



Intraoperative Neurophysiology Monitoring for Intra-axial Posterior Fossa Surgery

25

Sonia E. Q. Nunes and Francesco Sala

Key Learning Points

- It is important to understand which neural structures are at risk in order to plan the most appropriate IOM protocol during specific brainstem surgeries.
- Each IOM technique provides specific information on a particular pathway or anatomical area within the brainstem; however, a multi-modality approach is far superior in terms of reliability and safety.
- Mapping and monitoring techniques have different goals but their combined use is recommended.

Introduction

The brainstem is one of the most complex structures of the human body, with a multifaceted anatomy. Surgery of the brainstem is considered to be one of the most challenging neurosurgical procedures due to the significant risk of severe neurological deficits [1]. The approach to the

lesion is determined largely by the path that allows access to the lesion whilst causing the least significant risk to surrounding structures [2–4]. The brainstem is comprised of the mid-brain, pons, medulla oblongata; it is predominantly located in the posterior fossa region except for a small section which continues beyond the tentorial incisura and a short tract of the medulla oblongata which remains below the foramen magnum. It is rich in cranial nuclei, interconnecting fascicles, bundles and pathways, and the reticular formation, making the brainstem a complex structure both anatomically and physiologically. Moreover, surgical morbidity is substantially higher primarily due to the lack of structural redundancy and plasticity of this specific region [2, 3].

Tumor resection in the medulla oblongata requires great caution as the risk of compromising the respiratory center is a major concern as well as the patient's ability to swallow or protect airway. If the tumor is growing exophytically out from the brainstem surface, removal occurs at the location of the outgrowth; thus, the tumor creates its own entry into the brainstem where it can be accessed with less risk. However, with intrinsic tumors, the surgical approach requires a deep understanding of the functional anatomy. The direct surgical approach to brainstem tumors is like crossing a minefield as any manipulation, however delicate, in the brainstem area will

S. E. Q. Nunes · F. Sala (✉)
Department of Neurosciences,
Biomedicine and Movement Sciences,
Section of Neurosurgery,
University Hospital,
Verona, Italy
e-mail: soniaelizabeth.queiroznunes@univr.it;
francesco.sala@univr.it

potentially lead to high morbidity rates and significant mortality [4–6].

Safe entry zones have been established specifically for the posterior brainstem on the basis of specific landmarks, but these landmarks may be unreliable when the normal anatomy has been distorted due to the tumor [7, 8].

The advancement of intraoperative neuromonitoring (IOM) in the recent two decades has contributed to the feasibility and safety of brainstem surgery. IOM not only serves to predict postoperative outcomes but most importantly contributes to the prevention of neurological deficits. IOM includes various clinical neurophysiology techniques which have been tailored for surgery comprising of electromyography (EMG), and somatosensory (SEPs), brainstem auditory (BAEPs), and motor-evoked potentials (MEPs) to name a few.

SEPs and BAEPs were initially the only monitoring technique used in brainstem surgeries; however, it was later determined that these two techniques were only assessing function in 20% of areas within brainstem [9]. As a result, two new methods evolved, focusing on the functional integrity of motor pathways passing through the brainstem, where MEPs are recorded from the limb muscles and the corticobulbar MEPs (CoMEPs) from various cranial-nerve-innervated muscles [10–13]. Another significant technique involves mapping of the motor cranial nerve nuclei in brainstem surgery. Mapping focuses on the identification of anatomical landmarks to avoid injury especially when selecting the safest entry route to the brainstem [13].

The main focus of this chapter is to review IOM mapping and monitoring techniques (Figs. 25.1 and 25.2) which are indicated based

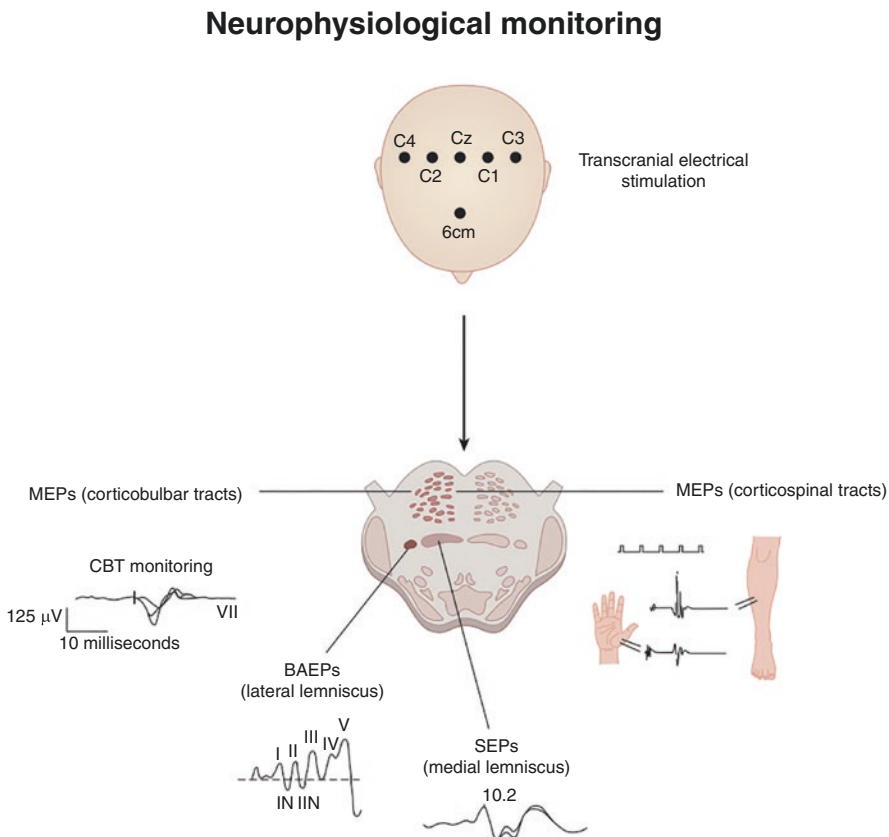


Fig. 25.1 Schematic illustration of neurophysiological monitoring techniques. These are monitored in real time, providing constant feedback on the functional integrity of the neural pathways within the brainstem (motor, sensory and auditory). See the text for further details on each mon-

itoring technique. MEPs, motor evoked potentials. SEPs, somatosensory evoked potentials. BAEPs, brainstem auditory evoked potentials. CBT, corticobulbar tract. (From Sala et al. [41]; with permission)

Neurophysiological mapping

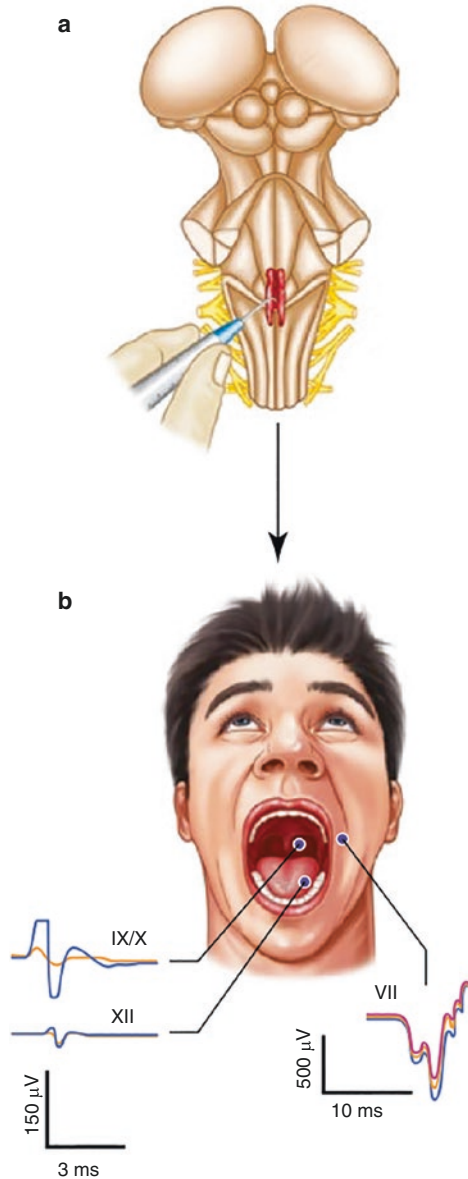


Fig. 25.2 Schematic illustration of intraoperative neurophysiology mapping techniques in the posterior fossa. These techniques are used to identify functional landmarks such as the motor nerve nuclei on the floor of the fourth ventricle. (a) A handheld monopolar (or bipolar concentric) probe is used 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. (From Sala et al. [41]; with permission)

on the anatomical location of the tumor in the midbrain, pons, and medulla oblongata.

Anesthesia

The anesthetic regime required for IOM is very specific due to the sensitivity and quality of the responses required for monitoring. All anesthetic drugs interfere with evoked potentials in some form or another and therefore it is imperative that anesthesia remains at constant levels. Intravenous bolus infusions or dramatic changes in the minimum alveolar concentration (MAC) of inhalation drugs may deleteriously affect the signals. Volatile anesthetics have a huge impact on SEPs and MEPs, impacting latencies and amplitudes. The current gold standard for IOM is total intravenous anesthesia (TIVA), with propofol as the hypnotic and remifentanyl as the analgesic drug [14]. The above anesthetic regime has little effect on the lower motor neurons, provided no muscle relaxants are administered [14–16].

Greunbaum et al., 2019, reviewed various IOM studies in neurosurgery and concluded that “in the event of a sudden intraoperative changes in electrophysiological signals; regardless of the IOM modality used, any sudden change in electrophysiological signal should prompt an immediate and appropriate intervention; a multimodal IOM approach is often, but not always, advantageous over a single IOM approach.” This further motivates the need for consistent communication between members of the surgical team in order to reduce any external factors that may influence the IOM and patient outcome [16].

Surgery of the Midbrain

Mapping

The midbrain occupies the notch of the tentorium and consists of three parts: a dorsal portion (the corpora quadrigemina or tectum), a large ventral portion (the tegmentum), and the cerebral peduncles. Posterior cerebral (PCA) and superior cerebellar (SCA) arteries surround the midbrain and

are in the close vicinity of the oculomotor (III) and trochlear (IV) cranial nerves. Minimizing manipulation of these neurovascular structures is imperative when removing tumors specific to this area. A dorsal approach through the supracerebellar infratentorial, an occipital transtentorial, or a subtemporal route has been used to approach intrinsic midbrain lesions.

The utilization of IOM through direct mapping of the tectal plate is used to identify safe entry zones when approaching intrinsic midbrain lesions, while mapping of peripheral oculomotor nerves may be used for tumors involving the cisternal, cavernous, or intraorbital segment of these nerves [2].

Mapping is performed with a monopolar or bipolar concentric handheld stimulating probe. Rectangular pulses of 0.2 ms duration at 1–2 Hz and intensity between 0.5 and 3 mA are recommended. Additionally, the use of a bipolar concentric probe is often preferred as it offers a higher focality of the stimulation and limited spread of the current. For direct stimulation of the brainstem, the current stimulation is recommended to remain very low, starting at 0.05 mA and not exceeding 1.5 mA [2].

Responses are obtained by placing small wire Teflon-coated electrodes in the 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. Placement of recording electrodes in the extrinsic ocular muscles requires great care and experience in order to avoid an injury to the ocular bulb.

The direct identification of the superior colliculi through brain mapping, however, has been mostly unsuccessful, likely because the nuclei of the oculomotor nerves are embedded in the periaqueductal gray matter, too deep to be activated by superficial stimulation [17, 18]. Also, muscle responses from extraocular muscles are usually of low amplitude because their 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 [19, 20], but recording monitorable MEPs from extraocular muscles remains challenging.

Avoiding injury to the oculomotor nerve nuclei and their relevant intramedullary tracts is paramount in preventing oculomotor deficits, but this remains still to be solved from a neuromonitoring perspective.

Corticospinal Tract Identification at the Level of the Cerebral Peduncle

The corticospinal tract (CST) is compressed within a small portion of the brainstem surface. It is exposed to injury when lesions are found lying in the region of the cerebral peduncle or the ventral section of the medulla. Mapping is strongly suggested to identify the CST [21]. In our unit, we have changed from the monopolar probe to the bipolar concentric probe. Compound muscle action potentials (CMAP) are recorded from the contralateral limb with a train of five stimuli of 0.5 ms duration at 1–2 Hz. Stimulation intensities begin at 0.5 mA and are increased in small increments up to 2 mA until a response is found. Once a response is attained, the probe should be moved in small increments of 1 mm in order to determine the lowest stimulation intensity required to elicit a response. This is done to ascertain the closest point to the CST. However, when removing a cystic lesion, mapping responses may produce negative results at the beginning of the procedure; therefore, it is important to map within the cystic cavity towards the CST, as CMAPs can be found inside the cystic cavity.

Monitoring

Motor-Evoked Potentials

Motor-evoked potentials (MEPs) have become the leading technique when evaluating the functional integrity of the CST. As with all IOM modalities, the relevance of each technique lies in the location of the lesion and the neuroanatomical structures affected during surgery, and the same can be said for MEPs in brainstem surgery.

Lesions involving the medulla oblongata and the cerebral peduncle require more aggressive MEP monitoring as opposed to pontine tumors, which are typically approached through the floor of the ventricle, with the CST located ventrally, thus less exposed to the risk of injury [2].

MEPs are generated by stimulating the primary motor cortex through transcranial electrical stimulation (TES) with a short train of stimuli. The short train of stimuli is necessary to record a muscle response, as it overcomes the blocking effects of anesthetic agents at the level of the motor neuron. TES is performed via corkscrew electrodes placed according to the international EEG 10–20 system, on the scalp at C1–C2 scalp sites for the upper extremities, whilst a midline montage consisting of an electrode at Cz and a second electrode 6 cm anterior to Cz is suggested for the lower extremities. A stimulus duration of 0.5 ms with an interstimulus interval of 4 ms is delivered, with a repetition rate of 1–2 Hz. Muscle responses are recorded via pairs of needle electrodes inserted into the upper and lower extremity muscles. Our monitoring protocol consists of the abductor pollicis brevis (APB) muscle for the upper extremity and the tibialis anterior (TA) or the abductor hallucis muscles for the lower extremity. Selective injury to either the upper or lower extremity is rare as CST fibers are primarily situated in a small ventral area in the brainstem.

Neuloh et al., 2009, recognized the predictive value MEPs have on the functional integrity of corticospinal tracts in brainstem surgeries, regardless of the type of lesion. Moreover, they noted that stable or transient MEP changes predicted unchanged motor outcomes, whilst an irreversible MEP loss (>50% amplitude drop) was indicative of severe postoperative paresis [10].

Brainstem Auditory-Evoked Potentials

Brainstem auditory-evoked potentials (BAEPs) reflect the neuronal activity from the auditory nerve, cochlear nucleus, superior olive and inferior colliculus of the brainstem. There are several

components to the BAEP that contribute to the successive excitation of the auditory nerve and the auditory nuclei in the caudal regions of the brainstem up to the midbrain structures. BAEPs are generated within the cochlea by transducing the mechanical acoustic stimulation of the hair cells.

BAEPs include seven waveforms which are identified by their latencies, generated from the stimulated ipsilateral ear. Wave (I) is the first negative near-field potential which arises from the distal auditory nerve action potential. Wave (II) is considered to be generated from the cochlear nucleus, yet a potential with a similar latency has been described as arising directly from the proximal portion of the auditory nerve and the presynaptic activity of the auditory nerve ending at the cochlear nucleus. Wave (III) arises from the lower pons, at the superior olivary complex. When analyzing this waveform, it is important to note that ascending projections from the cochlear nucleus are bilateral, therefore wave (III) may project responses from both the ipsilateral and contralateral stimulated ear. Stretching of the proximal part of the cranial nerve VIII in a cerebellopontine angle (CPA) surgery can cause changes or contribute to the loss of wave III [22]. Wave IV and V occur in the mid and upper pons/lower brain forming IV–V complex. Wave IV is considered to be generated from the high pons to lower midbrain level of the lateral lemniscus whilst wave V is generated at the inferior colliculus. Damage to these structures will compromise the IV–V wave complex, which can cause loss of responses. These two waveforms are not considered independent of each other, thus the dysfunction to either will affect the wave IV–V complex. The earliest sign of dysfunction is often noted with an increased latency in Wave V, typically observed during stretching of the tissues during cerebellar retraction in the suboccipital approach in CPA surgery. Waves VI and VII are thought to be generated at the medial geniculate nucleus of the auditory radiations but are less significant for their use in clinical practice [22, 23].

BAEPs are evoked by transient acoustic click stimuli at 90–100 dB to the ipsilateral ear, whilst the contralateral ear is stimulated with a white

masking noise of 60–70db simultaneously, in order to limit spread of stimulation from the side under evaluation. Due to the presence of cochlear microphonics and stimulus artifact, alternating stimulation polarities are often implemented to reduce stimulation artifact without affecting Wave I [22].

The recording of BAEPs requires the placement of electrodes at the CZ site according to the international 10–20 system. Monopolar needles are inserted on the ipsilateral and contralateral earlobe/mastoid to the lesion. As BAEPs signals are generated from anatomical structures far removed from the site of electrode placement on the head's surface, responses are small and require signal averaging of the responses of 1000 or more stimuli. The recommended bandpass is 100–150 Hz to 3000 Hz. Interpretation of waveforms is dependent on amplitude or latency changes in Waves I, III, and V. Amplitude changes are more prevalent than latency. Warning criteria comprises the following: A 50% decrease in amplitude and/or a 1 ms increase in the absolute latency of Wave V, or the I–V interpeak latency [22, 23].

In posterior fossa surgeries, various surgical maneuvers contribute to injury or malfunction of the auditory pathways. An abrupt drop in the BAEP amplitude is 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. Changes in BAEPs in some instances are indicative of brainstem injury and provide some detail on the location in 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. With this in mind, it is essential to recognize that the BAEP

is selective in its interpretation on the premise that BAEPs only focus on a limited area of the brainstem [22].

BAEPs are therefore better interpreted in the context of a multimodal monitoring approach, where this information is integrated with that from SEP and MEP monitoring.

Surgery of the Pons

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

Tumors in the pons are usually accessed through the floor of the fourth ventricle. This entry zone presents significant neurological risk due to the substantial amount of eloquent neural structures concentrated in a small area. One of the more dangerous entry points is the facial colliculus at the level of the pons, through the rhomboid fossa [24, 25]. Injury to this area produces facial and abducens nerve paralysis, as well as internuclear ophthalmoplegia if the fasciculus longitudinalis medialis is injured [26]. The identification of the facial colliculus often occurs with great ease as it is a well-defined anatomical landmark, provided it has not been distorted by the tumor. In these situations, neurophysiological mapping is the logical approach in identifying the functional nuclei or the intramedullary roots of the VI and VII cranial nerves (Fig. 25.3).

Mapping is performed with a bipolar concentric probe in order to avoid current spread to surrounding tissue with a single stimulus of 0.2 ms duration at a frequency of 1–2 Hz at a stimulation intensity of 0.5–1 mA. When mapping the floor of the fourth ventricle it is important to consider that the interpretation of mapping results has some limitations. It cannot detect injury to the supranuclear tracts deriving from the motor cortex and ending on the cranial nerve nuclei. Therefore, postoperative facial palsy cannot be excluded from the preservation of lower motor neurons if the corticobulbar pathway is injured proximal to the nuclei. It is also possible that when mapping, responses are attained from the intramedullary root of the facial nerve instead of

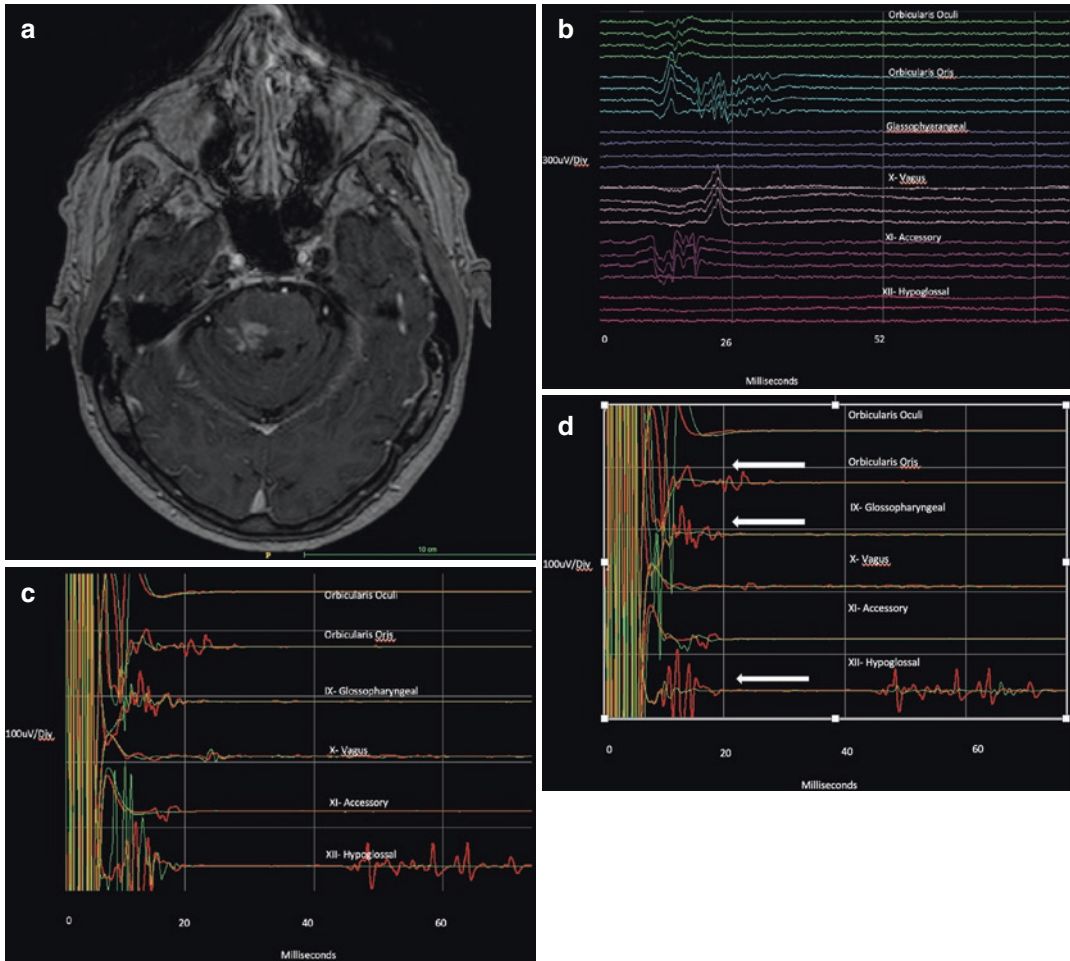


Fig. 25.3 (a–d) A 60-year-old male presented with progressive neurological deficits including right facial pain, ataxia and severe facial palsy. The MRI disclosed a patchily enhancing intrinsic brainstem lesion at the level of the right pons. (a) The patient continued to deteriorate clinically despite the use of corticosteroids and an open biopsy was planned for diagnosis. (b) Neurophysiological mapping near the infra-facial triangle was performed with a concentric bipolar probe at 0.1 mA. CMAP responses were obtained from the right side for the cranial nerve VII (Orbicularis Oris and Oculi), X and IX prior to biopsy. Threshold was therefore adjusted to a lower intensity (0.05 mA) and the surgeon continued to map more selectively until no responses were found, and the area with no CMAP responses was determined as the entry zone for biopsy. Opening baselines corticobulbar MEPs (CoMEPs) were recorded with a C3/CZ dipole, a train of 5 stimulation, duration 0.2 ms at 100 mA for cranial nerves VII,

IX-X, and XII (c). However, during the biopsy, a sudden amplitude decrease greater than 50% was observed, specifically for the facial (orbicularis oris), glossopharyngeal and hypoglossal nerve (d), arrows illustrate decrease in amplitude). The surgeon was immediately informed and the surgical field was irrigated with warm saline. Anesthetic and systemic baselines remained unchanged at the time of the event. Surgery was paused for a few minutes to allow responses to improve. Responses partially recovered in amplitude towards the end of surgery, but did not return to baseline values and required an increase in stimulation intensity in order to remain stable. Postoperatively the patient presented with only a moderate, transient, worsening of the preoperative facial palsy and a transitory weakness of the tongue muscles. Worsening of corticobulbar MEPs likely reflected a transient impairment of these tracts due to surgical maneuvers of traction to collect specimens for the biopsy

the nuclei, therefore resulting in a peripheral response despite injury to the motor nuclei leading to facial palsy [13].

Although mapping has its shortcomings it is still considered an indispensable tool for facial mapping, which makes identifying the facial nerve/nuclei possible when the anatomy is unclear.

Facial Nerve Monitoring: Free-Running Electromyography

Mapping serves only to identify the facial colliculus, whilst continuous monitoring techniques are necessary to assess the functional integrity of the facial nerve during surgery. Free-running electromyography (Fr-EMG) monitoring consists of spontaneous activity from the cranial nerves innervated by muscles of the facial nerve, in the absence of electrical stimulation. Neurotonic discharges can be seen in the Fr-EMG in response to surgical maneuvers that may indicate injury to the facial nerve. Irritation to the facial nerve produces either burst or train patterns [27]. Burst patterns are paroxysmal simple or polyphasic EMG patterns with a short duration which have been associated with direct mechanical trauma, irrigation, or electrocautery. Trains are more of a concern as they have a longer duration and are composed of repetitive high frequency discharges. Trains are divided into three categories: A, B, and C train. The A train is best described as a sinusoidal shape with a high inter-peak frequency with sudden onset and termination. The A train is considered the only pattern to clearly indicate postoperative paresis with high sensitivity and specificity. Yet, experience with the use and interpretation of A-trains refer almost exclusively to the facial nerve Fr-EMG during surgery for vestibular schwannomas [28], rather than brainstem surgery. Furthermore, no experience on A-train monitoring for other motor cranial nerves has been reported so far.

Facial Motor-Evoked Potentials

In the past two decades, there has been a greater focus on a more reliable technique to monitor the facial and lower cranial motor nerves known as corticobulbar MEPs [13]. Similarly, to the definition of A-trains, this technique was also originally implemented for the monitoring of the facial nerve during surgery for vestibular schwannomas [29]. CoMEPs assess the functional integrity of the entire corticobulbar pathway from the cortex to the muscle. It is valuable because on one hand it allows direct monitoring of an evoked potential throughout the entire corticobulbar pathway, rather than the registration of the spontaneous activity of the nerve and muscle. On the other hand, being a monitoring technique, it provides the continuous assessment of the functional integrity of this pathway, rather than only an intermittent mapping of the motor cranial nuclei or nerve. This technique represents, in fact, the extension of TES MEPs for limb muscles to the muscles innervated by motor cranial nerves. Facial CoMEPs are elicited through TES using a train of 4 stimuli, 0.5 ms duration at a rate of 1–2 Hz. Stimulus intensities can range from 60–150 mA. Recording electrodes are commonly placed in both orbicularis oris and oculi; however, they may be placed in any of the muscles innervated by the facial nerve. The stimulation electrode montage comprises C3/Cz for right sided muscles and C4/Cz for left side muscles. This particular montage is preferred as it reduces the spread of activation of the corticobulbar pathways deep in the brain or at the level of the brainstem which could lead to the direct stimulation of the peripheral facial nerve, producing false-negative results. A single versus train stimuli should be used to differentiate between centrally conducted and peripheral muscle responses [2, 30]. Warning criteria is not currently standardized; however, a baseline drop in amplitude of 50–80% is indicative of, at least, a transient facial palsy [29, 31].

Surgery of the Medulla Oblongata

Tumors located in the area of the foramen magnum or along the clivus often lead to surgery in the vicinity of the medulla oblongata. The medulla oblongata contains a high density of long tracts and lower cranial nerve nuclei which contribute to the significant risk of neurological morbidity. The lower cranial nerves consist of bilateral glossopharyngeal, vagus, accessory and hypoglossal nerves. The motor nuclei of these nerves are situated within the medulla oblongata. These nerves can be monitored [32] and need to be preserved as they are responsible for the functional gag reflex, swallowing, function of the vocal cords, and movement of the tongue and neck muscles. Damage to these nerves may lead to functional loss causing dysphagia, dysarthria, dysphonia, absent gag reflex, hypoglossal weakness as well as atrophy of the tongue [33, 34].

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

The mapping of the lower cranial nuclei is conducted in the same manner as the facial colliculus, with stimulation parameters remaining unchanged. It is important to keep in mind the location of the medulla, as it is situated in the region of the cardiovascular centers, therefore stimulation intensities should not exceed 2 mA as it can cause bradycardia or even cardiac arrest (Fig. 25.4) [27, 35].

Hook-wire electrodes are placed in the muscles innervated by the lower cranial nerves. Placement most often occurs in the posterior wall of the pharynx and on the tongue muscle, but in other instances, a recording electrode can be placed either directly on the endotracheal tube bilaterally or percutaneously at the level of the cricoid cartilage [27, 36]. The trapezius muscle is the muscle of choice when recording CMAPs from the accessory nerve [27].

Lower Cranial Nerve Monitoring

Free-running electromyography: Currently, the facial nerve in acoustic neuroma surgery is the only cranial nerve which has been found to present predictive values concerning outcomes. The reliability of free-running EMG for all other motor cranial nerves is still heavily debated [37].

Lower Cranial Corticobulbar-Evoked Potentials

Just as with the facial nerve, CoMEPs are performed on the lower cranial nerves with the same stimulation parameters and recordings are obtained from the same muscles used for mapping. CoMEPs can be difficult to obtain as responses can be unstable for IX/X cranial nerves due to the influence of spontaneous EMG activity, unlike the XII cranial nerve recorded from the tongue, which are usually more stable and reliable in CoMEP monitoring.

Brainstem Reflexes and Other Monitoring Techniques

In recent years, there has been an increased interest in monitoring brainstem reflexes when complex pathways are at severe risk. However, due to the polysynaptic organization of these pathways, responses can be unstable during general anesthesia, contributing to the difficulty of preserving or even eliciting responses.

The trigeminal somatosensory system is responsible for the sensation to the face and the anterior two thirds of the tongue. This is useful in surgeries involving the cavernous sinus or skull base surgeries. Recording electrodes are placed on the scalp in the area pertaining to the facial homunculus of the post central gyrus. Sensory nerves are tested by placing stimulation electrodes on the V2 and V3 branches of the trigeminal nerve [6].

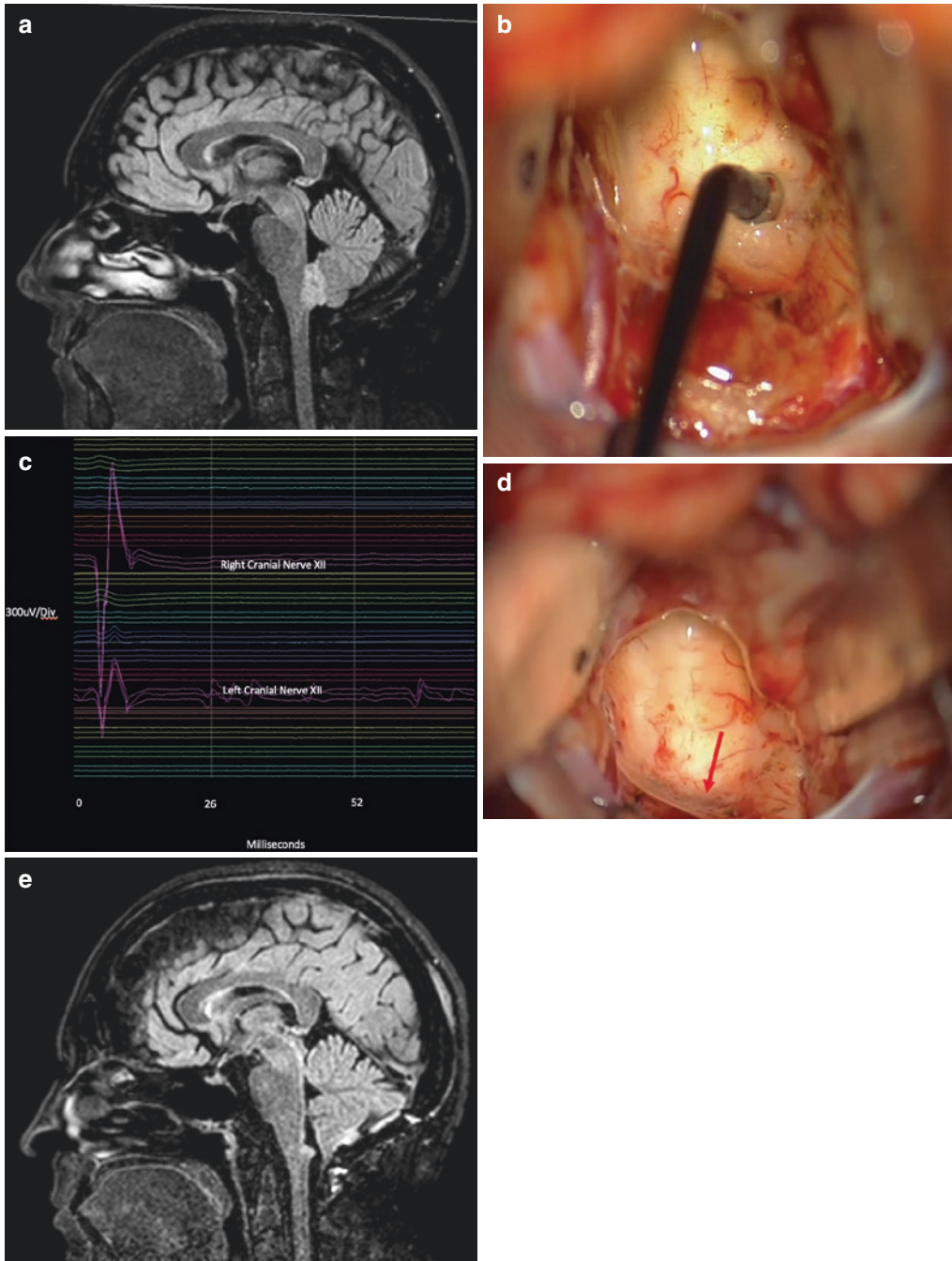


Fig. 25.4 (a) Preoperative sagittal flair MRI of a 50-year-old female incidentally diagnosed with a fourth ventricle lesion likely infiltrating the lower floor of the ventricle. (b) After 4 months, at a follow-up MRI the lesion appeared to have grown in size and surgery was therefore recommended. During surgery, mapping was performed using a bipolar concentric probe, on the floor of the fourth ventricle, to identify the motor nuclei of the lower cranial nerves. (c) A bilateral response was obtained from the cranial nerve XII at 0.5 mA, when stimulating the upper bor-

der of the infiltrating section of the tumor. A similar response was found when stimulating the infiltrating part. Traction in this area of tumor consistently resulted in marked bradycardia and even transitory cardiac arrest. The decision was therefore made to stop further resection of the tumor, leaving behind a small remnant of tumor (d, arrow). (e) Final pathology was ependymoma. The patients woke up with no neurological deficits and the postoperative MRI confirmed a near-total resection

The Blink Reflex has been well described by Deletis et al. in 2009, as a useful technique in the evaluation of the hyperexcitability of the motor axons of cranial nerve VII [38]. The Blink reflex corresponds to oligosynaptic reflex of the afferent pathway—the nasociliary branch of the ophthalmic branch (V1) of the trigeminal nerve, and an efferent pathway—temporal and zygomatic branches of the facial nerve. Stimulation occurs at the supraorbital nerve of either side of the face. Stimulation parameters are performed with a 1 to 7 rectangular constant-current stimulus with an interstimulus interval of 2 ms at an intensity ranging between 20 and 40 mA, and a repetition rate of 0.4 Hz. Recording electrodes are placed in the low lateral section of the orbicularis oculi muscle ipsilateral to the stimulation side.

Sinclair et al. 2017 [39] introduced a novel monitoring method which assesses the integrity of the laryngeal and vagus nerves by utilizing the laryngeal adductor reflex (LAR). The LAR has a vital role in protecting the larynx from aspiration. The LAR was obtained under general anesthesia, via the endotracheal tube-based surface electrodes. This technique monitors the complete vagal reflex arc, combining the sensory, motor, and brainstem pathways. The LAR is elicited by electrical stimulation of the laryngeal mucosa on the contralateral side of the operating field. Responses can be elicited either with a single stimulus with a 1 ms duration or stimulated with a train of 2 pulse stimuli with an ISI of 2–4 ms at a maximum intensity of 4 mA. In their study, they found that LAR responses which had a decrease in amplitude and increased latency were influenced by surgical maneuvers that either stretched or directly caused compression of the right laryngeal nerve (RLN). It was further noted that changes to the LAR only occurred when the RLN was in the range of the surgical field. None of their patients had intraoperative total reflex loss and postoperatively none had signs of vocal cord paralysis, further confirming the importance of this monitoring method as an adjunct to the current lower cranial nerve IOM techniques. Since the LAR is mediated at the level of the lower brainstem, it could indirectly provide information on its functional integrity. Recently, this

technique has been applied also during surgery in the brainstem and the cerebellopontine angle, with promising results [40].

Conclusion

The brainstem is known to have a complex intracranial anatomy along with being one of the most intricate structures in the human body. The risk of iatrogenic damage as a result of surgery in and around the brainstem remains very high even for the most experienced neurosurgeon.

Although maximum early resection improves the oncological prognosis, neurosurgical procedures are constrained by a rigorous evaluation of the compromise between radicality and preservation of healthy tissue: in defining the “safety margin,” the surgeon’s ability to map and monitor essential structures is fundamental to preserve a good quality of life for the patient and limit functional damage. Based on this, intraoperative monitoring (IOM) is a critical tool for indicating an impending intraoperative injury and as well as predicting postoperative outcomes.

IOM mapping techniques have been found to be particularly helpful in determining the safe entry zone with intrinsic and focal brainstem lesions. In order to achieve the best postoperative outcomes, a multimodality approach is required as unilaterally they might not provide sufficient information on the overall picture of the nervous system during surgery. This was found to be the case in SEPs and BAEPs techniques where these modalities only focus on a small section of the brainstem, without confirming the presence of focal injury despite preservation of responses. MEPs and CoMEPs are good indicators of motor outcome especially with Cranial nerves VII, IX/X, and XII. CoMEPs in the lower cranial nerves still present some challenges and further studies are required to produce more robust responses. With the recent novel techniques suggested for monitoring brainstem reflexes, we are beginning to have the techniques required to monitor the afferent pathways of the lower brainstem reflexes, further contributing to the reliability of brainstem monitoring.

References

- Cucu AI, et al. The brainstem and its neurosurgical history. *Neurosurg Rev.* 2021;44(6):3001–22.
- Sala F, D'Amico A. Intraoperative neurophysiological monitoring in brainstem surgery. In: Jallo G, Noureidine MHA, Shimony N, editors. *Brainstem tumors*. Springer; 2020. p. 109–30.
- Yang Y, et al. Analysis of safe entry zones into the brainstem. *Neurosurg Rev.* 2019;42(3):721–9.
- Cavalcanti DD, et al. Anatomical and objective evaluation of the main surgical approaches to pontine intraxial lesions. *World Neurosurg.* 2019;121:e207–14.
- Slotty PJ, et al. Intraoperative neurophysiological monitoring during resection of infratentorial lesions: the surgeon's view. *J Neurosurg.* 2017;126(1):281–8.
- Deletis V, Fernández-Conejero I. Intraoperative monitoring and mapping of the functional integrity of the brainstem. *J Clin Neurol (Seoul, Korea).* 2016;12(3):262–73.
- Sala F, Amico A, Bricolo A. Chapter 22: Surgery of brainstem lesions. Academic Press; 2020.
- Morota N, Deletis V. The importance of brainstem mapping in brainstem surgical anatomy before the fourth ventricle and implication for intraoperative neurophysiological mapping. *Acta Neurochir.* 2006;148(5):499–509.
- Fahlbusch R, Strauss C. Surgical significance of brainstem cavernous hemangiomas. *Zentralbl Neurochir.* 1991;52:25–32.
- Neuloh G, Bogucki J, Schramm J. Intraoperative preservation of corticospinal function in the brainstem. *J Neurol Neurosurg Psychiatry.* 2009;80(4):417–22.
- Kodama K, et al. Conjunct SEP and MEP monitoring in resection of infratentorial lesions: lessons learned in a cohort of 210 patients. *J Neurosurg.* 2014;121(6):1453–61.
- Dong CCJ, et al. Intraoperative facial motor evoked potential monitoring with transcranial electrical stimulation during skull base surgery. *Clin Neurophysiol.* 2005;116(3):588–96.
- Morota N, Ihara S, Deletis V. Intraoperative neurophysiology for surgery in and around the brainstem: role of brainstem mapping and corticobulbar tract motor-evoked potential monitoring. *Childs Nerv Syst.* 2010;26(4):513–21.
- Nunes RR, Bersot CDA, Garritano JG. Intraoperative neurophysiological monitoring in neuroanesthesia. *Curr Opin Anaesthesiol.* 2018;31(5):532–8.
- Koht A, Sloan TB, Toleikis JR. *Monitoring the nervous system for anesthesiologists and other health care professionals*. 2nd ed. Cham: Springer International Publishing AG; 2017.
- Gruenbaum BF, Gruenbaum SE. Neurophysiological monitoring during neurosurgery: anesthetic considerations based on outcome evidence. *Curr Opin Anaesthesiol.* 2019;32(5):580–4.
- Ishihara H, et al. The role of intraoperative monitoring of oculomotor and trochlear nuclei-safe entry zone to tegmental lesions. *Minim Invasive Neurosurg.* 2006;49(3):168–72.
- Sala F, Manganotti P, Tramontano V, Bricolo A, Gerosa M. Monitoring of motor pathways during brain stem surgery: what we have achieved and what we still miss? *Neurophysiol Clin.* 2007;37(6):399–406. <https://doi.org/10.1016/j.neucli.2007.09.013>.
- Schlacke HP, et al. Intra-operative electromyographic monitoring of extra-ocular motor nerves (Nn. III, VI) in skull base surgery. *Acta Neurochir.* 2001;143(3):251–61.
- Sekiya T, et al. Intraoperative electrophysiological monitoring of oculomotor nuclei and their intramedullary tracts during midbrain tumor surgery. *Neurosurgery.* 2000;47(5):1170–7.
- Deletis V, Sala F, Morota N. Intraoperative neurophysiological monitoring and mapping during brain stem surgery: a modern approach. *Oper Tech Neurosurg.* 2000;3:109–13.
- Legatt AD. Brainstem auditory evoked potentials: methodology, interpretation, and clinical application. In: Aminoff, editor. *Electrodiagnosis in clinical neurology*. New York: Churchill Livingstone; 2005. p. 489–523.
- Simon MV. Neurophysiologic intraoperative monitoring of the vestibulocochlear nerve. *J Clin Neurophysiol.* 2011;28(6):566–81.
- Strauss C, Romstöck J, Fahlbusch R. Pericolicular approaches to the rhomboid fossa. Part II. Neurophysiological basis. *J Neurosurg.* 1999;91(5):768–75.
- Lang JJ, Ohmachi N, Lang Sen J. Anatomical landmarks of the rhomboid fossa (floor of the 4th ventricle), its length its width. *Acta Neurochir.* 1991;113(1–2):84–90.
- Tanrikulu B, Özek MM. *Clinical presentation and assessment for brainstem tumors*. Cham: Springer International Publishing; 2020. p. 95–108.
- Skinner SA. Neurophysiologic monitoring of the spinal accessory nerve, hypoglossal nerve, and the spinomedullary region. *J Clin Neurophysiol.* 2011;28(6):587–98.
- Romstöck J, Strauss C, Fahlbusch R. Continuous electromyography monitoring of motor cranial nerves during cerebellopontine angle surgery. *J Neurosurg.* 2000;93(4):586–93.
- Dong CCJ, MacDonald DB, Akagami R, Westerberg B, AlKhani A, Kanaan I, et al. Intraoperative facial motor evoked potential monitoring with transcranial electrical stimulation during skull base surgery. *Clin Neurophysiol.* 2005;116:588–96.
- Téllez MJ, Ulkatan S, Urriza J, Arranz-Arranz B, Deletis V. Neurophysiological mechanism of possibly confounding peripheral activation of the facial nerve during corticobulbar tract monitoring. *Clin Neurophysiol.* 2016;127(2):1710–6.
- Acioly MA, et al. Facial nerve monitoring during cerebellopontine angle and skull base tumor surgery: a systematic review from description to current

- success on function prediction. *World Neurosurg.* 2013;80(6):e271–300.
32. Martinez ARM, et al. Electrophysiology of cranial nerve testing: cranial nerves IX and X. *J Clin Neurophysiol.* 2018;35(1):48–58.
33. Procaccio F, Gambin R, Gottin L, Bricolo A. Complications of brain stem surgery: prevention and treatment. *Oper Tech Neurosurg.* 2000;3:155–7.
34. Horn-Bochtler AKE, Büttner-Ennever JA. Neuroanatomy of the brainstem. In: *Brainstem disorders.* Springer; 2011. p. 1–35.
35. Suzuki K, Matsumoto M, Ohta M, Sasaki T, Kodama N. Experimental study for identification of the facial colliculus using electromyography and antidromic evoked potentials. *Neurosurgery.* 1997;41:1130–6.
36. Singh R, Husain AM. Neurophysiologic intraoperative monitoring of the glossopharyngeal and vagus nerves. *J Clin Neurophysiol.* 2011;28(6):582–6.
37. Schlake HP, Goldbrunner RH, Milewski C, Krauss J, Trautner H, Behr R, Sörensen N, Helms J, Roosen K. Intra-operative electromyographic monitoring of the lower cranial motor nerves (LCN IX–XII) in skull base surgery. *Clin Neurol Neurosurg.* 2001;103(2):72–82.
38. Deletis V, Urriza J, Ulkatan S, Fernandez-Conejero I, Lesser J, Misita D. The feasibility of recording blink reflexes under general anesthesia. *Muscle Nerve.* 2009;39:642–6.
39. Sinclair CF, et al. A novel methodology for assessing laryngeal and vagus nerve integrity in patients under general anesthesia. *Clin Neurophysiol.* 2017;128(7):1399–405.
40. Téllez MJ, et al. Neurophysiological monitoring of the laryngeal adductor reflex during cerebellar-pontine angle and brainstem surgery. *Clin Neurophysiol.* 2021;132(2):622–31.
41. Sala F, Gallo P, Tramontano V. Intraoperative neurophysiological monitoring in posterior fossa surgery. In: Ozek M, Cinalli G, Maixner WJ, Sainte-Rose C, editors. *Posterior fossa tumors in children.* Springer; 2015. p. 239–62.