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Intraoperative Neurophysiologic Monitoring and Mapping of the Motor System During Surgery for Supratentorial Lesions Under General Anesthesia

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Key Learning Points

- Postoperative neurological deficits after resection of brain tumors are caused by either direct tract injury or ischemic insults from proximal and distal arteries.
- Intraoperative monitoring for resection of brain tumors is feasible under general anesthesia in many cases. If speech or higher cognitive function is desired to be tested, an awake craniotomy is the preferred setting.
- Sensory-evoked potentials (SEP) may be used during surgery to identify the central sulcus and can detect cerebral ischemia.
- Motor-evoked potentials (MEP) may detect ischemia ahead of SEP and may detect ischemia occurring in a pure motor territory.
- Preservation or restoration of MEP at the end of the surgery indicates preserved motor function of the patient.
- Different subcortical mapping techniques have been developed. By applying cathodal high frequency short train monopolar stimulation, an estimation of distance to the corticospinal tract (CST) may be possible. If applied via a surgical instrument such as a suction aspirator or Cavitron ultrasonic surgical aspirator (CUSA), subcortical mapping can be applied continuously during critical surgical steps near the CST.

Introduction

The supratentorial space consists of both cerebral hemispheres and is separated from the infratentorial space by the tentorium (see Chaps. 25 and 26). Two-thirds of all adult central nervous system (CNS) tumors occur in the supratentorial space, whereas in children about only one-third of CNS tumors occur here. Common primary brain tumors in adults are gliomas (45–50%), meningiomas, pituitary adenomas, primary CNS lymphomas, medulloblastoma, and ependymomas. By far the most common brain tumors are metastases, notably lung cancer, breast cancer, and malignant melanoma. Fifty percent of patients with metastases have multiple lesions, and up to 50% of patients with cancer have brain metastases.

Supratentorial mass lesions can be in close proximity or attached to functionally important cortical areas and to subcortical fiber pathways. New neurological deficits, after surgery for such

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lesions, may occur in two ways: directly from a resection close to or within those functional areas and tracts or indirectly by inadvertent compromise of their remote vascular supply. Preserving their functional integrity during a maximal surgical resection [1, 2] requires both intermittent identification and delineation of critical regions and tracts (mapping) and continuous functional monitoring [3–5]. The continuous examination of language and higher cognitive function during surgery requires awake surgery (see Chap. 19), while primary motor and somatosensory functions may be tested with neurophysiological methods in patients under general anesthesia. Various mapping and monitoring techniques might be combined and several recent studies support this strategy [6–13]. These methods are employed for brain tumors and analogously for vascular and epilepsy surgery [14–17]. Here, we discuss a pertinent case of functional preservation during surgery for a glioma of the insula. This case illustrates typical conditions and methods for neurophysiological monitoring during brain surgery.

Case: Resection of an Insular Glioma

A 50-year-old male patient presented with a history of focal seizures and a mild sensorimotor right-sided hemisyndrome. Magnetic resonance imaging (MRI) showed an enhanced mass lesion of the left insular region without extension into the adjacent opercula (insular glioma Yasargil type 3b) [18]. Resection was performed with neurophysiologic motor mapping and monitoring as detailed below. Histology revealed a glioblastoma. There was a transient moderate postoperative aggravation of the hemiparesis that resolved by discharge. Early postoperative MRI revealed an ischemic lesion close to the corona radiata. The patient underwent radiochemotherapy and repeated cycles of temozolomide thereafter [19, 20].

Risks of Surgery for Insular Tumors and Other Supratentorial Mass Lesions

The major neurological risk of surgery for insular gliomas (about 10% of supratentorial gliomas) and many other deeply seated tumors is new hemiparesis. Those brain tumors are critically related to the primary motor system in two ways. Typically, they are near to the corona radiata at their dorsoapical extension [21]. In addition, insular and other tumors are surrounded by a variety of vessels, mainly branches from the middle cerebral artery, which supply the motor fibers along their supratentorial course [6, 21, 22]. The sylvian branches supply a major part of the motor cortex, the proximal perforating vessels supply the basal ganglia and the internal capsule, and the peripheral insular and the opercular perforators supply the corona radiata. Monitoring and preservation of the primary motor pathways are crucial because there is no functional substitute for the primary corticospinal projections as opposed to parts of the language and somatosensory networks. Secondary motor areas (supplementary motor area, premotor cortex) and their projections may be sacrificed unilaterally without significant permanent sequelae.

In general, similar risk factors apply to many deeply seated and even superficial supratentorial tumors. They are frequently located close to the corticospinal tract at its extended course. These tumors may also be adjacent to arteries that supply the corticospinal tract, including the lesser known opercular perforating vessels [23]. For example, temporomesial tumors may encroach on the cerebral peduncle and the vessels of the ambient cistern.

Preservation of Nonmotor Function Using Mapping and Monitoring Techniques

Nonmotor functional networks may require functional mapping and monitoring, depending on the location of the target lesion and the surgical approach (see Chap. 9). Mapping the cortex with cortical stimulation and functional monitoring during awake surgery for language and other functions is discussed in Chap. 19 [24–26]. The somatosensory fibers may be continuously monitored by SSEPs, which are also reliable indicators of central cortical perfusion. Limited resections of somatosensory cortex and its afferents might be possible without permanent deficits. In contrast, significant damage of the visual pathways results in visual field deficits that can be quite debilitating. Unfortunately, intraoperative monitoring of visual-evoked potentials (VEP) under general anesthesia has proven technically difficult and they are still of questionable clinical usefulness, although some progress seems to have been reported recently [27, 28] (see Chap. 4). For preservation of the visual pathway, diffusion tensor imaging-based tractography may be useful, particularly if it is fed into a neuronavigational, frameless stereotaxic system. This method is suitable for displaying other fiber tracts as well, including the CST or arcuate fascicle. However, there are still technical uncertainties regarding this method, with large, space-occupying lesions (brain shift) and peritumoral edema. Likewise, functional imaging (fMRI) may be useful for a rough allocation of functional areas but is not suited for sharp resection guidance. Recently, awake stimulation-based mapping has been shown to reliably identify optic radiations, which may be preserved depending on the oncological and functional goals of surgery [29]. At present, neurophysiological methods remain the "gold standard" for functional mapping and monitoring.

Motor Mapping and Monitoring

In centrally located tumors, safe resection requires initial identification of the primary motor cortex. Moreover, with insular and other deep lesions, motor mapping is a prerequisite for adequate positioning of the stimulating electrode for continuous motor monitoring. Neurophysiological mapping may be achieved mainly in two ways:

1. Stimulation mapping can be performed with either the Penfield technique (low frequency) as described in Chap. 18 [26] or as described below with the short train technique (high frequency) for the elicitation of motor-evoked potentials [30, 31]. Both methods can be used for the direct identification of the motor cortex and its projections; however, they do not unambiguously discriminate primary motor from premotor cortex. Nevertheless, first groups started to develop mapping protocols to differentiate primary motor from premotor projections based on the excitability and the latency of the observed responses [32, 33]. Interestingly, recent data indicate that in selected cases (such as recurrent gliomas and previously irradiated tumors), the classical Penfield technique (low frequency) might fail and the short train mapping MEP technique might be superior [8].
2. The identification of the central sulcus may be obtained by the indirect method of SSEP phase reversal mapping. Median nerve SSEPs are recorded from an electrode array positioned perpendicularly across the central sulcus over the motor hand area. The tangentially oriented overall source current of the primary postcentral cortical SSEP response generates a polarity-reversed mirror image at precentral recording positions, thus allowing identification of the central sulcus and, indirectly, of the primary motor cortex [34, 35]. In some cases, direct motor stimulation mapping usefully

complements the SSEP phase reversal recordings [36].

After identification of the primary motor cortex, MEP might be monitored by a multi-contact strip electrode placed on the precentral gyrus [37]. However, depending on the surgical approach and the cortical incision, for some deeply seated tumors, mapping of the motor cortex might not be necessary. Instead, MEP stimulation is performed transcranially at predefined positions according to anatomical landmarks [38].

After identification of the motor cortex, stimulation for eliciting motor-evoked potentials is repeated every 5–10 s throughout the resection via the cortical surface electrodes employed for phase reversal recording. Stimulation at higher frequencies of up to 2 Hz is mainly employed in spinal surgery but does not yield very stable MEP amplitudes and might even induce seizures. On the other hand, longer intervals between consecutive MEP recordings do not allow for continuous functional assessment. Every stimulus consists of a short train of four to seven electrical anodal pulses (of 300–1000 ms pulse duration) at an intensity of up to 20 mA during direct cortical stimulation (DCS) and up to 200 mA during transcranial electrical stimulation (TES). This pulse train elicits a series of action potentials that descend the corticospinal tract. Temporal summation of the burst of excitatory postsynaptic potentials at the alpha motoneuron overcomes the inhibitory effects of general anesthesia so as to elicit motor responses that can be recorded via surface or subdermal needle electrodes from the target muscles (muscle MEPs) [39]. Obviously, muscle relaxation should be avoided in such cases. Total intravenous anesthesia with propofol and opioids (e.g., remifentanil) is best suited and highly recommended for MEP monitoring; however, balanced anesthesia with low-dose (≤0.5 MAC) halogenated agents in combination with an opioid (e.g., remifentanil) is used in some surgical centers.

The MEP amplitude is the target parameter to be monitored in supratentorial surgery. In our experience, a decrease of 50% is a significant warning sign for impending motor damage [40]. Other groups rely on tighter criteria (a decrease in amplitude of up to 70–80%) with a higher risk of false-negative results [41]. An additional common MEP warning criteria is a sudden stimulation threshold elevation.

Irreversible MEP alterations are associated with a higher number of transient deficits compared with the reversible MEP changes and a higher likelihood that these motor deficits do persist. In almost all studies, MEPs show a high specificity and negative predictive value [17]. Thus, the absence of an irreversible alteration may reassure the surgeon that the patient will not suffer a motor deficit in the short-term and long-term follow-up. On the contrary, less consistency is reported for sensitivity estimates and the positive predictive value. This could probably be attributed to the low prevalence of reported alarming events in most series. MEPs seem to perform well as surrogate markers, as successful intervention followed by a reversal of MEP deterioration indicates postoperative motor function preservation [17].

Monitoring Results and Surgical Intervention

In the present case, arm muscle MEPs were monitored (Fig. 20.1). There were highly stable responses in two out of three muscles (I). During medial tumor resection, a significant drop of MEP amplitudes (II) occurred. Causes unrelated to the resection, such as positional, technical, physiological, and pharmacological, were examined and excluded. Once these causes were excluded, the surgeon was informed about the MEP changes. Resection of the tumor was temporarily halted and the site was inspected and irrigated; papaverine-soaked Gelfoam was applied, and the self-retaining retractor in the sylvian fissure was loosened and readjusted (III). After stabilization of the MEP responses (IV), the tumor resection was safely completed.

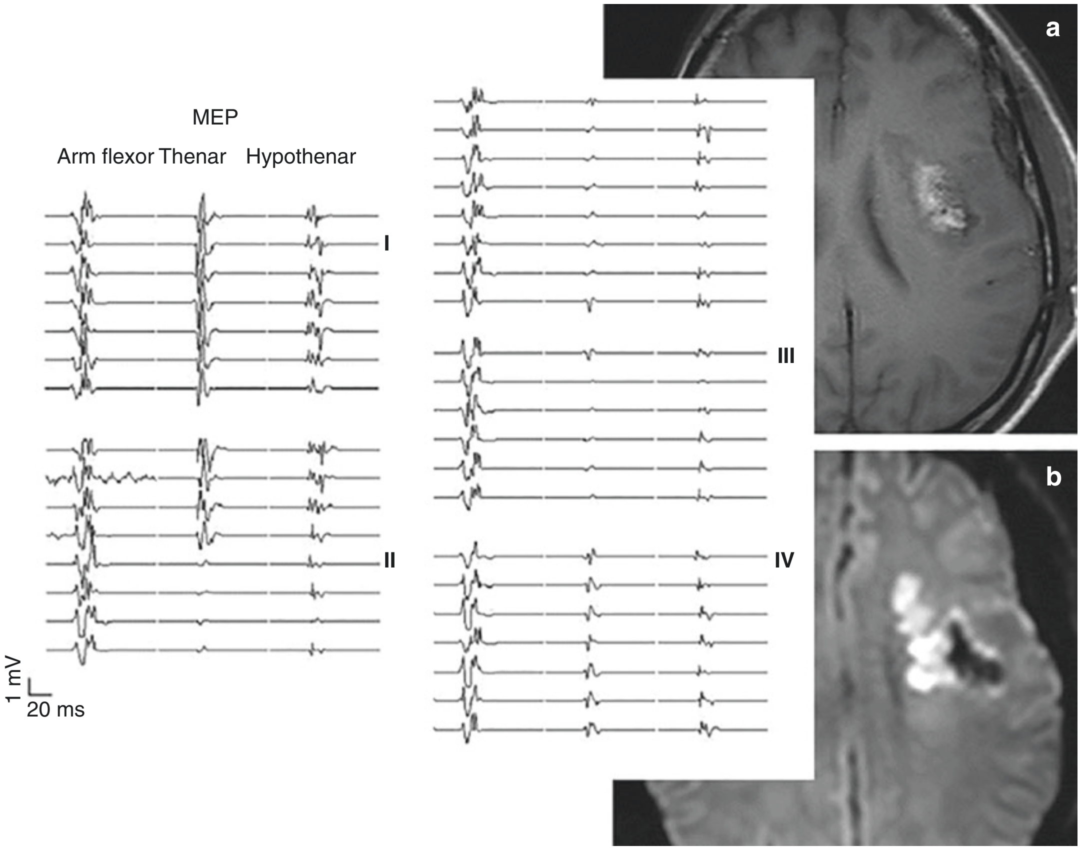

Fig. 20.1 MEP monitoring during surgery for supratentorial tumor surgery with MEP changes. Postoperative T1 (**a**) and DWI (**b**) MRI image

Possible Causes of the MEP Change and the Role of the Surgical Interventions

First, inadvertent bolus injections of anesthetics or muscle relaxation must be excluded, as well as a drop of blood pressure and body temperature, which all may significantly affect MEP amplitudes. A slow, gradual decrease of blood pressure and body temperature should be taken into account. The MEP parameters are not linearly related to cerebral perfusion but can change abruptly in a more stepwise fashion. When individual threshold values are encountered, MEP amplitude may have a sudden deterioration at an unpredictable point in time. For example, there is no absolute blood pressure threshold value. However, any mean arterial pressure below 70 mmHg may be critical, and significant drops in blood pressure must be avoided and reported when they do occur. Body temperature should be maintained above 36 °C by air-warming systems, if necessary. After this check for nonsurgical causes, a warning must be issued to the surgeon. Typically, resection or dissection is halted at this point. At the same time, inadvertent decreases of blood pressure or body temperature are reversed, and these measures should be communicated to the surgeon. The surgeon must exclude technical causes for MEP changes such as displacement of stimulation electrodes; poor contact of an electrode with the result of high impedance (subdural irrigation and wet cottonoids on top of the electrode are helpful); subdural air collection; or a shift of the motor cortex away from the stimulation electrodes after removal of a mass lesion. This might be even reconfirmed by redoing SEP phase reversal in some cases.

With the possibility of a surgically related cause for the MEP change, the surgeon's attention must be directed at specific surgical conditions that may have caused the monitoring alarm event. Obvious causes may be detected such as resection and electrocoagulation in close vicinity or within the CST as revealed by subcortical mapping, neuronavigation or anatomic criteria. The intervening activity is halted and may be resumed only after MEP changes have stabilized or recovered. A temporary halt of dissection and readjustment of the brain retraction is often sufficient to enable MEP recovery and further safe resection. Importantly, the previous surgical course of the procedure must be considered at this point. Extensive manipulation of remote blood vessels supplying the motor tract at some previous step of dissection is a typical cause of inexplicable MEP deterioration. It may be useful to place pieces of Gelfoam or cottonoids soaked with papaverine or nimodipine at sites of (previous) vascular manipulation. In some cases, a false positive alarm might occur and aborting tumor resection prematurely may compromise the oncological outcomes of the surgery such as progression-free survival. However, during tumor resection, in unclear cases, there is always the possibility to do a second surgery in the following days. Thus, all MEP alarms should be taken seriously and if non-reversible MEP alterations occur a postoperative motor deficit is expected in most cases.

The Role of Subcortical Mapping to Identify the CST During Brain Tumor Removal

During resection of tumors in the paracentral region as well as in deep-seated tumors close to the CST, the surgeon needs to know how distant the resection cavity is at a certain point to the CST. During subcortical stimulation, the MEP threshold depends on the charge applied to the brain tissue [42]. Obviously, charge density decreases with distance. The higher the stimulation intensity, the larger the area where MEPs can be generated, and vice versa [37]. Consequently, in case of higher stimulus intensity or charge, a positive stimulation is elicited at a greater distance from the CST. This "stimulation-strength-to-CST-distance" relationship has been increasingly investigated by many groups that have correlated the stimulation intensity in mA needed to elicit MEPs with distance in mm to the CST [43–48]. Notably these different studies applied a different number of stimuli, pulse duration, polarity, and therefore different charge. However, when applying subcortical mapping, it may be advisable to keep the number of stimuli and pulse duration constant [9, 37, 49, 50]. Further, for any distance estimation a constant-current cathodal stimulation is recommended. Even though no definitive statement on this relationship is possible, the rule of thumb "1 mA correlates to 1 mm" is increasingly being used when performing subcortical short train monopolar stimulation with five 0.5-ms cathodal constant-current pulses. The varying impedances of different tumour types (e.g., arterial venous malformation versus low grade glioma) should be considered when relying on this rule of thumb, especially when not applying constant current stimulation. The reliability of different stimulation paradigms to recognize essential motor fibers might depend on the clinical context, for example, infiltrative versus non-infiltrative tumors or prior radiation [8].

Applying this concept, the question arises which would be the lowest mapping threshold in mA for recommending discontinuing tumor removal. Different studies demonstrated that decreasing subcortical mapping thresholds correlate with an increasing risk of direct injury to the CST [7, 37, 46, 50–52]. Even subcortical mapping thresholds ≤ 3 mA might be safe if MEP monitoring remains stable at the same time and mapping is repeated frequently when approaching the CST [5, 37]. Anyhow, the subcortical alarm criterion to halt resection may depend on various factors like tumor histopathology, planned goal of tumor resection, infiltration of other eloquent areas, or the method of hemostasis. Thus, the subcortical mapping safety corridor varies among surgical centers [7–9, 37, 45–48, 50, 51, 53, 54].

However, the intermittent technique of conventional mapping may provide insufficient spatial and temporal coverage of the resection cavity. Consequently, subcortical mapping may fail to prevent direct injury of the CST despite discontinuing tumor removal at higher and apparently safe mapping thresholds. A noteworthy improvement might be using subcortical mapping continuously during critical surgical steps and directly at the site of tumor removal. This was achieved recently by integrating cathodal high frequency stimulation (five 0.5-ms pulses, 250 Hz) into the tip of the surgical suction device [9]. Positive MEP responses were coupled with an alarm sound to facilitate real-time feedback to the surgeon. Apparently so-called continuous "dynamic" mapping will not completely avoid direct injury of the CST; however, allowing mapping during every surgical step at every surgical site increases the mapping coverage with real-time feedback [55]. Later, the concept of continuous subcortical stimulation was used by stimulating directly via the Cavitron ultrasonic surgical aspirator (CUSA). This has been demonstrated a safe method as well [11, 56]. However, on rare occasions, CUSA activity might interfere with mapping results [57]. Further, implementation of mapping into a classical suction device will be available during all steps of tumor removal including subpial dissection and hemostasis, which may be performed with a variety of instruments [4, 9, 54, 55]. The integration of the stimulation probe into any surgical instrument (CUSA or suction probe) might increase the reliability, surgical acceptance, and clinical handling of subcortical mapping.

Why Is Neurophysiologic Monitoring Useful?

Clinical case series have shown that MEP deterioration occurs at stages when motor damage is imminent but still reversible. The clinical correlation of MEP recordings to motor function cannot be assessed at the time of monitoring unless an awake craniotomy is being performed. Thus, postoperative motor outcome is the best surrogate parameter. In large case series, the following correlation has been repeatedly confirmed: If MEP amplitudes recover or there is partial recovery because of surgical intervention, there is no deficit or only transient/minor new motor deficits postoperatively [17, 40]. Fortunately, MEP deterioration is reversible after surgical intervention in most cases. In many of those cases, diffusion-weighted MRI reveals ischemic lesions but not definite stroke affecting the corticospinal tract [6, 58, 59].

If there is an irreversible amplitude decrease and an irreversible MEP loss, there is a high probability of permanent new paresis, frequently associated with a stroke comprising the corticospinal tract. Conversely, stable MEP recordings point to a favorable motor outcome and allow for safe completion of critical steps of the procedure [3, 17, 60]. Therefore, there are three reasons for the use of monitoring: (1) prevention of new permanent deficits; (2) safe completion of critical procedures to achieve maximal tumor cytoreduction; and (3) an educational reason, which is to steepen the surgeon's individual learning curve and to improve the surgical skills for future cases. Monitored cases seem to have both a lower incidence of new postoperative deficits and better surgical resections, which ultimately benefit patients [6, 14, 61].

Conclusion

Resection of supratentorial lesions is associated with considerable functional morbidity, particularly when the lesions are located near blood vessels or near the eloquent cortices or tracts (e.g., the motor cortex or the CST). During surgery of insular tumors, new functional deficits are frequently caused by ischemic lesions that occur during tumor resection, as in the present case. During surgery of tumors in the paracentral area, direct mechanical injury of the motor cortex and the CST might occur. Therefore, motor preserva-

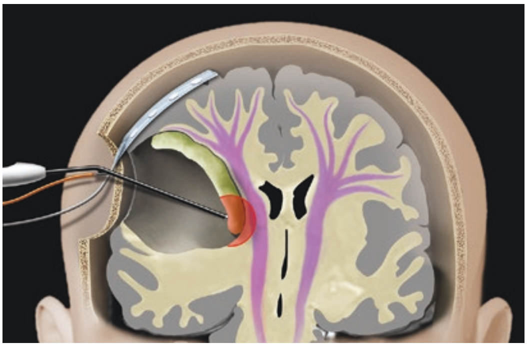

Fig. 20.2 A possible concept. The combined approach of MEP-monitoring techniques (here via a strip electrode placed on the motor cortex) for remote vascular injury and continuous subcortical short-train stimulation via a surgical instrument (here the electrified suction device) enables real-time functional feedback during tumor surgery close to the corticospinal tract. Coronal view of a right insular tumor, tumor tissue in green, corticospinal tract in violet. MEP, Motor-evoked potential. (*From* Seidel and Raabe [62]; *with permission*)

tion requires both mapping of the motor cortex and the CST as well as continuous monitoring using MEP recordings, which can both be performed with the patient under general anesthesia (Fig. 20.2). Other functions such as language, cognition, vision, and somatosensory perception may be mapped and monitored in awake procedures.

The causes of MEP changes may include nonsurgical conditions such as technical, physiological, pharmacological, and positional causes that need to be identified and excluded. Stable MEP recordings allow for safe completion of surgery whereas deterioration due to surgical causes should lead to early surgical intervention. Restoration of the MEP signals may prevent the occurrence of permanent new deficits.

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