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TECHNICAL NOTE

Direct cochlear nerve stimulation monitoring through evoked muscle responses during retrosigmoid vestibular schwannoma resection surgery: technical note

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OBJECTIVE Cochlear nerve preservation during surgery for vestibular schwannoma (VS) may be challenging. Brainstem auditory evoked potentials and cochlear compound nerve action potentials have clearly shown their limitations in surgeries for large VSs. In this paper, the authors report their preliminary results after direct electrical intraoperative cochlear nerve stimulation and recording of the postauricular muscle response (PAMR) during resection of large VSs.

METHODS The details for the electrode setup, stimulation, and recording parameters are provided. Data of patients for whom PAMR was recorded during surgery were prospectively collected and analyzed.

RESULTS PAMRs were recorded in all patients at the ipsilateral vertex-earlobe scalp electrode, and in 90% of the patients they were also observed in the contralateral electrode. The optimal stimulation intensity was found to be 1 mA at 1 Hz, with a good cochlear response and an absent response from other nerves. At that intensity, the ipsilateral cochlear response had an initial peak at a mean (± SEM) latency of 11.6 ± 1.5 msec with an average amplitude of 14.4 ± 5.4 μV. One patient experienced a significant improvement in his audition, while that of the other patients remained stable.

CONCLUSIONS PAMR monitoring may be useful in mapping the position and trajectory of the cochlear nerve to enable hearing preservation during surgery.

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KEYWORDS cochlear nerve; hearing preservation; intraoperative neuromonitoring; stimulation; surgery; vestibular schwannoma; surgical technique

Cochlear nerve monitoring and preservation during vestibular schwannoma (VS) resection surgery is often challenging, especially for large tumors (extrameatal diameter > 30 mm or grade IV according to the Koos grading scale).[1,2]

Brainstem auditory evoked potentials (BAEPs) and cochlear compound nerve action potentials (CNAPs) have been shown to be useful intraoperative tools to preserve cochlear nerve function. Their benefits are most significant in cases of small- to medium-sized tumors[3–5] and less useful in cases of large tumors. In this setting, BAEPs have been used in a continuous manner with defined alert criteria such as reduction of peak III amplitude of more than 50% to monitor the integrity of the cochlear nerve.[6,7] However, the delay in the response due to the data averaging (about 1000–2000 trials) that is required to assess any dysfunction is the main limitation of this technique. This is primarily due to the poor signal-to-noise ratio and poor temporal resolution, which cause inconsistent monitoring. Moreover, this technique only assesses the integrity of the acoustic pathway; it does not allow reliable identification of the cochlear nerve during tumor resection in cases of large tumors. BAEPs are also susceptible to disruption by various intraoperative factors, which limits the usefulness of intraoperative monitoring.[8,9]

Direct registration of CNAPs was introduced to overcome these limits, as it allows a real-time cochlear nerve assessment, with larger amplitudes and less averaging

ABBREVIATIONS BAEP = brainstem auditory evoked potential; CNAP = cochlear compound nerve action potential; EMG = electromyography; MFN = medial facial nucleus; PAMR = postauricular muscle response; VS = vestibular schwannoma.

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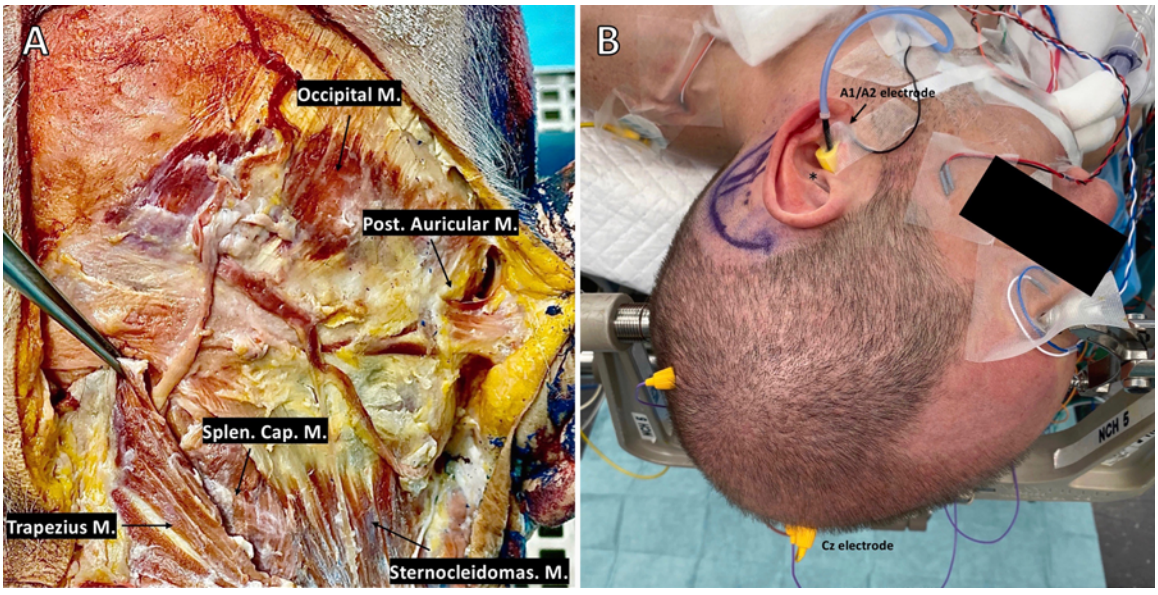

FIG. 1. A: Image of a cadaveric specimen in which a right suboccipital scalp flap is reflected to expose the suboccipital muscles and the posterior auricular muscle. The posterior auricular muscle consists of 2 or 3 fleshy fasciculi that arise from the mastoid part of the temporal bone by short aponeurotic fibers. They insert into the lower part of the cranial surface of the auricle of the outer ear. The muscle is innervated by the posterior auricular nerve, a branch of the facial nerve. **B:** Intraoperative photograph showing the placement of the electrodes at Cz-A1 and Cz-A2 on the ear lobe. The *asterisk* shows the stimulator that delivers the clicks for the BAEP. M. = muscle; N. = Nerve; Post. = posterior; Splen. Cap. = splenius capitis; Sternocleidomas. = sternocleidomastoid. Figure is available in color online only.

when compared with BAEP monitoring.[10] The recording of CNAPs is less affected by electrical artifacts. This technique is an intermittent recording in which the probe is left in place on the proximal part of the cochlear nerve, which may bother the surgeon during the procedure. The electrode can be displaced during surgical manipulation, leading to false-positive modifications of the recording potentials. Therefore, this technique is only applicable in cases in which at least some portion of the nerve is not covered by the tumor (close to the brainstem); it does not allow identification and assessment of the integrity of the nerve on the tumor capsule in cases of large VSs.[11] A large population of sound-evoked myogenic responses have been described, such as postauricular muscle response (PAMRs), stapedial reflex, jaw acoustic reflex, auditory blink reflex, or neck muscle responses.[12] PAMR is a large sound-evoked muscle action potential that is measured on the skin surface near the muscle behind the ear (Fig. 1A).[13] These responses are of muscular origin and often are much larger than the BAEPs. Their higher signal-to-noise ratio allows much less averaging to produce a stable waveform.[13] The PAMR can be evoked by monoaural or binaural stimuli and can be recorded using the same electrodes positioned for the recording of BAEPs, with a shorter latency. We explored the possibility of directly stimulating the cochlear nerve in our surgical cohort of large VSs, with recording electrodes placed at Cz and A1/A2 (Fig. 1B).

Methods

Electrode Setup

Scalp electrodes were positioned on Cz-A1 and Cz-A2 to record both cochlear evoked responses and BAEPs. The ground electrode was set on the sternum rostral to the stimulus-return electrode. In addition, continuous electromyography (EMG) was recorded with subdermal paired needle electrodes (Medtronic Xomed) positioned in 4 facial muscles (frontalis, orbicularis oculi, orbicularis oris, and mentalis), the masseter, and the trapezius to monitor the cranial nerve VII branches, cranial nerve V, and cranial nerve XI, respectively. Surface recording of the laryngeal mucosa by a NIM-Eclipse ENT intubation tube (Medtronic Xomed) was used to monitor cranial nerves IX and X.

Stimulation and Recording Parameters

General anesthesia and laryngotracheal intubation were achieved avoiding muscle relaxants to limit interference with the neurophysiological monitoring, which consisted of the following modalities: 1) direct cochlear nerve stimulation and triggered EMG recording were performed with a Prass probe monopolar electrode (Medtronic Xomed) using a negative, monopolar pulse (stimulation frequency 1 Hz, pulse duration 200 μsec, pulse intensity 0.1–2 mA); the acquisition time was 100 msec and the stimulation was performed at the cisternal portion of the cochlear nerve covering the tumor (Fig. 2A); 2) triggered EMG (for cranial nerves V, VII, IX, X, and XI) was performed using a cathodal current at 1 mA for 200 μsec at 1 Hz; 3) continuous EMG was performed with subdermal paired needle electrodes (Medtronic Xomed), positioned in relevant muscles for the other nerves as described above; and 4) BAEPs were recorded from Cz-A1 and Cz-A2 derivations by averaging 1000 responses after audio

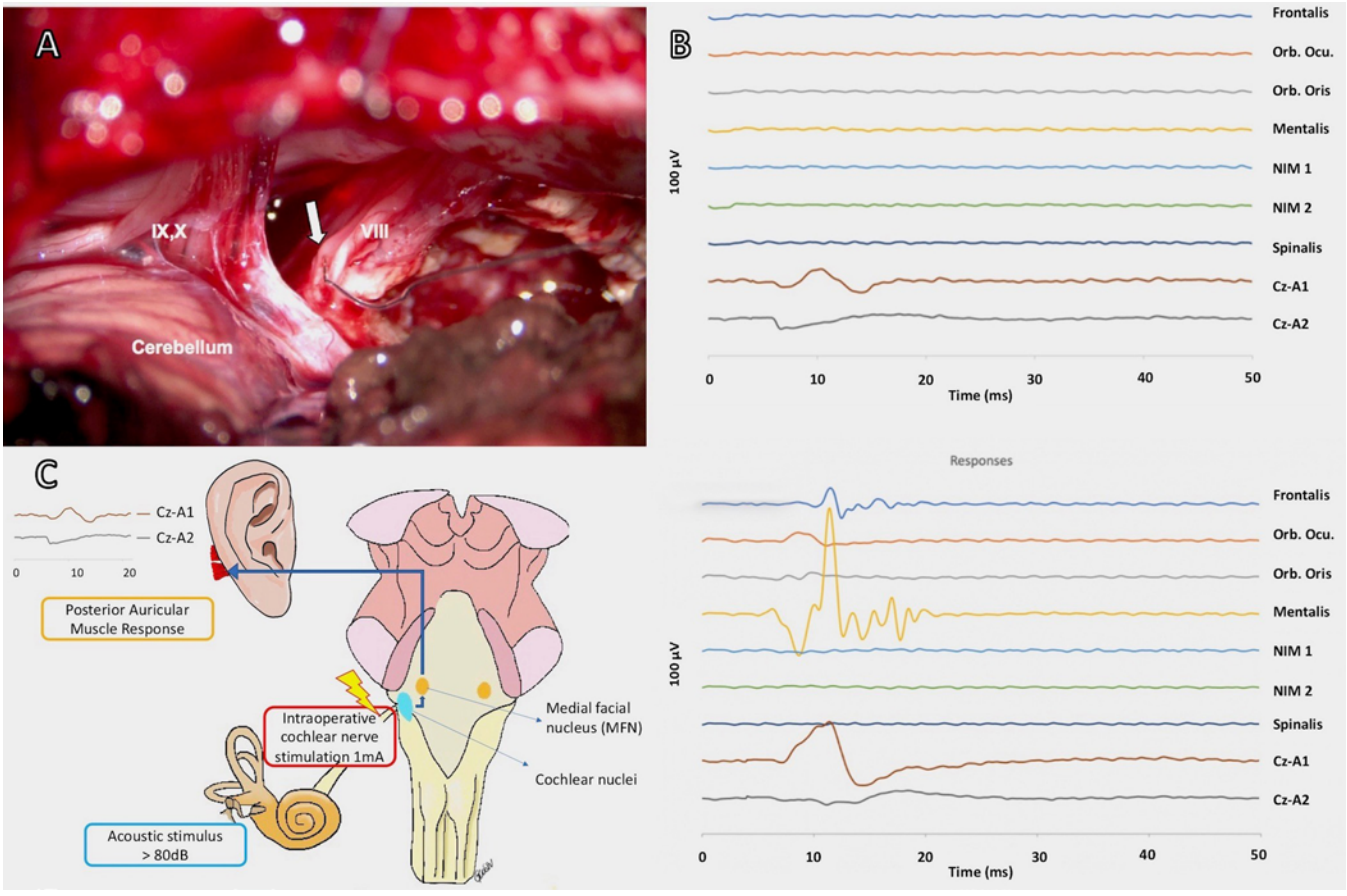

FIG. 2. A: Intraoperative image of the left cerebellopontine angle during planned subtotal resection of a large VS in the right park-bench position. The *arrow* denotes the stimulator for the monopolar stimulation. Note the proximity of the cochlear nerve to cranial nerves IX and X. **B:** PAMRs obtained from monopolar cochlear nerve stimulation at different current intensities. *Upper*: Cochlear stimulation at 1 mA induced responses on the ipsilateral Cz-A1 and Cz-A2 derivations but not on the other observed muscles. *Lower*: Cochlear stimulation at 2 mA induced responses on the ipsilateral Cz-A1 and Cz-A2 derivations and in the homolateral muscles innervated by cranial nerve VII. See text for details. **C:** Schematic drawing showing the anatomical basis of PAMR. Following a loud sound, the auditory nerve fibers simultaneously activate the cochlear nucleus, which projects to the MFN directly or bilaterally through the trapezoid body, which in turn innervates the muscles around the pinna. Ocu. = oculi; Orb. = orbicularis. Panel C: © Giulia Cossu, published with permission. Figure is available in color online only.

stimulations (clicks: 120- to 130-dB intensity; rarefaction: 10.1-Hz frequency).

Surgical Technique

Patients were all operated on using a standard retrosigmoid approach. The posterior capsule of the tumor was exposed and stimulated, searching for an aberrant course of the facial nerve. Secondarily, the cochlear nerve was also stimulated with our monopolar stimulator to elicit responses. If the stimulation was negative, the capsule was opened. The tumor debulking was coupled with stimulation of the internal part of the capsule covering the facial nerve at a current of 4–5 mA and progressively decreased to 2 mA. The thinned capsule of the tumor was progressively excised until the superior and inferior borders of the facial nerve were identified by stimulating the external part of the capsule. Mapping of the course of the facial nerve allows us to predict the course and localization of the cochlear nerve; it is usually located on the tumor surface inferior to the facial nerve.[14]

Results

We report our preliminary results obtained in a cohort of 10 consecutive patients with large VSs, in which we added direct stimulation of the cochlear nerve to our standard electrophysiological monitoring protocol. This study included only patients who had serviceable hearing prior to surgery (Gardner-Robertson grades 1–3). We were able to record evoked responses in all patients at the ipsilateral vertex-earlobe scalp electrode, and in 9 of 10 patients responses were also observed in the contralateral vertex-earlobe electrode. During the early part of our series, we explored gradually increasing stimulation intensities from 0.1 to 2 mA and different stimulation frequencies (1–30 Hz). With increasing intensities, we found that the adjacent nerves were also stimulated at the same time as the cochlear nerve. The most reliable stimulation intensity in our experience was found to be 1 mA at 1 Hz, for a good cochlear response with an absent response from other nerves. At 1-mA stimulation intensity, the ipsilateral cochlear response had an initial peak appearing at a mean (±

TABLE 1. Latencies and amplitudes of responses to direct nerve stimulation with 1-mA amplitude and 200-μsec duration at 1-Hz frequency

Cranial Nerve	Latency (msec)	Amplitude (μV)
VII	8.6 ± 1.7	210.8 ± 203.1
Cochlear	11.6 ± 1.5	14.4 ± 5.4
IX	9.7 ± 1.5	148.7 ± 135.7
XI	7.8 ± 1.2	2799 ± 1945

All values are given as mean ± SEM. An average of at least 30 measures was used for all values.

SEM) latency of 11.6 ± 1.5 msec with an average amplitude of 14.4 ± 5.4 μV (Tables 1–3). When the stimulation intensity was increased to 2 mA, responses from the facial nerve or cranial nerve X and/or XI were also recorded but with different morphology and latencies (Fig. 2B and Tables 1 and 2). These cochlear responses were found to be reversibly abolished by the use of neuromuscular blockers, which confirmed that the response recorded was of myogenic origin. One patient experienced a strong improvement in his audition, improving from Gardner-Robertson grade 3 in the preoperative period to grade 1 after surgery (Table 3). All the other patients were stable with no worsening in audition.

Discussion

In our surgical series, we were able to perform cochlear nerve monitoring through direct stimulation of the cisternal part of the cochlear nerve while recording with the same scalp electrodes used for BAEP recording. Responses recorded on the vertex-earlobe derivations could have originated from 6 different sources: 1) stimulation artifact, 2) contamination from other facial muscles, 3) auditory blink reflex, 4) other startle reflexes, 5) stapedial reflex, or 6) PAMR.

The stimulation artifact can be excluded based on the response latency (8.6 msec) and its independence from stimulation polarity and physiological variation with stimulation frequency.

Contamination from other facial muscles can also be excluded, as the cochlear responses were observed in the absence of other muscle responses at low stimulation intensities (≤ 1 mA). Furthermore, the responses observed in other muscles had different latencies and shapes (Tables 1 and 2).

TABLE 2. Cochlea-driven reflexes

	Afferent Nerve	Short Pathways	Efferent Nerve	Latency (msec)
Auditory blink reflex (orbicularis oris)	Cochlear	CN, PnC, VFN	Facial	20–40
Stapedial reflex	Cochlear	CN, SMN	Facial	7–15
PAMR	Cochlear	CN, MFN	Facial	10–15

CN = cochlear nucleus; PnC = caudal pontine reticular nucleus; SMN = stapedius motoneuron; VFN = ventral facial nucleus.

Auditory blink reflex is the electrophysiological correlate of the bilateral contraction of the orbicularis oculi muscle after a loud (> 80 dB) audio stimulation. This reflex belongs to the family of startle reflexes and, as such, shares some common pathways with PAMR. The neural pathway for this reflex begins in the cochlea and travels to the ventral cochlear nucleus and the superior olivary complex. The cochlear nucleus also projects to the caudal pontine reticular nucleus, which is involved in the whole-body startle,[15,16] and this in turn projects to the medial facial nucleus (MFN) as well as the dorsolateral facial nucleus, which innervates the orbicularis oculi muscle that is responsible for the acoustic blink reflex.[17] Auditory blink reflex can be ruled out based on its long latency of between 20 and 40 msec and the absence of orbicularis oculi muscle contraction during stimulation.

Other Startle Reflexes

The difference in the latency and the absence of recorded responses from muscles innervated by other cranial nerves such as the masseter (cranial nerve V) and trapezius (cranial nerve XI) allowed the exclusion of these potential sources.[12]

Stapedius reflex is one of the two middle ear reflexes, and it represents the involuntary contraction of the stapedius muscle that stiffens the stapes within the middle ear. It is a bilateral response that reduces the sound intensity reaching the inner ear and is a protective reflex mechanism. Once a loud sound is administered (70–90 dB above threshold), neural impulses from the cochlear nerves ascend from the cochlea to the ipsilateral ventral cochlear nucleus. Then the stimulus goes from the ventral cochlear nucleus to a bilateral stimulation of the facial nucleus, possible relaying through the trapezoid body bilaterally to the superior olivary complex.[18] The stapedius reflex latency varies with sound frequency and intensity and with the recording technique. In humans, stapedius reflex elicited by electrical cochlear stimulation can be recorded via EMG electrodes placed over the stapedius tendon. The experience from cochlear implant surgery shows that the latency of the stapedius reflex (elicited by a direct electrical stimulation) is around 11 msec,[19] which is in the range of the recorded responses in our series. Current electrophysiological literature does not show a comparable method of eliciting the stapedial reflex by scalp electrodes after a direct electrical stimulation of the cochlear nerve as performed in our surgical series.

The PAMR[20] is an auditory evoked vestigial muscle response that acts to pull the ear upward and backward[21] and an auditory localizing value. The cochlea is the receptor organ driving the PAMRs, since they can be obtained from subjects with abnormal vestibular function but normal hearing, but they are absent in deaf subjects with normal vestibular function.[22] The brainstem pathways of the PAMR remain debated, but a disynaptic transmission is hypothesized.[23,24] Following a loud sound, the auditory nerve fibers simultaneously activate the cochlear nucleus, which projects to the MFN directly or bilaterally through the trapezoid body, which in turn innervates the muscles around the pinna,[25] such as the PAM (Fig. 2C:)[24] The anatomical basis of the PAMR is akin to the pathway involved

TABLE 3. Demographic characteristics of the cohort, surgical outcome, and intraoperative electrophysiological findings

Patient No.	Age (yrs)	Sex	Koos Grade	Surgical Approach	EOR	Intraop BAEPs (wave III)		Intraop PAMRs		Preop GR Grade	Postop GR Grade	Preop HB Grade	Postop HB Grade	Follow-Up (mos)
						Latency (msec)	Amplitude (μV)	Latency (msec)	Amplitude (μV)					
1	45	M	IV	Retrosigmoid	STR + GK	3.1	0.6	12.0	6.3	1	1	I	I	19
2	45	F	IV	Retrosigmoid	STR + GK	3.3	0.1	11.0	13.5	2	2	I	I	6
3	39	F	IV	Retrosigmoid	STR + GK	3.2	0.8	11.0	13.5	1	1	I	I	17
4	42	F	IV	Retrosigmoid	STR + GK	2.9	0.3	13.4	8.0	1	1	I	I	17
5	74	M	IV	Retrosigmoid	STR + GK	3.2	0.7	15.0	15.6	3	3	I	I	13
6	55	M	IV	Retrosigmoid	STR + GK	3.1	0.1	11.0	10.6	3	1	I	I	4
7	33	F	IV	Retrosigmoid	STR + GK	3.3	0.6	12.0	22.8	1	1	I	I	19
8	51	F	IV	Retrosigmoid	STR + GK	3.3	0.4	10.0	12.0	2	2	I	I	32
9	42	M	IV	Retrosigmoid	STR + GK	3.2	0.6	11.0	22.8	2	2	I	I	5
10	40	F	IV	Retrosigmoid	STR + GK	3.3	2.4	10.0	18.8	2	2	I	I	19

EOR = extent of resection; GK = Gamma Knife; GR = Gardner-Robertson; HB = House-Brackmann; STR = subtotal resection.

in Preyer's reflex, a hybrid orienting and startle response to alerting sounds, evidenced by the twitching of the pinna induced by loud sounds (> 80 dB).[26] PAMR is seen as a biphasic electrical response consisting of two peaks: a negative peak between 10 and 15 msec and a positive peak between 15 and 18 msec, with amplitudes between 10 and 100 μV,[13,26] that correspond to the recorded responses in our series (Tables 1 and 2).

In the outpatient clinic, PAMRs are best recorded after a loud (> 80 dB) sound using an electrode placed on the midpoint of the postauricular muscle and another placed on the back of the pinna,[13] but they can also be recorded using the montage used for BAEP and a middle latency evoked auditory response,[26] similar to the setup used in our surgical series (Fig. 1B). PAMRs may be extremely variable across the population and within individuals.[27] As demonstrated by Cody et al., the response was absent in one ear in 32% of subjects and bilaterally in 7%.[20] It is important to note that the evidence of PAMR variability in the aforementioned study was obtained by stimulation studies with sound-evoked PAMR and not by direct electrical stimulation. Furthermore, responses may vary according to subject attention, emotion, anticipation, gaze direction (increasing response with the subject looking toward the recording electrode), or psychopathology.

Although the stapedial reflex cannot be formally ruled out, the PAMR could well represent the direct cochlear nerve stimulation responses that were recorded in our series. The direct stimulation of the cochlear nerve bypasses the cochlea and may explain the shorter latency that we report, when compared with data from the literature (8 msec vs 12 msec). To our knowledge, this is the first report of this specific technique with its intraoperative application, and it may represent a more reliable way to evoke PAMRs than a click administration. In our opinion, PAMR recordings after direct electrical stimulation of the cochlear nerve should be combined with BAEP during cerebellopontine angle surgery to enhance the chances of hearing preservation and in cases in which the PAMR is not elicited. BAEP monitoring represents a valid, well-studied neuromonitoring technique that signifies the integrity of the entire hearing pathway from the ear to the brainstem. While it is used essentially to avoid brainstem damage during surgery for large tumors, its utility to signal cochlear nerve damage is limited in surgery for large tumors because by the time wave III in BAEP disappears, nerve damage has already taken place and is generally irreversible.

PAMR has the distinct advantage of enabling us to accurately map the entire trajectory of the cochlear nerve on the tumor capsule without dissecting between the capsule and the nerve. This assumes great importance for cases in which a planned subtotal resection is performed.

Limitations of PAMR Monitoring

The interpatient variability described in the literature was not reported in our study, but this factor needs to be verified in a larger cohort. The PAMR technique only allows intermittent mapping of the position/trajectory of the cochlear nerve. This needs to be performed multiple times during surgery to achieve the maximal chance of nerve preservation in lieu of a method of continuous monitoring.

PAMRs are extremely sensitive to all muscle blocking agents administered during general anesthesia; thus, the choice of drugs for sedation needs to be discussed with the anesthesiologists preoperatively to avoid iatrogenic modification of the electrophysiological results. To date, the stimulation protocol for PAMR in the operating room is not standardized and the optimal stimulation parameters (current intensity, amplitude, and frequency) are not defined in the existing literature. An intraoperative monitoring protocol for PAMR needs to be standardized across patients in larger cohorts.

Conclusions

Hearing outcomes are assuming increasing importance in current surgical practice even for large VSs. The surgical paradigm of treatment of these tumors has shifted to a more nerve-centric approach whereby a less than total excision is planned. PAMR stimulation during surgery allows the identification of the entire cisternal course of the

cochlear nerve without entering into the plane between the tumor capsule and the nerve, thereby enabling preservation of neural function.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Daniel, Starnoni, Cossu, Pralong. Acquisition of data: Starnoni, Cossu, Pralong. Analysis and interpretation of data: Starnoni, Cossu, Pralong. Drafting the article: Starnoni, Cossu, Pralong. Critically revising the article: Daniel, Starnoni, Cossu, Maduri, Tuleasca, George, Maire, Messerer, Levivier. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Daniel. Study supervision: Daniel.

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