditory pathways, as they are obtained by ipsilateral and contralateral acoustic stimuli. This indicates that significant morbidity can occur in the absence of BAEP changes; therefore, BAEP is more important in showing significant auditory nerve changes.

Alterations in physiological parameters, such as hypothermia, may prolong the latency of BAEP. Irrigation of the surgical field with ice-cold saline may slow nerve conduction, prolong BAEP, and lead to false positives, which may lead to misinterpretation.

2. Somatosensory evoked potential (SSEP)

The somatosensory evoked potential is obtained by stimulating a peripheral sensory nerve, most commonly the median nerves in the upper limbs and the tibial nerves in the lower limbs and recording responses along the pathway in the dorsal column, medial lemniscus and especially the thalamocortical projections to the primary sensory cortex contralateral to the stimulation. Because it is a smallamplitude response, signal averaging is required to separate it from the EEG signals and noise. This prolongs the acquisition time and delays the feedback to the surgeon.

In general, a 50% reduction in the response amplitude and/or a 10% prolongation in latency is considered an alarm signal [16,17] (Fig.3).

For midbrain and pons surgeries, SSEP has little localization value in providing information about the functional integrity of the brainstem. In these cases, the SSEP of the upper limbs is sufficient. In cervicomedullary tumor surgeries, selective injuries of the upper and lower limb pathways can occur. In these cases, both upper and lower limb SSEPs should be performed together.

3. Motor evoked potential (MEP)

The MEP used in brainstem surgeries is similar to those used in supratentorial surgeries. The stimulus is applied with electrodes, preferably of the corkscrew type, positioned on the scalp over the motor areas according to 10-20 International System. Special care should be taken when positioning these electrodes in children with open fontanels and in patients with catheter and valve systems. Muscle





responses are recorded with needle electrodes positioned on the muscles of the upper and lower limbs. In posterior fossa surgeries, especially in the midbrain and pons, corticospinal fibers are concentrated in the ventral region, in a very small area, and selective injury is unlikely; therefore, monitoring only one upper muscle and one lower muscle is adequate.

The presence of MEP indicates that the functional integrity of the spinal cortical tract is preserved. A significant reduction in MEP amplitude, in the range of 50-80%, indicates of corticospinal tract impairment. Although only the disappearance of muscular MEP is strongly correlated with postoperative permanent paresis, a persistent decrease in amplitude may be correlated with a transient moderate deficit or, more rarely, with a mild permanent deficit [18,19].

MEPs are very sensitive to anesthetic effects, and careful protection of the tongue, lips, and endotracheal tube by positioning a bite block is important to avoid injuries caused by muscle contraction.

4. Corticobulbar motor evoked potential (CbMEP)

As the name implies, CbMEP has the potential to assess the integrity of a group of fibers that leaves the corticospinal tract at the midbrain level to reach each motor cranial nerve nucleus bilaterally [20]. Stimulation is hemispheric, and care should be taken because of the possibility of direct peripheral nerve activation by the stimulus. CbMEP is recorded with the same electrodes used to perform free and triggered EMG corresponding to the cranial nerves.

Most studies on the reliability of corticobulbar MEP in predicting postoperative deficits have been performed in adults for facial nerve assessment. The disappearance of a corticobulbar MEP during surgery is usually indicative of significant and long-lasting deficits. Transient loss and/or a permanent drop in amplitude is less of a concern but may still indicate some degree of worsening. A > 50% reduction in amplitude correlates with postoperative nerve dysfunction. Good functional outcomes are usually expected when these potentials remain stable throughout the surgery [21, 22, 23]. The presence of corticobulbar MEP in the IX/X and XII nerves at the end of surgery does not protect the functional integrity of complex circuits such as the swallowing and cough reflexes as CbMEP does not evaluate sensory pathways [24,25].

5. Free EMG

This technique is based on the observation of the spontaneous activity caused by mechanical irritation of the motor cranial nerves. This is called neurotonic discharge and is recorded with the same needle electrodes used for recording of triggered EMG and CbMep.

The appearance of high-frequency, homogeneous, sinusoidal neurotonic discharges during nerve manipulation suggests probable nerve injury and the manipulation should be stopped [26,27]. The absence of discharge may suggest the functional integrity of the nerve or may be due to electrical silencing caused by the acute section of the nerve that is not detected by free EMG.

Anesthesia, sitting position, and alarms

The same precautions used for anesthesia in supratentorial surgeries should be used for posterior fossa surgeries. Muscle relaxants should only be used during anesthesia induction. Total intravenous anesthesia with a constant infusion of propofol and opioids, preferably remifentanil, should be used [28,29]. Anesthesiologists should avoid bolus and be aware of blood pressure instability and bradycardia during brainstem manipulation.

Surgeries in the sitting position may cause changes in sensory and motor evoked potentials that are not related to neurological impairment. These changes are caused by the insulating effect of the subdural air collection [30,31].

What to do when intraoperative neurophysiological monitoring changes occur? The acronym TIP represents time, irrigation, and papaverine/pressure. The first action is to stop surgical manipulation and wait for signs of recovery. Irrigation of the surgical field with warm saline accelerates potential recovery. If arterial spasm is suspected, papaverine should be instilled locally to improve local perfusion; if hypotension is present, it should be corrected to prevent incipient ischemia.

Recently, techniques for the intraoperative evaluation of brainstem reflex pathways such as the blink reflex [32], laryngeal adductor reflex [33], and trigeminal hypoglossal reflex [34] have been described, which allow the evaluation of sensory afferent pathways. This will increase the safety of brainstem surgeries.

CONCLUSION

The primary goal of monitoring during neurosurgery is to prevent neurological deficits. The combination of the modalities described above allows real-time detection of alterations. When changes occur, they can often be reversed or minimized if corrective measures are taken promptly. Effective communication between neurophysiologists and surgeons is essential for successful intraoperative neurophysiological monitoring.

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DISCLOSURES

Ethical approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval is not appliable

Conflict of interest

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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CONTRIBUTIONS

-**Denise Pinheiro**: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing

-**Sergio Cavalheiro**: Conceptualization, Formal Analysis, Methodology, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing

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