Chapter 9
Motor Evoked Potential

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Abbreviations

BAEP	Brainstem auditory evoked potential
CBT	Corticobulbar tract
COR	Class of recommendation
CR	Corona radiata
CST	Corticospinal tract
CMAP	Compound motor unit action potential
DCS	Direct cortical stimulation
EEG	Electroencephalogram
EPSP	Excitatory postsynaptic potential
IOM	Intraoperative neurophysiologic monitoring
ISI	Interstimulus interval
LMN	Lower motor neurons
LOE	Level of evidence
MEP	Motor evoked potentials
MU	Motor unit
mMEP	Muscle motor evoked potentials
TES	Transcranial electrical stimulation
UMN	Upper motor neurons
SSEP	Somatosensory evoked potential

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Anatomic Review

Good knowledge about the anatomy and physiology of the motor system is crucial in the proper execution of the MEP. Its central components begin in the primary motor cortex (Brodmann area 4), usually located in the precentral gyrus, which works in association with other motor areas, including the premotor cortex, the supplementary motor area, posterior parietal cortex, somatosensory cortex, and several subcortical brain regions, to plan and execute movements. Damage to the primary motor cortex will result in permanent weakness. While lesions of the associated areas may also cause a motor disturbance, they tend to be transient as the remaining cortices can take over the lost function [1].

The connection between the motor cortex and motor neurons in the spine/brainstem is made by the pyramidal tract that is composed of the descending axons of the Betz cells, also known as upper motor neurons (UNM), which are part of the corticospinal tract (CST) and part of the corticobulbar tract (CBT) [2]. These descending axons in the corona radiata (CR) progressively converge at the posterior limb and genu of the internal capsule (IC) and continue their path inferiorly through the cerebral peduncle, the base of the pons, and medulla pyramids. Here, most of the CST fibers (80 to 90%) cross the midline constituting the pyramidal decussation and follow as lateral corticospinal tract or, in a smaller proportion, keep uncrossed as the anterior or lateral corticospinal tract. There are significant individual variations. The CST fibers descend along the spinal cord reaching the lower motor neurons (LMNs), whose cell body is located in the ventral gray matter of the spinal cord. A small percentage connects mono synaptically, whereas the majority terminate in propriospinal interneurons [3, 4]. In its turns, the CBT axons diverge from the pyramidal tract at the brainstem by synapse with the contralateral and ipsilateral motor nucleus of the cranial nerves via interneurons or directly (more details in Chap. 21).

Each of these levels is somatotopically organized. At the precentral gyrus, the foot and leg areas are located in the medial surface of the hemisphere, within the interhemispheric fissure. Towards the middle convexity, the thigh, trunk, arm, and forearm are represented, respectively. Further down, there are areas of the hand, face, and mouth; and lastly, next to the Sylvian fissure, it is the area of the tongue and pharynx (Fig. 9.1) [3]. The size of the representation is proportional to its functional importance, being much larger for distal limbs and face. A similar sequence can be seen at caudal levels where the pharyngeal, tongue, and facial muscles are at the genu and medial portion of the cerebral peduncle, distal/ proximal superior limb, trunk, and proximal/ distal inferior limb are represented in the anteroposterior direction of the posterior limb of the IC and mediolateral direction of the cerebral peduncle (Figs. 9.2 and 9.3).

Besides the corticospinal fibers, other indirect motor pathways travel to synapses with the LMNs mostly indirectly by interneurons, including the rubrospinal, reticulospinal, vestibulospinal, and tectospinal tracts. In addition, there are intrinsic spinal cord motor control systems like inputs from inhibitory interneurons and sensory Ia

Fig. 9.1 Cortical somatotopic representation of the Penfield motor homunculus

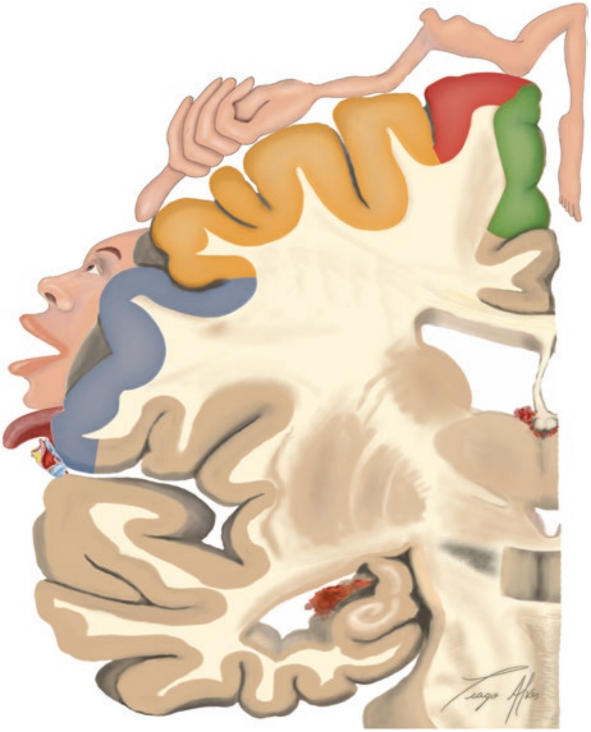
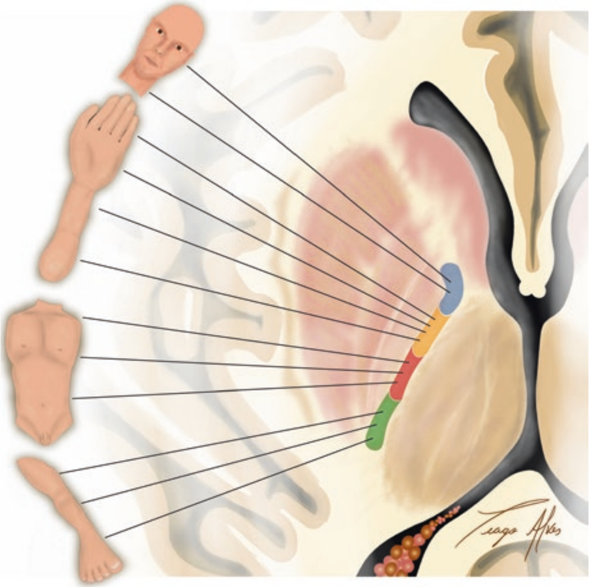


Fig. 9.2 Motor somatotopic representation at the level of the internal capsule



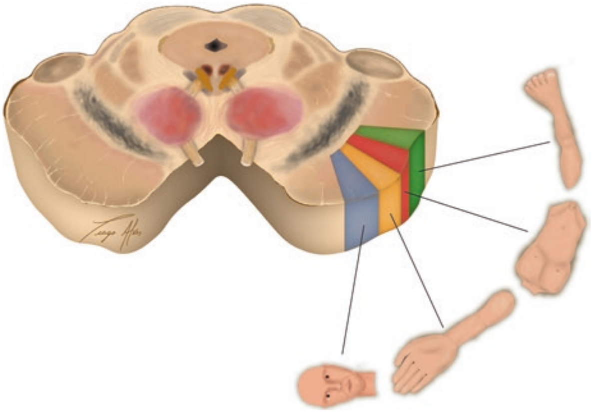


Fig. 9.3 Motor somatotopic representation at the level of the cerebral peduncle

and Ib fibers in addition to the propriospinal neurons, which provide an indirect disynaptic pathway for corticospinal volleys [5, 6].

Each axon of the LMNs will form a motor unit (MU) that includes the muscle fibers innervated and the neuromuscular junctions interposed. The more finely controlled a muscle is, the lesser the number of muscle fibers innervated by each motor unit. Thus, the proximal limb muscles have higher muscle fibers number per motor unit compared to distal muscles.

Brief Historical Review and Physiological Basis

The use of electrical stimulation by Penfield founded intraoperative brain mapping in the first half of the twenty century. However, more than fifty years would pass until the MEPs have become viable to be reliably used for IOM [4, 7–11].

The first neurophysiological registration of an MEP dates back to the 1950s when Patton and Amassian recorded direct traveling waves from the CST stimulating with a single electric pulse applied at the monkey's motor cortex [12]. Two types of waves were observed: the first was a short-latency response called D-wave (direct wave), interpreted as a result of the direct activation of the CST, followed by a set of waves termed I-waves (indirect waves), interpreted as trans-synaptic activation of motor neurons of the CST via cortical synaptic circuits.

The remaining motor path, including the lower spinal cord, nerve roots, and peripheral motor nerves, was not represented by these waves. Thus, different techniques have been tried in order to evaluate them. Stimulation of the spinal cord with recording at another level of the spine, nerves, or muscles was attempted. Even though muscle response could be evoked by spine stimulation, these recordings were not an accurate representation of the motor path since spinal cord stimulation activates other tracts in a non-selectively way, including antidromic volleys in the dorsal column ending at collateral synapses on LMNs [13–15].

Since the 1980s, we can elicit muscle response after transcranial stimulation both electrically and magnetically in conscious humans [11, 16]. However, due to the multi-synaptic nature of these evoked responses, these potentials did not persist under general anesthesia. Then, in 1993, Taniguchi broke this barrier by using a high-frequency train of 3–5 electric pulses with an inter-pulse interval of 2–4 ms applied directly to the human motor cortex, which evoked a muscle MEP (mMEP) intraoperatively in anesthetized patients. This sequence of stimulus in such a short interval seems to allow the summation of excitatory postsynaptic potential (EPSP) of the descendent volleys, mostly D-waves but probably also some I-waves, thus enabling the LMNs to fire [10].

Nowadays, MEP is widely used in the intraoperative practice at different types of surgeries threatening the motor system, either by transcranial electrical stimulation (TES) or by direct cortical stimulation (DCS). The muscle MEP is more versatile and most broadly employed, although the D-waves also have a specific but crucial role in some situations.

D-Waves

As a result of direct and selective activation of the axons of the CST, D-waves are a pure representation of the lateral system at the spinal cord. It comprises axons from the CST, responsible for sophisticated motor control of fine movements of the distal limbs and rubrospinal tract [3]. A single-pulse stimulus is applied over the motor cortex, while the descending volley of the CST is recorded over the spinal cord. I-waves are occasionally obtained in anesthetized patients; however, they are not stable enough to be followable. As the intensity of the stimulus increases, the greater the number of axons is recruited, increasing the amplitude of the registered potential until the maximum amount of CST is activated and the response reaches a point of stability without variation inter trials at the suprathreshold stimulation. An inverse relationship is also observed between the latency and the intensity of the stimulus. The greater the stimulus applied, the shorter the response latency, which can also bifurcate or even trifurcate into earlier components. Thus, it seems that higher intensities activate the CST deeper, and these shorter latencies and earlier components are nothing more than representations of activation at the level of the IC or brainstem [17–19].

The D-wave amplitude is also dependent on the pool of CST axons at the record level. Thus, the D-wave is bigger at cervical levels, and it gets smaller and smaller as the recording electrode goes down in the craniocaudal direction until it is no longer obtained generally around the T10 level [5, 20, 21].

Muscle MEP

Unlike the D-wave, the mMEP results from the activation of a multi-synaptic path mainly mediated by the propriospinal interneurons. This characteristic is of cornerstone importance in understanding the role of mMEP during intramedullary spinal cord tumor resection (more details in Chap. 28). The excitability of the interneurons and alpha motor neurons results from inhibitory and facilitatory impulses from supraspinal sources, such as rubrospinal, reticulospinal, and vestibulospinal tracts. Intraspinal propriospinal tracts are involved in reflexes, posture, and locomotor activity. They interconnect up to six spinal segments (short) and cervical and lumbar enlargements (long) [22]. Stimulation of the somatosensory cortex can also elicit mMEP, but it requires higher intensity.

Under anesthesia, mMEP only will be obtained efficiently if a short train at high frequency is used, thus allowing a temporal and spatial summation of LMN EPSPs [10]. The number of MU firing at intensities near the threshold is unknown and widely variable. Higher intensities of stimulation result in increased amplitude, polyphasia, duration, and short latencies by recruiting more MU and deeper until supramaximal intensity. Nevertheless, even in supramaximal levels, considerable trial to trial variation in amplitude and morphology occurs [5, 21, 23].

Methodology

Of paramount importance, while choosing a methodology, we point out that activated CST must be rostral to the lesion. This principle is going to rule all other variables: (1) DCS or TES, (2) electrode placement, (3) stimulus parameters, and (4) recording protocol. The goal is to match the highest amplitude of compound motor unit action potential (CMUAP) with the lowest intensity, leaving room for further intensity increase during the long-lasting surgery [24].

Electrode Placement

Cortical stimulation, either by DCS or by TES, works better utilizing anodal stimuli, whereas cathodal stimuli are more efficient for subcortical stimulation. Thus the montages are designed as anode-cathode for TES and DCS and vice versa for subcortical stimulation [21, 25]. For direct cortical stimulation, a subdural strip electrode is positioned over the primary motor cortex, and one or more contact can be used as an anode and other channels on the same strip or a subdermal needle, placed in the or near the surgical field, as a cathode [21, 24].

For TES, electroencephalogram (EEG) cups, needles, and corkscrew electrodes can be used. However, the last one provides better fixation and lower impedance and

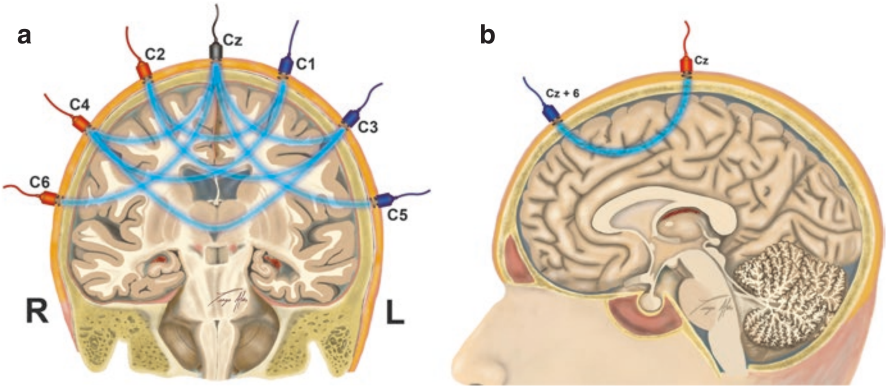


Fig. 9.4 The most used position for TES electrodes: C3, C4, C1, C2, Cz, and 6 cm anterior to Cz as well as C5 and C6, enabling multiple montages, such as C1-C2, C1-C4, C2-C3, C3-C4, C3/C4-Cz, C5/C6-Cz (**a**), and Cz-Cz + 6 cm (**b**). Right (R) and Left (L)

used to be preferred. Stimulation electrodes may be placed at the scalp in various positions, based on the 10–10 system (expanded 10–20) with the arrangement depending on the interest [26, 27]. The electrodes are most commonly placed at C3, C4, C1, C2, Cz, and 6 cm anterior to Cz, enabling multiple montages, such as C1-C2, C1-C4, C2-C3, C3-C4, C3/C4-Cz, and Cz-Cz + 6 cm (Fig. 9.4). Some have proposed a slight anterior positioning as M1, M2, M3, M4 (1cm in front of the traditional C position) [28], although there is no proven efficacy difference between the two sites (C versus M). Based on the motor homunculus distribution, the C3 and C4 positions tend to be more efficient to activate the motor path correspondent to the superior limbs at the same time that the electrodes placed at or near the middle line, namely, C1, C2, Cz, and Cz + 6 cm, preferably activate the lower limbs [20, 21, 29]. We have also suggested C5 and C6 as an interesting position to CBT due to the somatotopic organization of the cortical areas of the face and neck, allowing the use of lower stimulus intensities [30].

The montages are categorized according to their disposition on the scalp as hemispheric, interhemispheric, and midline. The hemispheric montages (C3/5-Cz, C4/6-Cz) activate the corresponding hemisphere, generating a predominantly contralateral response. These montages limit, at least in part, the depth of current penetration and allow the selective activation of upper limbs and face with low-intensity stimuli and minimal patient movement [21, 23, 29, 31]. The interhemispheric montages (C3-C4 and C1-C2) promote deeper current penetration evoking bilateral responses that include upper and lower limbs and often also sphincter and face, with lower threshold and higher amplitude contralateral to the anode [21, 23, 29, 31]. However, the interhemispheric montages are not advisable for CBT evaluation due to their potential to activate the facial nerve peripherally or supratentorial surgeries because of the high risk of bypassing the level of interest [5, 32]. The current shutting through the scalp makes C1-C2 a less efficient assembly than C3-C4, although, on the other hand, it induces less movement and may allow selective activation of the lower limbs [21, 29, 31]. Lastly, the midline montage (Cz-Cz + 6 cm) evokes symmetric leg mMEPs but is much less effective to hand and face [21, 29]. Even to selective leg responses, high intensities are often necessary because the electrical current induced occurs in an anterior-posterior direction, and this may preferentially activate neurons transynaptically since it might not evoke D waves as readily as coronal TES [33].

It is essential to highlight that activation happens already in the axon, not at the cell body. Furthermore, the level of activations depends on the stimulus intensity: the greater the intensity of the stimulus delivered, the deeper the CST activation point. So, keeping the same stimulator position, the depolarization would happen juxtacortical at the axon hillock, deeper at the IC, or even at the brainstem if progressively greater stimulus intensities are used [18–20] (Fig. 9.5).

Indeed, the neurophysiologist must always pay attention to the premise of *staying above the target* (see Fig. 9.6). For example, if the level at risk is the spinal cord, a C1-C2 or C3-C4 interhemispheric transcranial stimulation will activate the four limbs efficiently without major anatomic concerns. On the other side, if this same stimulation is used to evaluate a resection of a juxtacortical tumor, the activation will probably bypass the point of interest. Thus, it will only obtain an intraoperative mMEP registration without any predictive value, which cannot be called monitoring.

In order to avoid such pitfalls, we recommend a *topographic-physiological-guided MEP*. It is a more appropriate way to stimulate each level at risk, and the recorded response works as feedback of adequacy. Hence, we usually prefer

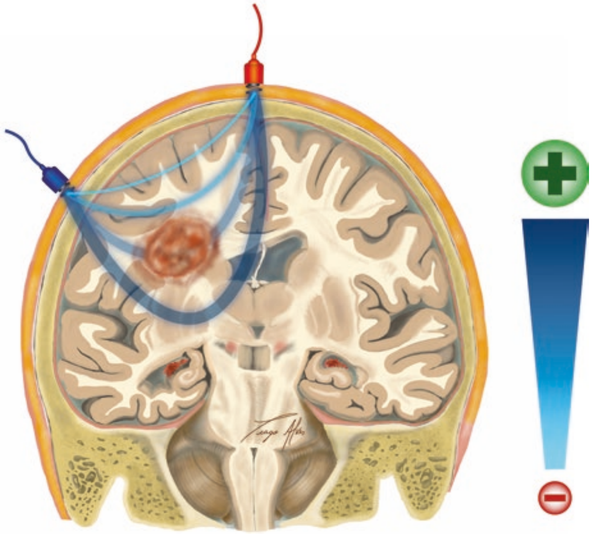


Fig. 9.5 The hemispheric montages activate the corresponding hemisphere, generating a predominantly contralateral response. These montages limit, at least in part, the depth of current penetration and allow the selective activation of upper limbs and face with low-intensity stimuli. Nevertheless, as long as the stimulus intensity increases, the stimulus loop tends to depolarize deeper levels being able to reach the IC or even the brainstem. Thus, is it crucial to stay careful in order to not allow the stimulus bypass the level of interest

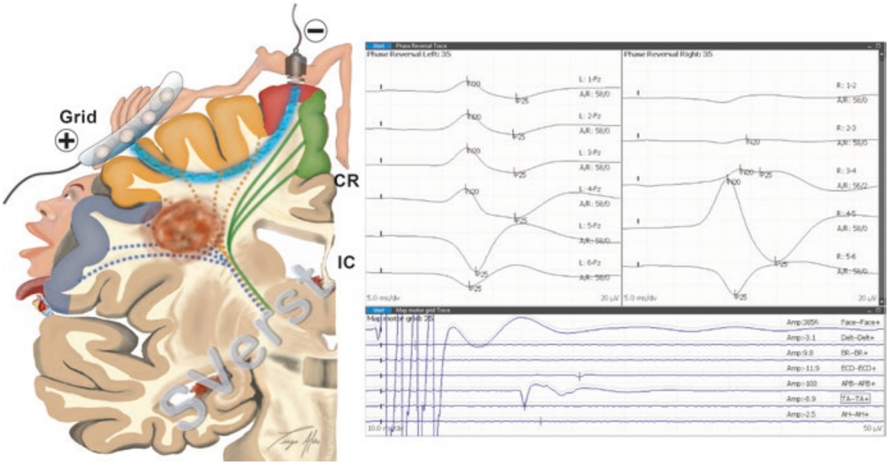


Fig. 9.6 Grid for upper limb: strip selective DCS MEP for upper extremity for lesions sitting at the level of CR. Strip position guided by phase reversal (see details about brain motor mapping technique at Chap. 14). MEP recording at contralateral *Mentalis (Face), Deltoide (Delt), Braquiorradialis (BR), Extensor digiti comunis (ECD), Abdutor pollicis brevis (APB), Tibialis anterior (TA),* and *Abductor hallucis (AH)*

Table 9.1 Reasoning between target and stimulation assembly

Target	Electrodes´ montage	Recording muscles	Notes
Corona radiata (CR)	DCS: Grid electrode Reference: Cz/ Fz or mc. If the tumor is large and separate upper and lower limb stimulation is needed, try to place the grid along the precentral gyrus and stimulate 2 different points of the grid or use 2 grids	A	Lesions in the vicinity of the convexity should always be monitored using DCS. Separate upper and lower limb mMEP should be achieved to infer stimulus is at CR
Internal capsula (CI)/ Insular tumor/ aneurysms/ anterior and media fossa approach	DCS or hemispheric TES: First option: C3 or C4-Cz for upper limbs and Cz-Cz + 6 for lower limbs. If Cz-Cz + 6 fails, try Cz-C4 Second option: C4-C1 and C3-C2	A and B	It is acceptable to get mMEP in all contralateral muscles, provided that ipsilateral mMEPs are absent. In this situation, only one-side IC is being activated
Infratentorial	Interhemispheric C1-C2 or C3-C4	C	

Recording muscles: (A) contralateral: Face, Deltoide, forearm flexor and extensor, *Abductor digiti minimi*, *Tibialis anterior and abductor hallucis. (AH)*; (B) ipsilateral: *Abductor digiti minimi*, *and Abductor halluces*; (C) bilateral *Abductor digiti minimi*, *Tibialis anterior, and abductor hallucis*

hemispheric stimulus for separate upper and lower limb mMEP for supratentorial approaches and interhemispheric assembly for infratentorial and spinal surgeries (Table 9.1). The supratentorial protocol is divided into cortical and CR versus IC. The former is always performed using DCS. So, lower intensities are necessary, and the activation usually happens juxtacortical, generating response in the muscle group represented in the cortex below the active grid (Fig. 9.6). If the IC is treated as surgeries for approaching an insular tumor or clipping an internal carotid or middle cerebral arteries aneurysm, the DCS is still recommended, although not always feasible, because often the primary motor cortex is not exposed by the craniotomy. In such situations, it is also possible to resort to TES stimulation as long as it stimulates upper or lower limbs selectively.

To ensure selective stimulation during the IC-target protocol, it is mandatory to record bilaterally (four limbs). The reasoning is based on the presence or absence of mMEP at the extremities. Since the first CST convergence happens at IC, we suppose that activation of IC results in simultaneous contralateral upper and lower mMEP but no ipsilateral mMEP. It means that only one IC is being stimulated. Eliciting simultaneous ipsilateral mMEP represents activation below IC, most probably by activating bilateral CST at the brainstem (Fig. 9.7).

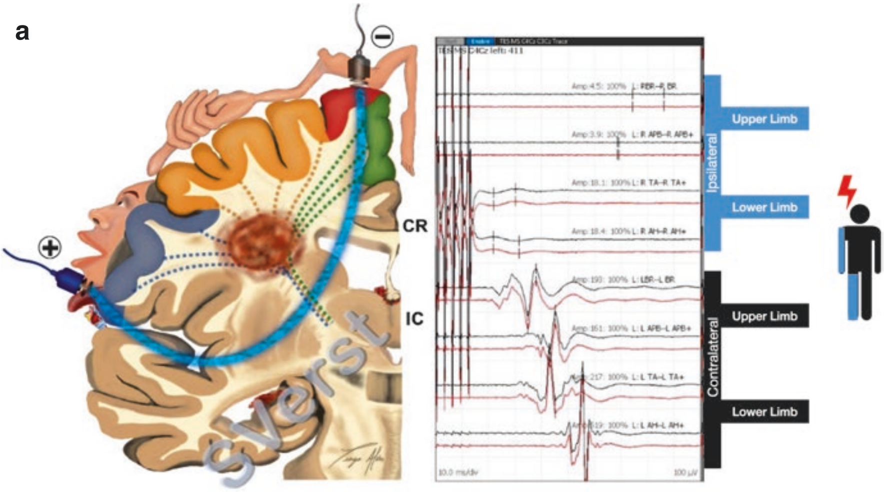


Fig. 9.7 Topographic-guided MEP protocol: bilateral muscle recordings and hemispheric stimulation in order to reach the level above the target. Recording at contralateral *Mentalis (Face), Deltoide (Delt), Braquiorradialis (BR), Extensor digiti comunis (ECD), Abdutor pollicis brevis (APB), Tibialis anterior (TA),* and *Abductor hallucis (AH)* in addition to *ipsilateral to stimulation Abdutor digiti minimi (ADMc)* and *Abductor hallucis (AHc)* or *BR, APB, TA, and AH bilateral.* (**a**) At lower intensity, mMEPs only from contralateral upper limb and face are recorded: probable stimulation site: CR, above the IC. Partial CR activation represented by dashed lines. (**b**) At median intensity, only mMEPs from contralateral upper and lower limb are recorded. There is mMEP response at the ipsilateral body. Probable stimulation site: IC. (**c**) At higher C3-Cz intensity stimulation, recordings of mMEP from contralateral upper and lower limbs + ipsilateral upper limb are present. Probable stimulation site: at the level of bilateral IC, or at the brainstem or below, where bilateral CSTs are being activated. ADM: *adductor digiti minimi*

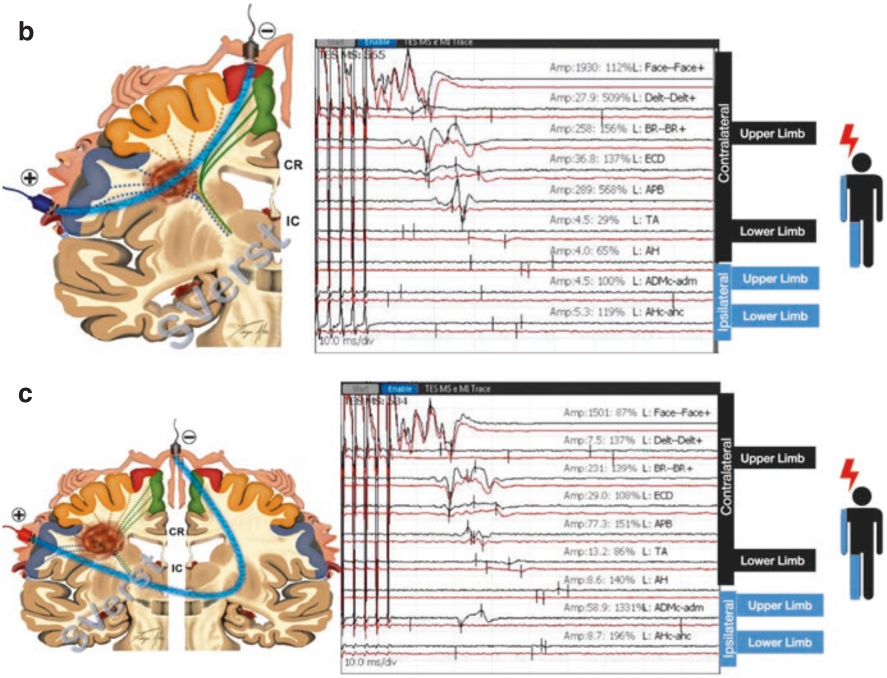


Fig. 9.7 (continued)

The biggest challenge is to achieve separate recordings for lower limbs. It relies on the sparse UMN population and depth of the interhemispheric sulcus. If the lesion is at CR, the grid electrode should be placed in the vicinity of the interhemispheric sulcus or slid inside the sulcus (Fig. 9.8). For lower limb mMEP activation nearby IC, Cz-Cz + 6 cm is effective in 68% [29]. Alternatively, Cz-C4 or C3, using Cz as the anode in the vertex and the cathode in the convexity, is sometimes effective to obtain a selective response of the lower limbs, although it often promotes deeper and less selective activation [5]. Most often, both lower limb mMEPs are recorded simultaneously due to the proximity of bilateral cortices. Yet, it does not compromise topographic-guided MEP (Fig. 9.9).

A combination of two electrodes in each hemisphere in parallel, called quadripolar (C1/M3 - C2/M4 or C3-M1/C4-M2), has recently been proposed by Schwartz and Husain [34]. The concept is expanding the current network to the same applied stimulation since the active electrodes are simultaneously positioned over the arm and leg area. The linked quadripolar method showed the most robust mMEP response in the foot, and the stimulation intensity was lower on average than any of the standard bipolar montages [34]. Some authors have also reported the same advantages to external anal sphincter MEPs with this electrode configuration [24].

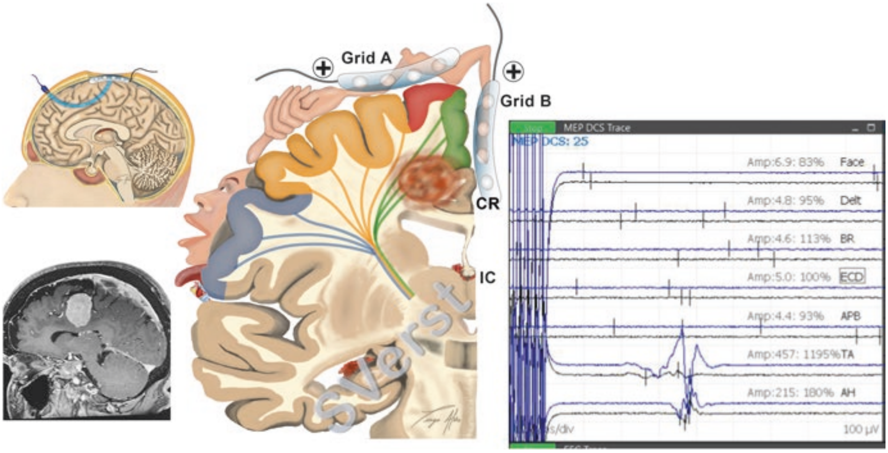


Fig. 9.8 Grid for lower limb: selective DCS MEP for lower extremity for lesions sitting at the level of CR: suggested positions for grid electrode: (A) or (B). Recording at contralateral *Mentalis (Face), Deltoide (Delt), Braquiorradialis (BR), Extensor digiti comunis (ECD), Abdutor pollicis brevis(APB), Tibialis anterior (TA),* and *Abductor hallucis (AH)*

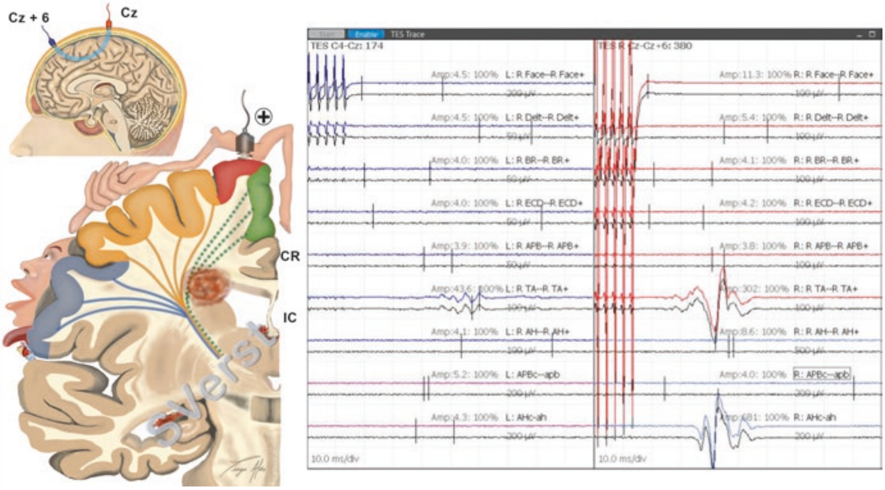


Fig. 9.9 Cz-Cz + 6: woman, 62 y.o., re-operation of glioma at right caudate nucleus. MEP protocol: C4-Cz for upper mMEP and Cz-Cz + 6 for lower limb mMEP. Recording at contralateral *Mentalis (Face), Deltoide (Delt), Braquiorradialis (BR), Extensor digiti comunis (ECD), Abdutor pollicis brevis (APB), Tibialis anterior (TA),* and *Abductor hallucis (AH)* in addition to *ipsilateral Abdutor digiti minimi (ADMc)* and *Abductor hallucis (AHc)* or *BR, APB, TA, and AH bilateral.* Stimulation Cz-Cz + 6 cm at lower intensity results in unilateral response; stimulation at higher intensity results in bilateral lower limb mMEP, without any response at upper limb, which is considered effective for topographic-guided MEP

Stimulus Parameters

When it comes to cortical stimulation, either by TES or ECD, anodal stimulation is more effective than cathodic because the dendrites on the surface of the cortex hyperpolarize under the anode, which depolarizes the descending axons of the CST, thus preferentially activating the D-waves. On the other hand, cathodic stimulation is more favorable to the depolarization of cortical interneurons, preferentially activating the I-waves. As it involves a greater number of synapses, the latter is more susceptible to anesthetic effects. Due to direct contact with the axon at the subcortical level, cathodal stimulation becomes the most effective [12, 35–38].

As pointed above, a high-frequency multipulse technique is necessary to elicit mMEP: multipulse stimulation (3 to 9 stimuli) delivered with a short interstimulus interval (ISI) 1–4 msec, duration of 0.05 to 0.5 msec, preferably at an inter-train frequency of 1 to 2 Hz. A minimum of 3 pulses is usually required to evoke mMEP. However, many patients may require a larger number of pulses, so 4 to 5 pulses seem to be a good starting point; thenceforth, this number can be adjusted as needed, with some practitioners using up to 9 pulses [5, 21, 24, 39]. The ISI is calculated by dividing 1000 by the stimulus frequency (Hz). Shorter ISI, such as 1 or 2 ms, increases the chance of subsequent pulses finding the pathway still in the relative refractory period, whereas ISI longer than 4 ms may not be favorable to the summation of the EPSPs. Therefore, ISI of 3, and especially 4 ms, generally provides the lowest motor thresholds at least for limb mMEP in patients with normal motor status under total intravenous anesthesia [20, 23, 29, 40]. For short-latency facial MEP, a 1-2 ms ISI can be helpful in separating the stimulation artefact at the same time that it brings responses with the highest amplitudes although with the simplest morphology [32]. We prefer to try the 2, 3, and 4 ms ISIs in each patient and choose the one that has worked better.

The stimulus can be delivered both as constant voltage or constant current. In the former, the stimulating current depends on the resistance, which, in its turns, can vary along with the procedure. At the constant current, the voltage fits according to the resistance to deliver the current chosen. The required intensity ranges a lot depending on age, electrode position, previous deficits, and anesthetic depth. It also depends on the other stimulus parameters. The use of a longer pulse duration has the strongest effect on the lowering of the motor threshold.

Nevertheless, the delivered charge increases proportionally by increasing the pulse duration [21, 29, 41]. Comparing slower (0.50 ms) and faster (0.05 ms) charges, there was no significant difference concerning MEP parameters (amplitude or latencies), MEP elicitability, and intraoperative MEP variability [41]. Rheobase is the smallest current value of a rectangular stimulus with pulse width considered infinite (from 250 to 1000 μs) that causes muscle contraction. Chronaxie is the smallest pulse width, also of a rectangular stimulus, but with twice the value of the rheobase, which causes muscle contraction. Short pulses save charge at the expense of a higher current whereas long pulses constrain current at the expense of a higher charge. The balance between current and charge, considered optimal, is in the pulse duration equal to the chronaxie. A pulse width of 0.2 ms has already been demonstrated to be most consistently optimal or near-optimal [21, 29, 40].

Sometimes, even the proper use of the pulse train technique is not enough to evoke robust muscle responses, especially in patients with previous motor pathway dysfunction or unavoidable unfavorable anesthetic regimens. In such situations, facilitation techniques may be saving. Recurrent pulse train stimulus at 1 or 2 Hz is often effective at enhancing mMEP. It has even been proposed using protocols with higher frequencies up to 5 Hz, which augmented the amplitude of the responses by about 2–3 times compared with 1 Hz. It is essential to point out that, in this same study, the facilitation effects tended to peak in the last half of the series of 10 TESs [42].

Another strategy uses the double train, which consists of applying a preconditioning stimulus before the test stimulus. The former would facilitate the action of the main stimulus by depolarizing the LMNs, thus maximizing its excitability. It is called homonymous stimulation because both conditioning and test stimuli are applied at the same site. From a practical point of view, this is done by applying a 3 to 4 pulse train as a conditioning stimulus followed by the 4–6 pulse test stimulus at specific inter-train intervals (ITI). The facilitation is optimal at short ITIs of 10 to 30 ms and longer ITIs of over 100 ms. It seems that short ITIs facilitate depolarization at the level of the LMNs, whereas the facilitation of longer ITIs is likely to be of cortical origin. It is important to be aware that there is a relatively inhibitory effect with an ITI between 30 and 100 ms [43, 44].

It is also possible to enhance the mMEP by employing a preconditioning stimulus delivered at the peripheral level, known as the heteronymous stimulus since the facilitating stimulus is performed in a different site than the test stimulus. Through it, it is possible to amplify the mMEP of a restricted muscle group corresponding to the conditioned nerve by producing a focal sensory afferent LMN facilitation. The advantage of this high spatial selectivity is that it makes possible the reduction of the TES threshold, consequently reducing a disturbing global movement of the patient in a context in which a segment is of particular interest [44, 45].

The stimulus to obtain the epidural motor evoked potential (wave D) is technically more straightforward because there is no synapse involved, and therefore it is little susceptible to anesthesia effects. A single pulse delivered through a C3-C4 montage is suitable. However, it is quite important to ensure that the stimulus intensity is sufficient to activate the CST bilaterally; otherwise, the fibers to the lower limbs or one CST side may be underrepresented. A practical manner to check which fibers are being activated is to record mMEP concomitantly, so it is possible to ensure that a given stimulus intensity is sufficient to elicit the entire path of interest. Another approach is to record separately left and right D-waves corresponding to right and left anodal TES, respectively, although it cannot be admitted that these are purely lateralized [20, 46].

Recording

The mMEP is recorded from muscles in the form of a CMUAP potential from limbs, sphincters, face, and bulbar muscles with surface, subdermal or intramuscular needle. The CMUAP tends to be more polyphasic and show a bigger amplitude when recorded with needle electrodes compared with surface recordings, although both can be considered effective [5]. Proper needling enhances the amplitude of the CMUAP and is discussed in Chap. 3. An atlas of muscle motor points is also available there.

Muscle recordings should be tailored to the procedure, taking into consideration the myotomes at risk. It is strategic to include in the protocol at least one muscle that is not at risk related to surgical manipulation. This channel works as a control, helping to differentiate between signal loss related to systemic/anesthetic changes and those related to direct neurological damage. When it comes to long paths, the distal muscle limbs would be preferred since they have optimal cortical representation in addition to subcutaneous tissue [47]. Therefore, in the upper limb, mMEPs are optimally recorded from hand muscles, as thenar eminence or abductor digiti minimi, and forearm muscles. In the lower limb, the tibialis anterior and abductor hallucis are the muscles most commonly used. Recording parameters include a sweep length of 50 to 200 msec, bandpass filter from 10–100 to 3KHz, and a sensitivity of 15 to 5.000⌈V/div according to the amplitude of the obtained responses. Averaging is not necessary due to the high signal-to-noise ratio [21, 23, 24, 29].

In comparison to SSEPs, brainstem auditory evoked potential (BAEP), and EEG, which are usually continually monitored throughout the procedure, TES muscle MEPs are usually acquired at certain periodic intervals due to patient movement induced by excessive muscle contraction, and thus, they are generally monitored intermittently. The use of selective montage as well as facilitation techniques are often effective in reducing the patient's movement, sometimes even allowing continuous or near-continuous stimulation without disturbing the surgeon [21, 24, 29–31].

For D-wave registration, a special bipolar recording electrode should be positioned near the spinal cord into the epidural or subdural space by the surgeon after spine exposure or percutaneously into the subarachnoid space through lumbar puncture followed by radiological confirmation of positioning in the last case. Long distances between the recording electrodes reduce in-phase cancellation, which could increase the D-wave amplitude; however, this favors the capture of more noise. Thus a 2 to 3 cm inter-electrode distance is considered appropriate. Recording parameters include a sweep length of 10 to 50 msec, bandpass filter from 0.2 to 3KHz, and a sensitivity of about 2 to 50 ⌈V/div. Few (5 to 20) if no sweep averaging is necessary [5, 20, 21, 48].

A proximal and a distal electrode should be positioned in relation to a medullary lesion so the former can be used as a reference. In some cases, as when there are tumors or the patient has undergone to radiation, there may be a desynchronization in the conduction of CST axons at a segmental level, and the distal D-wave may not be recordable from the beginning of surgery despite large mMEP and preserved cranial D-wave [20].

Interpretation and Alarm Criteria

When a multipulse technique is applied to anesthetized patients' brains, a limited subset of the largest axons of the CST is fired. Even though only a small part of the motor path is tested, the data obtained generally is enough to predict evolution accurately. The sensitivity of mMEP for the deficit is very high in such a way that preservation of MEPs is almost never associated with motor deficits. The rare false-negative results are better explained by technical and interpretive errors of professionals poorly trained in the use of semi-automated IONM devices [21, 49, 50].

Different alarm criteria have been proposed based on changes in amplitude, latency, duration, and complexity of the potential as well as the threshold stimulus intensity. The amplitude peak-to-peak measurement is the most widely used to assess both D-waves and mMEP [51–54].

There is an intrinsic variability of the mMEP trial to trial in the absence of any neurological damage. Therefore, changes until a 50% amplitude decrease are generally meaningless for all different kinds of surgeries. An amplitude decrement greater than 50% is considered critical to cranial procedures (class of recommendation (COR) III and level of evidence (LOE) C). However, it is usually not an appropriate alarm criterion for spinal cord monitoring because it could produce many false alarms. An "all or nothing" approach, i.e., notification only when the mMEP has completely disappeared, certainly is the most specific predictor of postoperative motor deficit (COR II and III and LOE B). However, a better alarm criterion also needs to be sensitive enough to allow that the surgical team is communicated before an irreversible injury is established when immediate and accurate corrective maneuvers can effectively be performed. Thereby, it seems preferable to notify the rest of the team before the disappearance of mMEP when the decrease reaches a limit percentage higher than 50% (e.g., 70%, 80%, or 90%) (COR II and III and LOE C). The criteria are still evolving, and currently, there is no consensus about the best alarm criterion for mMEP monitoring of the spinal cord [23].

An elevation of the stimulus threshold (100 V or greater) or simplification of the morphology (decrease of response duration or waveform complexity) may also be an indicator for impending neurological deficits. Although the correlation with the postoperative deficit is weaker than the amplitude criterion, it is rational to interpret these changes in the excitability, provided that they are focal as a subclinical or preclinical injury indicator. Therefore, changes in surgical strategy should be considered. It is essential to keep in mind that, from a predictive point of view, if the threshold shift does not progress to a significant drop in amplitude (not reversing with increasing stimulus intensity), then the patient will most likely have no clinical motor deficit postoperatively. These changes may be classified as a minor warning criterion in the intraoperative decision-making process (COR II and III and LOE B) [52, 55]. Changes in latency are generally useless in MEP monitoring [23].

The reliability of any of the warning criteria strongly depends on trial-to-trial variations of the responses. The range of these variations, in its turns, is determined by different factors, and anesthesia is one of the main variables, being a critical confounding factor in the interpretation of mMEP [56]. Therefore, it is essential to create steady-state conditions, preferably using total intravenous anesthesia (TIVA) and maintaining adequate blood pressure and hemoglobin levels as well as temperature and good ventilation parameters to minimize mMEP variations (COR II and III and LOE B). When steady-state conditions are maintained, the coefficient of variance of muscle MEPs tends to be minimal. Even with stable anesthetic conditions, it is also important to remember that it could tend to gradual amplitude fade and threshold elevation, a phenomenon called fading effect, particularly in long procedures or in muscle groups with previous dysfunction [20, 21, 46].

The TES parameters are also an important factor in the variation of the mMEP and are under the direct control of the neuromonitorist. Higher TES intensity reduces the trial-to-trial variability. At submaximal intensities levels, the mMEPs will be most sensitive to the contribution of any input giving space to a large variance of the response that is prone to false-positive findings. In such cases, only a lost of 100% of the response can be helpful as an alarm criterion. On the other hand, in the supramaximal voltage range, the sensitivity to the variations becomes reduced at most because the maximum number of LMNs that can be recruited has been reached. Thereby, supramaximal intensity levels allow proper use of more sensitive alarm criteria instead of only the mMEP disappearance [56].

The fact is that the surgical time, the anesthetic context, and the concomitant evolution of other neurophysiological modalities are much more relevant for interpreting the findings than a magic cut-off number itself. The greater the experience of the neurophysiologist, the greater the accuracy of the interpretation of the findings, whatever the threshold percentage the neuromonitorist has chosen as a reference point [21, 46].

Regarding the D-wave, its stability enables a more objective and reliable alarm criterion: a 50% drop in potential amplitude is widely accepted as such for spinal cord surgeries (COR II and III and LOE B). As mentioned above, the D-wave is the purest representation of the CST, and thus, it is considered the “gold standard” to the CST monitoring over mMEP, which receives a contribution from a supportive system. mMEP can disappear without significant changes in the D-wave during surgery for an intramedullary spinal cord tumor. In such cases, the patients wake up with paralysis, which invariably evolved with recovery within hours to days. This is because the support system can have its function assumed by the remaining tracts, while the CST is functionally irreplaceable. If, in addition to the loss of the mMEP, there was a significant drop in the amplitude D-wave, it means that the postoperative deficit will be permanent [20, 48]. In brain surgery, reduction of 30 to 40% in the cervical D-wave amplitude by DCS is a major alarm criterion (COR III and LOE C) [21, 23, 57].

For more details about interpretation in specific kinds of surgeries, see the corresponding chapter in this book.

Applications (Indications and Contraindications) and Safety

The use of MEP monitoring should be considered for any surgery where there is a risk of damage to the motor path at any level. The most common indications include neurosurgical, orthopedic, and vascular procedures: tumor or vascular malformations at or near the motor cortex and corticospinal tract, posterior fossa surgeries, craniocervical junction operations, aneurysm clipping, descending aortic procedures, carotid endarterectomy, spinal cord or cauda equina surgeries, spinal deformity, fracture or tumor vertebral surgeries and spine instrumentations among other procedures. There may be other procedures not cited in this list where potential damage to the motor system may demand MEP monitoring [21].

In some situations, MEP monitoring may not be required as when the patient already has chronic paralysis without any useful function or when the goal of the procedure is complete removal of certain types of pathologies regardless of postoperative paralysis. Therefore, the indication must be individualized for each case.

Intraoperative MEP monitoring is sufficiently safe for clinical use once taking the necessary precautions. Even so, it is not without complications. The most common complication is bite injuries, such as lip and tongue lacerations, with an estimated incidence rate of 0.2%. Most, with not all, of these injuries involve C3-C4 montage certainly because it tends to generate strong muscular contractions even due to its proximity to the temporal muscle and the trigeminal nerve [31, 58]. Most of these lesions are self-healing, although they may eventually require surgical repair. There are also reports of jaw fracture and endotracheal tube rupture. The use of bite blocks (rolled-up gazes or dental blocks) placed between the molars on both sides of the mouth is recommended to minimize this complication, but unfortunately, it does not eliminate these injuries [2, 21, 59].

Seizures are another possible complication that is rare (incidence of 0,03%), self-limited, and free of morbidity for TES but has a significant highest incidence during DCS. It is known that the Penfield technique is more epileptogenic than brief high-frequency pulse trains with incidences ranging from 5 to 20% and 1 to 4%, respectively. Epileptic patients are at higher risk, mainly if the seizure control is poor. Seizures are preferably treated with ice-cold irrigation if the cortex is exposed, which usually halts the seizure within a few seconds. In case of persistence, propofol bolus or benzodiazepines may be necessary, leading to the suppression of MEPs during a significant period for the procedure [39, 46, 58, 60, 61].

Other complications reported include burns under the stimulating electrodes possibly due to stray electrode current, hemorrhagic or infectious complications related to invasive electrodes, and transient cardiac arrhythmia. The movement induced by the stimulation can cause traumatic injuries to neurovascular structures, mainly during microscopic manipulation, so, in these cases, efforts must be made to minimize movements by optimizing the stimulus parameters and using more selective montages. When the movements are unavoidable, careful communication and surgical field video will be crucial to coordinate the time of the stimulus with the surgical manipulation [21, 58, 60].

Relative contraindications include epilepsy, skull defects, pacemakers or other implanted bioelectric devices, intracranial vascular clips, or electrodes but the real risks are uncertain. Moreover, patients with these conditions have had uneventful TES-MEP monitoring. Therefore, the benefits of MEP monitoring must be weighed against the potential risks in each patient [21, 23].

Conclusion

Despite the limitations regarding the quality of evidence and strength of the recommendations, MEP monitoring is strongly recommended by the main experts and medical societies. Proving a positive impact on outcome faces many challenges related to practical and ethical barriers to randomized and blind clinical trials. Furthermore, in most surgeries where the motor tract is threatened, it is much safer than risky to use intraoperative MEP monitoring techniques, provided it is conducted by qualified hands using the appropriate precautions. Therefore, it seems much more reasonable to use MEP monitoring than stay waiting for more robust evidence.

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