Intraoperative Neurophysiology During Intracranial Surgery in Children

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Introduction

Over the past 15 years, intraoperative neurophysiological monitoring (IONM) has established itself as an important clinical discipline. It aims, first, to prevent neurological deficits induced by surgery and, second, to predict functional outcome. IONM also documents the moment when injury to the neural pathways, if any, occurs. This last aspect, besides its medicolegal implications, retains educational value for young neurosurgeons. Nowadays, IONM is considered of great value during neurosurgical procedures in functionally eloquent areas of the nervous system, especially in pediatric neurosurgery.

IONM comprises two different though related aspects: monitoring and mapping. Monitoring

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continuously assesses the functional integrity of specific neural pathways by testing them as frequently as possible, giving a real-time feedback to the surgeon. Somatosensory evoked potentials (SEPs) and brainstem auditory evoked potentials (BAEPs) had been the only techniques available for many years. The advent of transcranial muscle motor evoked potentials (mMEPs) in the mid-1990s made possible the evaluation of the motor pathways under general anesthesia. In contrast, mapping enables the surgeon to localize neural structures in the midst of ambiguous tissues and whenever anatomical landmarks are not easily recognizable. As a consequence, a precise identification of these structures leads to safer surgery. For example, direct neurophysiological mapping localizes the primary motor cortex or the cranial nerve motor nuclei on the floor of the fourth ventricle, allowing the selection of safe entry zones by avoiding the motor strip and the brainstem motor nuclei, respectively.

In pediatric neurosurgery similar techniques can be used with certain limitations to adjust for the immaturity of the young nervous system, especially in infants.

Development of Motor Pathways in Children and Its Impact on IONM

The immaturity of the motor system in young children demands modifications of the IONM techniques used in pediatric neurosurgery.

Studies of human corticospinal tract (CST) development have shown that CST axons reach the medulla by 8 weeks postconceptional age (PCA) and the lower cervical spinal cord by 24 weeks PCA (Humphrey 1960; O'Rahilly and Muller 1994). Corticospinal connections reach the sacral levels between 18 and 28 weeks PCA and are completed at birth (Eyre et al. 2002, 2000), when the myelination process begins in earnest, and the expression of neurofilament is easily detectable.

These developmental findings are confirmed by neurophysiological studies, which show that functional synaptic corticospinal connections to the spinal motor neurons and interneurons are made mainly during the last trimester of pregnancy (Eyre et al. 2000). Such early connections appear to be important in the later activation of the corticospinal system and in guiding the development of the primary motor cortex and the spinal motor centers (Eyre et al. 2000, 2001).

There is, however, a discrepancy between the anatomical and neurophysiological development of the motor pathways. The neurophysiologic maturation of the CST progresses throughout childhood and adolescence, while the anatomic maturation is usually completed much earlier (Muller et al. 1991). The CST is the only spinal cord tract not fully myelinated at birth. Whereas myelination of the CST to the lumbar spinal cord occurs between the first 2 years of age (Kubis and Catala 2003), the electrophysiological maturation of the CST innervating the hand muscles is not complete till the age of 13 years (Armand et al. 1996; De Witt Hamer et al. 2012). Moreover, in the newborn there is bilateral innervation from each motor cortex to the spinal motor neuronal centers, so that focal transcranial magnetic stimulation (TMS) of one motor cortex evokes responses both in the ipsilateral and contralateral muscles. Interestingly, the responses from both sides have similar thresholds and amplitudes, but the onset latencies are shorter in the ipsilateral side, due to the shorter distance of the ipsilateral pathway (Eyre et al. 2001).

TMS studies also suggest that the motor threshold of the crossed CST increases during the first 3 months of age (Eyre et al. 2001) and then decreases gradually till early adolescence, when the adult value is reached (Masur et al. 1995; Muller et al. 1991; Nezu et al. 1997). The crossed central motor conduction time decreases accordingly during childhood (Eyre et al. 2001; Fietzek et al. 2000; Masur et al. 1995; Muller and Homberg 1992; Muller et al. 1991, 1997; Nezu et al. 1997, 1999), together with other age-related changes such as an increase in MEP amplitude and variable changes in MEP latencies depending on stimulation parameters (Caramia et al. 1993) and the subjects' heights (Koh and Eyre 1988). These electrophysiological changes correspond well with histological evidence of anatomic maturation of the motor tracts.

Supratentorial Surgery

The treatment of adult intracranial gliomas has significantly evolved over the past 15 years. In particular, there is a tendency toward a more aggressive surgical treatment of low-grade gliomas and increasing reluctance to adopt a "wait-and-see" policy. This is true also for pediatric brain tumors because of the strong association between extent of resection and good outcome (Berger et al. 1998; Duffner et al. 1998; Wisoff et al. 1998).

A recent large meta-analysis on the results of glioma surgery in adults has shown that tumor resection near eloquent areas of the brain using intraoperative brain mapping techniques showed a 50% reduction in the incidence of severe neurological deficits compared to equivalent surgery without IONM, with no compromise in the extent of resection (De Witt Hamer et al. 2012).

Thus, the goal of surgery is to maximize tumor resection while minimizing morbidity. To maintain the integrity of neurological functions is a prerequisite to warrant preservation of quality of life. Nowadays, considering the increase in survival rates of low-grade tumors, this aspect has become critical in pediatric brain tumor surgery.

The following is a summary of the main IONM techniques currently used in pediatric supratentorial surgery.

Somatosensory Evoked Potential (SEPs) and Phase Reversal Technique

SEPs are elicited when peripheral nerves are stimulated. The electrical stimulus causes a depolarization in proprioceptive fibers, and then the stimuli run along the ipsilateral dorsal column and cross the midline via the medial lemniscus to the contralateral ventral posterior lateral thalamic nucleus, eventually reaching the primary somatosensory cortex. The most common nerves used for SEP monitoring are the median nerve at the wrist and the posterior tibial nerve at the ankle. The intensity of stimulation ranges from 20 to 40 mA, with a 0.2-ms duration and 4.3 Hz repetition rate. Recordings are obtained at Cz-Fz for the lower extremity and C3/C4-Cz for the upper extremity.

Monitoring the SEPs can be useful during resection of tumors involving or adjacent to the medial lemniscal pathway or the primary sensory cortex. Furthermore, SEPs are extremely valuable in identifying the central sulcus and, indirectly, the adjacent primary motor cortex. The so-called phase reversal technique is used for central sulcus identification (Fig. 1a). The principle is that the polarity of the SEPs waveform is reversed when the recording electrodes are gradually moved from the primary sensory cortex posterior to the central sulcus to the primary motor cortex anterior to the sulcus (Cedzich et al. 1996; Wood et al. 1988). Once the craniotomy is made, a strip electrode with four to eight stainless steel contacts and an intercontact distance of 1 cm is placed perpendicularly across the suspected central sulcus. Recordings from the electrodes overlying the primary sensory cortex typically show a N20-P30 dipole where "N" and "P" indicate the polarity of the response (negative is upward, positive is downward), as well as the latency in milliseconds. Due to the cytoarchitecture of the central sulcus, a mirror-image waveform with reversed N and P potentials is typically recorded from the contacts overlying the primary motor cortex (Cedzich et al. 1996; Romstock et al. 2000). If a clear phase reversal is not obtained, the procedure can be repeated modifying the orientation of the strip electrode until the reversed dipole is identified. The success rate of this technique ranges between 91% (Cedzich et al. 1996; King and Schell 1987) and 97% (Kombos et al. 2000) and may be affected by the distortion of the normal anatomy due to the mass effect of intra-axial tumors. If the motor cortex is not directly exposed, as in a temporal craniotomy, the multicontact strip can still be slid underneath the dura and be advanced until it overlaps the central area (Berger 1996).

Once the motor strip has been identified by the phase reversal technique, the same contacts overlapping the primary motor cortex can be used as anode to stimulate the motor cortex directly, keeping Fz as cathode. At that point, the strip should be left in a position that does not interfere with the operation and reoriented along the length of the precentral gyrus. This would permit the use of different individual electrodes to stimulate

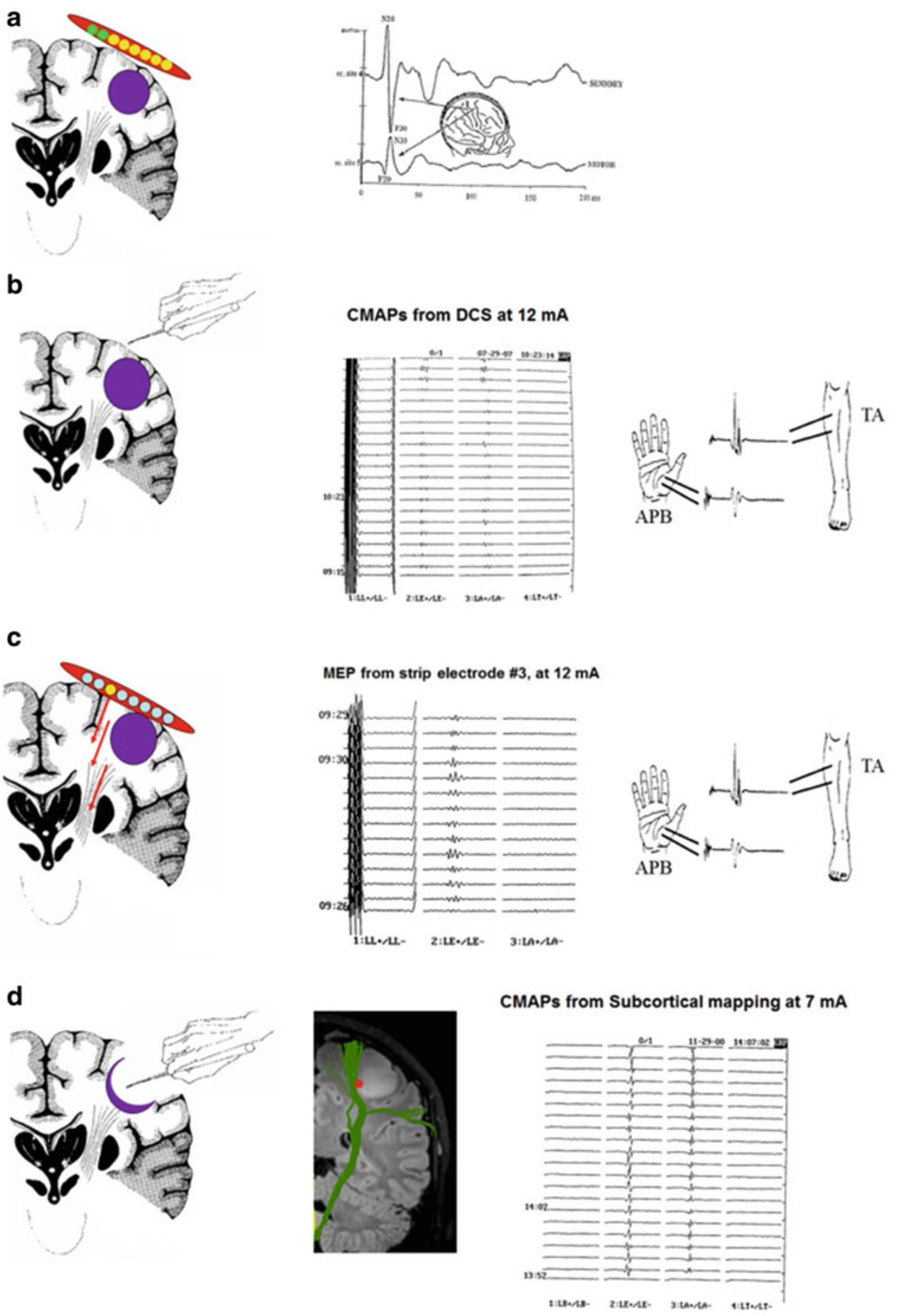


Fig. 1 Methodology for phase reversal, cortical mapping, MEP monitoring, and subcortical mapping. (**a**) Phase reversal technique. *Left:* an 8-contact strip electrode is placed across the expected central sulcus. (For purposes of illustration, the strip is seemingly placed along the coronal plane on the brain drawing, but is in fact in an oblique parasagittal plane, with its left side in a posterior position and its right side anterior.) Cortical somatosensory evoked potentials are recorded from the more posterior electrodes (*green*). *Right:* An inversion of the polarity

different parts of the motor homunculus (i.e., the medial electrodes for the lower extremity muscles and more lateral electrodes for the upper extremity and orofacial muscles). The best electrode to elicit a motor evoked potential is usually the one which generates the SEP mirror waves with the largest amplitude (Cedzich et al. 1996; Sala et al. 2002).

The phase reversal technique is of particular value in younger children where eliciting a motor response through direct cortical stimulation of the motor areas can be challenging due to the immaturity of the descending pathways.

Direct Cortical Stimulation, Subcortical Stimulation, and Motor Evoked Potential (MEP) Monitoring

Penfield's Technique Versus Short Train of Stimuli

Direct cortical stimulation (DCS) is an old technique, popularized in the first half of the last century by Wilder Penfield in Montreal (Penfield and Boldrey 1937), although it was already in use in Europe since the late nineteenth century (Bartholow 1874). The first report of the use of DCS in children is attributed to Penfield. In a 4-year-old girl with tuberous sclerosis, Penfield recorded by electrocorticography (ECoG) a well-localized spike focus over the right mid-central region of her primary motor cortex. While performing DCS of this area to reproduce her seizures and auras, he elicited a sensation in her left hand, followed by a left clonic seizure. Since then, DCS in children has been used mainly in epilepsy surgery, while reports of this technique in brain tumor surgery have remained anecdotal for a long time.

According to the 10–20 EEG system, the motor cortex is usually located around 45–50 mm behind the coronal suture in the midline. However, in young children the motor strip is often more anterior; in children younger than 3 years, the primary strip, or M1, can be located just 20 mm behind the coronal suture (Rivet et al. 2004). Thus, in young children, a craniotomy extending 2–3 cm behind the coronal suture may be enough to expose the motor cortex for placement of the stimulating electrodes.

For many years in pediatric neurosurgery, DCS has traditionally been performed using Penfield's technique (Berger et al. 1989; Jayakar 1993; Riviello et al. 2001; Stapleton et al. 1997), which is characterized by a continuous cortical stimulation over a few seconds with a frequency of 50–60 Hz and a biphasic stimulus of 0.5-millisecond (ms) duration. An initial intensity of 4 mA is used, and if no response is elicited, the intensity is increased in steps of 2 mA till movements are recorded in the contralateral muscles, up to a maximum current intensity of 18–20 mA. If no responses are recorded with intensity up to 20 mA, that part of the cortex is considered not functional. However, before labeling a cortical area as nonfunctional, it is essential to repeat the stimulation for consistency and to exclude any technical problem. In general, a stimulation study that is entirely negative never provides adequate security to plan a resection, unless there is a

Fig. 1 (continued) occurs across the central sulcus; the best electrode to perform a continuous MEP monitoring is the first one in front of the central sulcus (*yellow* electrode in panel **c**). (**b**) *Left*: A handheld monopolar stimulation probe with current of 12 mA is used to perform the direct cortical stimulation (*DCS*). *Middle:* compound muscle action potentials (*CMAPs*) are recorded from the contralateral APB and forarm extensor (in vertical column marked 2:LE+/LE) and abductor pollicis brevis (*APB*) (in vertical column marked 3: LA+/LA). *Right*: schematic illustration of recording needle electrodes inserted in contralateral APB and tibialis anterior (*TA*). (**c**) *Left:* Continuous monitoring of contralateral mMEPs is performed using direct cortical stimulation, obtained from the strip electrode number 3 (*yellow*) at 12 mA. *Middle:* response recorded from the left forarm extensor displayed in column marked 2: LE+/LE. *Right:* schematic illustration of recording needle electrodes inserted in contralateral APB and tibialis anterior (*TA*). (**d**) *Left:* Subcortical mapping is performed toward the end of tumor removal to localize the corticospinal tract. *Middle:* The point of subcortical stimulation is indicated in red in the neuronavigation system, proximal to the corticospinal tract. *Right: CMAPs* from contralateral upper extremity muscles are elicited through subcortical mapping, at 7 mA. (Reprinted from Sala et al. (2015b)) severe or even complete preoperative deficit. In children younger than 6–7 years, however, the functional immaturity of the motor system can further limit the success rate of DCS (Sala et al. 2002; Deletis and Sala 2012).

Penfield's technique, popularized by Ojemann (1991) and Berger et al. (1989) in the 1990s, was very popular in the past two decades, and it is still considered a standard method nowadays to perform cognitive mapping, but it has some disadvantages. The main problem is the very prolonged stimulation and, consequently, the high incidence of intraoperative seizures, with an incidence as high as 20% (Ojemann 1991; Szelényi et al. 2007). A prompt irrigation of the cortex with cold ringer lactate is usually effective in stopping seizures (Sartorius and Berger 1998) without using other pharmacological treatment such as short-acting barbiturates, which may decrease the excitability of the cortex and, consequently, interfere with further mapping and monitoring. The cortical stimulation is usually made under electrocorticographic monitoring in order to promptly identify afterdischarges, which anticipate clinical seizures. Electrocorticography also distinguishes afterdischarges from the actual mapping results and avoids misinterpretation (Blume et al. 2004; Chitoku et al. 2001; Gallentine and Mikati 2009). Another limitation of Penfield's technique is its inability to provide continuous monitoring because of its stimulation parameters, so that the functional integrity of the motor pathways cannot be assessed continuously during surgery. This may leave the patient exposed to the risk of undetected injury, such as due to vascular compromise. The third and most important limitation of this technique is the very low success rate when used in children under the age of 5–6 years (Duchowny and Jayakar 1993; Resnick et al. 1988; Riviello et al. 2001; Sala et al. 2002). Penfield's technique, therefore, remains valuable only for language and other cognitive mapping, and since this requires an awake and cooperative patient, it is of very limited use in the pediatric population.

For motor mapping, the so-called short train of stimuli technique became available in the mid-1990s, and, since then, it has progressively replaced Penfield's technique (Ng et al. 2010). The short-train technique was introduced to allow continuous monitoring of muscle motor evoked potentials (mMEPs) during transcranial electrical stimulation (TES) of the brain.

In the 1980s, Merton and Morton found that transcranial stimulations with a high-voltage single electrical pulse could activate the motor cortex and the motor pathways, generating mMEPs (Merton 1980). Unfortunately, TES in awake patients was very painful, and this technique could not be used during general anesthesia, because a single stimulus could not elicit a muscle response due to the blocking effect of anesthetics at the level of the alpha motor neurons. With the discovery of the multipulse technique (Pechstein et al. 1996), it became possible to elicit mMEPs under anesthesia using transcranial electrical stimulation, thanks to the generation of multiple descending volleys, which fire synchronously on the alpha motoneurons, therefore overcoming the effect of anesthesia. A short train of five to seven pulses (each of 0.5-msec duration and with interstimulus interval around 4.1 msec) applied to the skull is generally used to obtain mMEPs (Pechstein et al. 1996; Taniguchi et al. 1993). Following the International 10/20 EEG System, we usually place six electrodes for MEP monitoring: C1, C2, C3, C4, Cz-1 cm, and Cz + 6 cm. Corkscrew electrodes are preferentially used as these guarantee low impedance (Sala et al. 2010). To avoid penetrating injury, these electrodes should be carefully placed in infants under 12–18 months of age with open fontanels; when a shunt system is present, care should be taken to avoid intrusions into the tissues surrounding the subcutaneous catheter and/or valve. In these cases, the electrodes could be placed 2–3 cm away from their original position (Sala et al. 2010).

Muscle MEPs are recorded by placing needle electrodes in the contralateral limb muscles. The selection of muscles that have richer CST innervation is fundamental to obtain robust mMEPs during TES. The abductor pollicis brevis (APB) and the long forearm flexor or extensor have been shown to be good options for the upper limb (Taniguchi et al. 1993). Similarly, the abductor hallucis brevis is the best muscle for the lower extremities due to its dominant corticospinal innervation. For the orofacial muscles, the orbicularis oris and orbicularis oculi muscles are generally used, as well as the genioglossus and other muscles involved in the articulation of speech.

Different montages of the cranial electrodes can be used to optimize the elicitation of mMEPs without causing a vigorous muscle twitching, which can interfere with surgery. Usually, C1/C2 is a better electrode montage for eliciting mMEPs in the upper limb muscles, and a more median montage such as Cz-1 cm/Cz + 6 cm is advisable for the lower extremities. The more lateral electrode montages (C3/C4, C3/Cz, C4/Cz) can induce vigorous muscle twitching, and, if high stimulation intensities are used, these montages also incur a higher chance of activating the deeper portion of the corticospinal tract; the latter may result in false-negative results if the surgical trauma occurs more superficially, i.e., proximal to the point of activation of the corticospinal tract.

If the scalp electrodes interfere with the craniotomy incision, the electrodes have to be placed far from their standard position. As a consequence, obtaining mMEPs may require higher current intensities than usual, and this also may activate the CST deeper to the level of the surgery.

TES is considered a safe technique. Muscle MEPs elicited by multipulse transcranial electrical stimulation can be monitored during the surgical procedure even if the motor cortex is not exposed or when a direct cortical stimulation is not feasible, providing a continuous assessment of the motor pathways. In brain surgery and in brainstem surgery, the appearance of a significant drop in mMEP amplitude (range 50–80%) may be indicative of injury to the CST. A persistent decrease in amplitude or a reversible loss of the mMEPs may correlate with a transient motor deficit or, rarely, a permanent deficit. Complete disappearance of the mMEPs, on the other hand, strongly correlates with a permanent postoperative motor deficit (Neuloh et al. 2004).

In children younger than 4–5 years of age, higher stimulating thresholds may be needed due to the immaturity of the motor cortex and the subcortical motor pathways. However, this may be partially counterbalanced by the lower impedance of a thinner skull, which facilitates the activation of the motor cortex in TES (Sala et al. 2002, 2010).

Once the dura has been opened, mMEPs can be recorded following DCS from the strip electrodes. The advantage is that much lower current intensity is needed (less than 20 mA compared to up to 200 mA in TES), resulting in no muscle twitches and very low risk of distal activation of the CST.

The short-train technique, therefore, offers several advantages as it allows both continuous monitoring of mMEPs, through either TES or DCS, and mapping of the motor cortex through DCS (Fig. 1b, c). Anecdotal reports suggest that this technique has a significantly higher success rate for DCS than the traditional Penfield's technique, where the literature consistently reports poor efficacy in children younger than 5–6 years of age (Sala et al. 2002).

Bipolar Versus Monopolar Stimulation

Traditionally, Penfield's technique is performed using a bipolar handheld stimulator with two ball tips about 1 cm apart. In contrast, the short-train technique is usually performed through a monopolar probe, with a reference electrode that can be inserted in the temporalis muscle. It is important to clarify that *monopolar* and *bipolar* refer only to the characteristics of the stimulating probe but has nothing to do with the parameters of stimulation. With a monopolar stimulation, the current field is more diffuse, and the volume of brain tissue stimulated increases with the intensity of the stimulation, with the possibility of activating motor pathways at some distance (20–25 mm) from the point of stimulation. This lack of focality may be considered a disadvantage, but, in fact, it represents an advantage especially for subcortical stimulation because the surgeon can determine whether or not he is approaching the tract of interest judging by the threshold of stimulation. Conversely, with a bipolar stimulator, the electrical field is more circumscribed, and there is a lower risk of distal activation of the motor tracts, but the stimulation will produce no response unless the probe is almost directly on the tract, giving the surgeon a false sense of security operating close by.

Subcortical Mapping

The CST can be localized at a subcortical level using the same techniques for DCS (Fig. 1d). A short train of stimuli with the monopolar probe offers the best chance to obtain successful mapping (Szelenyi et al. 2011). In the past there was great interest to understand the relationship between the threshold current necessary to elicit a subcortical motor response (subcortical threshold) and the distance between the stimulation site and the CST itself. Although there are minor inconsistencies, current evidence suggests that a subcortical threshold current of 1 mA safely correlates with a 1 mm distance between stimulation site and the CST. In this regard, the lower the threshold is capable of eliciting a response, the higher is the risk of postoperative deficit; thus, if the threshold is lower than 3–4 mA, there is a significant risk of injury because the CST is only several millimeters away from the dissection (Nossek et al. 2011; Sala et al. 2003). Thresholds above 5 mA are usually considered safe (Figs. 2 and 3). While all these conclusions are culled from studies in adult patients, there are very scant data for subcortical mapping in children, and whether or not the same rule applies to children remains uncertain.

Mapping of Language

Nowadays, awake surgery is the gold standard when language and other cognitive functions are likely affected by the tumor. Modified anesthesia for awake surgery is well established for adult patients and has been used successfully in children aged 11–15 years (Soriano et al. 2000). Because awake surgery requires a cooperative and interactive patient, it is generally not feasible in young children (Balogun et al. 2014), particularly when subcortical stimulation, which is more time consuming, is required (Duffau et al. 2002; Keles et al. 2004). For children younger than 11 years and for those older children deemed unsuitable for awake surgery, a two-stage operation strategy can be applied. This consists in the implantation of subdural grids electrodes at the first operation, followed by selective grid electrode stimulation and cortical mapping after recovery from the first surgery (“extra-operative recording”), followed by the final surgical resection when all functional information has been acquired (Chitoku et al. 2001; Ojemann et al. 2003; Schevon et al. 2007).

In a study by Ojemann et al. (2003), localization of language function with awake DCS was possible in only 8 of 26 children, while in 18, the two-stage “extra-operative” functional localization technique had to be used. This study revealed that cortical language-related sites in younger children less than 8 years of age are mostly concentrated on the primary motor strip and the superior temporal gyrus, while in older children, the distribution of language-related cortical areas tends to be more diffuse, though not as widely distributed as in adults (Ojemann et al. 2003).

Extra-operative recordings with the subdural grid are especially indicated for epilepsy surgery, as it serves the dual purpose of functional mapping and accurate localization of seizure focus over a long period of time and under different physiological conditions. However, no information on the subcortical pathways can be acquired with the subdural grid.

Intraoperative neurophysiology for epilepsy surgery is beyond the scope of this chapter.

Infratentorial Surgery

The brainstem is a small but compact part of the central nervous system, with a high concentration of critical structures such as cranial nerve nuclei, neuronal circuits for the oculomotor and cough reflexes and swallowing mechanisms, sensory and motor pathways, cardiovascular and respiratory centers, and the reticular activating system. For this reason, surgical morbidity is significantly higher in the brainstem than in other brain areas, and a small injury can lead to debilitating functional deficits such as hemiplegia, dysphagia, and coma, or, in the worst case, death (Procaccio et al. 2000).

When the neurosurgeon approaches a tumor in the brainstem, the knowledge of its functional anatomy is fundamental while attempting to create a safe entry into the neural tissue, but such knowledge may not be enough when the normal anatomy

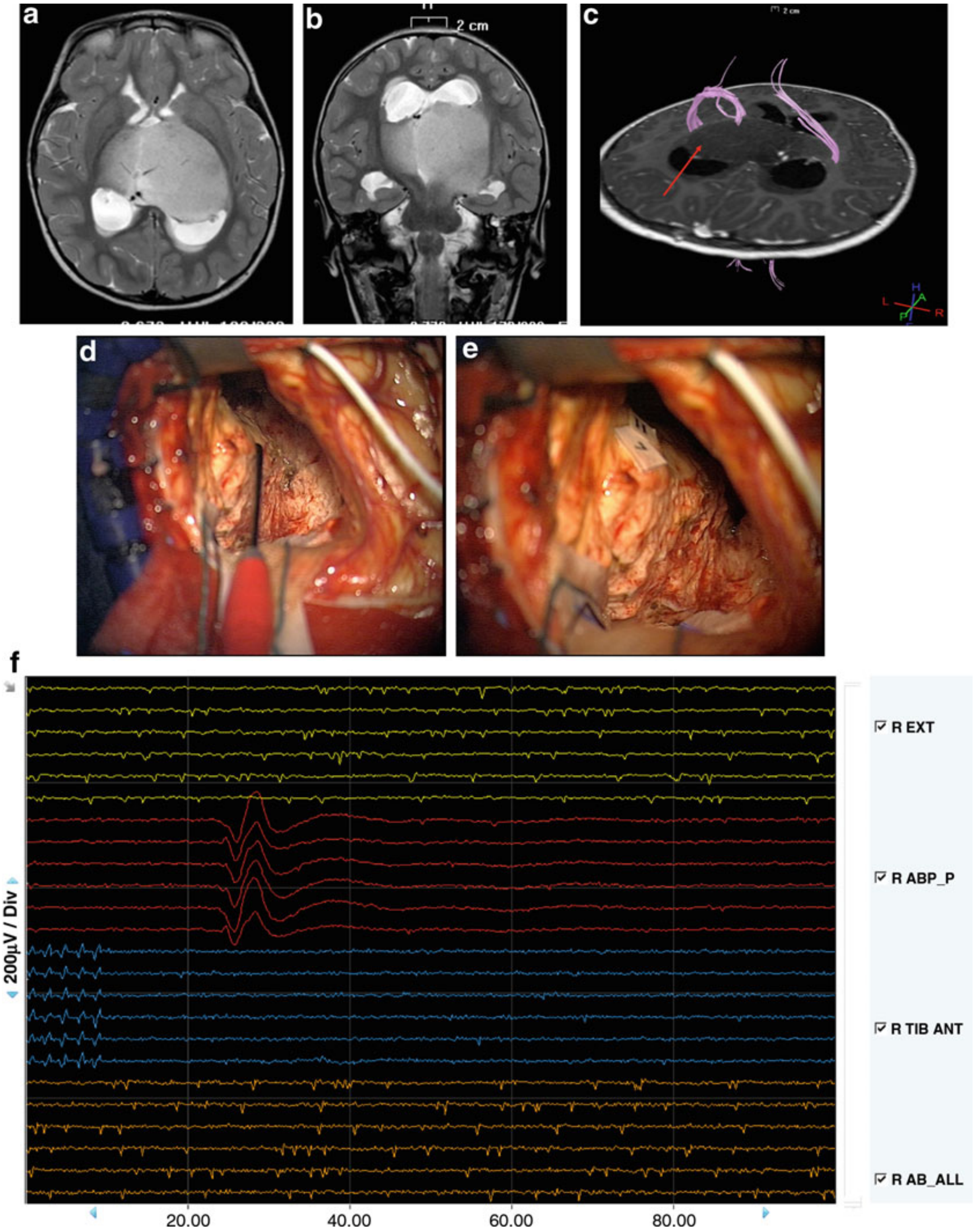


Fig. 2 (**a**–**b**) A T2-weighted MRI (axial and coronal views) showing a large bilateral thalamic tumor in a 2-year-old girl, who presented with a progressive history of delayed milestones achievement, mild right hemiparesis, and tremor on the right upper limb. (**c**) intraoperative neuronavigation snapshot. The tractography shows the corticospinal tract (*pink*) laterally displaced by the tumor on both sides. Surgery was planned to achieve a subtotal removal with the goal of preserving motor function. The *red arrow* indicates the location of the subcortical mapping during the surgery, illustrated in Fig. 2d–f. (**d**) Intraoperative view of the subcortical mapping performed through a handheld monopolar stimulation probe, with reference electrode in the temporalis muscle. (**e**)

is distorted by the lesion or when the tumor does not protrude through the surface of the brainstem. In the brainstem, probably more than in any other area of the nervous system, the role of IONM is to provide real-time information about the functional integrity of critical neural structures, thereby warning the surgeon of an impending injury caused, for example, by excessive coagulation or traction injury to perforating vessels. Conversely, stable electrophysiological signals encourage more aggressive maneuvers and consequently more radical and thorough resection of lesions. The following is a summary of the main IONM monitoring and mapping techniques that play vital roles in posterior fossa surgery (Fig. 4).

Monitoring in the Posterior Fossa

Brainstem Auditory Evoked Potentials (BAEPs)

Short latency auditory evoked potentials, also called BAEPs, are commonly used to monitor auditory pathways during brainstem surgery and to provide information on the general well-being of the brainstem. Recorded from scalp electrodes after a transient acoustic stimulus, BAEPs are not suppressed by conventional anesthetic agents (Banoub et al. 2003) and can be used to assess the integrity of the auditory nerve, the brainstem, and possibly also the higher subcortical centers. Normal BAEPs comprise seven different waves (I–VII), and a careful analysis of the individual waveforms and their neural generators can provide information about the localization of any prospective changes during surgery (Fig. 5). For example, damage to the eighth nerve near its cochlear organ end will lead to a prolongation of the interpeak intervals of waves I–III and an increase of the latencies of the III and V wave but would not alter the interpeak intervals of waves III–V. Complete disappearance of wave I would indicate a cochlear organ injury but not direct injury to the eighth nerve. Injury of the lower pons in the area of the cochlear nucleus or the superior olivary complex will prolong the III–V latency and cause a drop in their amplitudes. Injury to the midbrain will affect waves IV and V (Legatt 2008).

In spite of the theoretically clear-cut cascade of injury types, in reality, BAEPs monitoring is of limited value in brainstem surgery because it is difficult to extrapolate reliable information on the degree and location of the injury from BAEP waves alone. An exception may be in acoustic neuroma resection where BAEP monitoring has a role in assessing the integrity of the auditory nerve and indirectly in protecting against excessive cerebellar retraction, but this type of surgery is distinctly uncommon in children. The interpretation of BAEPs also requires an experienced neurophysiologist. Nevertheless, BAEP monitoring is usually included in a multimodality IONM approach for brainstem surgery.

Somatosensory Evoked Potentials (SEPs)

Monitoring of the SEPs during brainstem surgery has some value as any significant damage to the medial lemniscus pathways would be reflected by either a drop in the SEPs amplitude or a shift in their latencies. Yet, similar to BAEP monitoring, SEP per se does not provide specific information on the location of the injury within the brainstem; SEPs and BAEPs combined can evaluate only 20% of the brainstem pathways. In general, monitoring of upper extremity (median nerve) SEPs suffices during surgery of the midbrain and pons, as it is unlikely at this level to injure selectively proprioceptive pathways from either the lower or upper limbs while preserving the other. For

Fig. 2 (continued) Intraoperative view showing the site where a threshold current of 7 mA elicited a muscle response from the contralateral hand (H) muscle. (**f**) Muscle response recorded from the contralateral abductor pollicis brevis (APB-P). R EXT = right extensor digitorum communis; R APB_P = right abductor pollicis brevis; R TIB ANT = right tibialis anterior; R AB_ALL = right abductor hallucis. Pathology revealed a grade II astrocytoma. The patient woke up from surgery with a transient slight worsening of the preexisting right hemiparesis. She was then given adjuvant chemotherapy in order to postpone radiotherapy, given her very young age. (Reprinted Coppola et al. (2016))

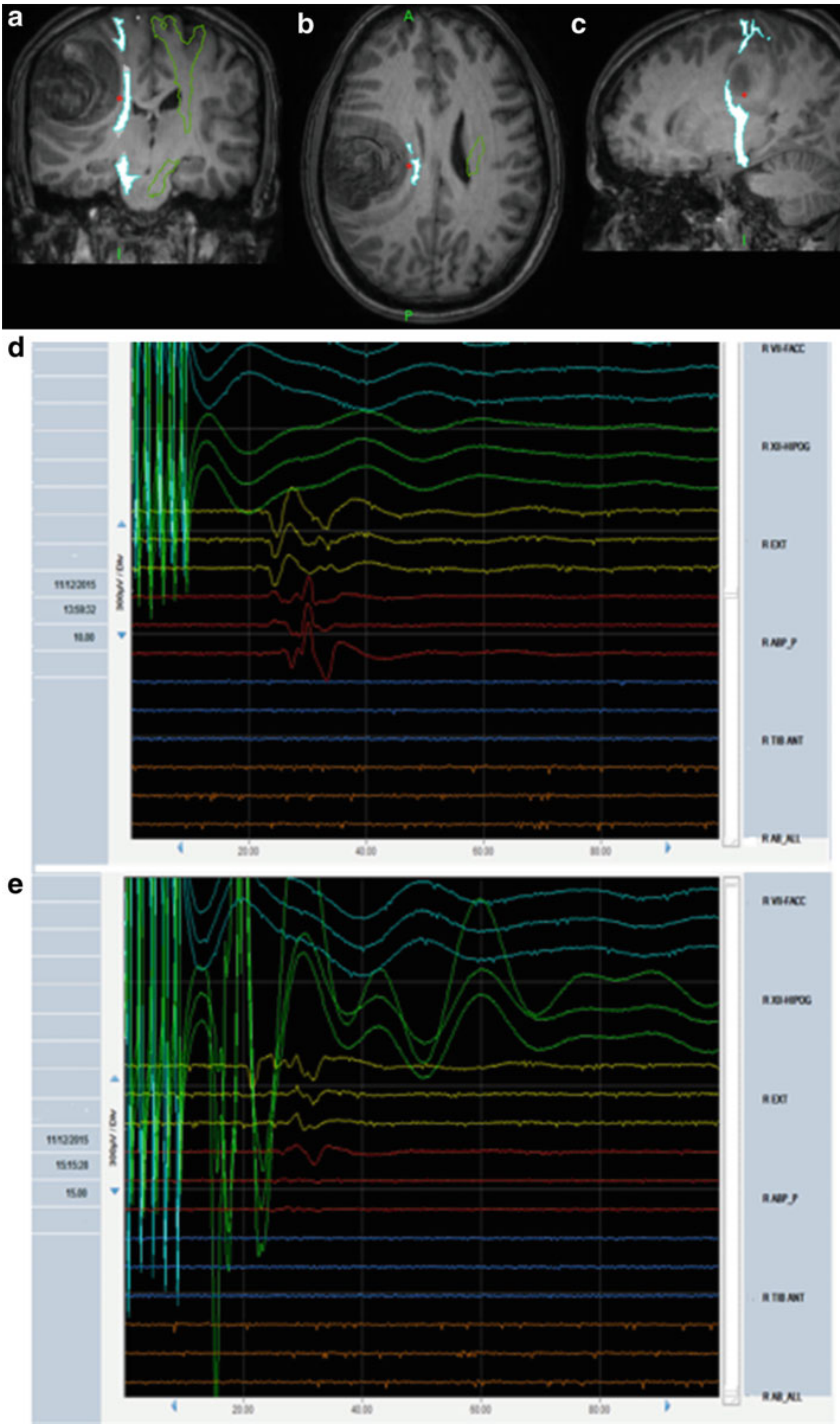


Fig. 3 (continued)

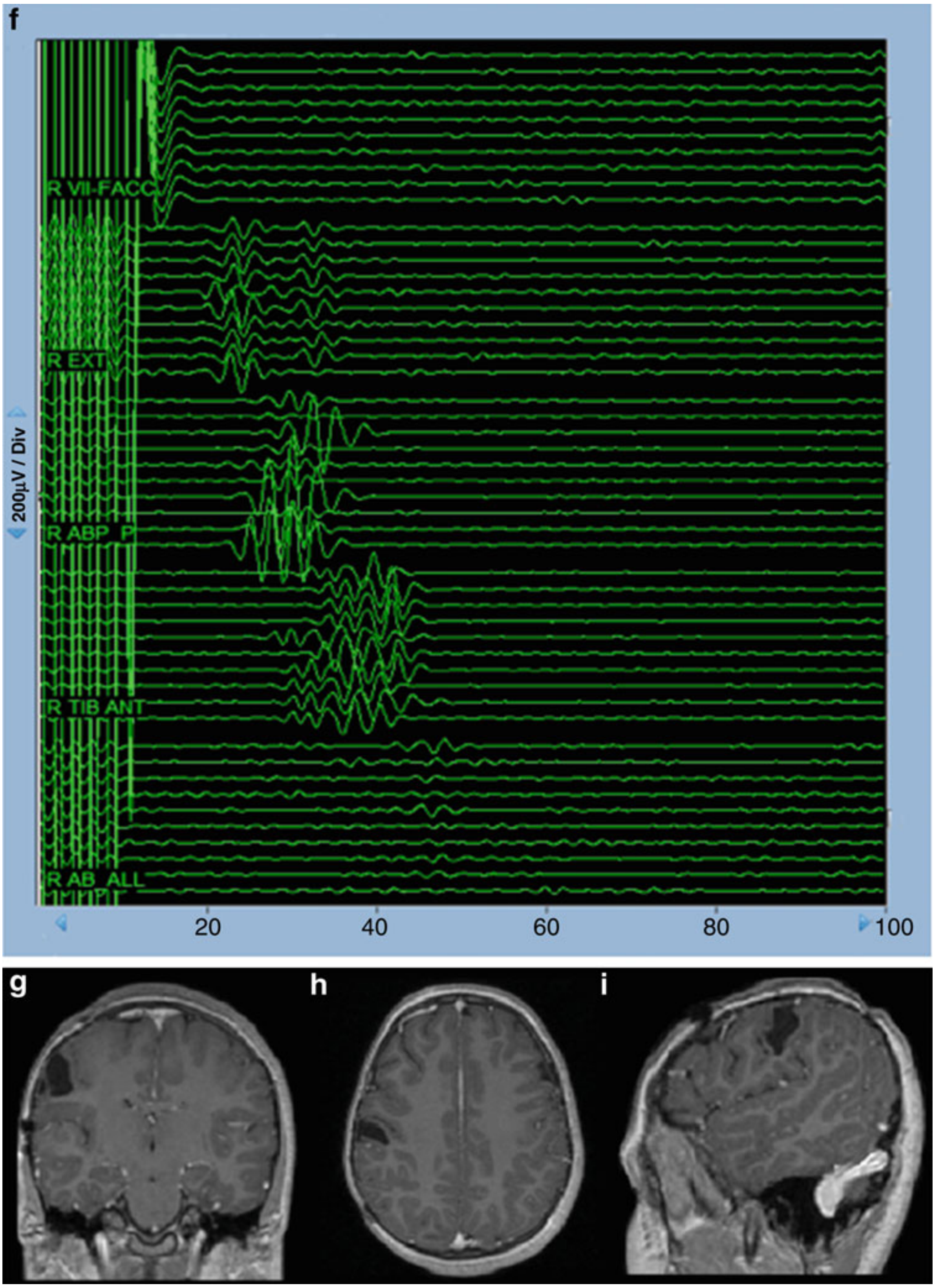


Fig. 3 (**a**–**c**) Intraoperative neuronavigation snapshots. The MRI with tractography shows a high-grade glioma of the Rolandic area in a 17-year-old boy who presented with a right-hand paresthesia. An anteromedial displacement of the corticospinal tract (*light blue*) is evident in coronal (**a**), axial (**b**), and sagittal (**c**) preoperative contrast-enhanced T1-weighted MRI. The *red* point indicates the site of intraoperative direct subcortical stimulation toward the end of the surgery. (**d**–**e**) Subcortical mapping showing the contralateral muscle responses. During the final part of the tumor removal, a consistent muscle response was recorded from the right abductor pollicis brevis (R APB-P) and extensor digitorum communis (R EXT) (**d**), as well as from the genioglossus muscle (R XII HPOG) (**e**). The stimulation intensities ranged from 10 to 15 mA (short train of five stimuli, 0.5-ms duration, interstimulus interval

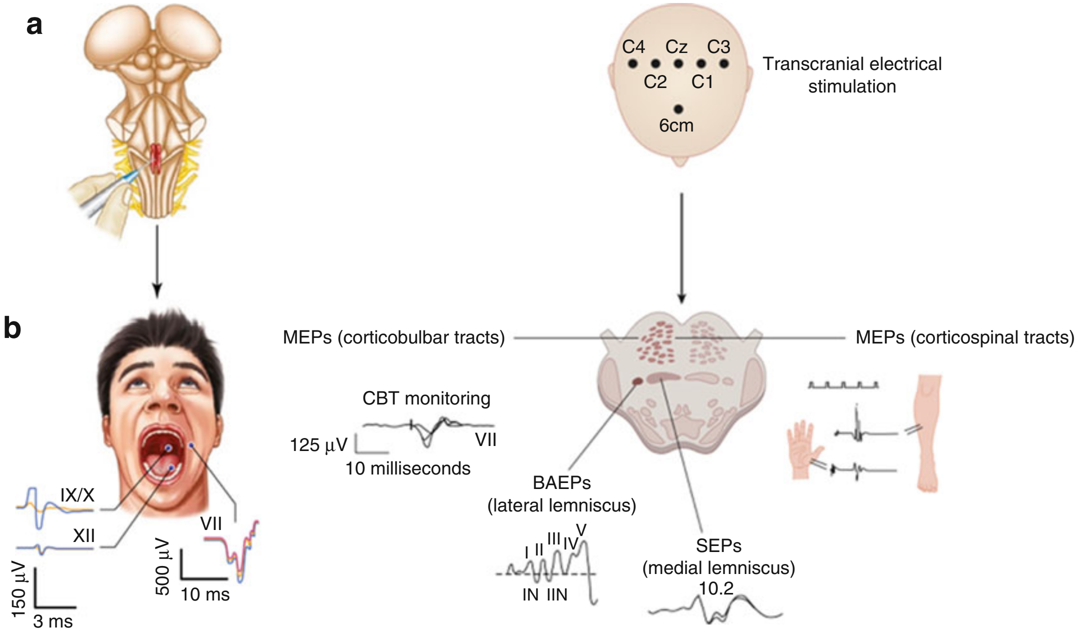


Fig. 4 Schematic illustration of intraoperative neurophysiology techniques in posterior fossa surgery. *Left panel*: Mapping of the floor of the fourth ventricle, which allows the identification of functional landmarks such as the nuclei of the motor cranial nerves: (**a**) A handheld monopolar probe is used to stimulate the rhomboid fossa. (**b**) Compound muscle action potentials are recorded from muscles innervated by the VII, IX, X, and XII cranial nerves. *Right panel*: Continuous monitoring of motor evoked potentials (*MEPs*), somatosensory evoked potentials (*SEPs*), and brainstem auditory evoked potentials (*BAEPs*) assess in real time the functional integrity of neural pathways during surgery. VII recording from the orbicularis oris for the facial nerve. IX/X recording from posterior wall of the pharynx for the glossopharyngeal/vagus complex. XII recording from the tongue muscles for the hypoglossal nerve. MEPs = motor evoked potentials. SEPs = somatosensory evoked potentials. BAEPs = brainstem auditory evoked potentials. CBT = corticobulbar tract (Modified from Sala et al. 2015a)

cervicomedullary tumor surgery, however, selective injuries to pathways from the upper and lower limbs are possible, so SEPs from both are used. At this level, SEPs can be temporarily compromised following the initial midline myelotomy and lateral displacement of the dorsal column and the Gall and Burdach nuclei (Deletis et al. 2000; Sala et al. 2015a). The SEPs usually recover later during surgery or the postoperative period, so a drop in the initial SEP amplitudes does not necessarily correlate with a permanent sensory deficit and is therefore not considered a criterion to abandon surgery.

Motor Evoked Potentials

From a methodological standpoint, brainstem MEP monitoring is similar to that described for supratentorial surgery, except that only

Fig. 3 (continued) of 0.4 ms, repetition rate of 1 Hz). The relatively high thresholds and the absence of significant preoperative motor deficits suggest that the corticospinal tract was displaced by the tumor. R VII-FACC = right orbicularis oris; R TIB ANT = right tibialis anterior; R AB_ALL = right abductor hallucis. (**f**) Continuous monitoring of muscle motor evoked potentials (mMEPs) in cascade mode, showing the stability of the mMEPs in real time during the surgical procedure. (**g**–**i**) Postoperative MRI in coronal (**g**), axial (**h**), and sagittal (**i**) sequences show complete tumor removal. The patient did not experience any additional neurological deficit after the surgery with a Karnofsky score of 100. (Reprinted from Coppola et al. (2016).

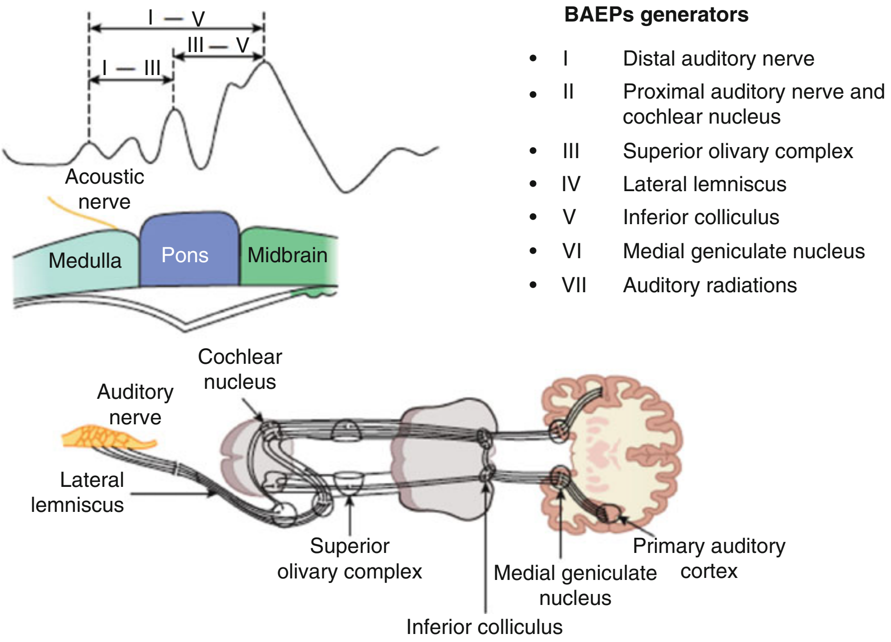


Fig. 5 Schematic illustration of brainstem auditory evoked potentials and the level in the brainstem where the individual waves are generated. The I–III, I–V, and III–V interpeak latencies are indicated

transcranial stimulation can be used for the former. The stimuli are applied through electrodes placed at C1 and C2 scalp sites according to the International 10/20 EEG system. The C1/C2 electrode montage elicits mMEPs preferentially in the right limb muscles and the C2/C1 montage does the same in the left limb muscles. In supratentorial surgery, it is important to monitor muscles from both the upper and lower extremities and the face in order to cover the entire homunculus. In the brainstem, the CST fibers are concentrated in a small ventral area, so an injury, however small, is unlikely to selectively affect just one group of muscles. Therefore, monitoring just the upper extremity mMEPs is acceptable. For transcortical MEP in children, the stimulation intensity seldom exceeds 150–200 mA, and in children without deficits, the upper limb mMEPs are often recordable with much lower stimulation intensities, around 40–50 mA, considering a train of 5 stimuli of 0.5 msec duration each (Sala et al. 2015a).

There is little information about the warning MEP criteria in brainstem surgery, and what is available comes from adult studies (Neuloh et al. 2004). Although new deficits from brainstem surgery correlate with more pronounced MEP changes than in supratentorial surgery, a complete loss of the MEP is not "required" (as in spinal cord surgery) to forecast postoperative deficits.

Corticobulbar Motor Evoked Potentials

Transcranial corticobulbar mMEPs are used to assess the functional integrity of the corticobulbar pathways. A short train of four stimuli is applied through scalp electrodes at a rate of 1–2 Hz with an intensity of 60–150 mA. Given the more lateral representation of orofacial muscles on the motor strip, the stimulating electrode montage is usually C3/Cz and C4/Cz for the right and left sides, respectively. Responses are recorded from wire or needle electrodes in the muscles innervated by the motor cranial nerves: superior rectus (III cranial nerve), lateral rectus (VI cranial nerve), masseter (V cranial nerve), orbicularis oris and oculi (VII cranial nerve), posterior walls of the pharynx (IX, X cranial nerves), trapezius (XI cranial nerve), and genioglossus (XII cranial nerve). To avoid swelling of the delicate eye muscles from direct wire implants, skin electrodes placed near the medial and lateral canthi are sometimes used to capture the far-field potentials from the medial rectus (III nerve) and lateral rectus (VI cranial nerve), respectively.

Corticobulbar mMEPs have the advantage of monitoring the entire pathway from the motor cortex through the corticobulbar tracts and the brainstem nuclei to the cranial nerves and muscles. Nevertheless, there are some limitations. First, the use of a lateral electrode montage (C3/Cz and C4/Cz) can induce vigorous muscle twitching which may interfere with microsurgery. Second, especially if the current intensity is high, the corticobulbar pathways may be activated directly at the level of the brainstem or even at the level of the peripheral nerve (Rothwell et al. 1994), masking an injury rostral to the point of activation. We have occasionally experienced false-negative results, and this possibility should be kept in mind. One strategy to decrease the risk of distal activation of the pathways is to eliminate all stimulation parameters that enable a single stimulus to elicit a muscle response. If a single stimulus elicits a muscle response, it is likely from distal activation because a single stimulus is unable to drive through a polysynaptic pathway especially under general anesthesia.

Clinical data on the reliability of corticobulbar mMEPs for predicting postoperative function of motor cranial nerves are incomplete, and most of the studies published over the past 15 years are on adults (Ito et al. 2013; Sala et al. 2007). What can be said is that if the corticobulbar mMEPs are preserved at the end of the surgery, the likelihood of normal function is very high, except perhaps for minor or transient deficits. Conversely, a complete loss of the MEP during surgery is a poor prognostic sign as most of these patients suffer from severe and/or long-lasting palsy. With regard to the lower cranial nerves, it is important to recognize that corticobulbar MEP monitoring, except for demonstrating the intactness of the motor axons of the IX, X, and XII nerves, does not safeguard the functional integrity of complex circuitries such as the swallowing and cough reflexes. As yet, we do not have reliable techniques to evaluate the sensory arms of these circuitries, which may explain the occasional discrepancies between intraoperative IONM data and postoperative clinical outcome.

Free-Running Electromyography

Evaluation of spontaneous electromyography (EMG) in muscles innervated by the motor cranial nerves is a technique that provides a continuous online monitoring of the integrity of the nerves or their nuclei within the brainstem (Eisner et al. 1995; Grabb et al. 1997; Schlake et al. 2001). EMG records spontaneous activity by the same needles used to record mMEPs during corticobulbar MEP monitoring, the spontaneous EMG presumably generated by potentially harmful manipulations of the nerve or its nucleus. However, this technique has limitations, and a robust correlation between these spontaneous “injury potentials” and clinical outcome is still lacking (Grabb et al. 1997; Schlake et al. 2001). For example, though the absence of spontaneous EMG activity supposedly implies functional integrity of the nerve, complete sectioning of the nerve has been associated with complete electrical silence. Vice versa, though a persistent irritative EMG pattern during and after surgical manipulation of cranial nerves usually warns of “near-injury” to the nerve, it can also be provoked by irrigation of the surgical field with cold saline solution. The reliability of free-running EMG appears to be highest for facial nerve monitoring, following the description of the so-called A-trains by Romstock et al. (2000) This EMG pattern consists of high-frequency trains, which retain a strong predictive value for postoperative facial palsy. However, the signal analysis is rather complicated; false-positive results are possible, and similar data have yet to be published for the other motor cranial nerves. The following is a case illustrating the usefulness of identifying spontaneous injury potentials of the medial rectus muscle in averting permanent damage to the oculomotor nerve during resection of an intrinsic midbrain tumor.

A 7-year-old boy with a right spastic hemiparesis of at least 4 years’ duration had been labeled to have spastic cerebral palsy. An MRI ordered because of progression of the right arm weakness showed a large intrinsic tumor in

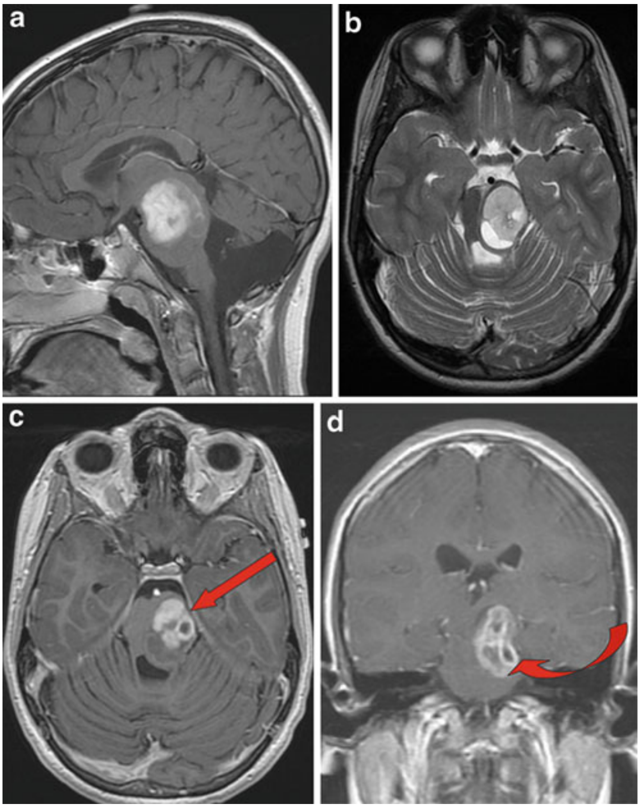


Fig. 6 MRI of a 7-year-old boy with long-standing right spastic hemiparesis. (**a**) Sagittal T1 image with gadolinium shows irregularly enhancing lesion in the ventral midbrain extending dorsally toward the quadrigeminal plate. (**b**) Axial T2 image shows the lesion with well-circumscribed borders and a thin rim of overlying left cerebral peduncle. A dorsal cystic portion is pushing against and distorting the superior colliculus and the oculomotor nucleus and its intramedullary nerve. (**c**–**d**) Axial and coronal T1 with contrast. The *red arrows* show the subtemporal, transtentorial approach to the left cerebral peduncle and tumor

the left peduncle of the midbrain, with irregular enhancement with gadolinium and well-circumscribed borders (Fig. 6a, b). The most dorsal margin of the lesion extended very close to the oculomotor nucleus and the intrinsic course of the oculomotor nerve though no oculomotor deficit was noted. A subtemporal transtentorial approach was selected for the resection (Fig. 6c, d).

At surgery, EMG needles were placed subcutaneously at the medial and lateral canthi to capture the far-field motor potentials from the medial and lateral recti, respectively. Following retraction of the temporal lobe, the IV cranial nerve was identified and preserved at the tentorial incisura (Fig. 7), which was then incised, and the cut edges were retracted with sutures to expose the midbrain peduncle, bulging with the underlying tumor (Fig. 8). After incising barely 1 mm of brainstem, soft grayish tumor was encountered, found to be a benign astrocytoma on frozen section (Fig. 9). The cavitron ultrasonic aspirator (CUSA) was used to assist in tumor removal till a clean tumor bed was achieved on the side of the cavity (Fig. 10). As the CUSA approached the very depth of the resection front, there was a sudden

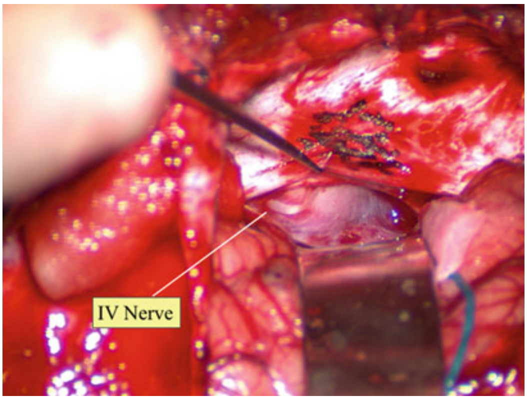


Fig. 7 Intraoperative exposure showing retraction of the inferior temporal gyrus and the fourth cranial nerve at the edge of the tentorial incisura, deep to which is the left cerebral peduncle still arachnoid-covered

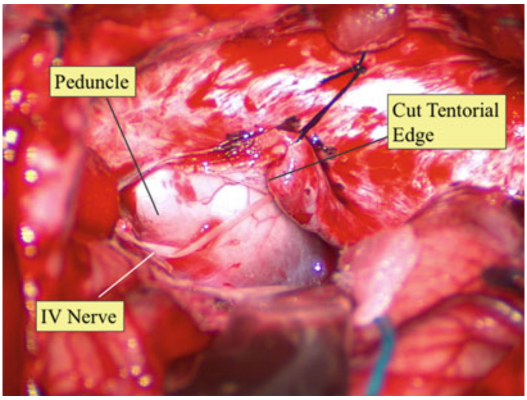


Fig. 8 The edge of the tentorial incisura is incised to expose more of the cerebral peduncle, bulging with intrinsic tumor

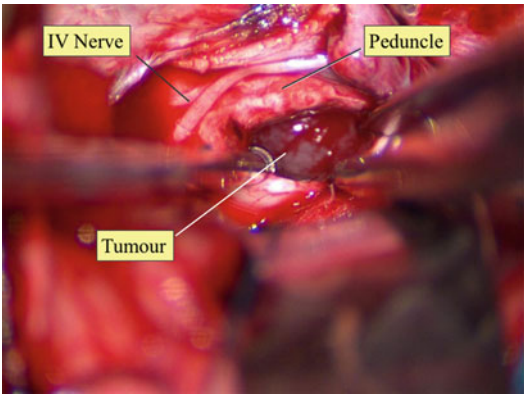


Fig. 9 Grayish tumor exposed after incising the barely 1 mm layer of overlying brainstem

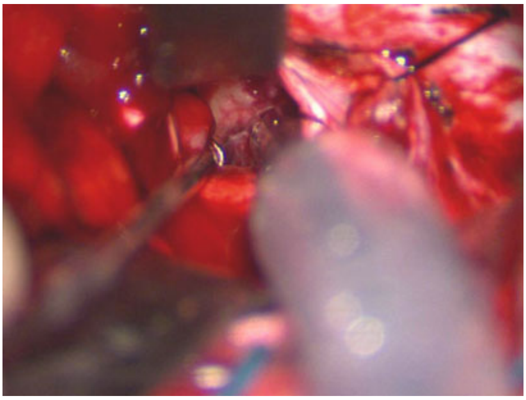


Fig. 10 The CUSA is used to remove the soft tumor. Sudden spontaneous EMG activities from the left medial rectus erupted at the deep extent of the resection cavity

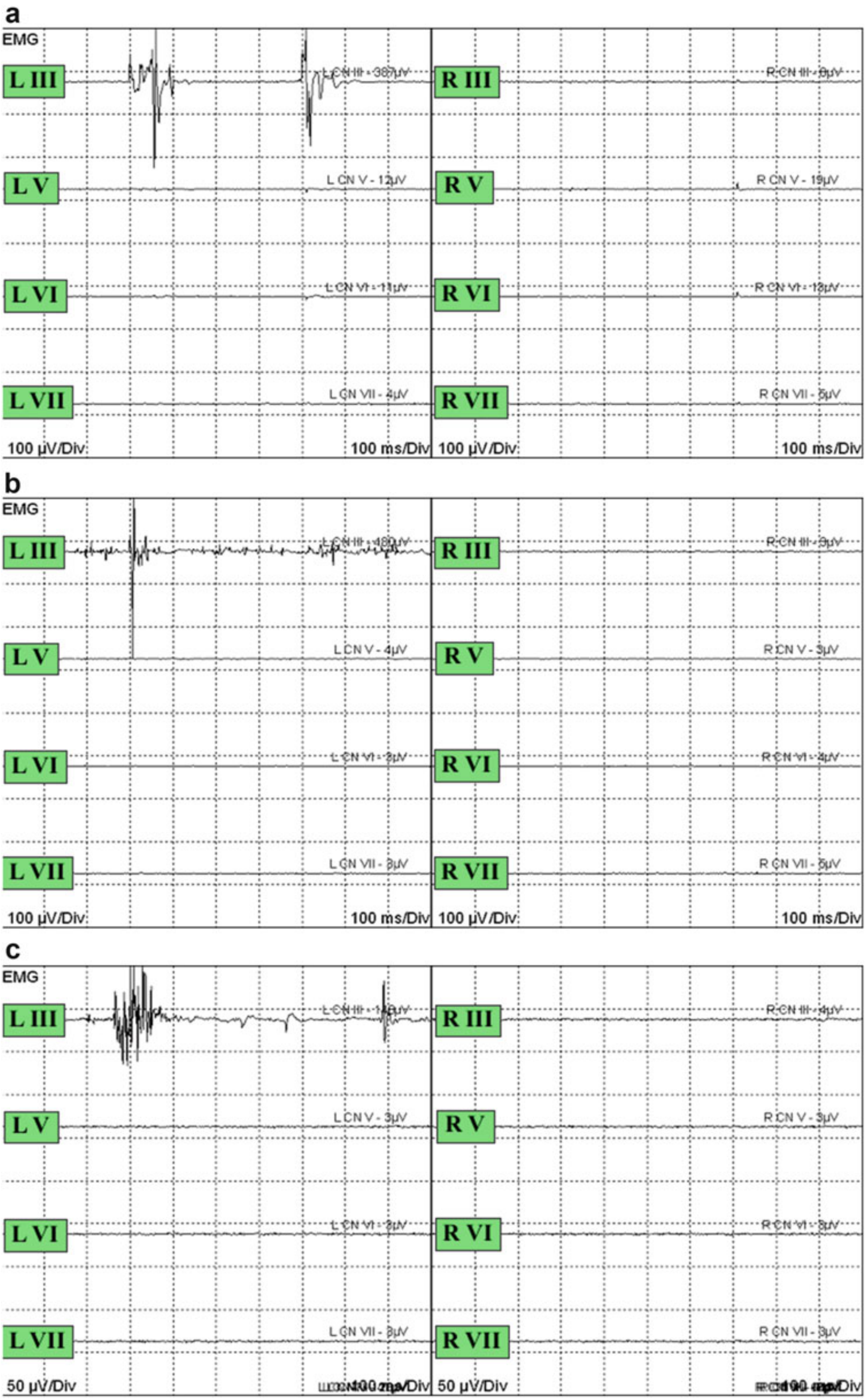
surge of spontaneous high-frequency discharges from the left (ipsilateral) medial rectus, signifying potentially deleterious manipulation (Fig. 11). Further resection was deemed too risky, and the procedure was halted, though a clean resection was accomplished (Fig. 12). Postoperatively, the boy suffered a transient weakness of all the eye muscles supplied by the III nerve, which completely resolved after a month. MRI confirmed gross total resection, and the deepest, i.e., the most dorsal tip, of the resection cavity was clearly very close to the left III nerve nucleus and its intramedullary nerve, where irritative "flutter" of the medial rectus apparently produced the putative EMG display (Fig. 13).

Mapping in the Posterior Fossa

During the 1990s, a number of skull base approaches to the brainstem have been developed, which naturally came with a zest to identify anatomical landmarks for safe entry zones to the brainstem. Yet, these landmarks are sometimes of little practical value as tumors often alter the local anatomy and render visual identification of these landmarks impossible. In such cases, neurophysiological mapping techniques can be useful in functionally (rather than anatomically) localizing motor cranial nerve nuclei and their projections within the brainstem whenever these are distorted by pathology.

Mapping of Peripheral Cranial Nerves

Peripheral motor cranial nerves can be identified in the surgical field through direct stimulation when these are encased in or dislocated by a tumor. Either a handheld monopolar probe or a bipolar concentric probe can be used. The advantage of bipolar stimulation is a limited spread of the current (rectangular pulses of 0.2-msec duration at 1–3 Hz and intensity up to 0.5–3 mA), hence reducing the risk of activation of nearby neuronal units. Recording electrodes are placed in the muscle innervated by their respective cranial nerves. Needle electrodes are used for larger muscles such as the masseter (V), orbicularis oculi and oris (VII), and trapezius (XI). For the



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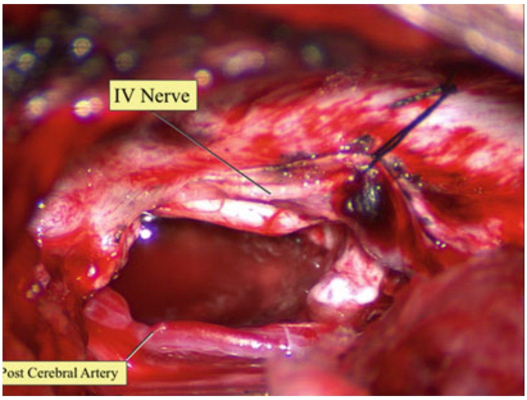

Fig. 12 The procedure was halted. Resection cavity with clean bed

genioglossus (XII) that is liable to bleed into itself when contracting against stiff needle electrodes, and muscles of small sizes such as the vocal cords (X) and oculomotor muscles (superior or medial rectus (III), lateral rectus (VI), and superior oblique (IV)), fine, pliable Teflon-coated wire electrodes are used instead.

The placement of wire electrodes in extrinsic oculomotor muscles may require the assistance of an ophthalmologist. One pair of electrodes is inserted into the superior rectus and one into the lateral rectus muscles to monitor the III and VI cranial nerve, respectively, and into the superior oblique for the trochlear nerve. The subcutaneous needles placed near the medial and lateral canthi are reasonable substitutes for intramuscular wires to avoid temporary postoperative palsy due to swelling.

When working in narrow spaces with high concentration of neural structures, it is important to adjust the stimulus intensity so that a response is obtained from only one muscle at a time. If the intensity is too high, the current may spread and the localizing value of the mapping vanishes. For extraocular muscles, the latency of the response obviously depends on the point of stimulation on the nerve, but in general it ranges between 2 and 5 ms (Sekiya et al. 2000). Mapping of the oculomotor nerves can be valuable during surgery for lesions involving the cisternal, cavernous, or intraorbital segment of these nerves.

Mapping of cranial nerves V–XII are routinely used during surgery for cerebellopontine angle and other skull base tumors. Usually, very low intensities (0.1–0.3 mA) are needed to elicit a compound muscle action potential (CMAP). In children, this technique may prove helpful during the removal of posterior fossa ependymomas, which often extend through the lateral recess and the foramen of Luschka to involve the facial and lower cranial nerves.

Mapping of the Corticospinal Tract at the Cerebral Peduncle

When a tumor involves the anterolateral part of the midbrain, careful precautions should be taken to avoid injuries to the CST. Anatomical landmarks such as the lateral mesencephalic vein described by Rhoton (2000) may be of some help to localize the CST, which usually lies anteromedial to this vein. When normal anatomy is distorted, the CST can be identified only through neurophysiological mapping. For this purpose, a handheld monopolar probe (tip diameter of 0.75 mm) can be used for cathodal stimulation, and a reference needle electrode is inserted in a muscle close to the surgical field as the anode. The CMAP response is recorded from one or more muscles of the contralateral limb. The stimulus intensity is progressively increased up to 2 mA or when the first response is obtained. The probe is then moved from that point in small steps of 1 mm in order to find the spot that generates a response with the largest amplitude. Alternatively, the moving probe will locate the site that requires the lowest threshold current to elicit a CMAP.

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Fig. 11 Free EMG recordings from the III, V, VI, and VII cranial nerve innervated muscles during surgery. (**a**) Clusters of high-frequency activities recorded from the left medial rectus muscle. Note quiescence in the ipsilateral V, VI, and VII innervated muscles and the contralateral III, V, VI, and VII innervated muscles. (**b**) Same as **a** with almost continuous low amplitude firing in the background. (**c**) Same as **b**

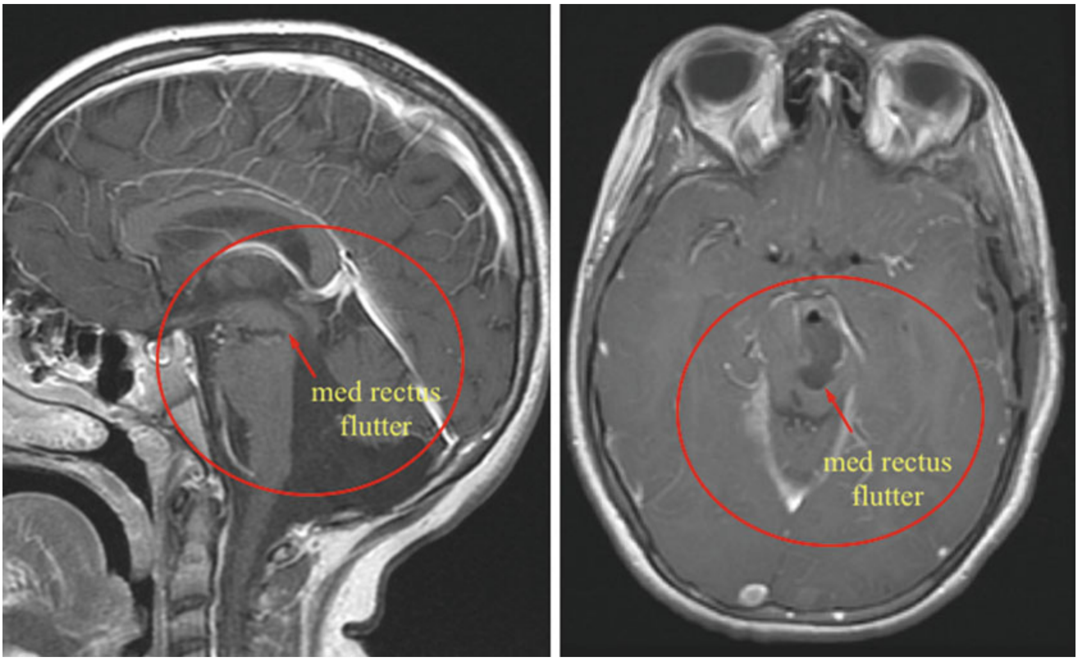


Fig. 13 Postoperative MRI, sagittal T1 (*left*), and axial T1 (*right*) show gross total resection of tumor and the deepest extent of the resection front adjacent to the left oculomotor nuclei and nerve (*red arrows*), corresponding to the occurrence of the "medial rectus flutter" during the resection

Direct Mapping of the Brainstem: Midbrain and Floor of the Fourth Ventricle

This is by far the most useful mapping technique in pediatric posterior fossa tumor surgery, given the high concentration of pediatric brain tumors in the brainstem and fourth ventricle. The role of neurophysiological mapping here is different depending on the location of the tumor.

If the tumor is exophytic, i.e., protruding outside the brainstem surface, its removal clearly begins at the outgrowth. In such cases, the tumor itself creates its own entry into the brainstem, and neurophysiological mapping may not be necessary. If the tumor is truly intrinsic and does not reach the surface of the brainstem, mapping is used to identify safe entry zones. Or when operating on medulloblastomas and ependymomas within the fourth ventricle, mapping can also assist in deciding when to stop aggressive resection if the tumor is infiltrating the ventricular floor.

The midbrain comprises a dorsal part, the tectal plate, a large ventral portion, the tegmentum, and the cerebral peduncles. During dorsal approaches to treat intrinsic midbrain lesions, it is important to minimize injury to the oculomotor nuclei and their intramedullary tracts. This is particularly relevant in children where a number of neoplastic lesions are found in this region, the great majority of which are focal, benign astrocytomas. These tumors usually arise from either the tectal plate or tegmentum and may extend rostrally to the thalamus or caudally to the pons, displacing but not infiltrating these structures.

Anecdotal reports (Duffau and Sichez 1998; Ishihara et al. 2006; Sekiya et al. 2000) as well as our own experience suggest that direct mapping of the superior colliculus is of little help to select the entry zone because the superficial layers of the colliculi connect the motor output from the III and IV nerves to the visual system via the thalamus and the lateral geniculate nuclei, while the nuclei themselves are embedded deep in the periaqueductal gray, too shielded to be activated by surface stimulation. However, once the dissection enters the tumor cavity within the dorsal midbrain, it is possible to use neurophysiological mapping to localize the oculomotor nuclei.

When the tumor involves the pons or the medulla, the most direct approach is by a suboccipital craniotomy to enter the fourth ventricle. At the level of the pons, the more prominent part of the median eminence, the facial colliculus, represents a highly vulnerable area during surgical entry (Lang et al. 1991). Damage to this area invariably causes simultaneous facial (VII) and abducens (VI) palsies, as well as lateral gaze paralysis from injury to the parapontine reticular formation. Here, the facial and abducens nuclei and the nuclei or intramedullary roots of cranial nerves IX to XII can be identified through direct stimulation on the fourth ventricular floor.

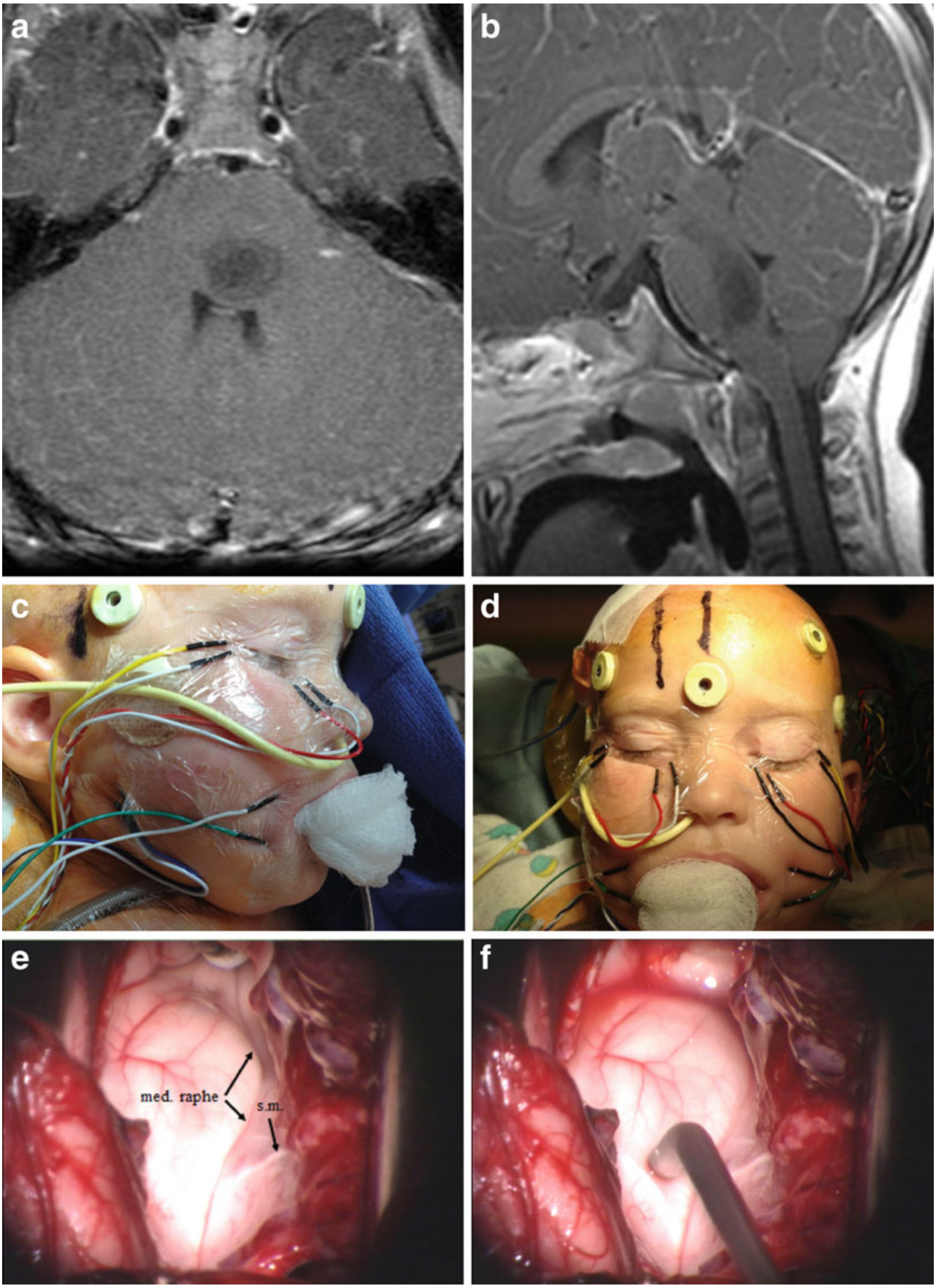
It is important to reiterate that the lowest current that elicits a muscle response should be used to locate the intended target, because higher stimulation intensities may activate the pathway at some distance from the point of stimulation. This is especially important when mapping the floor of the fourth ventricle, given the high concentration of motor nerves and nuclei here as compared to the cerebral peduncle. Therefore, rather than using a monopolar probe, we now exclusively use the bipolar concentric electrode which gives a much more focal activation.

A handheld concentric bipolar stimulating electrode is used with a stimulation intensity range of 0.1 to 2 mA, a rate of 3–5 Hz, and a duration of 150 μs. An initial current intensity of 0.5 mA is usually used for screen mapping, and once the intended motor cranial nerve nucleus is located, the stimulation current is lowered to the threshold level in order to obtain a clean, single motor recording without recruiting any adjacent nuclei. There are two different mapping strategies. One is to assess the threshold intensity that generates a recordable compound action potential (CMAP). By moving the tip of the stimulator in 1 mm steps over an area, it is possible to create a "threshold intensity map" for a particular target motor nucleus on the floor of the fourth ventricle. The lowest threshold marks the spot closest to the target nucleus (or its intramedullary root), and conversely, the highest threshold or no response at all marks the area farthest from the target nucleus, thus representing a safe zone of surgical entry into the brainstem. The other method uses a constant intensity of approximately 0.5–0.7 mA, and by sweeping the stimulating probe, one determines for each spot on the fourth ventricular floor the amplitude of the corresponding CMAP. The point corresponding to the highest amplitude indicates the vicinity of the target nucleus, while low amplitudes or, better, no response at all suggests a safe distance from the nucleus or its internal tracts.

For CMAP recordings, 13 mm subdermal needles are inserted in the following muscles: the masseter (V), orbicularis oculi and oris (VII), posterior wall of the pharynx (IX-X), vocal cords (X), and trapezius (XI). For the tongue (XII), wire electrodes are used to avoid hemorrhages within the substance of the tongue induced by contractions of the lingual musculature against the sharp needles.

The facial nucleus is the most superficial motor nucleus at the mid-pons level, usually with the lowest stimulation threshold and is usually the easiest to identify. However, nucleus VI is very close to nucleus VII, and responses from CN VI and VII are often elicited at the same time, though CMAP recording from VI is always slightly earlier than from CN VII. Nucleus V is deeper in the brainstem from the surface of the floor, so stimulation threshold is usually higher than for CN VI and VII (Fig. 14).

While mapping of the upper floor of the fourth ventricle is a well-established technique, in practice, some discrepancies exist between intraoperative IONM findings and postoperative functional outcome. In the case of the VII cranial nerve, brainstem mapping cannot exclude injury to the supranuclear corticobulbar fibers originating in the motor cortex and projecting to the facial nucleus. Consequently, a supranuclear facial paralysis could not be detected even though the integrity of the lower motoneuron has been "guaranteed" by brainstem mapping. Similarly, the nucleus itself could be destroyed, while CMAPs are being generated by stimulation of the intramedullary course of the VII nerve, but that is more theoretical than reality (Morota et al. 1995).



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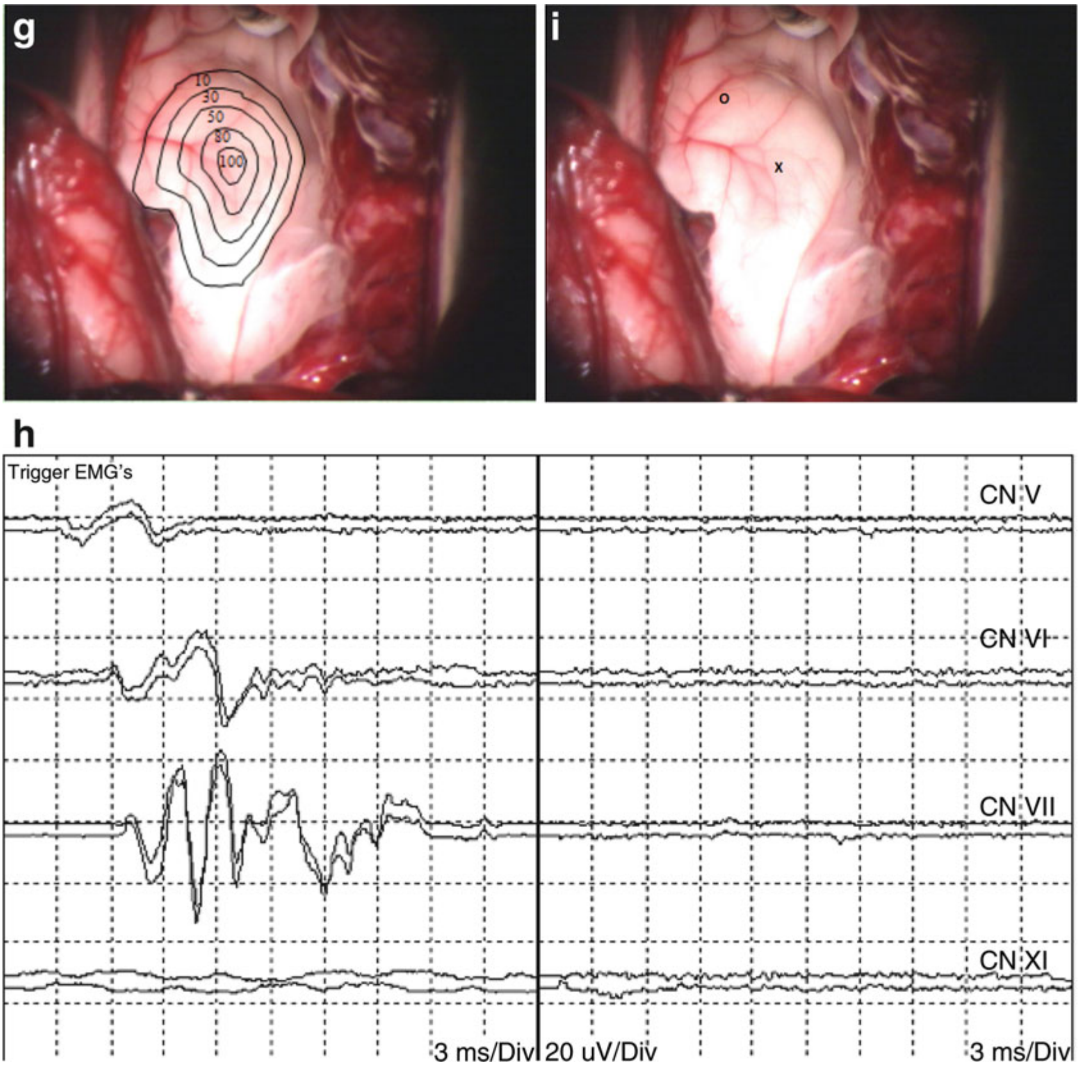

Fig. 14 (**a**–**b**). T1-weighted MRI with contrast (axial and sagittal views), showing a brainstem lesion in a 2-year-old boy with an intrinsic pontine tumor. (**c**–**d**) Subcutaneous needle electrodes are placed near the medial and lateral canthi to capture far-field muscle potentials from the medial rectus (III cranial nerve) and lateral rectus (VI cranial nerve), respectively. Intramuscular needle electrodes are inserted into the masseter (V cranial nerve) and orbicularis oris muscle (VII cranial nerve). Wire electrodes for the posterior pharynx (IX/X cranial nerves) are not shown. (**e**) Intraoperative view showing the normal anatomical landmarks of the fourth ventricular floor displaced by the tumor. Note deviation of the median raphe to the right, being displaced by the bulging tumor just rostral to the left stria medullaris (s.m.). (**f**) A handheld bipolar concentric stimulation probe is used to perform the neurophysiological mapping to localize the VII cranial nerve motor nuclei within the brainstem and identify a safe entry zone for tumor biopsy. (**g**) Left cranial nerve VII CMAP intensity distribution map. 100 = highest amplitudes and 10 = the lowest amplitudes. (**h**) Results of neurophysiological mapping showing a response for cranial nerves V, VI, and VII. (**i**) As a result of neurophysiological mapping, the safe entry zone is identified (O), while the facial colliculus (X) appears to be displaced caudally. Without mapping, the surgeon will likely enter the brainstem at the summit of the bulge, which would have destroyed the VII nerve nucleus

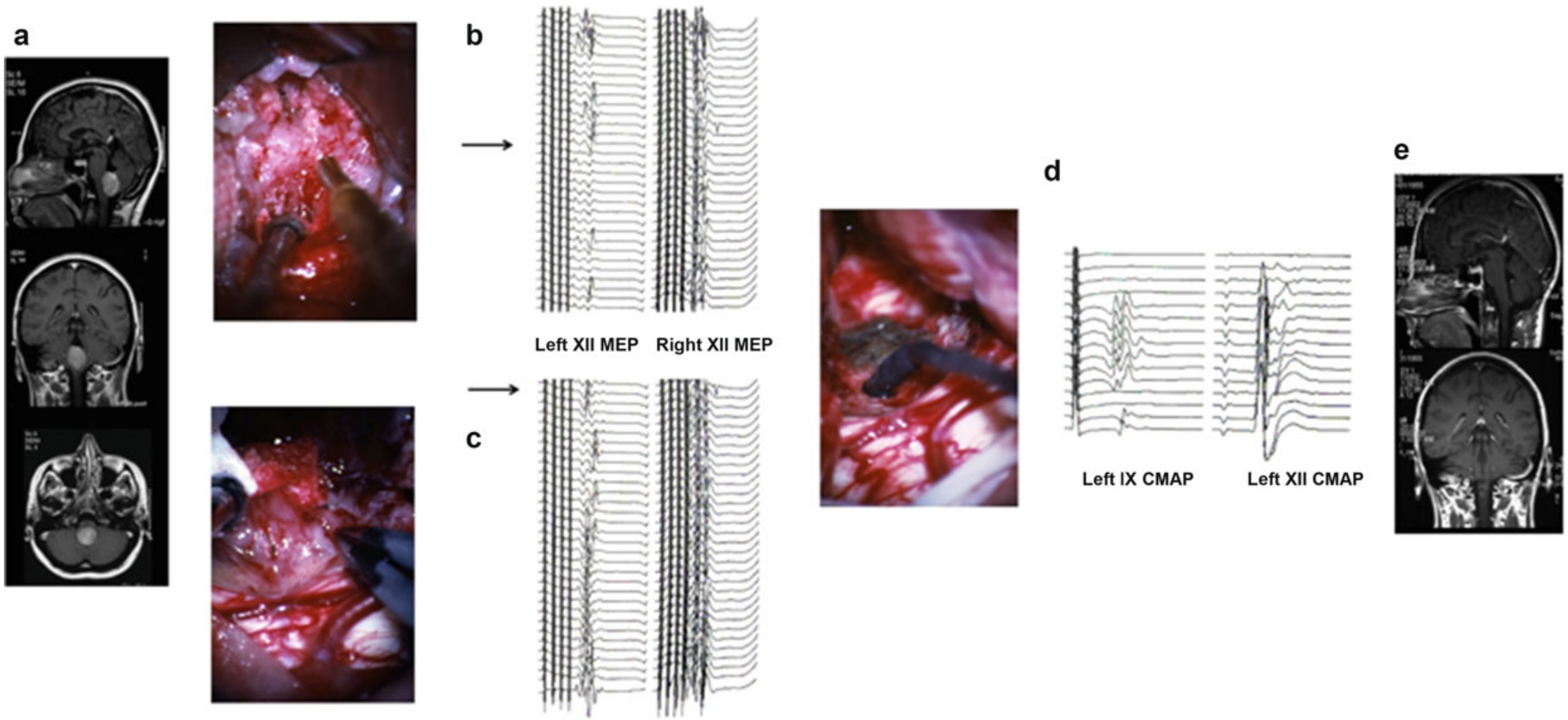

Fig. 15 (**a**) A T1-weighted gadolinium-enhanced MRI (sagittal, coronal, and axial views) showing a fourth ventricular ependymoma infiltrating the floor at the level of calamus scriptorius. During surgery, corticobulbar motor evoked potentials were continuously recorded from the genioglossus muscles (left XII MEP, right XII MEP in **b** and **c**). (**b**) While using the CUSA (*left panel*), a significant drop in the amplitude in the left hypoglossal MEP was recorded (*upper arrow*), which persisted for several minutes. For this reason, surgery was temporarily stopped to facilitate the recovery of the potentials. (**c**) Once the amplitude had recovered and a more repeatable left hypoglossal mMEPs was recorded (*lower arrow*), the surgery was resumed; the microscopic view suggested that the ependyma was infiltrated. (**d**) Removal of small amounts of tumor from the ependymal surface was alternated with direct stimulation of the floor of the fourth ventricle to localize the lower motor cranial nerve nuclei (*left panel*, surgical view). When clear compound muscle action potentials (*CMAPs*) were recorded from the left posterior pharyngeal wall muscles (glossopharyngeal/vagus nerves) and tongue muscles (hypoglossal nerve) (*right panel*), the surgery was stopped to avoid permanent damage to the underlying motor nuclei. (**e**) Postoperatively, a T1-weighted gadolinium-enhanced MRI (sagittal and coronal views) showing gross total removal of the tumor and a small enhancement at the calamus scriptorius, which may represent residual tumor. (Reprinted from Sala et al. 2014)

More caudally at the level of the medulla, both the hypoglossal and vagal nuclei are dorsally located near the “tip” of the calamus scriptorius and are therefore vulnerable to injury but also somewhat amenable to mapping. Immediately below the two slight prominence of the hypoglossal trigones lie the hypoglossal nuclei, which control the muscles of the tongue. Due to the close proximity of the two nuclei near the median raphe, surgical trauma to this area almost always results in bilateral injury and severe tongue paralysis and atrophy. Since this represents one of the most devastating cranial nerve deficits, even a minor injury to this area must be avoided.

Lateral to the hypoglossal trigones are the vagal triangles, and under these lie the dorsal vagal nuclei from which parasympathetic fibers to the bronchi, heart, and stomach originate. Slightly deeper and lateral lies the nucleus ambiguous, which gives rise to fibers of the glossopharyngeal (IX), accessory (XI) nerves, and somatic motor fibers of the vagus nerve, supplying musculature of the palate, pharynx, and larynx. Preservation of these neural structures is essential to avoid impairment of swallowing, phonation, and the cough reflex, with a consequent risk of aspiration pneumonia and inanition (Blessing 1997). To avoid cardiovascular instability including cardiac arrest, the maximum current intensity that should be used at the level of the lower brainstem is 2 mA (Suzuki et al. 1997).

It must be said that mapping of the glossopharyngeal nuclei does not guarantee successful swallowing since this only monitors the efferent arc of the swallowing reflex to the posterior pharyngeal muscles and does not in any way reflect the integrity of the afferent pathways and the complex internuncial connections within the brainstem that constitute successful swallowing and coughing and guard against aspiration. Therefore, even with preserved intraoperative XI and X nerve mMEPs, great care should be taken when managing extubation and postoperative airway clearance in children operated on for medullary tumors.

During resection of an intrinsic brainstem tumor, the riskiest part of the dissection is near the tumor-brain interface along the deep resection cavity. Here the potentially harmful manipulation may be millimeters from a cranial nerve nucleus. We recommend stopping the resection when an observable CMAP is elicited by a current at or below 0.5–0.7 mA, indicating extreme proximity to a depolarizable neural unit (Fig. 15). It is important to remember that most lesions of the medulla in children are benign astrocytomas or gangliogliomas, in which small remnants of residual tumors often remain stable and indolent for many years (Farmer et al. 1999) and occasionally may even disappear without adjuvant treatments.

Conclusions

The use of intraoperative neurophysiology has evolved significantly over the past two decades. It has become almost sine qua non in many procedures in pediatric neurosurgery. Virtually all IONM techniques that are currently used in adults can be used in the pediatric patient, with the exception of cognitive mapping during awake surgery, which is difficult in young children. Nevertheless, IONM in pediatric neurosurgery should be tailored to the peculiarity of the developing nervous system, and this implies technical adjustments.

References

Armand J, Olivier E, Edgley SA, Lemon RN (1996) The structure and function of the developing corticospinal tract: some key issues. In: Wing AM, Aggard P, Lanagan JR (eds) Hand and brain. Academic, San Diego, pp 125–145

Balogun JA, Khan OH, Taylor M, Dirks P, Der T, Carter Snead Iii O, Weiss S, Ochi A, Drake J, Rutka JT (2014) Pediatric awake craniotomy and intra-operative stimulation mapping. J Clin Neurosci 21:1891–4

Banoub M, Tetzlaff JE, Schubert A (2003) Pharmacologic and physiologic influences affecting sensory evoked potentials: implications for perioperative monitoring. Anesthesiology 99:716–737

Bartholow R (1874) Experimental investigations into the functions of the human brain. Am J Med Sci 67: 305–313

Berger MS (1996) The impact of technical adjuncts in the surgical management of cerebral hemispheric low grade gliomas of childhood. J Neuro-Oncol 28:129–155

Berger MS, Kincaid J, Ojemann GA, Lettich E (1989) Brain mapping techniques to maximize resection, safety, and seizure control in children with brain tumors. Neurosurgery 25:786–792

Berger C, Thiesse P, Lellouch-Tubiana A, Kalifa C, Pierre-Kahn A, Bouffet E (1998) Choroid plexus carcinomas in childhood: clinical features and prognostic factors. Neurosurgery 42:470–475

Blessing W (1997) The lower brainstem and bodily homeostasis. Oxford University Press, New York

Blume WT, Jones DC, Pathak P (2004) Properties of after-discharges from cortical electrical stimulation in focal epilepsies. Clin Neurophysiol 115:982–989

Caramia MD, Desiato MT, Cicinelli P, Iani C, Rossini PM (1993) Latency jump of “relaxed” versus “contracted” motor evoked potentials as a marker of cortico-spinal maturation. Electroencephalogr Clin Neurophysiol 89:61–66

Cedzich C, Taniguchi M, Schafer S, Schramm J (1996) Somatosensory evoked potential phase reversal and direct motor cortex stimulation during surgery in and around the central region. Neurosurgery 38:962–970

Chitoku S, Otsubo H, Harada Y, Jay V, Rutka JT, Weiss SK, Abdoll M, Snead OC 3rd (2001) Extraoperative cortical stimulation of motor function in children. Pediatr Neurol 24:344–350

Coppola A, Tramontano V, Basaldella F, Arcaro C, Squintani G, Sala F (2016) Intraoperative neurophysiological mapping and monitoring during brain tumor surgery in children: an update. Child Nerv Syst 32(10): 1849–1859

De Witt Hamer PC, Robles SG, Zwinderman AH, Duffau H, Berger MS (2012) Impact of intraoperative stimulation brain mapping on glioma surgery outcome: a meta-analysis. J Clin Oncol 30:2559–2565

Deletis V, Sala F (2012) Intraoperative neurophysiology: a tool to prevent and/or document intraoperative injury to the nervous system. In: Quinones-Hinojosa A (ed) Schmidek & sweet operative neurosurgical techniques: indication, methods and results, 6th edn. Elsevier Saunders, Philadelphia, pp 30–45

Deletis V, Sala F, Morota N (2000) Intraoperative neurophysiological monitoring and mapping during brain stem surgery: a modern approach. Oper Tech Neurosurg 3:109–113

Duchowny M, Jayakar P (1993) Functional cortical mapping in children. In: Devinsky O, Beric A, Dogali M (eds) Electrical and magnetic stimulation of the brain and spinal cord. Raven Press, New York, pp 149–154

Duffau H, Sichez JP (1998) Intraoperative direct electrical stimulation of the lamina quadrigemina in a case of deep tectal cavernoma. Acta Neurochir 140:1309–1312

Duffau H, Capelle L, Sichez N (2002) Intraoperative mapping of the subcortical language pathways using direct stimulations. An anatomo-functional study. Brain 125 (Pt 1):199–214

Duffner PK, Krischer JP, Sanford RA et al (1998) Prognostic factors in infants and very young children with intracranial ependymomas. Pediatr Neurosurg 28: 215–222

Eisner W, Schmid UD, Reulen HJ, Oeckler R, Olteanu-Nerbe V, Gall C, Kothbauer K (1995) The mapping and continuous monitoring of the intrinsic motor nuclei during brain stem surgery. Neurosurgery 37:255–265

Eyre JA, Miller S, Clowry GJ, Conway EA, Watts C (2000) Functional corticospinal projections are established prenatally in the human foetus permitting involvement in the development of spinal motor centres. Brain 123:51–64

Eyre JA, Taylor JP, Villagra F, Smith M, Miller S (2001) Evidence of activity-dependent withdrawal of corticospinal projections during human development. Neurology 57:1543–1554

Eyre JA, Miller S, Clowry GJ (2002) The development of the corticospinal tract in humans. In: Pascual-Leone A, Davey NJ, Rothwell J, Wassermann EM, Puri BKE (eds) Handbook of transcranial magnetic stimulation. Arnold, London, pp 235–249

Farmer JP, McNeely D, Freeman CR (1999) Brainstem gliomas. In: Albright AL, Pollack IF (eds) Principles and practice of pediatric neurosurgery. Thieme, New York, pp 640–654

Fietzek UM, Heinen F, Berweck S, Maute S, Hufschmidt A, Schulte-Monting J, Lucking CH, Korinthenberg R (2000) Development of the corticospinal system and hand motor function: central conduction times and motor performance tests. Dev Med Child Neurol 42:220–227

Gallentine WB, Mikati MA (2009) Intraoperative electrocorticography and cortical stimulation in children. J Clin Neurophysiol 26:95–108

Grabb PA, Albright L, Sclabassi RJ, Pollack IF (1997) Continuous intraoperative electromyographic monitoring of cranial nerves during resection of fourth ventricular tumors in children. J Neurosurg 86:1–4

Humphrey T (1960) The development of the pyramidal tracts in human fetuses correlated with cortical differentiation. In: Tower DB, Schade JB (eds) Structure and function of the cortex: proceedings of the second international meeting of neurobiologists. Elsevier, Amsterdam, pp 93–103

Ishihara H, Bjeljac M, Straumann D, Kaku J, Roth P, Yonekawa Y (2006) The role of intraoperative monitoring of oculomotor and trochlear nuclei -safe entry zone to tegmental lesions. Minim Invasive Neurosurg 49:168–172

Ito E, Ichikawa M, Itakura T, Ando H, Matsumoto Y, Oda K, Sato T, Watanabe T, Sakuma J, Saito K (2013) Motor evoked potential monitoring of the vagus nerve with transcranial electrical stimulation during skull base surgeries. J Neurosurg 118:195–201

Jayakar P (1993) Physiological principles of electrical stimulation. Adv Neurol 63:17–27

Keles GE, Lundin DA, Lamborn KR et al (2004) Intraoperative subcortical stimulation mapping for hemispherical perirolandic gliomas located within or adjacent to the descending motor pathways: evaluation of morbidity and assessment of functional outcome in 294 patients. J Neurosurg 100:369–375

King RB, Schell GR (1987) Cortical localization and monitoring during cerebral operations. J Neurosurg 67: 210–219

Koh TH, Eyre JA (1988) Maturation of corticospinal tracts assessed by electromagnetic stimulation of the motor cortex. Arch Dis Child 63:1347–1352

Kombos T, Suess O, Funk T, Kern BC, Brock M (2000) Intra-operative mapping of the motor cortex during surgery in and around the motor cortex. Acta Neurochir 142:263–268

Kubis N, Catala M (2003) Development and maturation of the pyramidal tract. Neurochirurgie 49:145–153

Lang J Jr, Ohmachi N, Lang J Sr (1991) Anatomical landmarks of the rhomboid fossa (floor of the 4th ventricle), its length and its width. Acta Neurochir 113:84–90

Legatt AD (2008) BAEPs in surgery. In: Nuwer MR (ed) Intraoperative monitoring of neural function. Handbook of clinical neurophysiology. Elsevier, Amsterdam, pp 334–349

Masur H, Althoff S, Kurlemann G, Strater R, Oberwittler C (1995) Inhibitory period and late muscular responses after transcranial magnetic stimulation in healthy children. Brain and Development 17:149–152

Merton PA, Morton HB (1980) Stimulation of the cerebral cortex in the intact human subject. Nature 285(5762):227

Morota N, Deletis V, Epstein FJ, Kofler M, Abbott R, Lee M, Ruskin K (1995) Brain stem mapping: neurophysiological localization of motor nuclei on the floor of the fourth ventricle. Neurosurgery 37:922–930

Muller K, Homberg V (1992) Development of speed of repetitive movements in children is determined by structural changes in corticospinal efferents. Neurosci Lett 144:57–60

Muller K, Homberg V, Lenard HG (1991) Magnetic stimulation of motor cortex and nerve roots in children. Maturation of cortico-motoneuronal projections. Electroencephalogr Clin Neurophysiol 81:63–70

Muller K, Kass-Iliyya F, Reitz M (1997) Ontogeny of ipsilateral corticospinal projections: a developmental study with transcranial magnetic stimulation. Ann Neurol 42:705–711

Neuloh G, Pechstein U, Cedzich C, Schramm J (2004) Motor evoked potential monitoring with supratentorial surgery. Neurosurgery 54:1061–1070

Nezu A, Kimura S, Ohtsuki N, Tanaka M (1997) Transcranial magnetic stimulation in benign childhood epilepsy with centro–temporal spikes. Brain and Development 19:134–137

Nezu A, Kimura S, Takeshita S (1999) Topographical differences in the developmental profile of central motor conduction time. Clin Neurophysiol 110: 1646–1649

Ng WH, Mukhida K, Rutka JTR (2010) Image guidance and neuromonitoring in neurosurgery. Child's Nerv Syst 26:491–502

Nossek E, Korn A, Shahar T, Kanner AA, Yaffe H, Marcovici D et al (2011) Intraoperative mapping and monitoring of the corticospinal tracts with neurophysiological assessment and 3-dimensional ultrasonography-based navigation. J Neurosurg 114:738–746

O'Rahilly R, Muller F (1994) Human embryonic brain. An atlas of developmental stages. Wiley-Liss, New York

Ojemann G (1991) Cortical organization of language. J Neurosci 11:2281–2287

Ojemann SG, Berger MS, Lettich E, Ojemann GA (2003) Localization of language function in children: results of electrical stimulation mapping. J Neurosurg 98: 465–470

Pechstein U, Cedzich C, Nadstawek J, Schramm J (1996) Transcranial high-frequency repetitive electrical stimulation for recording myogenic motor evoked potentials with the patients under general anesthesia. Neurosurgery 39:335–343

Penfield W, Boldrey E (1937) Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. Brain 60:389–443

Procaccio F, Gambin R, Gottin L, Bricolo A (2000) Complications of brain stem surgery: prevention and treatment. Oper Tech Neurosurg 3:155–157

Resnick TJ, Alvarez LA, Duchowny M (1988) Cortical stimulation thresholds in children being evaluated for resective surgery. Epilepsia 29:651–652

Rhoton AL (2000) The posterior fossa veins. Neurosurgery 47:S69–S92

Rivet DJ, O'Brien DF, Park TS, Ojemann JG (2004) Distance of the motor cortex from the coronal suture as a function of age. Pediatr Neurosurg 40:215–219

Riviello JJ, Kull L, Troup C, Holmes GL (2001) Cortical stimulation in children: techniques and precautions. Tech Neurosurg 7:12–18

Romstock J, Strauss C, Fahlbusch R (2000) Continuous electromyography monitoring of motor cranial nerves during cerebellopontine angle surgery. J Neurosurg 93:586–593

Rothwell J, Burke D, Hicks R, Stephen J, Woodforth I, Crawford M (1994) Transcranial electrical stimulation of the motor cortex in man: further evidence for the site of activation. J Physiol 481:243–250

Sala F, Lanteri P (2003) Brain surgery in motor areas: The invaluable assistance of intraoperative neurophysiological monitoring. J Neuros Sci 47(2):79–88

Sala F, Krzan MJ, Deletis V (2002) Intraoperative neurophysiological monitoring in pediatric neurosurgery: why, when, how? Childs Nerv Syst 18:264–287

Sala F, Manganotti P, Tramontano V, Bricolo A, Gerosa M (2007) Monitoring of motor pathways during brain stem surgery: what we have achieved and what we still miss? Neurophysiol Clin 37:399–406

Sala F, Manganotti P, Grossauer S, Tramontano V, Mazza C, Gerosa M (2010) Intraoperative neurophysiology of the motor system in children: a tailored approach. Childs Nerv Syst 26:473–490

Sala F, Squintani G, Tramontano V (2014) Intraoperative neurophysiological monitoring during brain stem surgery. In: Loftus CM, Biller J, Baron EM (eds) Intraoperative neuromonitoring. Mc Graw Hill, New York 285–297

Sala F, Gallo P, Tramontano V, Gerosa M (2015a) Intraoperative neurophysiological monitoring in posterior fossa surgery. In: Ozek MM, Cinalli G, Maixner W, Saint-Rose C (eds) Posterior fossa tumors in children, 1st edn. Springer, Cham 239–262

Sala F, Coppola A, Tramontano V, Babini M, Pinna G (2015b) Intraoperative neurophysiological monitoring for the resection of brain tumors in pediatric patients. J Neurosurg Sci 59(4):373–382

Sartorius CJ, Berger MS (1998) Rapid termination of intraoperative stimulation-evoked seizures with application of cold Ringer's lactate to the cortex. Technical note. J Neurosurg 88:349–351

Schevon CA, Carlson C, Zaroff CM, Weiner HJ, Doyle WK, Miles D et al (2007) Pediatric language mapping: sensitivity of neurostimulation and Wada testing in epilepsy surgery. Epilepsia 48:539–545

Schlake HP, Goldbrunner R, Siebert M, Behr R, Roosen K (2001) Intra-operative electromyographic monitoring of extra-ocular motor nerves (Nn. III, VI) in skull base surgery. Acta Neurochir 143:251–261

Sekiya T, Hatayama T, Shimamura N, Suzuki S (2000) Intraoperative electrophysiological monitoring of oculomotor nuclei and their intramedullary tracts during midbrain tumor surgery. Neurosurgery 47:1170–1176. discussion 1176–1177

Soriano SG, Eldredge EA, Wang FK, Kull L, Madsen JR, Black PM et al (2000) The effect of propofol on intraoperative electrocorticography and cortical stimulation during awake craniotomies in children. Paediatr Anaesth 10:29–34

Stapleton SR, Kiriakopoulos E, Mikulis D, Drake JM, Hoffmann HJ, Humphreys R, Hwang P, Otsubo H, Holowka S, Logan W, Rutka JT (1997) Combined utility of functional MRI, cortical mapping, and frameless stereotaxy in the resection of lesions in eloquent areas of brain in children. Pediatr Neurosurg 26:68–82

Suzuki K, Matsumoto M, Ohta M, Sasaki T, Kodama N (1997) Experimental study for identification of the facial colliculus using electromyography and antidromic-evoked potentials. Neuro- surgery 41:1130–1136

Szelényi A, Joksimovic B, Seifert V (2007) Intraoperative risk of seizures associated with transient direct cortical stimulation in patients with symptomatic epilepsy. J Clin Neurophysiol 24:39–43

Szelenyi A, Senft C, Jardan M, Forster MT, Franz K, Seifert V, Vatter H (2011) Intraoperative subcortical electrical stimulation: a comparison of two methods. Clin Neurophysiol 122:1470–1475

Taniguchi M, Cedzich C, Schramm J (1993) Modification of cortical stimulation for motor evoked potentials under general anesthesia; technical description. Neurosurgery 32:219–226

Wisoff JH, Boyett JM, Berger MS, Brant C, Li H, Yates AJ et al (1998) Current neurosurgical management and the impact of the extent of resection in the treatment of malignant gliomas of childhood: a report of the Children's cancer group trial no. CCG-945. J Neurosurg 89:52–59

Wood CC, Spencer DD, Allison T, McCarthy G, Williamson PD, Goff WR (1988) Localization of human sensorimotor cortex during surgery by cortical surface recording of somatosensory evoked potentials. J Neurosurg 68:99–111