Chapter 5
Intraoperative Neurophysiological Monitoring During Brainstem Surgery

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Abbreviations

APB	Abductor pollicis brevis
BAEPs	Brainstem auditory evoked potentials
CMAP	Compound muscle action potential
CSF	Cerebrospinal fluid
CSTs	Corticospinal tracts
DTI	Diffusor tensor imaging
EMG	Electromyography
ION	Intraoperative neurophysiology
MEPs	Motor evoked potentials
mMEP	Muscle motor evoked potential
SSEPs	Somatosensory evoked potentials
TA	Tibialis anterior
TES	Transcranial electrical stimulation

5.1 Introduction

Brainstem surgery is still considered among the most challenging neurosurgical procedures due to the significant risk of neurological morbidity. The high concentration of essential neural structures such as cranial nerve nuclei, sensorimotor and auditory pathways, as well as the reticular formation makes the brainstem a real minefield. Therefore, even a small injury to the brainstem can hinder the functional integrity of one or more of these neural pathways and result in neurological deficits. In fact, brainstem surgical morbidity is significantly higher than that of other areas of the central nervous system due to the lack of structural redundancy and plasticity.

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Aggressive surgical treatment of tumors in the medulla oblongata increases the risk of compromising the respiratory function and threatens the patient's ability to swallow or protect the airways; this may ultimately result in the need for gastrostomy and tracheostomy. An overall risk of 15% of permanent lower cranial nerve injury has been reported in children who underwent surgery for medullary tumors [1]. Rostrally, surgery in the pons and midbrain can result in diplopia – due to internuclear ophthalmoplegia – as well as sixth and seventh nerve palsy [2–4].

During the 90s, a number of authors discussed the functional anatomy of the brainstem, particularly with regards to the floor of the fourth ventricle, as most of the surgical approaches were through this posterior route. If the tumor is exophyting outside the brainstem surface, its removal begins at such outgrowth. In these cases, the tumor itself creates the entry path into the brainstem. However, when the tumor is truly intrinsic, i.e., lacking a surface component, a deep knowledge of the underlying local functional anatomy is required.

On the basis of a detailed map of the most dangerous surgical approaches to the brainstem, some relatively safe entry zones – mainly to the posterior brainstem – have been identified based on anatomical landmarks [5–7]. However, these landmarks turned out to often be unreliable due to the distortion of normal anatomy secondary to the tumor mass effect. For example, when approaching pontine tumors, the facial colliculus and/or striae medullaris were rarely recognizable at the beginning of the surgery and could not assist the surgeon in selecting the best entry zone [8].

Injury to brainstem neural structures can occur either during the attempt to approach an intrinsic lesion by selecting the wrong entry zone and/or during the removal of the lesion due to excessive manipulation of the brainstem, including traction, misplacement of retractors, and inadvertent coagulation of perforating vessels.

Intraoperative neurophysiology (ION) has emerged over the past two decades as a discipline aimed not merely to predict but also to prevent neurological injury, thanks to the tailored intraoperative use of standard clinical neurophysiological techniques such as electromyography (EMG), and somatosensory (SSEPs), brainstem auditory (BAEPs) and motor evoked potentials (MEPs). Monitoring these potentials allows to prevent an injury to the long pathways within the brainstem. In addition, the so-called mapping techniques provide a functional identification of critical anatomical landmarks – such as the facial colliculus, the cerebral peduncle or the lower motor cranial nerve nuclei – to avoid an injury to these structures when selecting the safest entry route to the brainstem [8–10] (Figs. 5.1 and 5.2).

Since the mid-90s, a number of ION monitoring and mapping techniques have been developed to assist neurosurgeons during brainstem surgery. Some of these techniques are nowadays considered standard and have well passed the test of time. Others are less popular and/or are considered less reliable because of the risk of false positive and false negative results.

In this chapter we will critically review, for each anatomical location – midbrain, pons, and medulla oblongata, the various ION mapping and monitoring techniques that can be used during surgery for brainstem lesions.

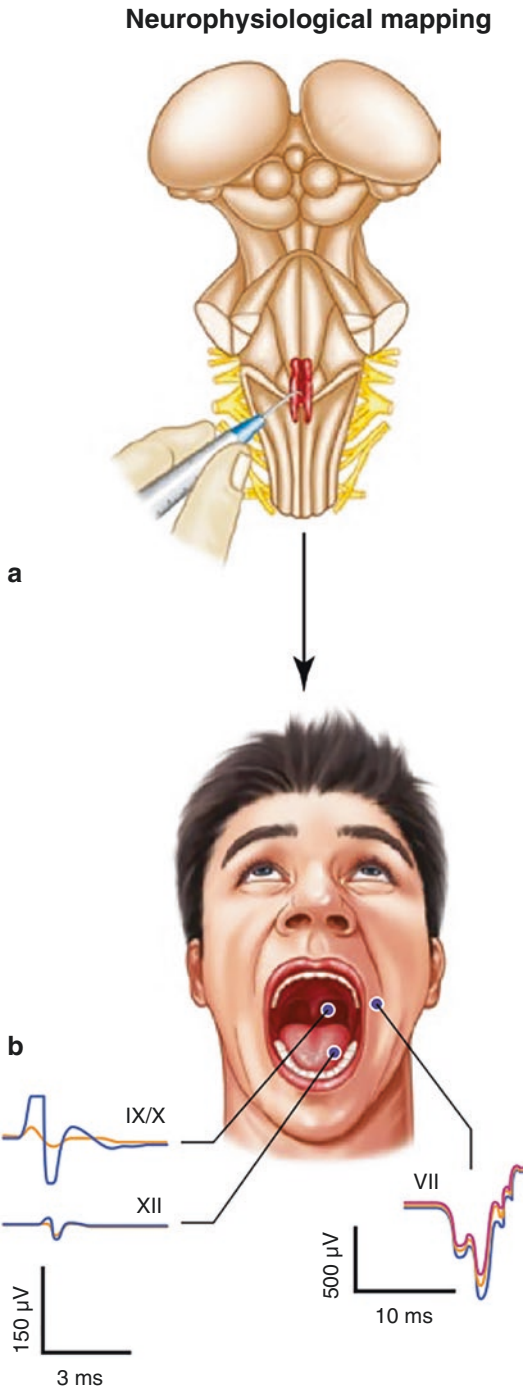

Fig. 5.1 Schematic classification of intraoperative neurophysiology mapping techniques in the posterior fossa. These techniques allow for the identification of functional landmarks such as the nuclei of motor cranial nerves on the floor of the fourth ventricle. (**a**) A handheld monopolar (or bipolar concentric) probe is used to electrically stimulate the rhomboid fossa. (**b**) Compound muscle action potentials (CMAPs) are recorded from the muscles innervated by motor cranial nerves (see text for details). VII: CMAP recorded from the orbicularis oris for the facial nerve. IX/X: CMAP recorded from the posterior wall of the pharynx for the glossopharyngeal/vagus complex. XII: CMAP recorded from the tongue muscles for the hypoglossal nerve. (Reprinted with permission from Sala et al. [56])

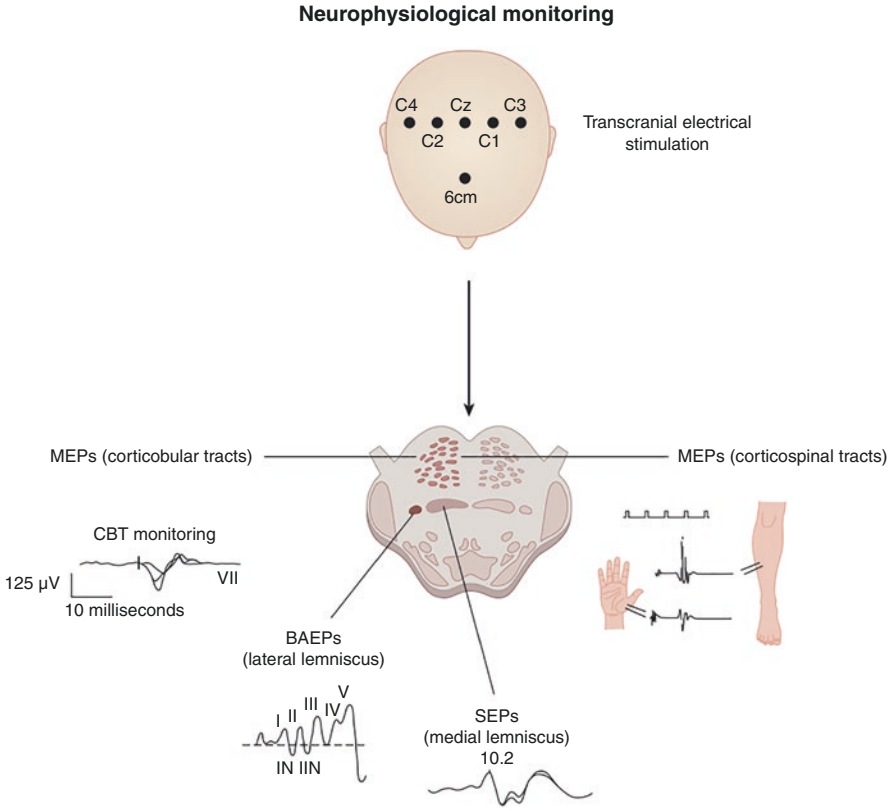

Fig. 5.2 Schematic classification of neurophysiological monitoring techniques. These allow to monitor the functional integrity of neural pathways (motor, sensory, auditory) within the brainstem on-line, throughout the surgery. See the text for further details on each monitoring technique. Abbreviations: MEPs, motor evoked potentials; SEPs, somatosensory evoked potentials; BAERs, brainstem auditory evoked responses; CBT, corticobulbar tract. (Modified with permission from Sala et al. [56])

5.2 Surgery of the Midbrain

5.2.1 Mapping

5.2.1.1 Identification of the Oculomotor Nerve Nuclei at the Level of the Tectal Plate

The midbrain occupies the notch of the tentorium and consists of a dorsal part (i.e., tectal plate), a large ventral portion (i.e., tegmentum), and the cerebral peduncles. Dorsal approaches, through either the supracerebellar infratentorial route or the occipital transtentorial route, can be used to approach intrinsic midbrain lesions.

Avoiding injury to the oculomotor nerve nuclei and their intramedullary tracts is important to avoid oculomotor deficits, such as Parinaud syndrome, which can compromise the quality of life of the patients. Midbrain tumors are quite common in the pediatric age group; while most of these lesions may have an indolent course with little tendency to grow and no surgical indication, surgery is indicated for growing lesions.

Direct neurophysiological mapping of the tectal plate can be used to identify safe entry zones to approach intrinsic midbrain lesions. Vice versa, the need for intraoperative mapping of peripheral oculomotor nerves is anecdotal in brainstem surgery, but it may be used for tumors involving the cisternal, cavernous or intraorbital segment of these nerves.

For direct identification of the peripheral cranial nerves III, IV, and VI, either a handheld monopolar probe or a bipolar concentric probe can be used. Rectangular pulses of 0.2 ms duration at 1–3 Hz and intensity up to 0.5–3 mA can be used. In general, the advantage of using a bipolar concentric probe is the higher focality of the stimulation and limited spreading of the current. For direct stimulation of the brainstem, the current is usually kept very low, starting at 0.05 mA and not exceeding 1–1.5 mA.

Recordings are obtained by placing tiny wire Teflon-coated electrodes in muscles innervated by the respective cranial nerves. Typically, responses are recorded from the external (lateral) rectus for cranial nerve VI, superior rectus for cranial nerve III, and superior oblique for cranial nerve IV. When placing the recording electrodes in extrinsic ocular muscles, care should be taken to avoid misplacement of the electrodes, which may cause an injury to the ocular bulb.

Muscle responses from extraocular muscles are usually of low amplitude because the muscle units have a small number of fibers innervated by a single axon. The latency of the response depends on the point of stimulation along the peripheral nerve or within the midbrain, ranging anywhere between 2 and 5 ms [11, 12].

We have repeatedly attempted direct identification of the superior colliculi through brain mapping. However, this has been mostly unsuccessful. One of the reasons could be related to the fact that the superficial layers of the colliculus connect to the visual system by projection to the thalamus and the lateral geniculate nuclei. Additionally, the nuclei of the oculomotor nerves are embedded in the periaqueductal grey matter, too deep to be activated by superficial stimulation (Fig. 5.3). Although reports on direct stimulation of the colliculi are anecdotal [12–14], similar limitations have been reported by Ishihara et al., who found that direct mapping is of little help to decide on the site of the incision [14].

5.2.1.2 Identification of the Corticospinal Tract at the Level of the Cerebral Peduncle

When dealing with lesions close to the cerebral peduncle or the ventral part of the medulla, injury to the corticospinal tracts (CSTs) is of concern. Mapping of the CST at the level of the cerebral peduncle is valuable to prevent injury.

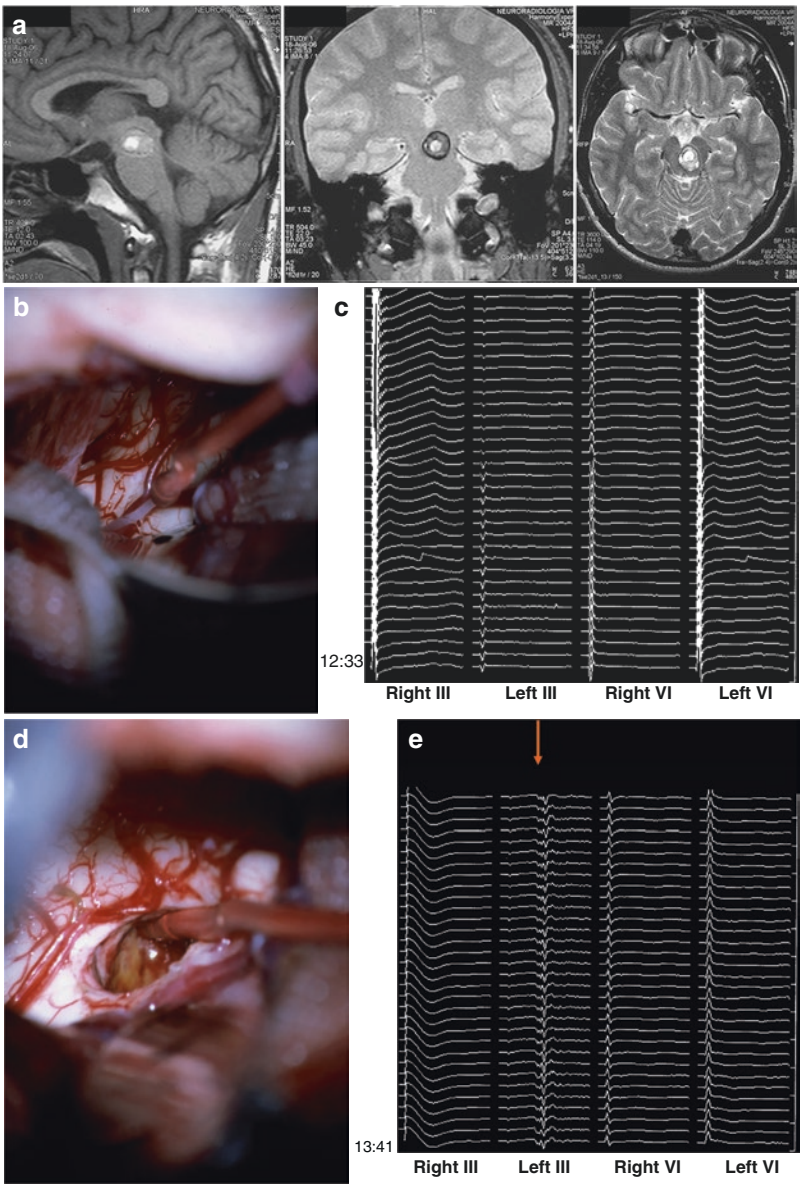

Fig. 5.3 Identification of the oculomotor nerve nuclei at the level of the tectal plate. (**a**) Sagittal (left), coronal (middle), and axial (right) magnetic resonance images of a left paramedian midbrain cavernoma. (**b**) Upon exposure of the superior colliculi, initial (time 12:33) direct stimulation of the left colliculus does not elicit any response from the oculomotor muscles innervated by the III and VI cranial nerves (**c**). (**d**) Later on (time 13:41), stimulation from inside the surgical cavity, during removal of the cavernoma, elicits a consistent response (red arrow) from the left upper rectus muscles (Left III), indicating stimulation of the nearby nuclei (**e**). Abbreviations: Right III, right upper rectus muscle; Left III, left upper rectus muscle; Right VI, right lateral rectus muscle; Left VI: left lateral rectus muscle. (Modified with permission from Sala et al. [36])

Nowadays, diffusor tensor imaging (DTI) plays an important role in the presurgical planning of surgery for brain gliomas to determine subcortical functional boundaries. The role of DTI in brainstem and spinal cord tumor surgery is more controversial; only few studies have specifically addressed the role of DTI in brainstem surgery [15, 16], but it is expected that DTI may guide neurophysiological mapping techniques, which remain the gold standard to localize the CST intraoperatively.

To identify the CST, we used for many years a handheld monopolar stimulator (tip diameter 0.75 mm) as cathode, with a needle electrode inserted in nearby muscles as anode (Fig. 5.4). More recently, we have switched to the use of a bipolar concentric electrode. The response is recorded as a compound muscle action potential (CMAP) from the contralateral limb, following a train of five stimuli of 0.5 ms duration at 1–2 Hz. Stimulation intensity is progressively increased up to 2 mA, starting from 0.5 mA, until a motor response is recorded. At this point, the probe is

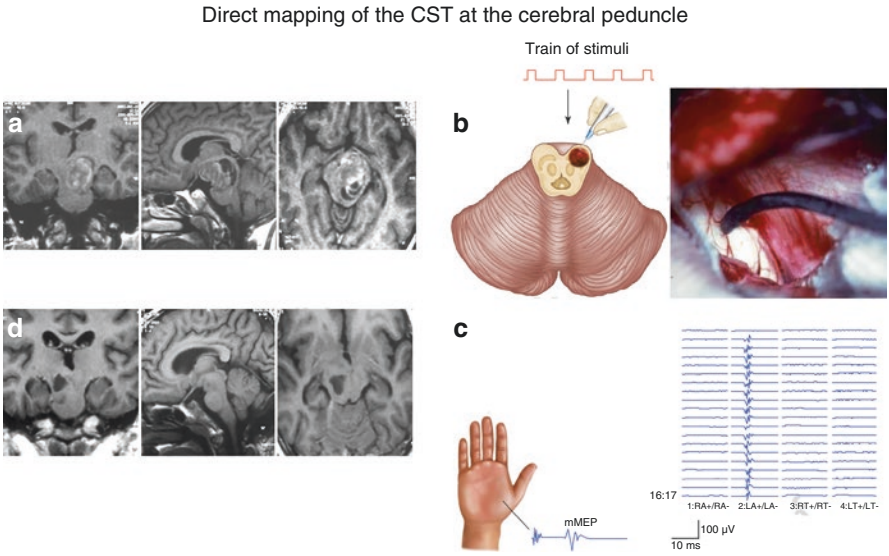

Fig. 5.4 Identification of the corticospinal tract at the level of the cerebral peduncle. (**a**) Enhanced T1-weighted images of a pilocytic astrocytoma of the left cerebral peduncle; coronal (left), sagittal (middle), and axial (right) view. (**b**) Schematic illustration of direct stimulation of the corticospinal tract at the level of the cerebral peduncle using a monopolar handheld probe (reference needle in the paraspinal muscles) with a short train of stimuli (each stimulus has a 0.5 ms duration) at 1 Hz and current up to 2 mA (left panel). Intraoperative view of stimulation of the left cerebral peduncle in the patient depicted in (**a**). The tumor was approached through a left lateral supracerebellar infratentorial route (right panel). (**c**) Muscle motor evoked potential (mMEP) recorded from the left abductor pollicis brevis (LA), while no responses were recorded in the left tibialis anterior muscle (LT) and right-sided muscles (RA and RT). (**d**) The tumor was then removed by entering the lateral midbrain posterior to the zone where the motor response was elicited. Postoperative gadolinium-enhanced T1-weighted images documented complete removal of the lesion. The patient presented with no additional motor deficits. (Modified with permission from Sala et al. [36])

moved in small increments of 1 mm in order to find the lowest threshold to elicit that response. The lowest threshold corresponds to the closest point to the CST. In the case of a cystic lesion, mapping is sometimes negative at the beginning of the procedure, but CMAPs can be recorded during mapping from within the cystic cavity towards the CST.

In principle, mapping of the CST along the brainstem is equivalent to subcortical CST mapping during brain tumor surgery. The technique is straightforward and well established. In supratentorial surgery, it is assumed that a roughly linear correlation exists between the threshold intensity in mA – to elicit a CMAP – and the distance from the CST in mm [17, 18]. This has not been investigated at the level of the brainstem, but one may expect a similar correlation.

5.2.2 Monitoring

5.2.2.1 Monitoring of Motor Evoked Potentials

Muscle motor evoked potential (mMEP) monitoring is a standard technique to assess the functional integrity of the CST.

During brainstem surgery, mMEP monitoring is likely more relevant for lesions involving or adjacent to the cerebral peduncle as well as during surgery in the medulla oblongata. Pontine tumors are mainly approached through the floor of the fourth ventricle, whereas the CSTs run ventrally, thus an injury to these pathways is quite unlikely.

To elicit mMEPs, the primary motor cortex is activated by a short train of stimuli delivered through transcranial electrical stimulation (TES). The short train of stimuli overcomes the blocking effects of anesthetic agents at the level of the alpha motoneuron and allows to record a muscle response [19–21]. TES is performed using scalp corkscrew-like electrodes placed at C1-C2 scalp sites for the upper extremities, while a Cz-C6 cm montage is usually preferred for the lower extremities, where Cz is placed at 1 cm behind the typical Cz point (see Fig. 5.2). A stimulus duration of 0.5 ms and an interstimulus interval of 4 ms is applied, at a repetition rate of 1–2 Hz. TES is usually safe [22], although a tongue bite block should always be inserted to avoid tongue injury by strong jaw muscle twitches that may occur during high intensity stimulation.

Muscle responses are recorded via pairs of needle electrodes inserted into the upper and lower extremity muscles. We usually monitor the abductor pollicis brevis (APB) for the upper extremity and the tibialis anterior (TA) or the abductor hallucis for the lower extremity. Since the CST fibers are concentrated in a very small ventral area in the brainstem, a selective injury to either upper extremity or lower extremity CST fibers is very unlikely to occur and, per se, monitoring the APB may suffice.

Warning criteria for mMEP monitoring during brainstem surgery are not well defined. Neuloh et al. [23] observed that stable or only transiently deteriorated MEPs warranted unchanged motor outcomes, while both irreversible deterioration

(namely, >50% drop in the amplitude) or a reversible loss were predictive of transient motor deficits in 37% of the cases; irreversible MEP loss was predictive of long-term, severe paresis. They concluded that, in comparison to supratentorial surgery, new deficits in brainstem surgery could occur only after more pronounced mMEP changes, but the "all or none" criterion – commonly used in spinal cord tumor surgery – was too little sensitive, potentially leading to false negative results.

Kodama et al. reported that SSEP and/or MEP decrements were observed during brainstem surgery at higher rates (47.5%) than in any other location within the posterior fossa [24]. In the same study, more than 50% of patients with SSEP and/or MEP decline during surgery had a hemiparesis at the time of hospital discharge, suggesting that MEP changes are indicative of at least short-term motor deficit.

In a surgical series focusing only on brainstem cavernomas, Shiban et al. observed an MEP sensitivity and specificity of 33% and 88%, respectively [25]. In general, low specificity may increase the risk of unjustified termination of surgery, potentially leading to incomplete tumor removal. Another observation by these authors was the fact that most of the MEP changes were rapid rather than progressive, with limited chances to alert the surgeon in time to take corrective measures. Overall, acute MEP deterioration is quite unusual and, when it occurs, is mainly due to a vascular injury that is related to arterial perforators during brainstem surgery. However, the main limitation of this study was the fact that because of MEP changes that occurred during non-critical stages of the operation, the surgeons never terminated the surgery prematurely despite ION alerts. Therefore, ION did not influence the surgical course.

In conclusion, during mMEP monitoring in brainstem surgery, the same limitations of MEP monitoring in supratentorial surgery apply, and quantitative warning criteria based on amplitude drop or increased threshold are still not ideal. Yet, in most studies, preservation of mMEPs remains a reliable predictor of good motor outcome.

5.2.2.2 Monitoring of Brainstem Auditory Evoked Potentials

Brainstem auditory evoked potentials (BAEPs) represent responses of the auditory nerve, the brainstem, and probably higher subcortical structures to acoustic stimuli. BAEPs are represented by seven different waves with different latencies [26] (Fig. 5.5).

The first wave (I) is the first negative near-field potential recorded near the ipsilateral stimulated ear and arises from the distal auditory nerve action potentials. The second wave (II) probably originates from both the proximal portion of the auditory nerve and the presynaptic activity of the auditory nerve ending at the cochlear nucleus. Wave III is thought to originate in the lower pons, at the level of the superior olivary complex. It is important to point out that ascending projections from the cochlear nucleus are bilateral, so wave III may receive contributions from brainstem auditory structures both ipsilateral and contralateral to the stimulated ear. The fourth and fifth waves usually join to form an IV-V complex, with anatomical generators

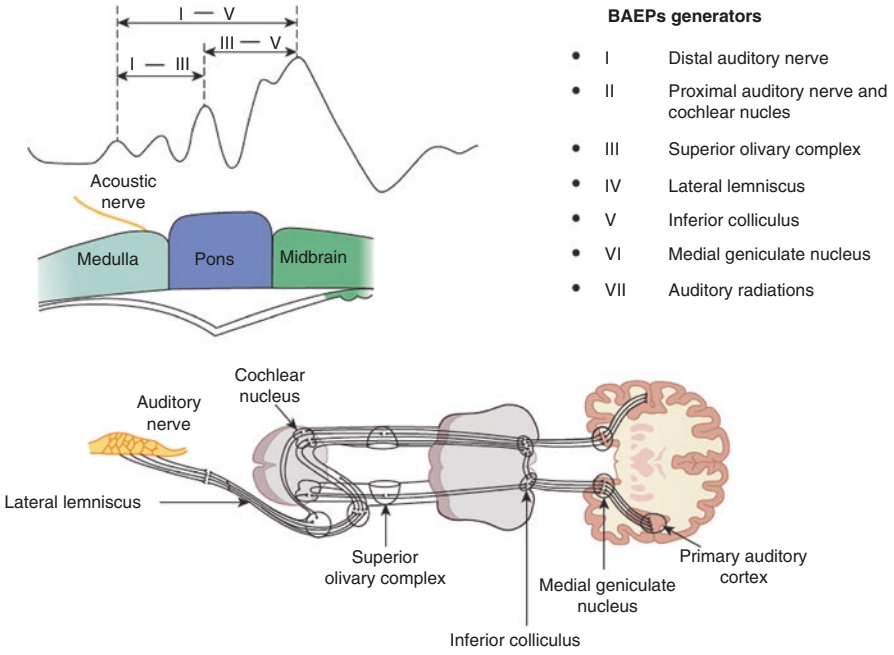

Fig. 5.5 Schematic illustration of brainstem auditory evoked potentials (BAEPs). Waves I to V and their generators are indicated (see text for details). (Republished with permission of McGraw-Hill Education, from Intraoperative Neuromonitoring, Christopher M. Loftus, Josè Biller, Eli M. Baron, 1st ed., 2014; permission conveyed through Copyright Clearance Center, Inc.)

that are in close proximity. Wave IV is thought to be generated in the high pons or lower midbrain at the level of the lateral lemniscus, and wave V is generated at the level of the inferior colliculus. During brainstem surgery, these two waves are commonly together either affected or unaffected, with some exceptions. Finally, waves VI and VII are supposed to arise at the level of the medial geniculate nucleus and auditory radiations, respectively, but these two waves are highly variable and not used in clinical practice.

BAEPs are elicited by transient acoustic 90–100 dB click stimuli (trains of 100-microsecond duration, electrical square pulses) delivered to the involved ear. White noise masking at 60–70 dB is simultaneously delivered to the contralateral ear. Alternating click polarities are often utilized during intraoperative BAEPs monitoring to minimize stimulus artefacts. Recording of BAEPs is performed with corkscrew/monopolar electrodes positioned at Cz (according to 10–20 International System) and monopolar needle at the earlobes (A1-generally left/A2-generally right, or Ai-ipsilateral/Ac-contralateral) or the mastoid process (Mi-ipsilateral/Mc-contralateral).

The recommended system bandpass for BAEPs is 100–150 Hz to 3000 Hz; BAEPs usually require 1000 or more acquisitions, with an adequate signal-to-noise ratio.

Standard criteria to interpret BAEP changes are based on amplitude and/or latency changes of waves I, III, and V. Changes in amplitude are more common than changes in latency. A 50% decrease in the amplitude and/or a 1-millisecond prolongation in the absolute latency of wave V or the I-V interpeak interval are considered warning criteria. A more sensitive criterion for changes in latency is a delay of more than 10% of the baseline peak V latency [27].

A number of surgical maneuvers can induce dysfunction or injury to the auditory pathways during posterior fossa surgery, including vascular derangements at the level of the cochlea, the auditory nerve, or the brainstem. Within the brainstem, the use of ultrasonic aspiration can also induce mechanical injury to the auditory pathways. An abrupt drop in the BAEP amplitude is more indicative of a vascular injury, but the majority of BAEP changes occur in a stepwise, reversible fashion. Therefore, if feedback to the neurosurgeon is promptly provided, there is enough time to take corrective measures and reverse an impending injury to the brainstem.

Some BAEP changes are more indicative of brainstem injury and retain some localizing value within the brainstem. For example, damage to the lower pons – near the area of the cochlear nucleus or the superior olivary complex – will induce a wave III and V delay or loss. Damage to the brainstem rostral to the lower pons, but below the level of the mesencephalon will affect wave V, but not waves I or III. Loss of wave V is not necessarily predictive of hearing loss, as it may just reflect temporal dispersion without a true, irreversible conduction block.

On the other hand, it should be pointed out that BAEPs assess only a very restricted area of the brainstem. At the level of the pons, likely no more than 20% of the brainstem area is covered by simultaneous SSEP and BAEP monitoring, suggesting that significant brainstem injury could occur in the absence of BAEP changes [28].

In our experience, while BAEP monitoring can offer an overview on the general "well-being" of the brainstem, it has rather been anecdotal to change the intraoperative surgical strategy exclusively on the basis of BAEP changes. BAEPs are therefore better interpreted in the context of a multimodal monitoring approach, where this information is integrated with that from SSEPs and mMEP monitoring.

5.3 Surgery of the Pons

5.3.1 Mapping

5.3.1.1 Mapping of the Facial Colliculus on the Floor of the Fourth Ventricle

Entering the floor of the fourth ventricle carries a significant risk of neurological injury due to the high concentration of eloquent neural structures in a very small area. At the level of the pons, the facial colliculus represents a highly dangerous brainstem "entry zone" through the rhomboid fossa [6]. Damage to this area causes

facial (VII) and abducens (VI) nerve paralysis as well as lateral gaze disturbances due to an injury to the paramedian pontine reticular formation. A midline injury involving the medial longitudinal fasciculus bilaterally may result in internuclear ophthalmoplegia.

Although the facial colliculus represents a classic anatomical landmark, its identification can be challenging when anatomy is significantly distorted by the tumor, and neurophysiological mapping could be the only way to functionally identify the nuclei or the intramedullary roots of the VI and VII cranial nerves.

A handheld bipolar concentric electrode could be used. A single stimulus of 0.2 ms duration is delivered at a frequency of 1–2 Hz. In general, two different mapping strategies can be used to identify the facial colliculus. In the first case, the surgeon looks for each site at the lowest threshold intensity, which allows to record a CMAP from the orbicularis oculi and/or the orbicularis oris muscles. By moving the stimulator 1 mm apart, it is possible to explore the floor of the fourth ventricle and identify the area closer to either the nucleus or the intramedullary root of the nerve. The other method is to work with a fixed intensity of approximately 0.5–1 mA and determine the amplitude of the muscle response for each point. The point corresponding to the highest amplitude indicates proximity to the mapped nucleus, while small amplitudes or no response at all suggest a safe distance from the nucleus or tracts.

There are yet two main limitations in the reliability of the mapping of the facial colliculus. The first is related to the fact that it cannot detect an injury to the supranuclear tracts originating in the motor cortex and ending on the cranial nerve motor nuclei. Therefore, preservation of the lower motoneuron per se may not exclude a postoperative facial palsy if the corticobulbar pathway has been injured proximal to the nucleus. The second limitation is that the possibility of stimulating the intramedullary root of the facial nerve, rather than the nuclei itself, exists. Therefore, this could result in a peripheral response that will still be recorded despite an injury to the motor nuclei [8] and, consequently, a postoperative facial palsy.

Even with these limitations, facial mapping remains a standard, very valuable ION technique, which undoubtedly facilitates the identification of the facial nerves/nuclei whenever the anatomy is ambiguous.

5.3.2 Monitoring

5.3.2.1 Monitoring of the Facial Nerve

Free-Running Electromyography While mapping techniques allow to identify the facial colliculus to select the safest entry zone through the floor of the fourth ventricle, only monitoring techniques can continuously assess the functional integrity of the facial nerve during surgery. Free-running EMG has been for many years the gold standard for facial nerve monitoring and is still widely used [11, 29, 30]. The spontaneous activity of the facial nerve is recorded through needle electrodes

placed in the muscles innervated by the facial nerve. Therefore, this is not an evoked potential. Different criteria have been proposed to interpret EMG activity, but convincing data regarding the correlation between EMG patterns and clinical outcome are still lacking [11, 30]. Paradoxically, the lack of spontaneous activity usually indicates no injury, but it could also be observed after a complete sectioning of the peripheral nerve. On the other hand, neurotonic discharges could reflect injury activity but sometimes occur following simple irrigation of the surgical field with cold saline. So, the real specificity and sensitivity of free-running EMG remains disputable. A higher degree of reliability has been documented for a specific pattern of high frequency, sustained neurotonic discharges, called A-trains. The occurrence and duration of A-trains has proved to be highly predictive of postoperative facial palsy. However, the A-train analysis is performed offline, and the predictive value of this specific pattern of EMG activity has been described only with regards to the surgery for vestibular schwannomas [31, 32], not in brainstem surgery.

Facial Motor Evoked Potentials A second method to monitor the functional integrity of the facial nerve is represented by corticobulbar MEPs (see Fig. 5.2). Essentially, the same principle of MEP monitoring for limb muscles is herein extended to the muscles innervated by motor cranial nerves. Facial MEPs are elicited through TES using a train of 4 stimuli, 0.5 ms each at a rate of 1–2 Hz and intensity ranging between 60 and 120 mA. The electrode montage is usually C3/Cz for right-sided muscles and C4/Cz for left-sided muscles. For recording, the same electrodes used during mapping of the facial nerve are used, and muscle responses can be recorded by both the orbicularis oris and oculi or any other muscle innervated by branches of the facial nerve. Facial MEPs are true evoked potentials, which assess the integrity of the corticobulbar pathway from the motor cortex to the muscles. Although there are no standard warning criteria for facial MEP interpretation, irreversible MEP loss is a poor prognostic sign, correlating with severe and long-lasting facial palsy [33]. The preservation of MEPs usually predicts no deficits or only minor and transient facial palsy, while significant amplitude drops – in our experience, in the range of 50% to 80% of baseline values – are indicative of at least a transient deficit.

One of the limitations of facial MEP monitoring is that the use of a lateral montage, with C3 or C4 as an anodal stimulating electrode, increases the risk that a strong TES may activate the corticobulbar pathways deep in the brain or at the level of the brainstem and foramen magnum [34]. This would increase the risk of a direct activation of the peripheral facial nerve. If this occurs, an injury to the corticobulbar pathway rostral to the point of activation of the facial nerve will not be recognized, and the patient will wake up from surgery with a facial palsy in spite of the preservation of facial MEPs. To minimize the risk of these false-negative results, it is always recommended to keep the stimulation intensity as low as possible. However, the only possibility to predict the threshold for peripheral activation is to repeat the same stimulation while keeping the same parameters (stimulus duration, intensity,

and frequency), except for the number of stimuli, which is decreased from 4 to 1. A single pulse TES should not elicit muscle MEPs during general anesthesia because neural transmission through a polysynaptic pathway would be blocked by the anesthetics; if a muscle response is still present, this response should be interpreted as a direct activation of the cranial nerve and is, therefore, not reliable for monitoring. Alternatively, a muscle response that is present with a train of stimuli and absent following a single stimulus is likely generated by a true corticobulbar activation and can be used for monitoring [35, 36]. Due to the physiological variation of this threshold during surgery, secondary to anesthesia, room temperature or other factors, it is important to re-check the threshold for peripheral activation several times during surgery. For example, if surgery is performed in a semi-sitting position, a significant cerebrospinal fluid (CSF) leak occurs after opening the dura and may produce pneumocephalus; the presence of air between the cortex and the skull will increase the threshold for TES and, therefore, new corticobulbar MEP baselines should be taken after the dura is opened.

Acioly et al. [37] have recently reviewed the literature on facial nerve monitoring in skull base and cerebellopontine angle surgery, concluding that: "Although there is a general agreement on the satisfactory functional prediction of different electrophysiological criteria, the lack of standardization in electrode montage and stimulation parameters precludes a definite conclusion regarding the best method." These considerations can certainly be extended to facial nerve monitoring in brainstem surgery.

5.4 Surgery of the Medulla Oblongata

Surgery of the medulla carries a significant risk of neurological morbidity because an injury to the lower cranial nerves or the cardiorespiratory centers can be life-threatening. Here, within the small concavity of the calamus scriptorius, between the obex and the striae medullaris, lie the hypoglossal and vagal triangles. Immediately below the two medial triangles lie the hypoglossal nuclei, which control the muscles of the tongue. Severe tongue paralysis and atrophy secondary to hypoglossal injury represents one of the most devastating cranial nerve deficits, and even a minor injury in this area must be avoided. Lateral to the hypoglossal triangles are the vagal triangles and under these triangles lie the dorsal nuclei of the vagus nerves. These provide motor fibers to the bronchi, heart, and stomach. Slightly deeper and lateral lies the nucleus ambiguous, which provides fibers to the glossopharyngeal (IX), vagus (X), and accessory (XI) nerves. These fibers ultimately innervate the musculature of the palate, pharynx, and larynx. Therefore, even a small injury to this area can cause dysphonia and may impair the swallowing and coughing reflexes, exposing the patient to the risk of aspiration pneumonia and/or inability to eat or drink [38, 39].

5.4.1 Mapping

5.4.1.1 Mapping the IX/X, XI and XII Cranial Nerve Nuclei

Neurophysiological mapping of the lower motor cranial nerves is performed similarly to mapping of the facial colliculus. The stimulating parameters are the same, with emphasis that at the level of the medulla – due to the close proximity of the cardiovascular centers – no intensity higher than 2 mA should be used as it may induce severe bradycardia and even cardiac arrest [40]. A bipolar concentric electrode is preferred for more focal stimulation. CMAPs are recorded from wire electrodes inserted in the muscles innervated by the lower cranial nerves. It should be pointed out that the glossopharyngeal nerve provides motor fibers only to the stylopharyngeus muscle, which elevates the pharynx during swallowing and speech. However, selective placement of recording electrodes in the stylopharyngeus muscle only is not possible, and it is expected that most of the muscle activity recorded from the pharyngeal muscles or soft palate likely reflects a mixed activation of both the IX and X cranial nerves. Another limitation of mapping of the glossopharyngeal nuclei is that stimulation on the floor of the fourth ventricle assesses only the functional integrity of the efferent arc of the swallowing reflex, while no information on the integrity of afferent pathways and afferent/efferent connections within the brainstem is obtained [41].

To record CMAPs for the IX/X and XII cranial nerves, we generally prefer to use tiny wire electrodes inserted in the posterior wall of the pharynx (inserted lateral to the endotracheal tube, bilaterally) and the tongue muscles, respectively. Other techniques to place recording electrodes either directly on the endotracheal tube or transcutaneously in other vocalis muscles can be used [42–44]. For the accessory nerve, regular needle recording electrodes are inserted in the trapezius muscle.

Morota et al. [8, 45] suggested that medullary tumors tend to displace the motor cranial nerve nuclei ventrally. So, whether the tumor is intra-axial or a fourth ventricular tumor – such as a medulloblastoma or an ependymoma – infiltrating the floor, neurophysiological mapping can be used to select the entry zone in the first case and to determine when to stop resection in both cases (Figs. 5.6 and 5.7). It should be considered that a positive mapping response with a low threshold intensity, lower than 0.5 mA, suggests a close proximity to the nuclei, which lie just a few millimeters below the ependyma. In this case, we recommend abandoning tumor resection as the risk of injuring the nuclei and/or the intramedullary roots is high, and this will expose the patient to life-threatening conditions. While a subtotal removal may be undesirable for medulloblastomas and ependymomas, most of the intra-axial medullary tumors, especially in children, are low-grade gliomas, and even if a tiny sole of the tumor is left on the floor of the fourth ventricle, close neuroradiological follow-up may suffice with no need to start adjuvant therapies upfront [46].

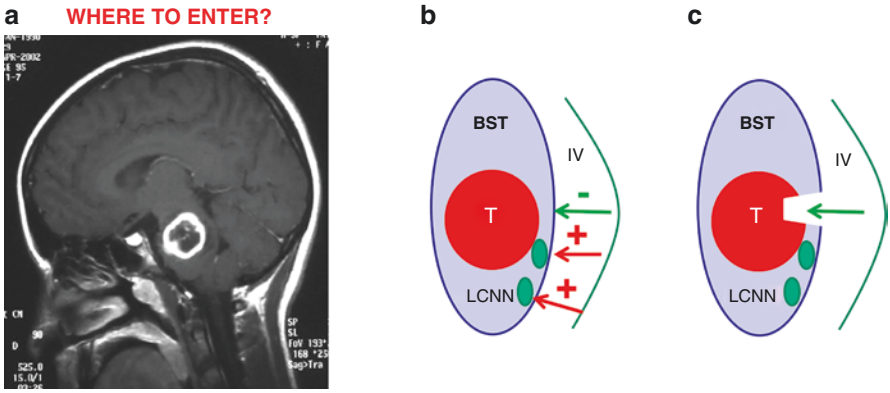

Fig. 5.6 Schematic illustration of the role of neurophysiological mapping on the floor of the fourth ventricle, for fully intra-axial brainstem tumors (**a**). Direct stimulation of the floor of the fourth ventricle is performed with either a monopolar or bipolar concentric stimulator (arrows). A positive mapping result (red arrow) indicates proximity to either cranial nerve nuclei or their intra-axial roots. Therefore, this is not a safe entry zone (**b**). Alternatively, negative stimulation (green arrow) or a stimulation requiring much higher intensity, indicates safe distance from the nuclei or their intra-axial roots, and can be used as an entry zone to the brainstem and the tumor (**c**)

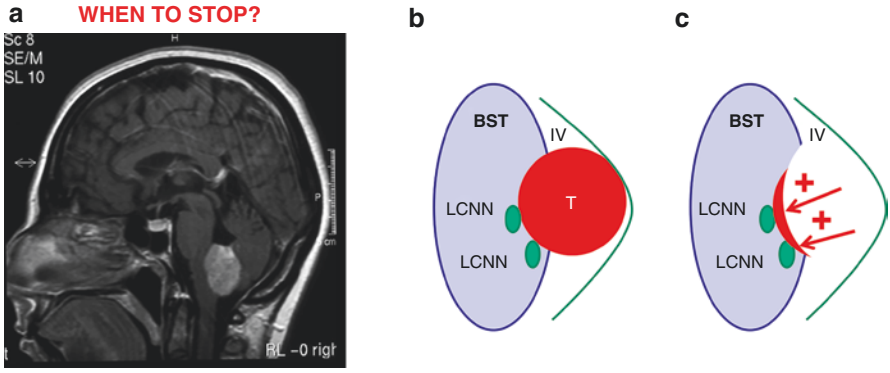

Fig. 5.7 Schematic illustration of the role of neurophysiological mapping on the floor of the fourth ventricle, for dorsally exophytic brainstem tumors or for fourth ventricular tumors infiltrating the floor (**a**). In these cases, neurophysiological mapping is often negative at the beginning of the case because the nuclei are displaced ventral to the tumor, especially at the level of the medulla (**b**). However, when stimulation of the last sole of tumor elicits a positive mapping response at low intensity (**c**), this is the time to stop resection in order not to violate and injure the lower cranial nerve nuclei or their intra-axial roots, which are only few millimeters underneath

5.4.2 Monitoring

5.4.2.1 Lower Cranial Nerve Monitoring

Free-Running Electromyography Despite the fact that recording of free-running EMG for the facial nerve in vestibular schwannoma surgery has proved to be reliable [31, 32, 47], the overall reliability of free-running EMG for other motor cranial

nerves remains controversial [11, 30]. In particular, Schlake et al. [48] observed rather high rates of false positive and, of most concern, false negative results, concluding that the predictive value of free-running EMG is limited.

Corticobulbar Motor Evoked Potentials As an alternative to free-running EMG, some authors [36, 49, 50] in the past 20 years have extended the use of facial nerve corticobulbar MEPs to the lower cranial nerves. The same parameters of stimulation and the same criteria (namely, a single stimulus versus a train of stimuli) to differentiate a real corticobulbar response from a peripheral activation of lower cranial nerves apply. Recordings are obtained from the same wire electrodes used for neurophysiological mapping. In our experience, MEPs from the hypoglossal nerve, recorded from the tongue, are very stable with little spontaneous activity and can be well monitored throughout the surgical procedure. Alternatively, MEPs for the IX/X nerves are unstable, and their interpretation is sometimes complicated by a more frequent spontaneous activity as compared to cranial nerve XII.

Finally, it should be considered that at the current state-of-the-art ION techniques, only efferent pathways are monitorable for the lower cranial nerve-mediated reflexes such as swallowing and coughing. Therefore, an injury to the afferent arch of these reflexes will not be recognized by current monitoring and mapping techniques [41]. This explains why discrepancies between ION data and postoperative neurological outcomes can occur. Very recently, Sinclair et al. [51] documented the possibility to monitor the laryngeal abductor reflex during thyroid surgery. Since this reflex is mediated at the level of the lower brainstem, it can indirectly provide information on the functional integrity of the involved area. Although this is still a very preliminary report on a small number of patients, it has certainly shed new light on the ION monitoring of the lower brainstem [52]. Hopefully, monitoring of brainstem-mediated reflexes, such as the laryngeal abductor reflex or the blink reflex, will improve the reliability of ION monitoring in surgeries of the pons and medulla oblongata.

5.5 Other Monitoring Techniques in the Brainstem

Some other methodologies related to the monitoring of trigeminal SSEPs (T-SSEPs) and brainstem reflexes have emerged over the past few years. A reliable methodology for eliciting T-SSEPs under general anesthesia was described by Malcharek et al. [53]. They recorded long-latency T-SSEPs from the scalp after simultaneously stimulating V2 and V3 branches of the trigeminal nerve. Although this method was tested in patients undergoing carotid endarterectomy, it may be important to assess the functional integrity of sensory fibers of the trigeminal nerve during brainstem surgery.

The blink reflex has also been monitored under general anesthesia [54]. This reflex is mediated by an afferent pathway – the nasociliary branch of the ophthalmic branch (V1) of the trigeminal nerve, and an efferent pathway – the temporal and zygomatic branches of the facial nerve. Deletis et al. were able to elicit the R1 com-

ponent in 86% of 27 patients aged 1 to 78 years. They applied one to seven rectangular constant-current stimuli with an interstimulus interval of 2 ms, an intensity of 20–40 mA, and a train repetition rate of 0.4 Hz over the supraorbital nerve. Recording was done from the ipsilateral orbicularis oculi muscle [54]. The integrity of this reflex reflects the functional integrity of the neural structures involved at the level of the pons.

Finally, the masseter reflex, also known as the jaw jerk reflex, can be monitored intraoperatively by inserting percutaneous hook-wire electrodes just under the zygomatic arch, approximately 5 mm lateral to the temporomandibular joint. Single stimuli with a duration of 0.2–0.5 ms and progressively increasing intensity are applied. The insertion depth of the stimulating wire electrode is determined when the stimulation elicits a response in the masseter and temporalis muscles. Recordings are obtained by inserting subdermal needle electrodes into the ipsilateral masseter and temporalis muscles [55].

5.6 Conclusion

Surgery of brainstem lesions remains challenging despite all the remarkable advancements in the field of neuroanesthesia, postoperative intensive care, and presurgical planning, including tractography. This small region of the central nervous system represents a minefield even for the experienced neurosurgeon.

To date, ION remains essential to improve the safety of brainstem surgery. With the only exception of the localization of oculomotor nerve nuclei following stimulation of the superior colliculi, mapping techniques are reliable and very useful in determining the safest entry route for intrinsic, focal brainstem lesions. Additionally, these techniques help to decide when to stop the removal of fourth ventricular tumors infiltrating the floor, in order to avoid an injury to the VII, IX/X and XII cranial nerve nuclei.

ION monitoring can nowadays support the surgeon in two ways: (1) by providing functional information aimed to identify ambiguous neural structures – this may assist in identifying the safest entry zone to intra-axial lesions and/or determine the proximity of cranial nerve nuclei to stop the resection of brainstem exophytic tumors or fourth ventricular tumors infiltrating the ependyma; and (2) by on-line monitoring of the functional integrity of somatosensory, motor and auditory pathways to minimize the risk of a permanent injury.

SSEPs and BAERs are well established techniques since many years but only cover a small area of the brainstem, and focal injury may occur despite their preservation. Therefore, a multimodal neuromonitoring approach, including corticospinal and corticobulbar MEPs, should be used instead. MEPs, in general, are good predictors of motor outcome, though warning criteria in the brainstem are not well set, especially for corticobulbar MEPs of the lower cranial nerves, where only few studies are reported in the literature. Nevertheless,

corticobulbar MEPs, for the VII and especially for the IX/X and XII cranial nerves, are a valid alternative to free-running EMG, which often lacks specificity and sensitivity.

The lack of ION techniques to reliably monitor afferent pathways of the lower brainstem mediated reflexes, such as swallowing and coughing, remains problematic. Recently, however, novel techniques have been proposed to monitor brainstem reflexes at the level of the pons and medulla oblongata, and these developments are opening new perspectives to further enhance the reliability of brainstem monitoring in neurosurgery.

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