Somatosensory- and Motor-Evoked Potentials in Surgery of Eloquent Cortex Under General Anesthesia: Advantages and Limitations

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In this chapter we will discuss two neurophysiological tools: somatosensory-evoked potentials (scalp and cortically recorded) and motor-evoked potentials (transcranial stimulation, direct cortical stimulation, and direct subcortical white matter stimulation), which assist the neurological surgeon operating under general anesthesia upon a patient with a cerebral lesion in proximity to eloquent cortex. We define eloquent cortex as a region whose damage may likely result in a neurological deficit within the realm of motor (paralysis, weakness, coordination), or sensory discrimination (perceptual, visual, spatial orientation, agnosia, apraxia).

Due to the inter-connectivity of the precentral and postcentral gyri, combined motor/sensory deficits can appear. Stable SSEP and MEP monitoring often correlate with a lack of clinical deficit, though false negatives can occur. Accessory pre-motor cortical regions and the frontal motor eye fields are not tested by present techniques under general anesthesia, but postoperative deficits in these areas often improve if SEPs and MEPs have been stable.

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Short-Latency Somatosensory-Evoked Potentials (SSEPs)

Somatosensory-evoked potentials have been utilized intraoperatively to assess real-time function of somatosensory pathways since the early 1970s [1]. Currently, surgical procedures in which SSEPs are routinely used include any which may affect structures in the SSEP pathway: peripheral nerve or plexus, spinal cord, brainstem, or brain [2–4]. This may directly or indirectly affect the central nervous system-generated SSEP waveforms by jeopardizing the vascular territory relating to these structures.

The following professional societies have guidelines, policies, or position statements regarding the use of SSEPs: American Society of Neurophysiological Monitoring [5], American Clinical Neurophysiology Society (ACNS) [6], International Federation of Clinical Neurophysiology (IFCN) [7], American Society of Electroneurodiagnostic Technologists (ASET) [8], and the International Organization of Societies for Electrophysiological Technology

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(OSET) [9]. These guidelines, positions, or policies represent the recommended best practices of utility, methodology, and interpretive criteria for intraoperative SSEPs.

Anatomy and Physiology

The large fiber sensory system, which is responsible for proprioception and perception of vibration, is assessed during SSEP testing. Stimulation of peripheral nerves conducts signal to the spinal cord via dorsal roots, and ascends through multiple pathways, though the general consensus is that SSEPs are primarily mediated by the ipsilateral dorsal column. Nerve fibers originating from thoracic and cervical innervation terminate in the cuneate nucleus, and nerve fibers originating from the lower body terminate in the gracillis nucleus. Fibers cross to the contralateral side of the medulla upon exiting the dorsal column to form the ascending medial lemniscus, which terminates in the somatosensory nuclei located in the ventral posterior lateral nucleus of the thalamus. The primary somatosensory cortex receives input from the thalamus in a somatotopic distribution: the lower extremity is closest to midline, followed in the lateral direction by the trunk, upper extremities, and face [2, 4, 5].

The middle cerebral artery, which is the terminal territory of the carotid artery, provides blood supply to the area of cortex mediating upper extremity SSEPs, while the cortex mediating lower extremity SSEPs is supplied by the anterior cerebral artery. The vertebral arteries supply the upper cervical cord and medulla, while the basilar arteries largely supply the pons and midbrain, and perforating arteries off the proximal portions of the above-mentioned arteries or their communicating arteries supply the deep paramedian areas of the diencephalon and cerebral hemispheres.

Stimulation and Recording

A number of FDA-approved multimodal intraoperative neurophysiological monitoring systems are available for stimulation and recording of SSEPs simultaneously with other evoked potentials. The recommended SSEP stimulation sequence is to interleave stimulation and recording for each limb individually. Cathodic rectangular current pulses are used to stimulate peripheral nerves and generate SSEP responses. Disposable conductive solid-gel surface electrodes or disposable subdermal needle electrodes may be used to deliver constant-current stimuli.

Stimulation sites are most commonly located at the median or ulnar nerve at the wrist for upper SSEP responses, and at the posterior tibial nerve at the ankle for lower SSEP responses. Possible alternative sites for lower SSEP stimulation are the peroneal nerve at the knee, or posterior tibial nerve at the popliteal fossa. It is important to note that when proximal alternative stimulation sites are utilized, that the latency of SSEP responses will be shortened, and latencies are increased for tall or long-limbed individuals [2–5].

The ranges of recommended stimulus parameters are as follows:

- Pulse width: 200–300 μs.
- Frequency: 1.5–5 Hz.
- Amplitude intensity: Supramaximal, <60 mA for surface electrodes, <40 mA for subdermal electrodes.

Supramaximal stimulation is recommended to minimize response variation. Sufficient intensity can be selected by a number of methods. One common method is to incrementally increase the stimulus amplitude until a repeatable, visible twitch in the thumb or toe is present (assuming median and posterior tibial nerve stimulation). Though this method is only useful in the absence of muscle relaxation, it indicates adequate stimulation of the nerve. To verify if the stimulus is supramaximal, another technique that can be used is the incrementing of stimulus intensity to the point where further increments do not appreciably increase the amplitude of recorded responses. This can be done in the presence of muscle relaxants, and eliminates any induced asymmetries in recording from differing levels of stimulation in each nerve.

The frequency of stimuli is recommended to not be a factor of 60, as this is a frequently encountered source of electrical artifact. Selecting a frequency that is not a factor of 60 allows for signal averaging to effectively remove this out-of-phase noise from the averaged signal.

All SSEP responses are on the order of microvolts when recorded from an electrode with appropriate electrode impedance (ideally below 5 kΩ). Electrical artifact and interference from other equipment or electrical lines in or near the OR makes averaging necessary to obtain an appropriate signal-to-noise (SNR). Typically, several hundred to one thousand responses are averaged before analyzing a waveform. Bandpass filter settings are typically 30–500 Hz for upper and lower SSEP cortical recording.

In order to isolate any observed changes in SSEP responses, recording at various locations in the SSEP pathway is essential. This gives information regarding the level at which potential injury has occurred. It is also recommended to record individual responses from bilateral upper extremity and lower extremity nerve stimulation regardless of the location that is at risk for injury. Bilateral upper and lower recording allows for determination of global versus local signal changes. This will be further discussed in the Interpretation section.

Cephalic SSEP electrode positions are located according to the 10–20 International System of EEG electrode placements.

SSEP waveform features are identified as positive or negative deflections at their usual post-stimulus latency. Some examples are: N13, P19/N22, and P37/N45. Differing sources of literature may label these peaks at a slightly different latency: for example P19 is sometimes referred to as P20. However, these are both referring to the positive deflection in the cortical potential from median stimulation. By knowing which waveform is being referred to, it should be intuitive which waveform feature is being discussed [2–5].

SSEP signal recording utilizes high gain amplifiers, and bandpass filtering. A low-cut filter between 10–30 Hz and a high-cut filter between 300–500 Hz is recommended for the cortical responses, while the recommendations for subcortical and peripheral responses is a band-pass filter with cutoffs between 10–30 and 1000–3000 Hz.

Technical considerations that can cause false positives in recording may arise from electrodes becoming displaced or equipment malfunction in the acquisition system and software. It is crucial for neurophysiology team personnel to be properly trained with the commercial system, as well as the availability of technical experts with extensive computer troubleshooting skills to remedy issues. Utilizing checks such as verifying stimulus artifacts and measuring electrode impedance values can aid in identifying confounding technical issues.

Brachial Plexus/Erb's Point Potential: The ascending upper SSEP is generally first recorded at the level of Erb's point. Subdermal or solid-gel electrodes can be used for the recording of this signal. It is picked up from electrodes located approximately 2 cm superior to the midpoint of the clavicle. The Erb's point waveform is recorded referentially, with the reference electrode being placed at the contralateral Erb's point. The recorded signal reflects the activity at the brachial plexus. The waveform consists of one negative peak located approximately at 9 ms (N9) post median or ulnar nerve stimulus.

Subcortical Potential: The subcortical potential, or cervicomedullary potential, is generally recorded from an active electrode located on the posterior neck at the location of C5 or C2, referenced to an electrode placed at Fpz or a noncephalic reference. The peak commonly used for interpretation in this montage is the P/N13. There are multiple generators for this deflection, including the root entry zone in the dorsal horns, dorsal columns, and the cuneate nucleus. Peaks after 12 ms contribute to the waveform from Fz when it is used as a reference, but are not as routinely used for interpretation as P/N13.

Thalamocortical (cortical) Potential: Subdermal spiral electrodes or gold-cup electrodes are typically used for recording thalamocortical potentials. The active electrode is placed at either C3′ or C4′, which is 2 cm posterior to C3/C4 respectively, contralateral to the upper SSEP stimulus to record from the somatosensory

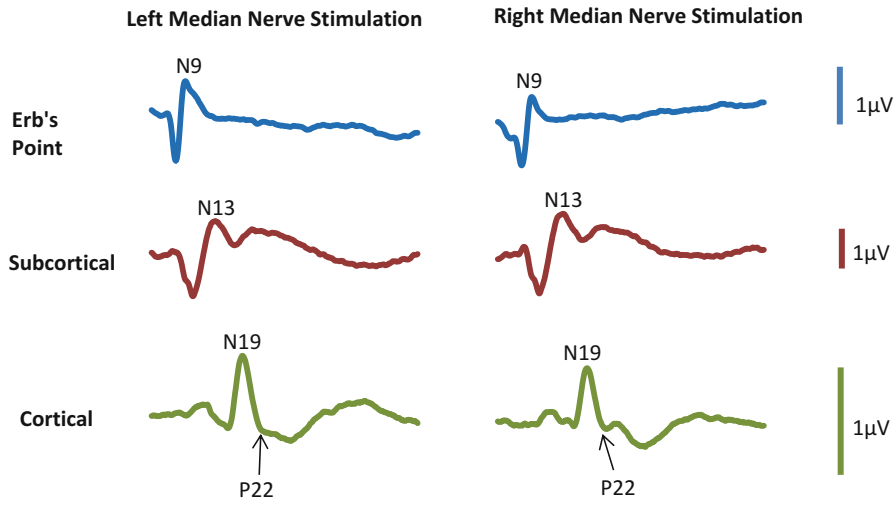

Fig. 1 Median nerve SSEP responses recorded from a patient with no neurological deficits, 500 responses averaged. Scale bars for each set of left and right responses are indicated. Standard polarity convention shows N-peaks as an upward deflection, and P-peaks as a downward deflection

parietal cortex. Either the ipsilateral C3′/C4′ electrode, Fz, or the earlobe can be used as the referential recording electrode. N19 (or N20) and P22 are the deflections typically analyzed for interpretation of the cortical potentials, which are mostly thought to be generated by the electrical volleys in the thalamocortical fibers, which synapse in the primary somatosensory parietal cortex (Fig. 1).

Lower Limb SSEPs

Popliteal Fossa potential: The first ascending potential typically measured in lower extremity SSEP recording with posterior tibial nerve stimulation is located peripherally at the popliteal fossa. This potential is analogous to the Erb's Point recording in upper SSEP recording. The active electrode is placed in the posterior crease of the knee, with the reference 3–5 cm superior to it. The recorded negative deflection at approximately 8 ms is a sensory nerve action potential (SNAP) of the posterior tibial nerve, proximal to the stimulation site.

Subcortical Potential: The subcortical potential for lower SSEP responses utilizes the same active and reference electrodes as the upper SSEP: C5/C2 and Fpz. The most commonly interpreted deflection in this waveform is referred to as N34, sometimes N30. It is thought to be the equivalent of P/N13 in the upper SSEP response, though there is debate whether this is the case.

Thalamocortical (cortical) Potential: Two montages can be used for capturing the lower SSEP thalamocortical potential: Cz′-Fz or C3′-C4′ (for the left lower response, and inverted to C4-C3 for the right). C3′, C4′ and Cz′ are approximately 2 cm posterior to C3, C4, and Cz in the EEG International 10–20 System. The deflections in the waveform observed at approximately 37 and 45 ms post-stimulus are thought to be the analog of N19/P22 in the upper SSEP recordings, corresponding to the electrical volleys in the thalamocortical pathways. For the lower SSEP waveform, the electrode ipsilateral to the site of stimulation is first more electropositive than the reference, in contrast to the upper SSEP waveform. Thus, the deflections used for interpretation for lower SSEPs are P37 and N45 (Fig. 2).

Anesthetic Considerations

Anesthetic agents can have varying effects on recorded SSEP responses, depending on the com-

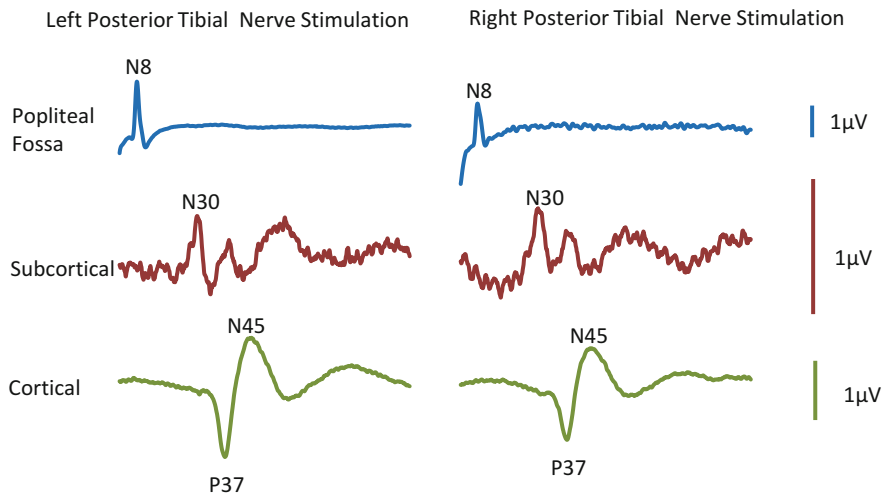

Fig. 2 Posterior tibial nerve SSEP responses recorded from a patient with no neurological deficits, 500 responses averaged. Scale bars for each set of left and right responses are indicated. Standard polarity convention shows N-peaks as an upward deflection, and P-peaks as a downward deflection

bination of agents used. It is therefore crucial for the neurophysiology team to communicate with the anesthesia team in order to optimize the anesthetic plan for intraoperative neurophysiologic recording [5, 10–12]. For more detailed information pertaining to the mechanism of actions causing influence in the SSEP pathway, please refer to the references at end of the chapter. The following table is a summary of anesthetic agents commonly used and their impact on SSEP recordings (Table 1).

Muscle relaxants may be used in the presence of SSEP recordings, and may enhance the signal clarity. However, if motor-evoked potentials are simultaneously recorded, muscle relaxants decrease the compound muscle action potential. This will be discussed in the next section.

Interpretation and Application during Lesion Resection in Proximity to Eloquent Cortex

It is advantageous to obtain peripheral, subcortical, and cortical SSEP responses during intracranial surgery as opposed to cortical responses alone. The same holds true for lesions located in either the right or left hemisphere: recording contralateral as well as ipsilateral responses aids in interpretation.

When identifying a change in SSEP responses, it is important to determine if localized change(s) proximal to the operative site are present, or if observed changes are a result of an anesthetic or technical issue. This can be done by analyzing the level of the signal change (peripheral, subcortical, or cortical), and whether the change occurred unilaterally or bilaterally. Systemic signal changes, limb malpositioning, or cerebral infarcts can potentially be identified when bilateral peripheral, subcortical, and cortical recording is performed.

The generally accepted criterion for significant intraoperative SSEP changes during intracranial surgery is the 50/10 rule: an amplitude reduction equal or greater than 50 % or 10 % latency increase for a waveform compared to its baseline should be reported immediately to the surgical team [2–6, 12].

Systemic factors that can lead to signal changes are: temperature, hypotension, or hypoxia. Hypotension and hypoxia are associated with amplitude decrease or loss. Decreases in temperature cause increased SSEP latencies in

Table 1 Anesthetic agents and their effects on SSEP recording

Anesthetic agent	Effects on SSEP recording
Benzodiazepines	Mild reduction of cortical amplitudes [92, 93]
Barbiturates	Reduction of cortical amplitudes, increase of cortical latencies [5, 10, 92]
Propofol	Progressive reduction of cortical amplitudes, increase of cortical latencies [5, 10, 11, 92]
Opioids	Mild increase in cortical latencies [92, 94]
Inhalational agents	Dose-dependent reduction of cortical amplitudes Concomitant use of nitrous oxide and halogenated agents compounds amplitude reduction [5, 10, 92]
Etomidate	Increase of cortical amplitudes at low doses [95–97]
Ketamine	Increase of cortical amplitudes [98]
Dexmedetomidine	No significant effect [99]

affected limbs. Cold IV fluid injection may increase the latency only in the limb of injection site. Pre-existing neurologic deficits that are detectable with SSEP responses can be amplified such that the response in the affected limb is more sensitive to minor degrees of hypotension compared to unaffected limbs [2–5].

Limb malpositioning is highly suspected, by comparing postpositioning responses to baselines and identifying signal deterioration at a peripheral site and ascending recording sites. In this regard, SSEPs are very valuable for any time which prolonged surgical positioning will put the patient at risk for a postoperative compressive or stretch-related nerve injury.

For procedures in which the patient is in sitting position, the presence of intracranial air correlates with deterioration of cortical SSEP amplitudes. SSEP recording is of particular value when neurovascular structures are at risk, since there is a near linear correlation between cortical amplitudes and cerebral blood flow (CBF) when decreased below 15 ml per 100 g of brain parenchyma per minute. Cortical amplitude loss shows correlation with middle cerebral artery and carotid artery infarcts; however, cortical SSEP responses remain relatively insensitive to subcortical ischemia [2, 13–15]. EEG also may be utilized to identify diminished CBF, as ipsilateral slowing and amplitude decreases can be sensitive indicators. However, this is less commonly used during lesion resection proximal to eloquent cortex, due to placement of recording electrodes located in the way of the surgical site.

Practical Limitations

The most obvious limitation to intraoperative SSEPs as a monitoring tool near eloquent cortex is that they can only be obtained from scalp recordings if electrode positions are not in the surgical field. Scalp-recorded SSEPs serve a monitoring purpose as opposed to mapping or a direct localization technique. If the somatosensory cortex is exposed during surgery, SSEP postcentral gyrus localization/mapping and monitoring may be performed via direct cortical recording, while scalp recording is not possible.

Another limitation of SSEP responses intraoperatively is the variation between observed deficit and clinical correlation. As previously mentioned, mixed nerve SSEP responses are conducted via the large-fiber sensory system, responsible for vibration sensation and proprioception. A common misconception is that clinically symptomatic decreased sensation or pain will de detectable with SSEP responses. This can sometimes be the case, but only if the underlying cause of neurological symptoms also affects the specific large fiber pathway being tested.

SSEP responses are averaged signals, so there is a limit to how immediately responses can be obtained and analyzed. Depending on the frequency of stimulation and number of averages being used, signals can be obtained for interpretation between 1 and 5 min. Higher stimulation frequencies and lower number of averages can correspond to lower response amplitudes and more noise in the signal, making interpretation less clear. Optimizing stimulation and recording parameters for every patient, such that an adequate signal-to-noise ratio is achieved

with consistent responses for interpretation will achieve the best trade-off for signal acquisition time versus signal clarity. Well-trained personnel are essential.

Effective and frequent communication between the surgical and neurophysiology teams can reduce the delay between averaged signal interpretations and critical surgical steps. Changes in SSEP signals can be masked during signal averaging, which can further delay the detection of changes. The neurophysiology team must have a clear understanding of critical structures in the nearby vicinity of the surgical field or dissection and correlate particular vigilance to the pertinent monitoring modalities. If the neurophysiology team does not have a clear view of the surgical field, this delay can be avoided if the surgical team announces when a critical manipulation or resection occurs. The neurophysiology team will then immediately begin a new series of averaging responses, such that waveforms collected before that manipulation or resection will not average in the interpreted response, and potentially mask any changes.

Reports of SSEP sensitivity for neurophysiological monitoring vary depending on the type of surgical procedure being studied; however, most reported series are around 80 %. In a review concerning the predictive values of SSEPs only, SSEP sensitivity and negative predictive value for minor cerebral hemisphere deficits were 64 and 95 %. When severe deficits only were considered, the sensitivity and negative predictive values were 81 and 98 % [16]. In general, when using the 50/10 rule, false positives are more likely to occur than false negatives. However, careful attention to possible systemic and anesthetic confounds may identify potential false positive results intraoperatively.

Localization of the Somatosensory and Motor Cortex with SSEPs

In contrast to the use of SSEP responses for monitoring functional integrity of the somatosensory pathway, the phase-reversal technique can be used for mapping the location of the central sulcus intraoperatively. The phase reversal technique, first introduced in the late 1970s, has since been described by numerous studies for its application during cranial lesion resections [17–24]. Many, if not most, will also stimulate the precentral gyrus for motor movement verification, which is discussed in Section "Direct Cortical Motor Mapping."

Stimulation and Recording

Stimulation is typically performed at the contralateral median nerve, with settings analogous to scalp SSEP recordings. Commercially available grid or strip electrodes are placed on the cortical surface, at the anticipated location of the hand sensorimotor gyri (approximately 3–8 cm from midline) across the central sulcus with an optimal angle of 15°. If a lesion is present, the strip should be placed adjacent to the visible margins of the lesion. The placement of the grid/strip should then be adjusted to maintain peak amplitudes by rotating or displacing the grid/strip [25–27]. Communication with the neurophysiology team is again essential, and patience is required from the surgical team.

Posterior tibial SSEP phase reversal can also be performed, but the cortical representation is limited to a much smaller area, closer to midline. Furthermore, alternative peripheral nerve sites have been used for central sulcus localization, including the femoral, peroneal, and ulnar. A group in 2005 successfully localized the phase reversal utilizing stimulation of the contralateral lower lip mucosa [25–28].

Each electrode site within the strip/grid serves as an active recording site, with a common reference. The reference electrode is typically a subdermal needle or solid-gel electrode placed on the contralateral mastoid or cephalic reference, or a needle electrode placed in the exposed temporalis muscle. Impedance checks should routinely be performed to verify the electrodes are making adequate contact. Saline irrigation can improve impedance; however, excess irrigation can lead to shunting between electrode sites (Fig. 3).

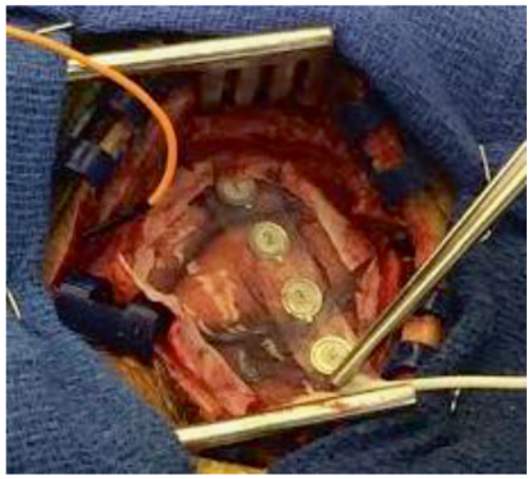

Fig. 3 Subdural electrode strip placed on exposed sensorimotor gyri for direct cortical recording. The reference electrode is the orange subdermal needle inserted into exposed temporalis muscle. Diameter of strip electrode is 6 mm

Interpretation and Application during Lesion Resection in Proximity to Eloquent Cortex

The recorded thalamocortical potentials in the postcentral gyrus have the characteristic N19 and P22 components, as previously discussed. Electrodes located anterior to the central sulcus exhibit an inverse polarity: at approximately 19 ms post-stimulus: they become more electropositive than the reference electrode. The reason for this phase reversal is based on the perpendicular electrical dipole generated on the postcentral gyrus relative to the central sulcus from median nerve stimulation: the polarity of the dipole changes on the adjacent precentral gyrus [29]. The phase-reversal technique is dependent on the neurophysiology team identifying the electrode locations where the reversal of phase is observed. The pre-central electrodes exhibit a peak positivity at a slightly increased latency when compared to the peak negativity (N19) of the post-central electrodes. Figures 4 and 5 are examples of cortical median nerve SSEP phase reversal waveforms. In Fig. 4 two 1×4 electrode strips were placed across the central sulcus in the hand sensorimotor region. Phase reversals are observed in between electrode positions 2 and 3 for both electrode strips. In Fig. 5 two 1×4 electrode strips were placed parallel to the central sulcus, and a phase reversal can be observed between the two electrode strips.

In situations where a clear phase reversal cannot be adequately identified, increasing the number of grid or strip electrode contacts, and utilizing a bipolar montage where adjacent electrode positions are differentially amplified can provide a clearer phase reversal.

Once the central sulcus has been identified, it is recommended to adjust the position of the electrode grid/strip such that the localized sulcus is situated between different electrode positions, to verify the cortical potentials again identify the same location.

Practical Limitations

Though the central sulcus can often be identified using anatomical landmarks and MRI images, the SSEP phase reversal technique is regarded as one of the most reliable tools for identifying the central sulcus. Distorted anatomy resulting from displaced cortical structures in the presence of a lesion, individual variations in functional organization and anatomy, and limitations of spatial sensitivity in preoperative imaging studies all support the complementary use of SSEP phase reversal intraoperatively for increased accuracy of central sulcus identification [25–27].

Reports of success rates for identification of the central sulcus with the SSEP phase reversal technique range from 90 to 97 % [23, 30–32]. Situations in which SSEP phase reversal cannot identify the central sulcus include lesion-related displacement of the central sulcus, anesthetic, or technical confounds analogous to those relating to scalp SSEP recording, and pre-existing marked sensorimotor deficits.

The proposed causes for absent or distorted cortical potentials in tumor patients are: (1) the tumor desynchronizes propagated afferent electrical volleys along the thalamocortical pathway, (2) the mass effect of the lesion distorts the spatiotemporal projection of cortical electrical

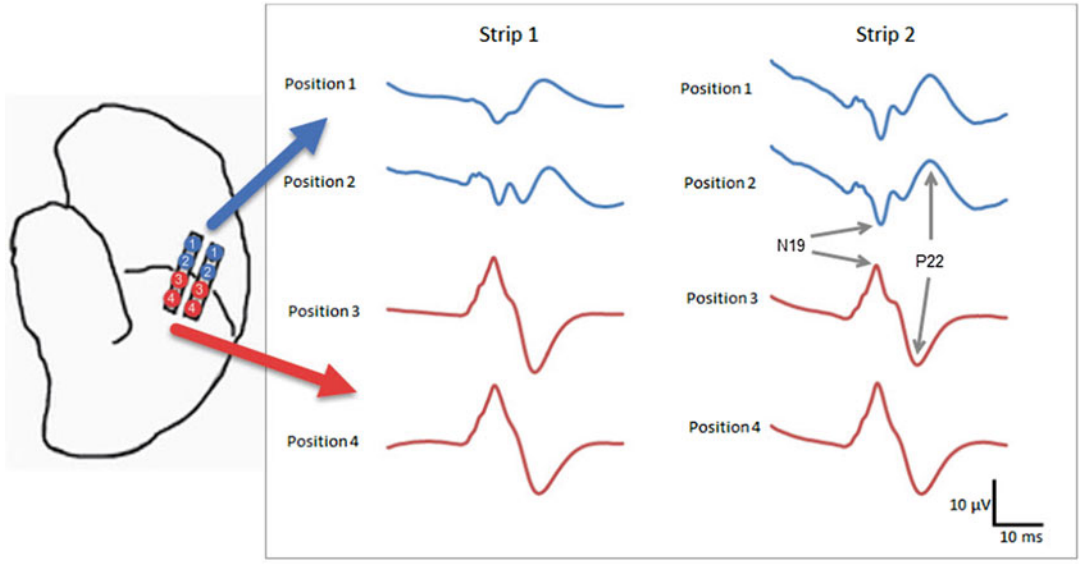

Fig. 4 Two 1×4 electrode strips were placed across the central sulcus in the hand sensorimotor area of an adult patient with no sensory deficits as indicated, and median nerve cortical responses were recorded. Positions 1–2 for each strip show an early positivity (precentral) and positions 3–4 show an early negativity (postcentral). The central sulcus was identified to be located in between electrode positions 2 and 3. Standard polarity convention shows N-peaks as an upward deflection, and P-peaks as a downward deflection. The phase reversal of N19 and P22 is labeled between position 2 and 3 on strip 2

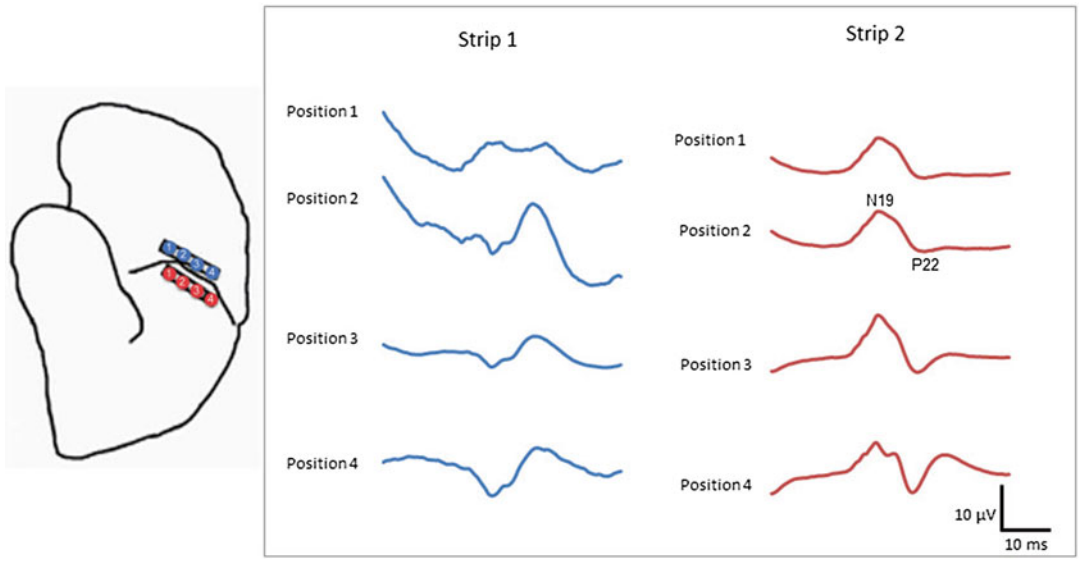

Fig. 5 Two 1×4 electrode strips were placed parallel to the central sulcus in the hand sensorimotor area of an adult patient with no sensory deficits as indicated, and median nerve cortical responses were recorded. All positions on strip 1 show an early positivity (precentral) and all positions on strip 2 show an early negativity (postcentral). Standard polarity convention shows N-peaks as an upward deflection, and P-peaks as a downward deflection. The central sulcus was identified to be located in between strip 1 and strip 2. N19 and P22 are labeled on position 2 for strip 2

dipoles to the brain surface and (3) the recording site may not be appropriate for recording a potential generated in the hand area of the postcentral gyrus [25].

Most importantly, although SSEP phase reversal is reliable for verifying the location of the central sulcus, it does not identify motor function, and when used alone is inadequate for preventing postoperative motor deficits: motor mapping methods are also indicated.

Transcranial Motor-Evoked Potentials (tcMEPs)

Due to multiple technical difficulties in the application of magnetic stimulation, the preferred intraoperative stimulation method for motor-evoked potentials is electrical cortical stimulation. Nevertheless, the lessons learned from magnetic tcMEP in experimental primates and man for optimization of anesthetic agents used has carried over to electrical tcMEPS [33–40]. In 1996, three groups first demonstrated the now clinically standard pulse train technique under anesthesia [41–43]. After the 2002 report by MacDonald alleviating safety concerns regarding transcranial electrical stimulation, and the first government approved commercial stimulator that same year, tcMEPs began to increase in intraoperative clinical use and research [44, 45]. Under general anesthesia, this electrical stimulation can be performed transcranially or directly on the primary motor cortex (discussed in Section "Direct Cortical Motor Mapping"), with compound muscle action potentials recorded in response.

Anatomy and Physiology

The motor-evoked pathway monitored intraoperatively originates with stimulation at the primary motor cortex, which is located on the pre-central gyrus and responsible for voluntary movements. Not unlike the somatosensory cortex, the primary motor cortex is organized somatotopically, with the tongue and face motor neurons near the sylvian fissure, hand and arm neurons in its middle convexity, and leg and foot neurons from its crest to mesial parasaggital region. The primary motor cortex is selected for electrical stimulation due to the low electrical threshold necessary to induce muscle responses [45].

The large myelinated axons in or just below the primary motor cortex are thought to be the predominantly activated fibers during tcMEP stimulation, consisting of the corticospinal and corticobulbar pathways, which conduct action potentials to lower motor neurons without intervening synapses [45–48]. These large fibers converge in the corona radiata, and travel through the internal capsule, to form the crus cerebri. Next the fibers travel through the cerebral peduncle of the midbrain, descend the pons and medulla where the major of fibers decussate, forming the large lateral corticospinal tract (CST). The CST descends via the lateral funniculus, mainly terminating in dorsolateral lamina IX and VII. The CST branches off at spinal segments, primarily at the cervical and lumbar levels. The majority of axons synaptically transmit to interneurons, then alpha motor neurons, while some synapse directly on the alpha motor neurons, which in turn innervate upper and lower limb muscles. Compound muscle action potentials are recorded as a result of the temporal and spatial summation of lower motor neuron excitatory postsynaptic potentials [4, 45].

Corticobulbar tract fibers originating in the motor cortex travel alongside CST fibers, until they diverge into the brainstem and terminate on interneurons, and to a smaller extent directly to motor neurons to generate cranial muscle movements [45].

Indirect motor pathways, the propriospinal system and neuromodulatory pathways might influence MEPs, but are not thought to significantly contribute to them [45].

The middle cerebral artery and the anterior cerebral artery primarily supply blood to the motor cortex, lenticulostriate perforators and the anterior choroidal artery supply the internal capsule, and vertebral and basilar artery branches supply the brainstem, all of which may produce distinct changes to MEP responses in the presence of ischemia [15, 45].

Stimulation and Recording

Studies in monkeys showed direct waves (D-waves) recorded from the corticospinal tract are produced as a result of a single pulse transcranial electrical stimulus, and have been verified in humans during intramedullary tumor surgery. However single electrical pulses are typically insufficient under general anesthesia to elicit muscle responses. Multipulse stimulation elicits a series of descending volleys (D-waves), produced by direct axonal stimulation. I-waves (Indirect waves), which are produced by intracortical circuits that incite additional cortico-motor neuron discharges, follow D-waves in conscious patients, or under anesthetized patients when a sufficiently strong pulse-train stimuli are used. Stimuli with adequate activation of D-waves along with some I-wave recruitment produces enough temporal summation of excitatory postsynaptic potentials (EPSPs) which summate to activate some lower motor neurons, ultimately resulting in CMAP potentials [4, 15, 45–47].

Anodal monophasic trains of rectangular pulses are delivered through the scalp to the motor cortex in each hemisphere for tcMEP stimulation. C1, C2, C3, and C4 may all be used as active stimulation sites. It is recommended that during baseline testing, optimal electrode sites are selected which minimize threshold current for repeatable maximized muscle responses. Hemispheric, inter-hemispheric, and midline stimulation montages optimize CMAP recording for different applications. It is recommended to use a hemispheric montage for supratentorial procedures. However, the hemispheric montage will preferentially activate facial and arm responses, therefore optimal settings would include the ability to stimulate with an additional montage to optimize leg responses as well. Spiral (corkscrew) needle electrodes are best suited for stimulation during craniotomies, since they are self-securing and rarely become displaced during surgery [45, 47, 49].

Typical parameters for tcMEP stimulation are: 3–8 pulses, 50–1000 μs pulse widths, and interstimulus intervals of 3.0–4.0 ms. Constant current and constant voltage stimulus generators are commercially available, with upper safety limits of 200 mA or 1000 V. However, the exact combination of pulse width and number of pulses may limit current or voltage amplitudes, so that the overall delivered charge does not exceed maximum safety limits [4, 44, 45, 50].

Because the skull has very high impedance, it is estimated that only 10–20 % of delivered current reaches the motor cortex, resulting in maximum safety limits for transcranial stimulation that significantly exceed those for direct cortical stimulation [51].

tcMEP stimulation occurs axonally, in the white matter, but the exact site of stimulation is critical for supratentorial procedures. As stimulation is increased, the latency of the D-wave shortens, which indicates stimulation occurring at an increased depth within the white matter. With high levels of stimulation, near the maximum settings of commercially available equipment, stimulation may occur as deep as the foramen magnum. This reinforces the importance of optimizing stimulation montages and minimizing stimulating charge delivered, in order to avoid stimulation occurring distal to the site of surgical manipulations [15, 52, 53].

Compound muscle action potentials (CMAPs) are typically obtained by needle electrodes in response to tcMEP stimulation. Muscle recording sites used in supratentorial procedures are generally selected according to area of representation on the motor homunculus. Areas that are well represented, such as hands and feet, are more easily activated and therefore provide more reliable responses. Commonly used muscle sites include: abductor pollicis brevis, abductor digiti minimi, brachioradialis, abductor hallucis, and anterior tibialis. Pairs of solid-gel surface electrode or subdermal needles may be used, both placed in the muscle belly of interest, approximately 2–4 cm apart. Recording is performed referentially between the 2 electrodes, to minimize electric artifacts. CMAPs should be band-pass filtered between 10 and 100 Hz, and 1500–3000 Hz [4, 45]. Although stimulus artifact may still be present with these settings, the presence of artifact is often useful to confirm the stimulus has been delivered. CMAPs, which are polyphasic waveforms with varying amplitudes, in

the absence of motor pathway deficits or muscle atrophy, range between 10 and 1000 μV. CMAP latencies vary between ~10–40 ms for cervically innervated muscles and increase in latency within a patient inferiorly for lumbosacrally innervated muscles. CMAP amplitudes are large enough that single responses are generally interpreted, as opposed to averaging techniques that are used during SSEP testing [4, 45].

The short pulses used during tcMEP stimulation are considered safe, as electrochemical injury occurs only with >1 ms pulse duration of prolonged monophasic train stimuli. Commercially available tcMEP stimulators are in accordance with the 50 mJ IEC safety limit, and therefore scalp burns due to thermal injury are exceptionally rare. Induced seizures as a result of tcMEP stimulation have a reported occurrence of 0.03 %, as seizures are very unlikely with the brief, high-frequency trains utilized. The most common tcMEP complications are bite injuries associated with jaw muscle contractions. These muscle contractions are likely mediated via the corticobulbar pathway, trigeminal nerve and/or direct jaw muscle stimulation. To minimize bite injuries, soft bite blocks are recommended to be placed between both sets of molars, though they may not necessarily eliminate injury [45, 54] (Fig. 6).

Anesthetic Considerations

Analogous to the effect of anesthesia on SSEP recording, tcMEPs are altered by certain anesthetics [111, 112]. The neurophysiology and anesthesia team must work closely to ensure that tcMEP recording is feasible, and avoid any confounds which make CMAP interpretation uncertain. The following chart is a summary of these effects (Table 2).

tcMEP responses are more sensitive to inhalational agents than SSEP responses. In some cases, administering 0.5 MAC is tolerable for SSEP responses, but may result inability to elicit repeatable tcMEP responses. The widely recommended anesthetic for tcMEP recording is a propofol and opioid TIVA (total intravenous anesthesia) [10, 11, 45, 47, 48, 55–60].

Muscle relaxants are not recommended during tcMEP testing, although some reports indicate that low levels of relaxants may be used if they are kept constant in conjunction with the neurophysiology team monitoring train of four responses [45, 61].

Interpretation and Application during Lesion Resection in Proximity to Eloquent Cortex

Similarly to SSEP interpretation, confounding factors may result in tcMEP changes that are unrelated to surgical maneuvers, and rostral or contralateral responses can aid in identifying these confounds.

Gradual reduction of amplitudes generalized to all muscle groups is often a result of anesthesia or what is commonly referred to as “muscle MEP fade.” This observed fade refers to the gradual progressive decrease of CMAP amplitudes, and/or increase of stimulating thresholds over the duration of time under general anesthesia. The likely cause of this phenomenon is due to decreased lower motor neuron excitability, possibly also contributed by D-wave or I-wave fade. MEP fade varies between patients, and may be absent or marked. Increments of stimulus intensity may be needed during long procedures, and it is recommended to frequently acquire MEP signals, so that this gradual fade is observed, and not attributed to significant surgically related changes [15, 48, 62, 63].

Systemic factors that will result in generalized tcMEP amplitude deterioration or loss are hypotension, drug bolus, or intracranial air if the patient is in sitting position. Limb ischemia or malpositioning can also be detected by tcMEPs, resulting in focal CMAP amplitude loss. Body or limb decreased temperature results in increased CMAP latencies. Simultaneously acquiring SSEP responses can further help identify these confounds. Depending on the time course of these systemic factors, the observed CMAP amplitude loss may appear more acutely or gradually, contributing to the “muscle MEP fade” [45, 48, 64].

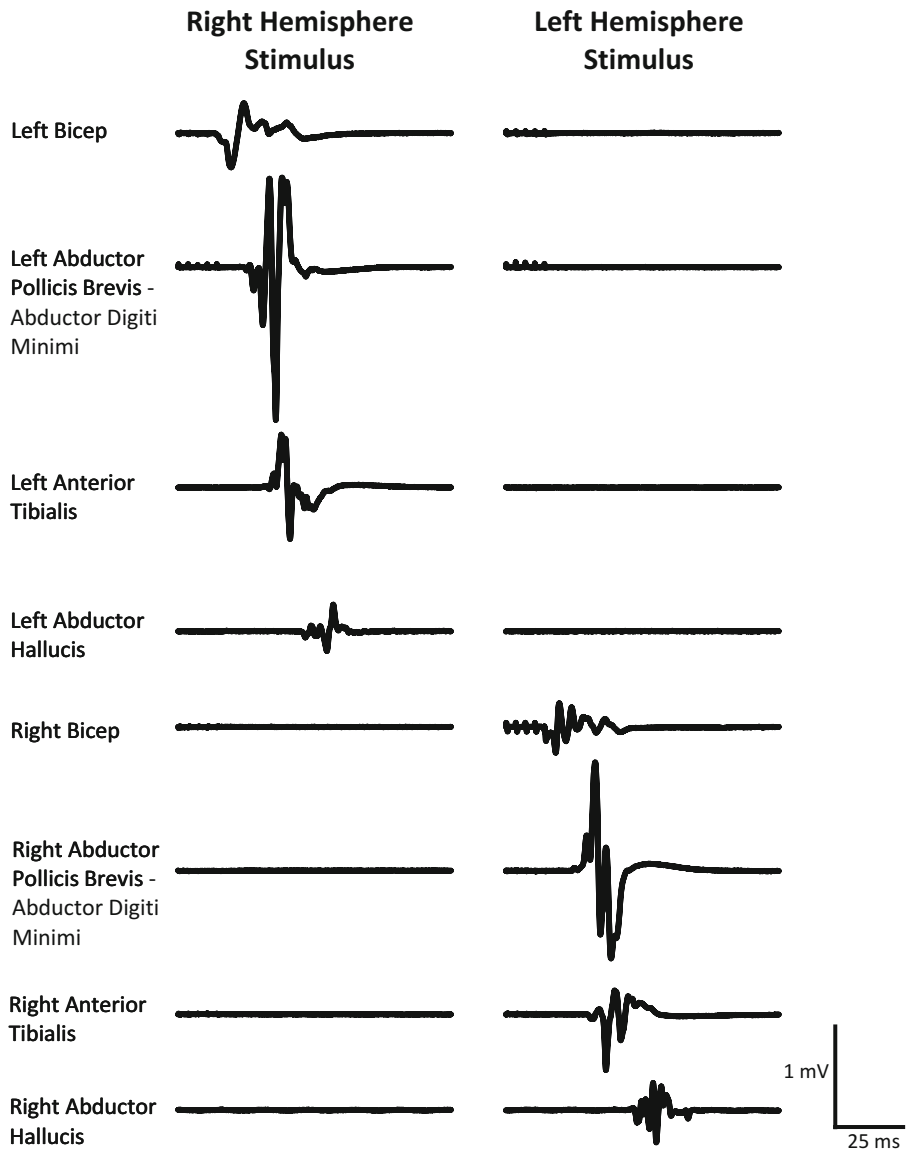

Fig. 6 tcMEP CMAP responses in an adult patient with no motor deficit. Contralateral activation is isolated for both right and left hemisphere stimulus settings. Anodic stimulation occurred at C3 and C4 for left and right hemispheres, respectively

CMAP interpretation is dependent on the neuromuscular junction, therefore it is recommended to include a train-of-four testing modality during the use of tcMEPs. The train-of-four should be performed at a peripheral nerve site, as peripheral muscles are generally recorded during tcMEP use. The train-of-four is useful for identifying any anesthetic or systemic confounds leading to CMAP deterioration due to decreased peripheral transmission.

The following are pathologic mechanisms that may result in intraoperative deterioration of tcMEP responses: (1) cortical I-wave circuit disruption, (2) corticomotor neuron failure, (3) corticospinal tract conduction failure, (4) background

Table 2 Anesthetic agents and their effects on tcMEP recording

Anesthetic agent	Effects on TcMEP recording
Benzodiazepines	Significant reduction of CMAP amplitudes [10, 11]
Barbiturates	Significant reduction of CMAP amplitudes, disappearance of CMAPs [100]
Propofol	Progressive CMAP amplitude reduction [10, 11]
Opioids	Minimal effects [10, 11, 34, 45, 100, 101]
Inhalational agents	Dose-dependent reduction of cortical amplitudes Concomitant use of nitrous oxide and halogenated agents compounds amplitude reduction [10, 11, 33, 45, 102–105]
Etomidate	May enhance CMAP responses [10, 11, 35, 106, 107]
Ketamine	Negligible effect at low doses, reduction of CMAP amplitude at high doses [10, 11, 39, 45, 100, 108]
Dexmedetomidine	No significant effects[a] [10, 99, 109]

[a]One case report of MEP loss associated with dexmedetomidine during pediatric spine surgery

facilitation system disruption, (5) lower motor neuron failure, and (6) peripheral conduction failure [45]. There are numerous reports suggesting interpretive warning criteria indicating tcMEP deterioration. These include:

- *Presence or Absence:* Amplitude, latency, threshold stimulus, and CMAP waveform are not analyzed, and the interpretation based solely on the absence of a CMAP response present at baseline is considered a significant change [63–65].
- *Amplitude Reduction:* Peak-to-peak amplitudes of CMAP responses are interpreted, and decreased amplitude beyond a percentage of baseline amplitude is considered significantly changed from baseline. Published reports suggest ranges between 50 and 80 % reduction should be used for warning criteria. 50 % is the most commonly accepted warning criteria for supratentorial procedures [15, 45, 66, 67].
- *Threshold Amplitude:* Current or voltage stimulus thresholds needed intraoperatively to evoke CMAP responses that are a set limit greater than baseline thresholds are considered significantly changed from baseline [55, 65, 68].

The presence or absence approach has only been suggested for use in spinal surgery, and is inadequate for supratentorial procedures [63–65]. Threshold testing requires slightly increased intraoperative testing time, and thresholds are known to vary with anesthetic depth [4, 55]. Amplitude reduction is the most commonly used criterion for supratentorial procedures [45, 66, 67]. However, it is recommended that any warning criteria decisions are discussed with the surgical team preoperatively during surgical planning, and any amplitude or threshold changes not explicitly related to known anesthetic or systemic changes are reported to the surgical team intraoperatively. However the surgical team leader must be made aware (by the neurophysiology team if not anesthesia) that anesthetic, muscle relaxant, or systemic changes have occurred or are suspected to have occurred that may jeopardize monitoring capabilities.

Practical Limitations

As with scalp SSEP recording, tcMEP testing requires that the stimulating electrodes placed over the primary motor cortex are not in the surgical field. If this is not possible, direct cortical stimulation techniques must be used instead, discussed in Section "Direct Cortical Motor Mapping." Also analogous to scalp versus direct SSEP recording, tcMEP stimulation serves as a monitoring technique, and direct cortical methods must be employed for any localization information.

CMAP responses can have high trial-to-trial variability, especially in the presence of any preexisting motor deficits. Therefore, interpretation criteria should always account for a patient's CMAP variability observed during baseline testing. Due to this variability, signal averaging is not advanta-

geous for CMAP recording; however, it is unnecessary as the signal-to-noise ratio is typically adequate for single responses to be reliably interpreted.

As previously mentioned, the amount of voltage or current needed to stimulate transcranially is orders of magnitude greater than with direct stimulation. Although there are no electrochemical safety hazards with the tcMEP stimulus, there is contraction of the jaw and facial muscles during stimulation. Depending on the exact stimulating electrode montage and threshold intensity needed, this patient movement during stimulation can interfere with surgical manipulations. Therefore, although there is negligible delay between testing and interpretation, as opposed to SSEPs, continuous testing of tcMEP responses is not often feasible, and testing must be communicated to the surgeon so that there are no unexpected patient movements. It is recommended that tcMEP responses be obtained frequently, to account for any confounding factors, such as MEP fade, and before and after any crucial surgical maneuvers. Constant communication between the surgical and neurophysiology team is necessary, to ensure that tcMEP responses are obtained in a fashion that minimizes delay between potential surgically related injury and observed signal changes.

Preservation or Irreversible Complete Deterioration of MEP Responses

During insular glioma and central-region tumor surgery, up to 44 % of patients might exhibit intraoperative MEP alteration [66, 69]. MEP responses with unchanged response parameters (amplitude and stimulation thresholds) correlate with no new postoperative motor deficits. The exception to this is supplementary motor area lesions; in which intraoperative MEP preservation is clinically predictive of complete or near-complete recovery of voluntary movements [70, 71]. Complete and irreversible loss of tcMEP responses is clinically predictive of a postoperative motor deficit, with a report of 42 % patients having severe permanent deficits [15].

Reversible or Incomplete MEP Deterioration

Reversible deterioration in compound muscle action potentials is observed when intraoperative signal amplitude reduction, or complete signal loss is followed by subsequent full or partial recovery of amplitude.

There are a number of confounding factors that may affect CMAP amplitudes intraoperatively aside from those due to surgical manipulation and lesion resection. Limb pressure and malpositioning can case CMAP decrease, which can be confirmed with simultaneous SSEP recording.

Reversible deterioration or incomplete deterioration (either judged by amplitude loss or increased stimulation thresholds) are clinically correlated to postoperative motor deficits ranging from transient deficits to moderate permanent deficits [66, 67, 69, 70].

Irreversible MEP changes are more often correlated with postoperative deficits than reversible alterations, frequently with confirmatory brain MRI findings. Complete CMAP loss has been shown to significantly correlate more with subcortical MRI signal alterations, whereas CMAP incomplete deterioration correlated more often with precentral gyrus signal alterations [15, 67].

At present, although reversible or incomplete MEP deterioration lacks the sensitivity to accurately predict postoperative motor outcome, simply monitoring the presence or absence of responses is insufficient for supratentorial procedures.

Direct Cortical Motor Mapping

Direct cortical stimulation (DCS) is a mapping and monitoring technique, in which constant current stimulation is applied directly to the cortex. Handheld monopolar, bipolar, and subdural strip or grid electrodes may all be used as stimulating electrodes. Activated pathways are identical to transcranial stimulation techniques; however, with smaller employed current fields focal activation of somatotopic axons may be elicited. Although direct cortical stimulation may be utilized during awake craniotomies with cooperative patient feedback, this chapter will only discuss methods under general anesthesia which relies on electromyographic CMAP responses.

Stimulation and Recording

Under general anesthesia, two stimulation techniques may be employed: bipolar cortex stimulation (Penfield's Technique) and MEP mapping (Taniguchi method).

Bipolar Cortex Stimulation (Penfield's Technique)

Bipolar rectangular pulses with 0.5–1 ms duration are delivered via a bipolar handheld probe with ~5 mm spacing or subdural grid to the exposed motor cortex at 50–60 Hz for approximately 1–4 s. Threshold intensities for eliciting a motor response are determined by starting at 3–5 mA, and increasing by increments of 0.5–2 mA. Threshold amplitudes for evoking a)motor response are typically less than 10 mA [15, 18, 24, 26, 45, 72–77].

Multi-pulse Train Technique (Taniguchi Method)

Trains of four to nine (typically 5) monophasic anodal rectangular pulses 200–500 μs in duration with an inter-stimulus interval of 2–4 ms are delivered via a hand-held probe or subdural grid to the exposed motor cortex. Threshold amplitudes are identified by increasing amplitude by increments of 0.5–2 mA but not exceeding 25 mA. The mean threshold for motor gyrus stimulation is reported to be 6–12 mA [78]. This stimulation technique can be applied in a monopolar fashion with the return electrode in exposed temporalis muscle or scalp, or in a bipolar fashion, between two sites on a subdural grid or via a bipolar handheld probe [15, 26, 27, 45].

In both cases, it is recommended to stimulate the entire are of interest before increasing the stimulus amplitude incrementally. Penfield's technique is associated with a higher risk of induced seizure than the multi-pulse train technique. However in both cases it is recommended to place a subdural grid or strip on exposed cortex adjacent to stimulation, in order to monitor electrocorticography (ECoG) for the presence of after discharges (ADs). With either stimulating technique, although reported incidence of seizure is only 1 % it is advised to preventatively take precautions so that the surgical, anesthesia, and neurophysiology team is prepared to respond to intraoperative electrographic and/or clinical seizure, with ice cold saline or Ringers' solution quickly applied to the cortical surface [15, 26, 27, 60, 79, 113].

Recording

Under general anesthesia motor responses to direct cortical stimulation are evaluated by subdermal needle electrodes placed in contralateral muscle groups of areas which are at the highest risk for damage, and/or visual inspection of contralateral muscle groups during stimulation. Penfield stimulation typically elicits a tonic muscle response, whereas the multi-pulse technique elicits a single CMAP response [80] (Figs. 7 and 8).

Interpretation and Application during Lesion Resection in Proximity to Eloquent Cortex

Distorted anatomy due to lesions may make anatomical landmarks for identification of the central sulcus unreliable. Anatomical and functional imaging techniques enable the identification of the precentral gyrus, although intraoperative direct cortical stimulation remains the gold standard for functionally verifying motor cortex.

DCS is performed after central sulcus localization, when possible. The pre-central sulcus location of the largest N25 peak (which is the phase reversal of the P22 post-central sulcus peak, illus-

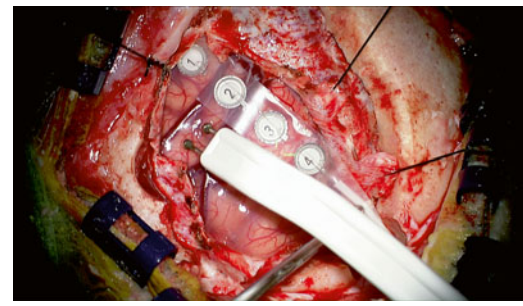

Fig. 7 Direct cortical stimulation via handheld bipolar probe, with ECoG monitoring via subdural strip prior to resection of low-grade glioma in adult patient. Diameter of strip electrode is 6 mm

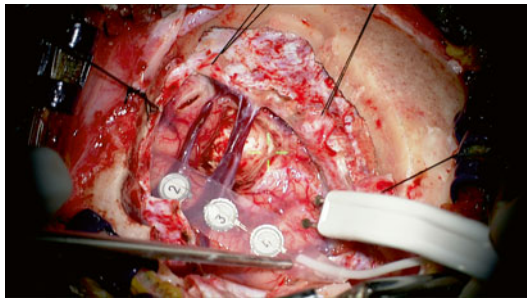

Fig. 8 Direct cortical stimulation via handheld bipolar probe, with ECoG monitoring via subdural strip after partial resection of low-grade astrocytoma. Bipolar probe position indicates location of stimulation which evoked involuntary contralateral dorsiflexion. Diameter of strip electrode is 6 mm

trated in Figure 4) can be used as an ideal starting location to begin DCS stimulation [15, 26, 27].

The multipulse train technique is increasing in popularity, due to the decreased incidence of induced seizure, lower delivered total charge during stimulation, and more minimal stimulus artifact on ECoG recording. Furthermore, the multi-pulse technique has allowed for a more quantitative analysis of elicited responses, increasing the value of DCS as a monitoring technique as well as a mapping technique. Once DCS has successfully localized motor function, a grid or strip may be placed to stimulate and evoke CMAP responses to monitor the functional integrity of the CST during resection utilizing the multi-pulse technique, if the placement does not interfere with resection [19, 70, 78, 80–85]. An increase in stimulus-threshold of 4 mA necessary to evoke CMAP responses has been suggested as a criterion indicating significant change; however, currently there are not reports confirming or suggesting otherwise [84, 86].

When DCS is used for mapping purposes, threshold values of less than 10 mA are generally accepted as indicative of eloquent motor cortex localization, for either Penfield or multi-pulse stimulation methods.

Practical Limitations

While under general anesthesia, motor mapping is limited to muscle groups that are monitored with electromyography, or those that are visible without disturbing the surgical drapes. With a cooperative awake patient, feedback regarding all muscle groups is available.

To maximize specificity of localization, it is important to continually use threshold or near-threshold settings, as supramaximal DCS settings may activate axons adjacent to the anodic stimulation site, decreasing specificity. When DCS is used as a monitoring tool during resection, reports have shown that only patients with significant signal deterioration or increased threshold experienced motor deficits 3 months postoperatively [82–84].

Direct cortical stimulation under general anesthesia is confined to the primary motor area. Stimulation of the supplementary motor area rarely activates involuntary CMAP responses. Intraoperative functional mapping of language, sensory, and supplementary motor area in response to direct electrical stimulation currently all require an awake cooperative patient.

Due to the great difference in stimulus amplitude parameters between DCS and tcMEP, patient movement during DCS is minimal and of less concern than tcMEP.

In the case that no CMAPs are evoked during stimulation, the function of the stimulating probe can be verified by checking for stimulation artifact on the ECoG recording montage, or stimulating the exposed temporalis and verifying a muscle twitch response. It is also possible to stimulate adjacent cortex that is not exposed when stimulating via grid electrodes, as they can be carefully slid subdurally under adjacent bone (Fig. 9). Systemic and anesthetic confounds that deteriorate tcMEP CMAPs can also deteriorate DCS CMAPs, therefore the anesthetic and troubleshooting recommendations are the same for DCS under general anesthesia as those for tcMEP.

The most likely complication of DCS is the occurrence of focal or generalized seizure. Administering bolus sedatives in response can impair continual motor mapping by decreasing neuron excitability. Instead, administering ice cold saline or Ringer's solution directly to the cortex will terminate the seizure.

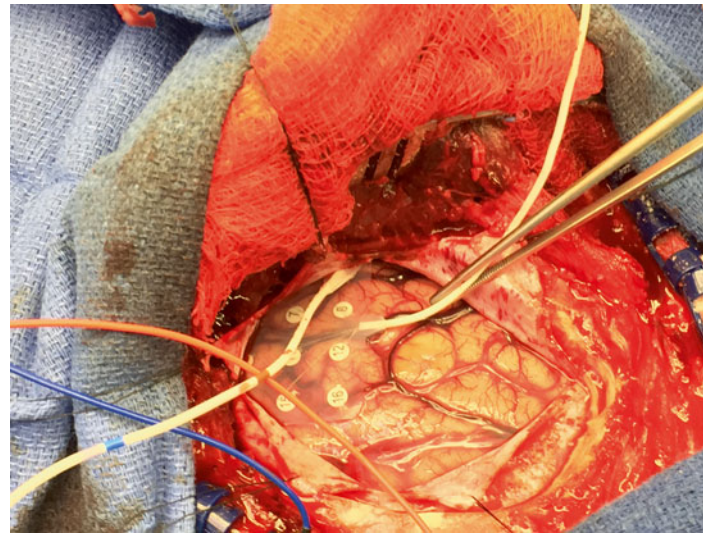

Fig. 9 4×4 Contact subdural grid positioned beyond the boundary of exposed cortex, underneath temporal bone for ECoG recording

Subcortical Stimulation

During direct subcortical stimulation, white matter tracts are regularly stimulated all along the resection margin or wall during surgery of tumors in eloquent areas [110]. While sensory, speech, and language subcortical stimulation techniques all involve the cooperation of a patient under local anesthetic; subcortical motor stimulation can be performed under general anesthesia [87].

After direct cortical stimulation and mapping of the primary motor cortical areas, subcortical direct electric stimulation may be used to detect corresponding descending motor pathways. Stimulation techniques used are identical to DCS parameters for Penfield's technique or the multi-pulse train technique used for cortical stimulation, with the exception that stimulation is via the cathode.

Bipolar stimulation provides the most precise results, as the current field produced during stimulation is smaller than with monopolar stimulation; however the eloquent tissue must be situated between the two probe tips to evoke a response. Some experts prefer monopolar stimulation due to the homogeneous current field created by radial current spread [80, 84].

Subcortical stimulation can be used to estimate the distance between stimulation site and corticospinal tract (CST). Estimates of the ratio of threshold current to distance from CST during subcortical stimulation, are approximately 1.0–1.5 mA/1.0 mm. A recent report suggested that resection should be stopped when subcortical stimulation thresholds are 2 mA, and that higher thresholds indicate safe distance from CST [86, 88–90].

Subcortical stimulation used in addition to DCS monitoring during resection has shown a combined sensitivity and specificity of 66.67 and 96.84 % for prediction of iatrogenic injury in a study of 100 patients [84, 86].

Pitfalls in the Usage of Somatosensory- and Motor-Evoked Potentials in Surgery of Eloquent Cortex under General Anesthesia

Obviously the use of these neurophysiological tools does not take the place of sound surgical experience, careful and delicate surgical technique, extensive knowledge of neuroanatomy, and particularly our newer appreciation of the subcortical white matter fiber tracts. Image guidance including the fiber tracts, functional MRI, and other modalities to preserve eloquent cortex, have shown immense value, but at present should be used in conjunction with neurophysiologic techniques, and not replace them.

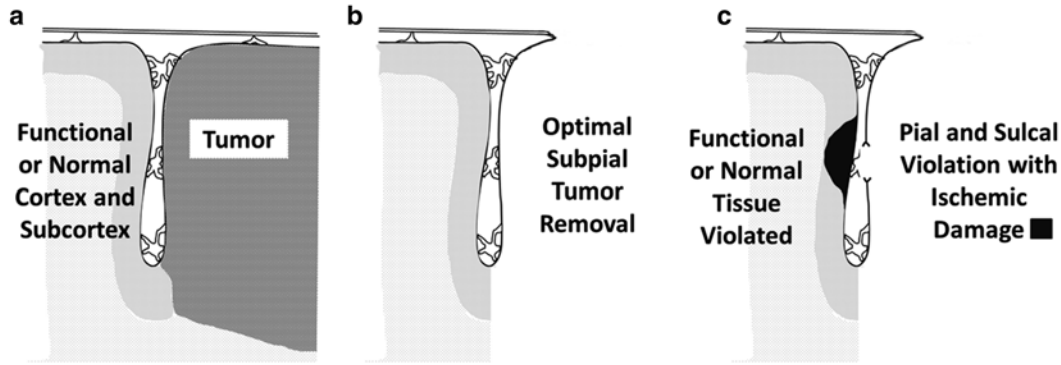

Fig. 10 (**a**) Schematic cortical sulcus with normal or eloquent cortex on the left bank and cerebral gyrus invaded by tumor on the right. (**b**) Optimal removal of tumor on the right respecting the pial border. (**c**) Violation of the pial surface, occlusion of a sulcal artery, and ischemic injury to the normal or eloquent left cortical bank

A number of our surgical strategies and neurophysiological techniques for safe brain tumor removal in proximity to eloquent cortex come from our experience gained in epilepsy surgery. Similarly, we must be reminded of particular cautions in relation to the handling of cortical gyri and sulci, and the technique of subpial dissection. Thus eloquent cortical and subcortical tissue can be inadvertently damaged if careful subpial tumor resection is not carried out and the pial borders and vasculature in the sulci are not preserved (Fig. 10). It must be recalled that with direct cortical stimulation and SSEP recordings we are predominately only visualizing, stimulating, or recording from the crest of the particular gyrus. An equal amount or more of eloquent cortex may well be buried in the continuous cortical sulcal wall of that gyrus (Fig. 11). Similar unexpected deficits can be encountered in resections adjacent to the pre-central and post-central gyri, as eloquent cortex may occasionally continue up the other sulcal side of an adjacent gyrus whose crest would not be recognized as eloquent [91]. Additionally in the Rolandic area, the posterior angulation of the afferent primary sensory fibers to the post-central gyrus; and the pyramidal tract outflow from the pre-central gyrus through the corona radiata to the internal capsule must be appreciated and respected [91], ideally along with subcortical motor stimulation being performed (Fig. 12).

Conclusions and Future Advancements of Somatosensory- and Motor-Evoked Potentials in Surgery of Eloquent Cortex under General Anesthesia

A number of experienced anesthesiologists are not comfortable with full general anesthesia by total intravenous anesthesia (TIVA)—being sedative/hypnotics, analgesic narcotics, with minimal muscle paralysis. For a number of good reasons they prefer to augment with inhalational agents albeit at lower percentages than routinely used for general anesthesia. However, standardized, well-accepted neuroanesthesia protocols to optimize SSEP and MEP recordings under general anesthesia are now well documented, and coordination and communication between anesthesiologists, neurosurgeons, and the neurophysiological monitoring team is essential to optimize monitoring and patient protection. Yet there is no doubt that fluctuations in anesthetic agent concentrations and the mixture of general anesthetic agents may affect neurophysiologic monitoring.

The ability for "real-time," ongoing blood concentrations of all intravenous, inhalational, and muscle paralyzing agents utilized during general anesthesia could advance neurophysiologic monitoring sensitivity and specificity. Increased understanding of the specific effects of these agents and how they may interact with each

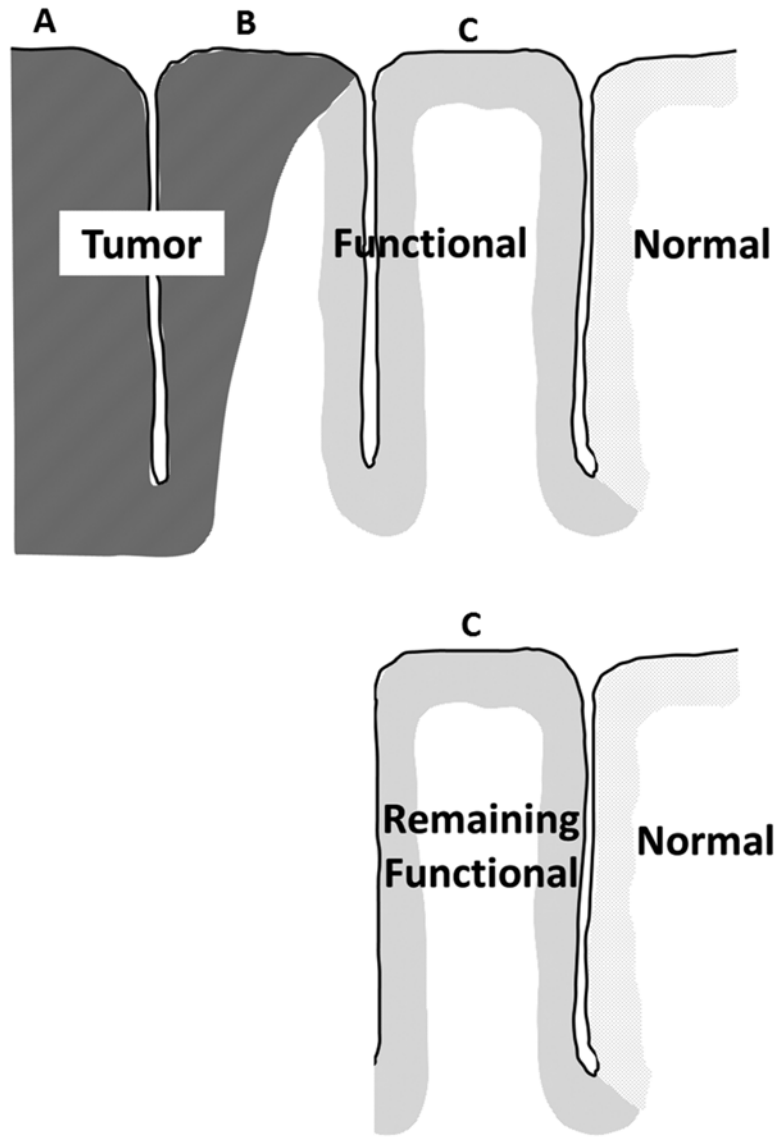

Fig. 11 *Top*: schematic of cortical surfaces with Gyrus C having eloquent motor and sensory function revealed by surface stimulation and SSEP recording. Gyrus B is partly invaded by tumor on the left, but has eloquent cortex on its right bank not revealed by cortical surface stimulation. *Bottom*: excision of Gyrus A and B removes the right bank of B, containing eloquent function in the cortex

other would improve the ability to account for response variability due to anesthetic agents. The phenomena of MEP "fade" discussed previously with prolonged operations, may involve accumulation of drug or metabolites within muscle cells or their receptors. This information would allow the monitoring team to optimize interpretation of CMAP responses, and also likely lead to lower and better controlled dosing titrated to the individual patient. If anesthetic and muscle paralytic control could be stabilized, or become homeostatic, accurate automated quantitative waveform analysis of recorded tcMEPs and SSEPs may be possible, dramatically standardizing monitoring ability.

Cerebral cortical regions in man in general have a varied, but yet rather consistent regional cortical nerve cell and nerve fiber structural organization (i.e. pre- and post-central, primary visual, associational, etc) . There is some evidence in animals and man that each such specialized cortical area may possess a particular "neurophysiological signature" which could be used to surgically identify a particular eloquent

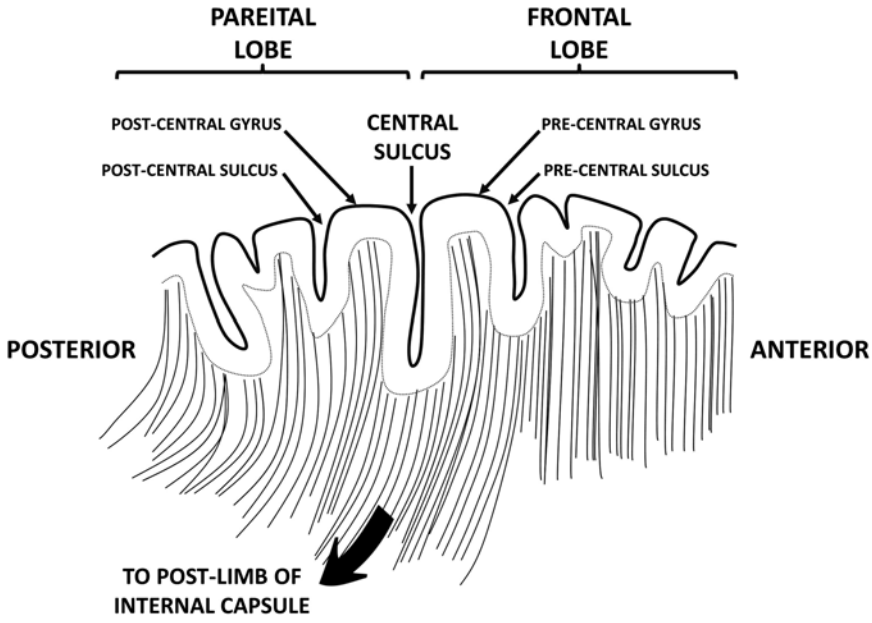

Fig. 12 Parasagittal section through the central hemispheric region. Schematic representation of the posterior course of Rolandic cortical fibers to reach the posterior limb of the internal capsule

cortical region. Electrocorticographic (ECoG) broadband evoked responses to motor, sensory, verbal, or complex behavioral tasks in awake patients has shown promise in identifying eloquent cortical regions, which could improve the safety of subsequent tumor excision under general anesthesia. Such techniques may improve in the near future and be added to our neurosurgical armamentarium.

For the foreseeable future, somatosensory- and motor-evoked potentials under general anesthesia as an aid to cerebral hemispheric tumor surgery near eloquent cortex will likely remain a mainstay. We envision improvement in our understanding and usage of these currently accepted techniques, and better consistency in managing the variable factors in our methodologies. We also anticipate increased accuracy of automated latency and amplitude alerts, at which point: (1) all neurophysiological tests have evidence-based, agreed-upon, procedure dependent threshold warning criteria, and (2) any waveform variation due to an anesthetic agent can be accurately quantified and factored into automated algorithms.

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