Microvascular decompression (MVD) is a widely used surgical intervention to relieve the abnormal compression of a facial nerve caused by an artery or vein that results in hemifacial spasm (HFS). Various intraoperative neurophysiologic monitoring (ION) and mapping methodologies have been used since the 1980s, including brainstem auditory evoked potentials, lateral-spread responses, Z-L responses, facial corticobulbar motor evoked potentials, and blink reflexes. These methods have been applied to detect neuronal damage, to optimize the successful decompression of a facial nerve, to predict clinical outcomes, and to identify changes in the excitability of a facial nerve and its nucleus during MVD. This has resulted in multiple studies continuously investigating the clinical application of ION during MVD in patients with HFS. In this study we aimed to review the specific advances in methodologies and clinical research related to ION techniques used in MVD surgery for HFS over the last decade. These advances have enabled clinicians to improve the efficacy and surgical outcomes of MVD, and they provide deeper insight into the pathophysiology of the disease.

Keywords microvascular decompression; hemifacial spasm; intraoperative neurophysiologic monitoring.

INTRODUCTION

Hemifacial spasm (HFS) is a rare condition that causes involuntary contraction of facial muscles, usually on one side of the face, accompanied by abnormal compression of the adjacent facial nerve near the brainstem by a vein or artery. HFS is known to develop via two representative pathologic mechanisms: 1) peripheral ephaptic transmission and 2) central hyperexcitability of the facial motor nucleus (FMN). The symptoms can be controlled by pharmacologic treatment or local botulinum toxin injection in some patients, but microvascular decompression (MVD) surgery can be considered in patients exhibiting a poor response to such nonsurgical treatments. MVD involves separating the affected facial nerve from the adjacent blood vessels causing the compression, and it has a high success rate in removing the spasm.1,2

Since Møller and Jannetta3 first performed electrophysiologic recordings of facial nerves and muscles during MVD in 1984, various intraoperative neurophysiologic monitoring (ION) methodologies have been applied during MVD, including brainstem auditory evoked potentials (BAEPs), lateral-spread response (LSR), Z-L response (ZLR), blink reflex (BR), and facial corticobulbar motor evoked potentials (FCoMEPs). These techniques not only made it possible to monitor for damaged nerves, including the facial nerve and cochlear nerve, but they also enable real-time evaluation of the success of decompression.4-7 More...
over, many research groups have used ION to provide deeper insights into the pathologic mechanisms of HFS and to analyze the predictive value of ION data for long-term postoperative neurologic outcomes.8–12 Fernandez-Conejero et al.13 published a well-organized review article in 2012 describing detailed methodologies and interpretations of ION techniques used during MVD for HFS. However, they focused mainly on the utilization of ION to advance the understanding of the pathophysiology of HFS. There have been new advances reported in this field since that time. Therefore, this article aimed to review and present advances in ION techniques and evaluate their electrophysiological/clinical significance in MVD for HFS based on studies published after 2012.

ION DURING MVD

BAEPs

Since the cochlear nerve lies directly adjacent to the facial nerve, postoperative hearing loss frequently occurs due to injury to the cochlear nerve during MVD surgery for HFS. Several events can result in such injuries,14 including traction during cerebellar retraction (CR), ischemia due to vasospasm when manipulating the compressive vessel loops, mechanical or thermal trauma during vessel and nerve dissection, or compression caused by the insertion of a Teflon pad. Postoperative hearing loss after MVD reportedly occurs in 7.7% to 20% of cases when BAEPs are not monitored; however, since introducing the ION of BAEPs, the rate of postoperative hearing loss has decreased to no more than 2%.15 Therefore, the ION of BAEPs is now considered essential during MVD for HFS.

Changes in stimulation methods

BAEPs are usually evoked by broadband click stimuli typically generated by passing 100-μs square-wave electrical pulses to a transducer to generate acoustic signals. The stimulus intensity is chosen so as to produce clear BAEPs, with a click intensity of 100 dB SPL (sound pressure level) or 60–70 dB HL (hearing level) commonly being utilized. To prevent crossover responses, white noise at 60 dB SPL or 30–35 dB HL is applied to the contralateral ear. Also, alternating the click polarity may be helpful for minimizing problematic electrical stimulus artifacts during ION. Stimulus frequencies of 5 Hz to 30 Hz have been reported in the literature, but the American Clinical Neurophysiology Society (ACNS) recommends stimulus rates of 5–12 Hz because faster rates can degrade the BAEP waveforms. According to the ACNS guideline, 500–1,000 repetitions are generally recommended to obtain interpretable and reproducible BAEPs.16 However, using a stimulus rate of 10 Hz over an average of 1,000 trials means that it takes approximately 100 seconds to obtain interpretable BAEPs. Since the cochlear nerve can be damaged within a very short time during MVD, postoperative hearing loss cannot be sufficiently prevented when using a method that requires approximately 100 seconds to obtain BAEPs.

Developing ION instruments with high signal-to-noise ratios has significantly reduced the disintegration of the waveform amplitude that occurs with a higher stimulation rate. For example, Joo et al.17 reported no significant difference in the disintegration of the waveforms obtained using stimulation rates of 10 Hz and ~40 Hz. Those authors also found it possible to obtain reliable waveforms when using an average of 400 trials with a stimulation rate of 43.9 Hz. Using a real-time monitoring protocol during MVD for HFS reduced the time required to obtain reliable BAEPs to less than 10 seconds. The new protocol has also reduced the time required to detect injury to the cochlear nerve during MVD surgery, and so has significantly decreased the rate of postoperative hearing loss (4.02% vs. 0.39%, p=0.002). Over the last decade, there has been agreement among some researchers that there are limitations to preventing postoperative hearing loss when a relatively long period time is required to obtain reliable BAEP waveforms and that obtaining BAEPs in a shorter time is possible by applying a higher frequency stimulation rate and a lower average number of trials.17,14 The differences in methodologies that have been used to obtain reliable BAEPs are summarized in Table 1.

Changes in recording methods

To obtain BAEPs, the standard recording derivations consist of a preauricular or mastoid electrode that is referenced to Cz’ according to the 10–20 electrode placement system for electroencephalography. Using the conventional methods, waves I and II represent near-field potentials, whereas waves III–V represent far-field potentials. Unlike near-field potentials, far-field potentials are susceptible to amplitude reductions under anesthesia.19 To improve the consistency and amplitude of BAEPs, Greve et al.20 placed an electrode on Erb’s point (EP) instead of the preauricular or mastoid area in 30 patients undergoing infratentorial surgeries (15 of whom underwent MVD), and found that the amplitudes of wave IV (left +65%, p<0.001; right +43%, p=0.002) and wave V (left +54%, p<0.001; right +48%, p<0.001) were significantly increased using EP–Cz’/EP2–Cz’ derivations compared with those obtained using A1–Cz’/A2–Cz’. When using an extracephalic electrode placed at EP, the amplitudes of waves III–V in BAEP recordings were significantly higher than those obtained using the preauricular-vertex derivations.
Changes in warning criteria
Despite the numerous studies investigating the use of BAEPs as an ION tool during MVD, there is no consensus on the warning criteria that are predictive of postoperative hearing loss. Polo et al. postulated that a wave-V latency prolongation of 0.6 ms represented a significant change in BAEPs that was likely to be associated with hearing loss, while Grundy et al. suggested that the surgeon should be alerted when a 1.5-ms delay in wave V is observed. In contrast, Hatayama and Möller reported that a prolongation of wave V latency was always accompanied by a reduction in wave V amplitude. Such decrements were significantly more common than the prolongation of the latency of wave V in patients with postoperative hearing loss, and so those authors suggested that a decrease in amplitude was a more-reliable indicator of postoperative hearing loss. Thirumala et al. recently reported that the loss of wave V during MVD surgery was a significant predictor of postoperative hearing loss, since the probabilities of this complication were 60%, 25%, and 10.2% in cases with a persistent loss, transient loss, and significant change in wave V, respectively.

Despite considerable efforts to identify significant warning signs, the results of some of the previous studies have been inconsistent. Thus, many researchers still consider a latency prolongation of 1 ms or an amplitude decrease of at least 50% on two successive trials as a warning sign of hearing loss. However, since inaccurate warning criteria based on BAEPs can prolong operation times and even actually induce postoperative hearing loss due to unnecessary additional manipulations, it is critical to establish the critical warning signs during ION for predicting this postoperative complication. Therefore, Park et al. reported critical warning criteria for predicting postoperative hearing loss based on BAEPs in 932 patients with HFS. When applying a real-time protocol for obtaining a reliable BAEP waveform within 10 seconds during MVD in patients with HFS, postoperative hearing loss occurred in 11 (1.2%) patients and was most commonly observed in those exhibiting a persistent loss of wave V (n=6, 54.5%). Postoperative hearing loss occurred in 7.4% of patients who showed a transient loss of wave V and 2.0% of patients exhibiting a latency prolongation of at least 1 ms combined with an amplitude decrease of at least 50%. In addition, 194 of the 932 patients in the study of Park et al. experienced a latency prolongation (≥1 ms) of wave V without an amplitude reduction of at least 50% during MVD surgery, and 30 of those 194 patients exhibited only a latency prolongation >2 ms; however, none of these patients experienced postoperative hearing loss. Their study also validated the warning criteria for predicting postoperative hearing loss based on BAEPs during MVD surgery for patients with HFS. More specifically, the authors reported that the permanent loss of wave V showed the highest specificity (99.4%) for predicting postoperative hearing loss, while transient loss and latency prolongation (≥1 ms) with an amplitude reduction (≥50%) exhibited high accuracy. In summary, the authors concluded that the currently adopted ‘significant warning signs’ of postoperative hearing loss, such as a latency prolongation of at least 1 ms or an amplitude decrease of at least 50%, were inappropriate criteria for preventing postoperative hearing impairment during MVD surgery, and that relying on a single warning sign alone would not provide sufficient accuracy. Park et al. therefore suggested using a sliding scale for the critical warning signs based on BAEPs as follows: 1) the observation sign (attention sign), comprising a latency prolongation of at least 1 ms without an amplitude decrease of at least 50%; 2) the warning sign, comprising a latency prolongation of at least 1 ms with an amplitude decrease of at least 50%; and 3) the critical sign, comprising the complete loss of wave V. When the observation sign is detected during MVD surgery, the neurophysiologist should notify the surgeon immediately, although no corrective actions are necessary. The surgeon should again be notified when either the warning or critical sign appears, and more-aggressive measures should be instigated to prevent damage to the cochlear nerve when the critical sign occurs.

Importance of waveforms other than wave V
While a latency prolongation of at least 1 ms or an amplitude decrease of at least 50% of wave V has been used as the warning criteria during MVD for HFS, recent studies have confirmed that the loss of wave V is more important than other waveform changes. When wave V is lost during MVD for HFS, two distinct patterns have been observed: 1) total wave loss (including of wave I), or 2) loss of wave V but not of wave I. Since wave I is generated in the cochlea, damage to that organ can lead to the total loss of BAEPs. During MVD, cochlear infarction secondary to vasospasm can lead to to-

Table 1. Methodologies for intraoperative neurophysiologic monitoring of BAEPs

| ACNS  | Real-time protocol | University of Pittsburgh Medical Center |
|-------|-------------------|----------------------------------------|
| Stimulus rate | 5–12 Hz | 43.9 Hz | 17.5 Hz |
| Average number of trials | 500–1,000 | 400 | 256 |
| Time to obtain BAEPs | About 100 seconds | About 9.1 seconds | About 14.6 seconds |

ACNS, American Clinical Neurophysiology Society; BAEPs, brainstem auditory evoked potentials.
tal wave loss, including of wave I. Also, if the proximal portion of the cochlear nerve is damaged during MVD, wave I may persist despite the loss of wave V if the cochlea remains intact. Joo et al. analyzed data from 36 patients who experienced wave-V loss during MVD for HFS, and found that 12 (33.3%) presented with total wave loss (including wave I). These patients were significantly more likely to experience postoperative hearing loss ($p=0.009$) and a significantly higher frequency of postoperative complications such as dizziness and tinnitus. That study also investigated the timing of wave-V loss, and found that total wave loss occurred more frequently after the decompressive procedure of MVD, suggesting that severe changes in BAEPs could happen later, including after completing the procedure, and hence that continuous attention was required until the end of MVD surgery.

The use of CR to access the cerebellopontine angle is known to be the leading cause of postoperative hearing loss during MVD surgery. Two patterns of BAEPs can appear during the CR step depending on the direction in which the cochlear nerve is pulled: 1) wave I of the BAEPs can change if the cochlear nerve is pulled toward the brainstem, whereas 2) wave III changes if the cochlear nerve is pulled away from the brainstem. Park et al. investigated the predictive value of the initial change in wave I or wave III during CR in MVD surgery. They analyzed the data of 241 patients who exhibited a latency prolongation of at least 1 ms or an amplitude decrease of 50% of wave V during MVD for HFS. The patients were categorized into the following two groups based on significant changes in BAEPs during CR: 1) latency prolongation of wave I of $\geq 0.5$ ms with prolongation of the interpeak interval between waves I and III of $<0.5$ ms, and 2) latency prolongation of wave I of $<0.5$ ms with prolongation of this interpeak interval of $\geq 0.5$ ms. The results of that study suggested that two-thirds of all patients experienced Group-B changes during the CR component of MVD. Eleven of the 241 patients exhibited the loss of wave V at the end of the surgery, although 10 of them belonged to Group B. Also, five patients experienced postoperative hearing loss, all of whom were in Group B. Based on these results, the authors concluded that a latency prolongation of wave III during CR was a significant prewarning sign of BAEPs for postoperative hearing loss (Fig. 2).

**LSR**

The LSR is an abnormal muscle response recorded from facial muscles innervated by another branch that is induced by stimulating the facial nerve branch. The LSR is known to be a specific electrophysiologic finding for HFS. There is a positive correlation between the disappearance of the LSR dur-

![Fig. 1. Examples of brainstem auditory evoked potentials with (A) and without (B) the persistence of wave I (black triangle) in patients experiencing the loss of wave V (red triangle) during microvascular decompression surgery.](image)
ing MVD and a favorable outcome in patients with HFS, and so disappearance of the LSR has been used as an indicator of complete facial nerve decompression. However, there have also frequently been unexpected observations such as the absence of the LSR before MVD or the persistence of the LSR after MVD. Also, several studies have suggested that a residual LSR after MVD is not related to the long-term outcome following HFS treatment.

Changes in methodology
The LSR is usually recorded by stimulating the temporal or zygomatic branch of the facial nerve at approximately 3 cm lateral to the lateral margin of the orbit. Electromyography (EMG) recordings of the facial nerve can be made from the frontalis, orbicularis oculi, orbicularis oris, and mentalis muscles. The direction of stimulation to induce the LSR is centripetal toward the brainstem, with the cathode positioned proximally. The disappearance of the LSR has been utilized as an indicator of adequate decompression, and so accurate measurements of the LSR during MVD are crucial, and these are difficult using the conventional evaluation method for several reasons, including 1) variations in the anatomical distribution of the facial nerve branch, and 2) the difficulty of evaluating whether a branch of the facial nerve is fully stimulated to elicit the maximal LSR.

Lee et al. recently suggested that a new LSR monitoring method is more reliable than the conventional methods. To achieve this improvement, they conducted preoperative LSR testing in an outpatient clinic to map the anatomy of the facial nerve branch of each individual patient. After identifying the patient-specific location, they stimulated the facial nerve branch in the centrifugal direction, with the anode located proximally over the area just anterior to the mandibular fossa and with the cathode located distally in the temporal or zygomatic branch of the facial nerve. This new method resulted in LSR disappearing significantly more often after MVD compared with the conventional method (98.2% vs. 61.8%, p=0.0012). Furthermore, the persistence of the LSR after MVD (1.8% vs. 29.1%, p=0.0051) and the absence of the LSR (0.0% vs. 9.1%, p<0.0001) were both significantly less common with the new method than with the conventional method. The authors explained why the new method of stimulating the nerve in the centrifugal direction resulted in greater efficacy during MVD. In bipolar stimulation of a peripheral nerve, depolarization occurs at the cathode; conversely, hyperpolarization occurs at the anode. Therefore, the cathode must be placed closer to the recording electrode to elicit a more appropriate excitation of the peripheral nerve. The authors suggested the new method could primarily allow for more accurate stimulation of the facial nerve branches, which could in turn also lead to a secondary increase in the accuracy of measurements of the LSR. However, further measurements in more patients are needed to confirm the usefulness of these new methods.

Prognostic value of the LSR
As mentioned above, while the LSR has been used as an indicator of adequate MVD for HFS, there is still considerable debate about its prognostic value for predicting long-term spasm-free status following MVD. Liu et al. investigated the prognostic value of intraoperative LSR measurements in 332 patients with HFS who had undergone MVD surgery.
erative LSR changes were classified into complete disappearance, amplitude change ≥50%, and amplitude change <50%. Almost all (98.4%) of the 316 patients who exhibited a reduction in the LSR of at least 50% (including complete disappearance) experienced relief on the immediate postoperative day and over a long period of time after surgery (an average of 34.1 months). However, of those who experienced a decrease in the LSR of less than 50%, 18.8% and 25% achieved good outcomes on the first postoperative day and at the latest follow-up, respectively ($p<0.01$). These findings suggest that a reduction in the LSR of at least 50% could be useful as a predictor of good long-term outcomes following MVD.

However, Thirumala et al.\textsuperscript{35} obtained conflicting results regarding the prognostic value of the LSR in a study that also analyzed the long-term outcome according to the disappearance of the LSR following adequate MVD for HFS. In that study, 40 (17%) patients exhibited a residual LSR after adequate decompression. The analysis of the long-term postoperative outcomes revealed no difference in spasm-free status between patients who experienced the disappearance of the LSR and those with persistent LSR; however, the disappearance of the LSR was correlated with immediate postoperative spasm relief. Therefore, the authors concluded that although the disappearance of the LSR was associated with immediate relief, it was less strongly associated with long-term clinical improvement after MVD. El Damaty et al.\textsuperscript{36} also studied the value of intraoperative LSR for predicting clinical outcomes after MVD. In that study, the LSR completely disappeared in 56 of 100 patients with HFS, partially disappeared in 14, persisted in 10, and was not detected in 20 patients. There was no significant association between the disappearance of the LSR and the clinical outcome at 1 year after surgery ($p=0.9$). Those authors concluded that the LSR was valuable only as an intraoperative guidance tool to ensure adequate decompression, and that it was not a reliable predictor of the prognosis after MVD surgery.

A 2020 meta-analysis of the prognostic value of the intraoperative LSR for predicting clinical outcomes after MVD analyzed data from 26 studies involving 7,479 patients with HFS.\textsuperscript{37} Overall, the intraoperative LSR status had a high specificity but only a moderate sensitivity in predicting the spasm-free status after MVD, with the following specificities and sensitivities reported at various time points: 89% and 40%, respectively, at discharge, 90% and 41% at 3 months postsurgery, and 89% and 40% at 1 year postsurgery. For the patients who experienced a persistent LSR after MVD, the probability of persistent HFS was 47.8% at discharge, 40.8% at 3 months, and 24.4% at 1 year postsurgery. Those authors considered that the primary cause of the low sensitivity of intraoperative LSR as a prognostic factor after MVD was the high cure rate of HFS (≥90%) and the low incidence of a persistent LSR following MVD, followed by the unique pathogenesis of HFS.

Two distinct pathologic mechanisms are known to contribute to the genesis of HFS: vascular compression and the hy-

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**Fig. 3.** The facial nerve mapping and the comparison of stimulation direction for lateral spread response. A: Facial nerve mapping performed preoperatively. The locations of maximal lateral-spread response elicitation are divided into the following three regions: F (directed toward the frontalis muscle, which is almost vertical to the anode), O (directed toward the orbicularis oculi muscle), and F-O (between F and O). B: The direction of stimulation in the new methodologies. Electrodes are inserted intradermally, with the anode located proximally over the area just anterior to the mandibular fossa. The cathode is located distally in the temporal branch of the facial nerve. The direction of stimulation is centrifugal, projecting outward from the brainstem (red arrow). Centripetal impulses are transmitted toward the brainstem in the conventional method, with the cathode positioned proximally (black arrow).
perexcitability of the FMN. Any residual LSR could be attributed to the central mechanism of HFS pathophysiology, including the hyperexcitability of the FMN in the brainstem. The pulsatile impulse to the root entry/exit zone (REZ) was immediately removed once MVD was performed, and the hyperexcitability of the FMN began to decline and normalize slowly over a few months, or even a few years in some patients.

**ZLR**

The ZLR is an alternative intraoperative EMG measurement of the facial nerve for HFS. This response can be evoked by stimulating the adjacent facial nerve branch when the wall of the offending artery is electrically stimulated. The ZLR is known to be a useful measurement when the LSR cannot be evaluated or is unstable, such as when this response is absent before MVD or persists after MVD. In addition, measuring the ZLR can help identify the offending vessel when there are multiple potential offending vessels.

**Methodology**

ZLR measurements involve inserting subdermal needle reference electrodes into the frontal muscle, with the needle recording electrodes inserted into the orbicularis oculi, orbicularis oris, and mentalis muscles. The stimulating electrode is a noninvasive concentric electrode used intracranially. This method involves bipolar stimulation. Before detaching the offending artery from the facial nerve, the stimulating electrode is placed on the offending artery wall within 5 mm of the compression site of the REZ, a square-wave impulse (1–2 mA, 0.2 ms, 3 Hz) is delivered, and facial EMG signals are recorded. This recording procedure is repeated for every offending vessel until the facial nerve is completely decompressed.

**Practical value**

The ZLR may be useful when there are limitations to measuring the LSR. Zheng et al. suggested that measuring both the LSR and ZLR could provide more useful information than measuring the LSR alone, since the ZLR may be the only useful intraoperative facial EMG metric in some cases. In addition, the ZLR can differentiate the offending vessel when multiple vessels are present or when the offending vessel is concealed by a tandem vertebral artery. However, the ZLR should be measured carefully, since it is an orthodromic facial EMG measurement based on a current that spreads to the facial nerve from an electrically stimulated arterial wall that lies within several millimeters from the facial nerve. Therefore, the ZLR would be elicited irrespective of the stimulation location along the course of the artery in cases in which there is any mechanical contact between the electrically stimulated arteries and the facial nerve. For example, the ZLR could persist if the distal cisternal portion of the offending arteries were in contact with the distal facial nerve in addition to any vascular contact at the REZ, despite the disappearance of the LSR after complete decompression. Also, some experts consider that one possible drawback of measuring the ZLR is that a larger craniectomy than usual is needed in order to be able to stimulate the offending vessel using a bipolar stimulator.

**FCoMEPs**

Since the development of an intraoperative facial nerve-related corticobulbar tract monitoring method, FCoMEP monitoring has been widely used in various types of neurosurgical approaches applied to treat lesions involving the facial nucleus and/or facial nerve. Considering that the established pathophysiology of HFS is related to both the facial nucleus and the peripheral facial nerve, the application of FC0MEP monitoring during HFS surgery could be very useful for evaluating electrophysiologic changes of the entire pathway related to the facial nerve.

The first study to employ FC0MEP monitoring in MVD surgery was reported in 2005 by Wilkinson and Kaufmann. When FC0MEPs were monitored during surgery in patients diagnosed with HFS and trigeminal neuralgia, the amplitude and duration of the FC0MEPs significantly decreased after decompression on the side affected by spasms in patients with HFS.

In 2012, Fernández-Conejero et al. revealed that FC0MEPs could be generated in response to even a single transcranial stimulus at a relatively low intensity before the facial nerve decompression could not be reproduced following the decompression in patients with HFS. A response originating from transcranial motor cortex activation from a single stimulus could be differentiated from the 'peripheral' response, which came from the directly activated facial nerve by a distally spreading current and could be elicited by a single pulse (as is well known) based on the latency of waves, since a 'peripheral' response usually has a short onset latency (<10 ms). After successful decompression, only multipulse transcranial stimuli could elicit FC0MEPs, and each elicitation required a higher stimulus intensity than before the decompression, indicating an increased threshold.

Since then similar findings related to FC0MEPs have been obtained in studies involving MVD surgery in patients with HFS, some of which also analyzed facial motor evoked potentials (MEPs) data to assess correlations with other neuro-monitoring data, such as free-running EMG (fEMG) or abnormal motor responses (AMRs), and to evaluate the predictive value for postoperative symptom relief.

Fukuda et al. classified patients with HFS (n=45) into two groups based on the ratio of the final (post-MVD) to base-
line (pre-MVD) FCoMEP amplitudes recorded from the orbicularis oculi muscle: <50% (FCoMEP-A, n=30) and ≥50% (FCoMEP-B, n=15). In group FCoMEP-A, there was a significant correlation between the amplitude and the disappearance of AMRs during MVD (p<0.05), and this group also contained a higher proportion of patients whose symptom disappeared ‘immediately’ postoperatively compared with the proportion in group FCoMEP-B. However, the difference was not statistically significant (p=0.19). The same research team also investigated the relationship between the change in the FCoMEP amplitude ratio and fREMG activity, which was defined as the integral value of the maximum fREMG amplitude induced by saline injection before and after MVD.43 The FCoMEP amplitude ratios (post-MVD/pre-MVD) in the mentalis muscles were significantly lower in the group with fREMG ratios <50% (59.0%±31.0%, mean±SD) than in the group with fREMG ratios ≥50% (92.6%±32.1%, p<0.05).

Wilkinson and Kaufmann45 compared the thresholds for FCoMEPs during surgery in patients with HFS (n=65) and those with skull-base tumors (n=29). The proportion of FCoMEPs generated by single-pulse stimulation was higher in patients with HFS than in patients with skull-base tumors (87% vs. 10%), while a significantly lower stimulating voltage (multipulse) was required to elicit the response in the former group (111.3±49.0 V vs. 182.8±70.2 V, p<0.001). In another recent study performed by the same research group, the authors compared the activation threshold voltages and the mean amplitudes of FCoMEPs using the nonspasm (asymptomatic) side as a control.46 The activation threshold of MEPs was significantly lower on the HFS side than on the nonspasm side (162.9±10.1 V vs. 198.3±10.1 V, p=0.01), and the addition of desflurane (a centrally acting anesthetic agent) to the total intravenous anesthesia protocol resulted in a significantly smaller reduction in the amplitude of facial MEPs on the HFS side than on the nonspasm control side (59% vs. 79%, p=0.03), which supported the central hyperexcitability of the facial nucleus theory of HFS.

While FCoMEPs have recently been increasingly applied in MVD surgery for patients with HFS, more well-designed controlled studies are needed to establish the clinical usefulness of FCoMEP monitoring as a predictor of postoperative outcomes.

**BR**

Attempts have also been made to utilize a brainstem reflex in ION during MVD for HFS. Møller and Jannetta47 first reported the elicitation of the BR response intraoperatively as well as its disappearance after decompression of the facial nerve in patients with HFS. However, it was subsequently suggested that the electrical response induced by their methodology could result from the lateral axon-to-axon spread of excitation in the facial nerve fibers instead of the trigeminal afferent nerve.48

In 2009, Deletis et al.49 reported a new methodology for eliciting the early response (R1) component of the BR in anesthetized patients by applying a train of electrical stimuli to the supraorbital nerve. That research group also described intraoperative recordings of the BR during MVD surgery. They found that increasing the stimuli intensity or the number of stimuli within the train was necessary to elicit a BR immediately after MVD in patients with HFS, and they attributed these changes in the BR to the immediate decrease in the hyperexcitability of the FMN following effective decompression of the facial nerve.13

Choi et al.12 recently investigated the prognostic and predictive values of utilizing the BR as an ION technique during MVD in 41 patients with HFS. They compared BR and LSR monitoring results with clinical outcomes at 1 day, 1 month, and 6 months postoperatively. The outcome of spasm resolution differed significantly between the groups exhibiting a persistent BR and a resolved BR at all three time points. However, the same outcome differed significantly between patients with a persistent LSR and a resolved LSR only at 1 day and 1 month postoperatively, while BR monitoring was significantly better than LSR monitoring for predicting surgical outcomes only at 6 months after surgery. Those authors suggested that the BR could be a more-reliable predictor of surgical outcomes than the LSR, and a potentially useful method for ensuring adequate decompression of the facial nerve during this type of surgery. They also observed a difference in the pattern of change between these two methodologies throughout the surgical procedures (i.e., the BR disappeared almost simultaneously or before the LSR in most cases). They proposed a mechanistic explanation for this phenomenon from a neurophysiologic perspective. A representative case is illustrated in Fig. 4.

Blink synkinesis (BS) can be demonstrated by the presence of electrical responses not only in the orbicularis oculi but also in the orbicularis oris or other facial muscles during electrical stimulation of the supraorbital nerve in patients with HFS.50,51 Møller and Jannetta47 found that decompression of the facial nerve led to the disappearance of both BS and the LSR. They hypothesized that the underlying pathophysiological mechanism of HFS is related to the hyperexcitability of the FMN. In 2019, Hsu et al.52 evaluated the utility of BS monitoring during MVD for HFS relative to that of the conventional ION methodologies; ultimately, they concluded that BS showed the highest sensitivity and predictive values among the three methodologies they compared, including BS, the LSR, and facial nerve MEP.
While their potential value has yet to be fully elucidated, BR and BS monitoring are promising candidates for new ION methodologies, not only for predicting surgical outcomes but also as indicators of adequate decompression of the facial nerve during MVD for HFS, which could compensate for the shortcomings of the LSR. Moreover, these reflex-based methodologies can also facilitate the additional and simultaneous monitoring of the trigeminal afferents and brainstem connections comprising the reflex arc. To date, the number of studies using BR or BS has been quite limited; therefore, further prospective studies with larger sample sizes and more extended follow-up periods are required to confirm the usefulness of these reflex monitoring techniques.
CONCLUSION

The application of the new advances in ION methodologies used during MVD for HFS summarized in this review have not only provided clinicians with deeper insights into the pathophysiology of HFS, but they have also led to improvements in the efficacy of MVD and the prognosis of HFS after treatment. Future studies on developing novel monitoring techniques and the modification/optimization of existing ION methodologies will continue to improve clinical outcomes following MVD for HFS.

Availability of Data and Material
The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

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Conflicts of Interest
Kyung Seok Park, a contributing editor of the Journal of Clinical Neurology, was not involved in the editorial evaluation or decision to publish this article. All remaining authors have declared no conflicts of interest.

Funding Statement
This work was supported by the Soonchunhyang University Research Fund.

Acknowledgements
The authors thank Jong suk Choi, M.D. and technologist Byung-Hwa Park for their help in preparing the figures.

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