Intraoperative neuromonitoring techniques in the surgical management of acoustic neuromas

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Unfavorable outcomes such as facial paralysis and deafness were once unfortunate probable complications following resection of acoustic neuromas. However, the implementation of intraoperative neuromonitoring during acoustic neuroma surgery has demonstrated placing more emphasis on quality of life and preserving neurological function. A modern review demonstrates a great degree of recent success in this regard. In facial nerve monitoring, the use of modern electromyography along with improvements in microneurosurgery has significantly improved preservation. Recent studies have evaluated the use of video monitoring as an adjunctive tool to further improve outcomes for patients undergoing surgery. Vestibulocochlear nerve monitoring has also been extensively studied, with the most popular techniques including brainstem auditory evoked potential monitoring, electrocochleography, and direct compound nerve action potential monitoring. Among them, direct recording remains the most promising and preferred monitoring method for functional acoustic preservation. However, when compared with postoperative facial nerve function, the hearing preservation is only maintained at a lower rate. Here, the authors analyze the major intraoperative neuromonitoring techniques available for acoustic neuroma resection.

KEY WORDS • acoustic neuroma • vestibular schwannoma • intraoperative neuromonitoring • microneurosurgery • tumor resection • hearing preservation • facial nerve preservation

ACOUSTIC neuromas (vestibular schwannomas) are categorized as benign, extraxial brain tumors (Fig. 1) developing near the internal auditory canal, typically with involvement of the cerebellopontine angle. Advances in treatment modalities have popularized the application of less invasive management methods such as radiotherapy and radiosurgery, which carry high efficacy and low morbidity. However, many acoustic neuromas, particularly those that are large in size, necessitate surgical intervention.

The primary operative goals are gross tumor debulking while safeguarding the adjacent cranial nerves (Fig. 1). Neural preservation is particularly important in the contemporary management of acoustic neuromas. By virtue of their location, these tumors are close to the facial and vestibulocochlear cranial nerves (Fig. 1), and can thus severely impair the nerve function at the time of initial presentation. The neuroma can directly impinge, tightly adhere to, or overtly damage the nerves. These tumors often present as operative challenges, as resection may cause nerve irritation or injury leading to neurapraxia, axonotmesis, or neurotmesis.

The various options of surgical approaches (translabyrinthine vs middle fossa vs retrosigmoid) for acoustic neuromas and their respective patterns of postoperative cranial nerve preservation have been described. However, IONM may demonstrate improvements in structural and functional preservation of the cranial nerves during these operations. Several IONM techniques have been developed and evaluated with particular focus on CN VII and VIII preservation. Among these methods, the most frequently

Abbreviations used in this paper: BAEP = brainstem auditory evoked potential; CN = cranial nerve; CNAP = compound nerve action potential; ECOG = electrocochleography; EMG = electromyography; IONM = intraoperative neuromonitoring; IOVM = intraoperative video monitoring; MUP = motor unit potential.
used are EMG for the facial nerve and BAEP monitoring for the vestibulocochlear nerve. Here, we assess the fundamental characteristics underlying the major techniques available in IONM, emphasizing specific advantages and limitations of their utilization for optimal patient management.

Intraoperative Monitoring of the Facial Nerve (CN VII)

Cranial nerve VII plays a critical role in facial muscle function and one’s cosmetic appearance, and its weakness can have severe and profound implications on a patient’s quality of life. For instance, loss of facial nerve function can ultimately result in an inability to blink, secrete tears, or speak properly, thus imposing a significant burden on the patient. Such significant outcomes were once considered a probable morbidity. However, with the advent of facial neuromonitoring, the morbidity once associated with acoustic neuroma resection has been drastically reduced. The House-Brackmann Grading Scale, which ranges in increasing severity of deficits from Grade I through Grade VI, serves as a standardized method for analyzing postoperative outcomes of facial nerve function. As a result of advances in micro-neurosurgery and facial nerve IONM, many patients with smaller tumors have minimal functional loss of the nerve, as indicated by low House-Brackmann grades. In patients with larger tumors, the outcomes are not as optimistic, as these patients are at an increased risk of postoperative facial nerve deficits. Electromyography

The use of EMG to monitor facial nerve function has been well documented, leading to its widespread application in modern practice. The operative EMG device consists of a stimulator probe and a “sensor” that detects contractions of the facial muscles. Most operations use a minimum of 2 channels to observe the activity of the orbicularis oris and orbicularis oculi muscles, although the use of additional channels to observe other facial muscles may provide further benefit. Prior to the operation, the baseline electrical parameters, including MUPs and insertional activity, of these muscles are measured and recorded for future comparisons. The stimulator probe is applied to determine the location of the facial nerve. During an operation, the ideal location for applying the probe on the facial nerve is near the brainstem because it is proximal to the area of resection. Distal stimulation, while possible, yields limited data, as stimulation is being directed on the portion of the nerve that is virtually unaffected by resection. However, distal stimulation is not to be ignored, as several studies have found that higher proximal-to-distal EMG amplitude ratios successfully predict postoperative facial nerve function. When delivering the stimulus, the amount of current that is administered by the probe can be adjusted. Once the amount of current applied exceeds the action potential threshold of the patient’s facial nerve, an action potential is fired that causes twitching of the facial muscles. The sensor detects these facial movements and emits a sound alarm, thereby providing direct, immediate, and real-time feedback. The facial muscle MUPs corresponding to this stimulation are also projected onto an oscilloscope to facilitate visualization.

The electrical morphology, frequency, and characteristics of the MUPs vary greatly, and such divergences offer insights into possible abnormal nerve activity.
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nals can be observed on an intraoperative EMG study. A single MUP wave is referred to as a “spike,” while a short chain of MUPs is classified as a “burst.” When a sustained streak of MUPs is distinguished, it is designated as a “train,” which is shown in Fig. 3. Train MUPs possessing a particularly high frequency (greater than 30 Hz) are termed “neurotonic.”

Neurotonic train activity typically serves as an indicator of intense nerve stimulation, as robust nerve stimulation correlates with greater MUP activation. During an operation, neurotonic discharges can occur in the context of nerve stimulation, irritation, or damage. However, not all neurotonic train waves carry equal clinical significance. The A-train pattern has been most substantially affiliated with postoperative facial nerve deficits (Fig. 3).

The A trains are characterized as a high-frequency train pattern with the following features: a duration lasting milliseconds to seconds, an amplitude in the range of 100–200 μV, and a short onset and offset. The duration of “train time,” as quantified by the seconds of A-train activity, has been shown to translate to worse postoperative facial nerve paresis. Other train patterns that may be encountered on an EMG include the B and C trains, although they have not been shown to carry significant value in predicting postoperative nerve function. As described by Romstöck et al., B trains manifest either in a spike or burst pattern and are distinguished by their gradual onset, low amplitudes, and average duration lasting minutes to hours. C trains, on the other hand, are irregular waveforms of varying amplitudes that bear resemblance to interference. Aside from train time and activity, other electrical EMG findings bear clinical importance as well. Mandpe et al. reported that low immediate postoperative stimulation thresholds in combination with a response amplitude appeared to reliably foretell excellent postoperative facial nerve function. Neff et al. reached similar conclusions but with stimulation thresholds of 0.05 mA or lower and amplitudes greater than 240 μV.

Electromyography provides several benefits. One of its main functions is determining the anatomical location of the facial nerve. Direct, pinpoint visualization of the nerve may often prove difficult, as the tumor, its capsule, and bone may interject along the nerve’s trajectory. By adjusting and determining the current required for muscle stimulation, however, the relative proximity of the nerve to the probe can be deduced. If there is very little tumor, tissue, or bone covering the nerve, the facial nerve will be more prone to stimulation at lower currents, such as lower than 0.2 mA, thereby implying that the nerve is highly exposed, close to the probe, and in danger of being manipulated. Conversely, stimulation at higher currents, such as greater than 0.5 mA, suggests the presence of a sizable tissue or bone barrier between the nerve from the probe. Highly adherent tumors have a tendency for creating thicker barriers from the probe, thus resulting in higher mean stimulation thresholds.

In addition, EMG helps prevent unplanned manipulation of the facial nerve by emitting a warning noise whenever muscle stimulation is detected. This can warn the surgeon of impending danger and thus advise cessation of current actions or recommend extreme caution. By doing so, EMG directly influences surgical planning and strategy, as the surgeon can appropriately alter the surgical ap-
proach to avoid causing damage to the nerve.\textsuperscript{9,25,46,82,111,125} A-train activity or other abnormal EMG patterns may also encourage caution,\textsuperscript{42} although they must be placed in context: neurotonic discharges can sometimes fire even in the presence of a transected nerve.\textsuperscript{42} In addition to perioperative nerve preservation, EMG can help clarify the residual function of the nerve postoperatively.\textsuperscript{46,54} When comparing postoperative and baseline stimulation threshold, patients who require high or higher postoperative currents may have endured some degree of nerve injury.\textsuperscript{54,70,93,123,126,128,150}

Despite its benefits, EMG is not an infallible monitoring system. During resection, the facial nerve may appear grossly intact; however, this finding does not necessarily convert to true nerve functionality.\textsuperscript{1,11,22,60,70,95} One possible explanation for this phenomenon is that EMG can sometimes receive poor data input. This issue is particularly salient with the application of microinstruments to cauterize tissue or tumor surrounding the facial nerve.\textsuperscript{41,85} The generated electrical signal may create artifact, signal interference, and distortion.

Electromyography also runs the added risk of instigating electrical injury from overstimulation. As general principle, application of the stimulator probe should be done conservatively to avoid inducing iatrogenic injury to the facial nerve. Intense or prolonged stimulation theoretically increases the risk of causing irreparable nerve injury.\textsuperscript{106,127} To that end, several techniques are encouraged to diminish the risk of injury. Pulsed stimulation, for example, appears to have a lower injury risk than constant stimulation.\textsuperscript{26,60} In addition, monopolar stimulation with constant voltage may be superior to bipolar constant-current stimulation.\textsuperscript{82} However, the majority of experimental studies done to examine the potential for overstimulation have been conducted in animal models. Through these studies, one of the emerging general principles has been the greater influence of stimulus frequency on the degree of nerve injury. In rats, Sapmaz et al.\textsuperscript{199} investigated the respective effects of stimulus amplitude (mA) and frequency on histological axonal degeneration. The authors’ results demonstrated that frequency, but not amplitude, was statistically significant in causing greater axonal degeneration. In other words, rats with 20 stimulations had more degeneration than those that underwent 10 stimulations (p < 0.05), while rats with 30 stimulations had more degeneration than those that received 20 stimulations (p < 0.05).\textsuperscript{199} In a cat model, McCreery et al.\textsuperscript{26} obtained similar results: stimulation at 100 Hz versus 50 Hz caused greater axonal degeneration, while stimulus amplitude did not appear to have much effect. Another important principle is the superiority of pulsed stimulation when compared with constant stimulation. In mice, pulsed stimulation was associated with less myelin and axonal degeneration.\textsuperscript{42} In a cat study, investigators found that extended periods of high frequency stimulation caused greater injury and that pulsed stimulations can reduce the risk of damage.\textsuperscript{42} Interestingly, Kartush et al.\textsuperscript{28} found that constant current stimulation can be safely applied in guinea pig models as long as the electrode is properly insulated to preclude shunting. In summary, low stimulus frequencies and pulsed stimulations can be applied clinically to minimize the risk of injury from overstimulation.

**Direct Observation/Video Monitoring**

To increase the sensitivity of facial nerve IONM, recent studies have proposed implementing direct observation of facial muscle movement or intraoperative video monitoring (IOVM).\textsuperscript{21,28,29,85} Theoretically, IOVM would supplement EMG by allowing better visualization of facial muscle contractions, thus providing an additional aid in the operating room. During IOVM, an anesthesia mask containing several infrared cameras is fastened to the patient’s face, and the infrared properties of these cameras allow video recording under the operative drapes.\textsuperscript{28,85} The camera view can be magnified such that even minute movements may be detected by the naked eye.\textsuperscript{85} The images are projected on a 4-way split screen: 2 focus on movements of the facial muscles, another displays the microscopic operating field, and the remaining screen projects the EMG tracings.\textsuperscript{28,29} These simultaneously derived images are thus juxtaposed next to each other, with a sound alarm triggered by facial muscle contractions.\textsuperscript{28,29}

Although IOVM may prove useful, the full utility of this tool remains to be characterized. In a study comparing EMG with IOVM, the use of EMG alone exhibited higher sensitivity in detecting facial nerve activation: EMG detected facial muscle movement at a stimulation of 0.3 mA, whereas IOVM required a minimum of 0.5 mA.\textsuperscript{29} De Seta et al.\textsuperscript{29} obtained similar results, finding EMG alone to be more sensitive than IOVM. Thus, EMG appears more effective than IOVM based on current data. However, further studies must evaluate the validity of IOVM as a supplementary tool in the operating room.

**Intraoperative Monitoring of the Vestibulocochlear Nerve (CN VIII)**

Even with modern IONM, current vestibulocochlear nerve retention rates do not compare favorably with the excellent outcomes seen with the facial nerve.\textsuperscript{5,12,16,36,49,52,62,75,88,94,99,103,115,116,120,130,132,139,147} Although this discrepancy may highlight the need for improvement in IONM of CN VIII,\textsuperscript{29} it may also reflect the inherent difficulty in preserving auditory function, as large tumors are more highly associated with postoperative deficits.\textsuperscript{1,11,20,23,88,103,116} and tumors with extensive infiltration into the cerebellopontine angle render acoustic preservation an arduous task.\textsuperscript{23,89,147}

Operative damage to the vestibulocochlear nerve can be induced in various ways.\textsuperscript{83,64,149} Direct operative trauma is a potential avenue, with the nerve most prone to exposure during maneuvers, such as drilling into the internal auditory canal, operative traction, or subsequent tumor resection.\textsuperscript{1,17,19,51,79,96,129} Cranial nerves are inherently more susceptible to trauma because they are ensheathed in central myelin, thus lacking the extra protective layers, such as the perineurium, that are more prevalent in peripheral myelin.\textsuperscript{8,17,91,64,79,123} Ischemic damage also presents further risk of injury. More specifically, vascular changes to the internal auditory artery, such as occlusion, rupture, or vasospasm, are believed to induce postoperative hearing deficits.\textsuperscript{17,97,84,88,122} Strauss et al.\textsuperscript{15} found that applying medical therapy to preclude such vasospasms produced
preservation rates that were more than twice as high when compared with controls.

**Brainstem Auditory Evoked Potentials**

Brainstem auditory evoked potentials are defined as the bioelectric neural activity that materializes in response to stimulation of the vestibulocochlear nerve. In comparison with the background electrical brain activity, these BAEP waves are diminutive and difficult to detect. To facilitate distinction between BAEPs and background “noise,” several thousand samples of the electrical stimulus must be acquired and subsequently averaged to create a distinct auditory evoked potential. On BAEP recordings, the auditory response is extracted from several locations in the entire vestibular nerve pathway, as it travels peripherally to centrally. The peaks of the evoked electrical potentials are classified as Wave I through Wave V, which correspond to the peripheral cochlear nerve and the inferior colliculus, respectively. These waves can be seen in Fig. 4.80

In BAEP monitoring, scalp and earlobe electrodes are placed, and an auditory stimulator discharges acoustic clicks to the operated ear through an earphone-transducer apparatus. The electrical pulse rate is set at a range of 20–50 clicks per second. Before commencing with the operation, the stimulus intensity, as measured in decibels, is adjusted until the patient can hear the click; the stimulus is eventually delivered at several decibels higher than the measured threshold. Upon delivery of the stimulus, the ears are stimulated bilaterally so white noise is applied at an intensity several decibels lower to obscure the response of the contralateral ear.

**Fig. 4.** Figure demonstrating direct CNAPs (A), direct recording from the lateral recess of the fourth ventricle (B), and BAEPs (C). Note the 2 negative peaks seen on direct CNAPs and the relative coincidence of the first negative peak on direct CNAP to Wave I on BAEP monitoring. Roman numerals indicate the waves. Reproduced with permission from Møller and Jannetta: J Neurosurg 59:1013–1018, 1983.

When considering BAEP waveform shifts, Waves I, III, and V carry the most clinical significance. Changes in their amplitude, peak latency, or presence of the peak are heavily scrutinized and compared with baseline BAEPs. More specifically, increased peak latencies of Waves I, III, and V; high interaural latency differences; decreased amplitudes of Waves I and V; increased interpeak latencies between Waves I–III, III–V, and I–V; are examples of potentially concerning wave changes. Between peak latencies and interpeak latencies, the latter is the more clinically useful marker because peak latencies are more susceptible to influence from external factors such as age, thus rendering them less reliable. However, the majority of these parameters are, at best, warning signs that alert the surgeon; among them, only maintenance of Waves I and V has been consistently shown to correlate with better postoperative hearing preservation rates, although others have found poor hearing outcomes despite wave preservation.

The use of BAEPs comes with several limitations. Because the stimulus response must be summed and averaged to obtain a wave of sufficiently high amplitude, the tradeoff to this process is a significant time delay that can last up to several seconds to minutes. Naturally, such a delay can negatively influence the course of surgery, as BAEPs effectively provide data that were applicable several seconds or minutes prior. Matthis and Samii reported that direct BAEP monitoring was able to reduce the lag time to 5–15 seconds, suggesting that considerable improvements may be possible. In addition, BAEP recordings are prone to presenting false-positive results. Trauma is not the only causative agent of BAEP waveform shifts, with other physiological or intraoperative processes such as anesthesia, hypothermia, and irrigation all capable of inducing waveform changes. Such a wide range of artifact sources can create great difficulty with respect to surgical decision making. The utility of BAEPs may also be patient dependent, as some do not have detectable BAEPs while others have abnormal baseline BAEPs. Without a clear starting point, BAEP monitoring may prove too difficult a task to complete. Measuring CNAPs may be more beneficial in such cases, as patients occasionally have BAEP waveform normalization postoperatively despite preoperative absence.
Electrocochleography and Direct CNAPs

Brain auditory evoked potential monitoring is considered a “far-field” technique because the auditory response is measured on the scalp, which is distal from the neural auditory response. In contrast, ECOG and direct CNAPs are “near-field” techniques because the stimulation evokes and records an electrical response close to its origin on the auditory nerve. Because these techniques record from the nerve itself, near-field IONM bypasses the noise and artifact created in far-field IONM, which translates to reducing the number of stimuli averaged required in addition to affording a larger amplitude for facile visualization. Ultimately, this leads to a much quicker assessment of nerve function.

In principle, both ECOG and direct CNAPs use electrodes to measure potentials generated from the auditory nerve, with some minor differences in operative setup. For ECOG, electrodes are typically positioned trans tympanically on the middle ear promontory of the pathological ear. Reference and ground electrodes are placed on the ipsilateral earlobe and on the forehead, respectively. A foam ear plug not only holds the electrode firmly in place but also impedes foreign substances from breaching into the ear canal. Similar to the BAEP, the stimulating electrode administers click impulses, and multiple responses must be averaged for a distinct wave pattern to emerge.

As its name suggests, in direct CNAPs, the action potential is measured directly from the acoustic nerve itself. The recording electrode is placed directly on the acoustic nerve, the negative electrode is attached to the mastoid of the contralateral ear, and a reference electrode is placed on the scalp. It is common practice to place the recording electrode proximal to the tumor being resected, with adhesive such as Gelfoam applied between the electrode and nerve to reinforce the placement. Like the BAEP and ECOG, a click stimulus is applied through an earphone, and the resulting compound action potential is measured.

Electrocochleography and direct CNAP monitoring are both techniques that rely on deducing the compound action potential, which represents a summation of all the action potentials, from the vestibulocochlear nerve. These CNAPs, as they are known, are visualized as negative peaks distinguishable by their high amplitudes. In ECOGs, they consist of 2 action potential peaks designated “N1” and “N2,” and in direct CNAP monitoring, comparable peaks are obtained. Because ECOG involves peripheral nerve stimulation, the N1 waveform seen on ECOG is congruent with Wave I on BAEP monitoring. The absolute loss of N1 on ECOG is frequently associated with postoperative hearing deficiency. Changes to the latency or amplitude of N1 on either ECOG or direct recording are also electrophysiological signs suggestive of injury. Further electrical waveforms are seen in ECOG, thus differentiating it from a direct CNAP reading. The cochlear microphonic and summation potential are both electrical responses generated from the organ of Corti, and lower cochlear microphonic detection thresholds may be involved in prognosticating postoperative hearing function. In the overall context of ECOG monitoring, however, cochlear microphonics and summation potentials are generally considered less important than the N1 peak.

The primary advantages of ECOG and direct CNAPs are derived from their near-field designation. With shorter latency periods, they reflect pertinent information much faster than BAEPs and provide immediate feedback on the state of the auditory system. Changes seen on compound action potentials also tend to occur immediately, a helpful trait when considering vascular etiologies of dysfunction: vascular changes cause immediate effects that may not be detected quickly enough on BAEP monitoring. The quick response time in conjunction with larger amplitudes than BAEPs has strengthened the reputation of measuring CNAPs as the most preferred monitoring method of choice. When comparing direct CNAPs with ECOG, direct CNAPs possess higher predictive value of postoperative functionality, with lower false-positive and higher true-positive rates.

Electrocochleography and direct CNAPs have unique disadvantages. Because the recording electrode is placed peripherally, ECOG is unable to provide information about the entirety of the auditory nerve, particularly the more central portions of the auditory pathway. As a result, it is possible to completely transect the nerve centrally without observing any credible change on the ECOG study. Due to its rather invasive nature, ECOG also presents an increased risk of CSF otorrhea due to tympanic membrane perforation during electrode placement. To circumvent this issue, alternative but visible options include tympanic or extratympanic electrode placement. Electrocochleography can prove technically challenging as well. The electrode must be held securely in place; moving it manually or unintentionally can induce changes in the baseline amplitude and latency, thus exacerbating the difficulty of making subsequent comparisons.

The disadvantage of using direct CNAPs is mainly practical. In larger tumors, there is very little operating space to place the recording electrode without sacrificing visibility of the surgical field. As a result, direct CNAPs are generally reserved for patients presenting with smaller tumors.

Conclusions

Implementation of facial and vestibulocochlear nerve IONM, in combination with the development of improved modern microneurosurgical techniques, has led to a dramatic reduction in the morbidity once associated with acoustic neuroma surgery. The facial nerve, in particular, has shown higher rates of preservation with the use of EMGs. The vestibulocochlear nerve, on the other hand, may be important to investigate as an avenue for further improvement. Despite the combined techniques of BAEPs, ECOG, and direct CNAPs, auditory preservation rates do not yet approximate those of facial nerve preservation. Further efforts and investigations are needed to study and incorporate other adjunctive IONM techniques in an attempt to improve preservation of auditory function.
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