Detailed insight into transtympanic electrocochleography (TT-ECochG) and direct cochlear nerve action potential (CNAP) for intraoperative hearing monitoring in patients with vestibular schwannoma – methodology of measurements and interpretation of results

Izabela Pobożny, Magdalena Lachowska, Robert Bartoszewicz, Kazimierz Niemczyk
Department of Otorhinolaryngology, Head and Neck Surgery, Medical University of Warsaw, Poland; Head: prof. Kazimierz Niemczyk MD PhD

ABSTRACT:
Background: The aim was to present the methodology and interpretation of intraoperative hearing monitoring with simultaneous Transtympanic Electrocochleography (TT-ECochG) and direct Cochlear Nerve Action Potential (CNAP) measurements during vestibular schwannoma removal.

Materials and Methods: Detailed methodology of measurements and interpretation of results are presented in three exemplary patients who underwent tumor removal via middle fossa approach (MFA) with the use of intraoperative monitoring of hearing with TT-ECochG and direct CNAP performed in real time. In addition, all responses were automatically recorded and stored along with surgical information and subjected to detailed analyses and calculation after surgery.

Results: The following changes in TT-ECochG and direct CNAP responses were observed: Patient #1 – TT-ECochG and CNAP responses with minor, but transient, morphology changes (hearing was preserved); Patient #2 – CNAP responses changed significantly but, temporarily, from triphasic into biphasic responses later, with marked but partially reversible desynchronization of CNAP; changes in TT-ECochG responses were also observed but, at the end, returned to baseline (surgery-related deterioration of hearing); Patient #3 – irreversible changes of TT-ECochG and direct CNAP (complete loss of hearing).

Conclusions: A combination of TT-ECochG and direct CNAP allows for real-time monitoring of auditory function during vestibular schwannoma resection and surgical manipulation which contribute to the risk of hearing loss. Therefore, the surgeon can be instantly informed about changes which could increase the possibility of preserving the patient’s hearing.

KEYWORDS: acoustic neuroma, action potential, cochlear nerve, evoked response, hearing loss

ABBREVIATIONS
ABR – Auditory Brainstem Responses
AP – action potential
CPAT – cerebellopontine angle tumor
CNAP – cochlear nerve action potential
direct CNAP – direct Cochlear Nerve Action Potential
EANO – European Association of Neuro-Oncology
MFA – middle fossa approach
MRI – magnetic resonance imaging
PTA – pure tone audiometry
SNR – signal-to-noise ratio
TT-ECochG – Transtympanic Electrocochleography

INTRODUCTION
Vestibular schwannoma is a benign, slowly-growing tumor developing from the Schwann's sheath. According to recommendations from the National Institutes of Health Consensus Development Conference on Acoustic Neuroma in 1991 [1], microsurgery was assumed to be the best modality in the treatment of vestibular schwannoma. The goal of this surgery is total tumor removal with preservation of neurological function of adjacent structures, including hearing. Selecting the surgical removal of a cerebellopontine angle tumor (CPAT) via the middle or posterior cranial fossa allows for complete tumor removal and hearing preservation. Intraoperative monitoring of hearing is used for maximal increase in the probability of hearing preservation in case of both above-mentioned surgical accesses [2]. The most commonly used electrophysiological
tests include Auditory Brainstem Responses (ABR), Transtympanic Electrocochleography (TT-ECochG) [3–11], and direct Cochlear Nerve Action Potential (direct CNAP) [3, 5, 8, 10–17].

The aim of the study was to present the methodology and interpretation of the findings of intraoperative hearing monitoring with a simultaneous measurement with TT-ECochG and direct CNAP throughout vestibular schwannoma removal in exemplary patients whose hearing was preserved or lost due to the surgery.

MATERIAL AND METHODS

Ethical consideration

The study was reviewed and approved by the local Institutional Ethics Committee (KB/142/2017 and KB/11/A/2019). All patients gave their informed consent. The project conforms to The Code of Ethics of the World Medical Association (Declaration of Helsinki).

The methodology of intraoperative monitoring of hearing

In this paper, the participating patients were selected to illustrate methodology and detailed interpretation of results of the intraoperative monitoring of hearing with TT-ECochG and direct CNAP. Intraoperative electrophysiological assessments were performed with a two-channel SmartBox device integrated with SmartEP software (Intelligent Hearing Systems, Miami, FL, USA). Each TT-ECochG test was performed with the non-inverting electrode (−) applied via the posteroinferior quadrant of the tympanic membrane and supported on the promontory at the beginning of the surgery. The direct CNAP non-inverting electrode (−) was situated on the proximal portion of the cochlear nerve (next to the brainstem) after exposing the internal auditory meatus. A grounding needle electrode was placed on the border of the forehead and hairy scalp and the inverting needle electrode (+) was placed on top of the head at vertex. All electrode impedances were kept at 1-3 kiloohm (kΩ) or less. Simultaneous TT-ECochG and direct CNAP measurements were initiated after developing access to the tumor (after exposing the internal auditory meatus via the middle cranial fossa).

Initially, auditory responses were registered with TT-ECochG from one channel while developing access to the tumor and exposing the internal auditory meatus. Subsequently, after exposing the internal auditory meatus and vestibulocochlear nerve, a needle electrode was placed in the area of the cochlear nerve and a two-channel measurement was started from the promontory (TT-ECochG) and the cochlear nerve (direct CNAP).

In order to obtain evoked auditory potentials from the promontory (TT-ECochG) and direct CNAP, acoustic stimulation was performed with an 80-dBnHL (decibel above normal adult hearing level) click using ER3 insert earphones (Etymotic Research, Elk Grove Village, IL, USA). The rate of stimulus presentation was 21.17/s, the number of averaged signal samples ranged from 128 to 256 sweeps, and alternating polarization was used. Such a number of averaged signal samples facilitated readable and repeatable responses both from TT-ECochG and direct CNAP measurements. The TT-ECochG and CNAP recordings were amplified 100.000 times and band-pass filtered from 30 to 3.000 hertz (Hz). The analysis (time) window of 12.8 ms was used. Selection of the analysis time window was based on physiological and measurement parameters (adequate time window to observe all the TT-ECochG and direct CNAP waves, no secondary overlap, no conflict with recording filters, etc.).

SmartEP software enables real-time monitoring with TT-ECochG and direct CNAP responses obtained every five to six seconds. Therefore, it is possible to perform ongoing assessment of the auditory organ status and inform the surgeon about changes in the morphology of TT-ECochG or direct CNAP response without interruption of measurement and no loss of current data. All responses are automatically recorded in the system’s memory. Therefore, they may be reanalyzed at any moment after the operation and subjected to detailed analyses and calculations.

Patient descriptions

In this paper, we present three patients chosen from a larger group to show methodology of intraoperative monitoring of hearing and detailed insight into the interpretation of electrophysiological results. The presented three patients were chosen as examples to illustrate and discuss in detail the results of TT-ECochG and direct CNAP measurements in case of: 1) hearing preservation at good level but with some disturbances in electrophysiological recordings during the surgery (patient #1); 2) hearing preservation at good level but with some disturbances in electrophysiological recordings during the surgery (patient #2); and 3) total hearing loss due to the vestibular schwannoma removal (patient #3).

Before surgery, all three patients underwent contrast-enhanced magnetic resonance imaging (MRI) assessment which confirmed existence of a tumor of the eighth cranial nerve. The tumor filled
Patient #1 presents the example of hearing preservation at a very good level after vestibular schwannoma removal. The patient was a 49-year-old female with a 4 x 6 x 7 mm tumor located on the right side with vertigo, headaches, and equilibrium problems for a year but no history of tinnitus or hearing impairment. According to the Koos classification [18], it was a grade I tumor while, pursuant to the guidelines by Matthies et al. [19], it was a T1 intrameatal tumor. Fig. 2. presents the pure tone audiometry (PTA) hearing threshold and speech audiometry in this patient pre- and postoperatively. Postoperative audiologic tests confirmed hearing preservation at a very good level.

Patient #2 presents the example of hearing preservation at a good level after vestibular schwannoma removal. The patient was a 50-year-old female with left-side hearing loss (Fig. 2.) and tinnitus for the previous two years but no vertigo. The size of the tumor was 14 x 8.8 x 15 mm and was located on the left side. It was classified as Koos grade II [18] and T2 according to the classification by Matthies et al. [19]. The postoperative hearing threshold remained almost at the baseline level, with minimal increase of approximately 5 to 10 dB HL. Speech discrimination reached 80% at the maximal intensity of 110 dB SPL (Fig. 2.).

Patient #3 presents the example of total hearing loss due to vestibular schwannoma removal. The patient was a 57-year-old female with a right-side tumor. The size of the tumor was 9.6 x 4.9 x 9.4 mm. The patient reported right-side hearing loss (Fig. 3.), tinnitus, and headaches for two years. She experienced no vertigo or equilibrium disorders. It was a Koos grade I tumor [18] and, according to Matthies et al. [19], it was classified as T1. Postoperatively, no response to any acoustic stimuli was observed on the right side. Postoperative speech audiometry also showed no response (Fig. 3.).
RESULTS

Fig. 4. presents recorded TT-ECochG and direct CNAP responses throughout tumor removal with minor changes in the morphology in Patient #1, whose hearing was preserved postoperatively. Initially, the AP amplitude of the TT-ECochG read-out was 10.18 μV with the latency of 1.95 ms. Direct CNAP had been triphasic since the beginning of the measurements, with visible P1, N1, and P2 peaks. Visible changes in CNAP morphology were observable at the initial stages of tumor removal during cochlear nerve stretching. The P1, N1, and P2 peaks decreased and appeared at longer time intervals. Triphasic responses changed into biphasic responses with only P1 and N1 peaks visible. The AP amplitude of TT-ECochG was then slightly decreased to 9.47 μV and the latency extended to 2.02 ms. During subsequent surgical manipulations of the tumor, CNAP responses improved and became triphasic with visible P1, N1, and P2 peaks. At the final stage, following complete tumor resection, individual CNAP potentials were triphasic and stable. As regards TT-ECochG, the amplitude of AP was stabilized at 9.47 μV and the latency was 1.85 ms. Minor, short-lasting changes in TT-ECochG and CNAP morphology indicated temporary disruptions affecting auditory organ status which remained almost unchanged when comparing pre- and postoperative values (Fig. 1.).

The hearing of Patient #2 was also preserved after surgery. This example indicates considerable but temporary changes in the morphology of TT-ECochG, direct CNAP responses during tumor removal, and for a short period after the resection when slight hemorrhage occurred in the labyrinthine artery (Fig. 5.). Initial direct CNAP responses were triphasic. However, since the beginning of tumor resection, the P2 peak presented a low amplitude. In this case, one-third of tumor volume was located in the cerebellopontine angle, so the responses had been morphologically changed since the beginning of the measurements. The AP amplitude of TT-ECochG read-out was 8.86 μV with the latency of 2.15 ms. The initial stages of tumor resection brought no significant changes in TT-ECochG and CNAP morphology with visible changes in CNAP morphology occurring only during tumor stretching and removing its marked portion. The responses became wider, altered into biphasic responses with only P1 and N1 peaks remaining visible. The P2 was desynchronized (its peak was poorly visible and response latency was extended). The AP amplitude of TT-ECochG was slightly decreased and the latency was extended but morphology remained unchanged. The otosurgeon was instantly informed of the changes in the recorded electrophysiological responses. Therefore, any activity was momentarily paused in the area of the tumor and the eighth cranial nerve. After a short period, CNAP responses resumed a triphasic pattern and the otosurgeon continued tumor resection. Another deterioration of the response and a change in CNAP morphology occurred immediately following complete tumor resection, during a minor hemorrhage from the labyrinthine artery. The CNAP response pattern became biphasic again with extended latency and poorly visible P1, N1, and P2 peaks. Moreover, CNAP responses were biphasic during hemostasis with bipolar coagulation. However, at the final stage, they started to stabilize and change into triphasic responses. At the same time, the AP amplitude of TT-ECochG was slightly reduced to 8.00 μV and latency extended to 2.25 ms. After achieving hemorrhage...
control, CNAP responses became triphasic. The AP amplitude of TT-ECochG increased to 9.02 μV and the latency was 2.17 ms again.

The comparison of responses before and after tumor removal (Fig. 5.) showed that direct CNAP responses were triphasic although response morphology following complete tumor resection changed. The peaks of P1, N1, and P2 potentials had extended latency and the P2 peak was less visible than P1 and N1. The changes indicated a minimal injury to the auditory pathway which led to hearing deterioration visible in the postoperative results of audiologic tests (Fig. 2.).

The third case (Patient #3) manifested permanent changes in the morphology of TT-ECochG and direct CNAP response which were due to irreversible changes and injuries sustained during the resection of vestibular schwannoma. Fig. 6. presents the stages of CPAT removal along with visible changes in TT-ECochG and direct CNAP morphology indicating permanent injuries to the auditory pathway. At the initial stage of CPAT removal, the CNAP responses were triphasic. However, since the beginning, their morphology had been slightly changed; the responses occurred with extended latency and the morphology of P2 peak was markedly changed. The AP amplitude of TT-ECochG was 3.47 μV with latency of 2.00 ms. Subsequent surgical manipulations associated with tumor resection and direct stretching of the cochlear nerve changed CNAP responses into biphasic responses. The AP amplitude in TT-ECochG decreased to 3.05 μV and the latency extended by 0.10 ms. Rapid changes in CNAP and TT-ECochG morphology directly followed the complete resection of the tumor. Cochlear nerve action potential altered into monophasic responses before disappearing completely. In TT-ECochG, the value of AP amplitude also decreased markedly and latency extended considerably. Finally, no response was recorded. In this case, permanent changes occurred in the auditory pathway, which indicated possibility of complete hearing loss, which was subsequently confirmed with postoperative pure tone audiometry (Fig. 3.).

**DISCUSSION**

Intraoperative monitoring of hearing is used during CPAT resection via MFA in order to increase the possibility of preserving the patient’s hearing at the best possible level. It is most commonly performed with TT-ECochG and ABR [3, 4, 6, 7, 20–23]. Professional literature includes reports on the intraoperative monitoring of hearing using a combination of ABR and direct CNAP or TT-ECochG and direct CNAP [2–5, 8–12, 15, 17]. Transtympanic electrocochleography provides an almost-real-time response from the peripheral segment of the vestibulocochlear nerve. Direct CNAP also provides real-time responses from the proximal cochlear nerve. Therefore, both methods are useful tools in the intraoperative monitoring of hearing in clinical practice.

Auditory brainstem responses are used to assess neuronal conduction in the vestibulocochlear nerve and the brainstem which, theoretically, makes it an excellent testing method. However, a significant limitation associated with ABR use for the intraoperative monitoring of hearing is the necessity to average a large number of samples (several hundred repetitions) of the recorded electrophysiological signal in order to obtain an optimal signal-to-noise ratio (SNR), thereby achieving readable and repeatable responses. One serious disadvantage of the ABR technique is its inability to provide real-time results [24]. Moreover, ABR is a far-field recorded potential with low-amplitude responses which makes it more susceptible to various artifacts, including those from the electrical network [10, 12]. The above-mentioned problems may be overcome by using auditory potential measurement from the promontory (TT-ECochG). Due to the measurement of potentials near their source, the amplitude of the electrophysiological response is several times higher, making it easier to obtain a favorable SNR ratio to receive a readable AP from nerve VIII. Achieving a readable and repeatable averaged measurement requires a relatively low number of collected samples and the responses are obtained every few seconds. Therefore, it may be assumed that TT-ECochG monitoring is an almost-real-time procedure [24]. Intraoperative TT-ECochG assessment provides information only about the vestibulocochlear nerve and the cochlea so its implementation as the only test is not the optimal method for intraoperative monitoring of hearing.

Direct CNAP measurements also provide real-time information (every few seconds) concerning auditory function [10, 24]. The analyzed parameters include response morphology and amplitude changes. Direct CNAP is also subjected to qualitative analysis according to the classification into various response phases: mono-, bi- and triphasic, or no response [12]. Triphasic responses with visible P1, N1, and P2 potentials reflect the presence of three synchronized peaks which confirm the appropriate response of the peripheral part of the auditory pathway from the respective structures: the spiral ganglion, vestibulocochlear nerve, and cochlear nuclei. In case of biphasic responses, P1 and N1 peaks present extended latency and lower amplitude, which most commonly takes place during tumor removal and usually indicates disrupted information transfer along the vestibulocochlear nerve, which then desynchronizes response in the cochlear nuclei. A monophasic response (one with largely extended latency and low amplitude) indicates the disrupted activity of spiral ganglion neurons. Injury to the vestibulocochlear nerve renders the neurons unable to transfer bioelectrical information to the cochlear nuclei or the information is abnormally desynchronized so it may not trigger readable and recordable responses. The lack of response (flat read-out) shows the lack of potential generation in the spiral ganglion following acoustic stimulation. Such a situation is usually observed in the case of prolonged disruption of inner ear perfusion, which may result from damage to the labyrinthine artery or, less frequently, the anterior inferior cerebellar artery [13]. Lowered amplitudes of P1, N1, and P2 potentials and their extended latencies may suggest a reduction in the number of neurons and fibers as well as the disruption of stimulation and response obtained from the neurons of the spiral ganglion and cochlear nuclei [13]. The CPAT evacuation is associated with stretching and damaging the individual fibers of the vestibulocochlear nerve and generating episodes of inner ear or cochlear nerve ischemia. Therefore, disrupted intraoperative CNAP response results from the disturbed production of normal responses from the individual neurons of the auditory pathway with a subsequent prolongation of the latency and reduction of the amplitudes of those responses from the peripheral areas of the auditory pathway [12, 13].
Based on the types of direct CNAP response phases, it may be assumed which area of the auditory pathway sustained injury. Importantly, direct CNAP responses are measured via an electrode located proximally to the tumor [3, 5, 10, 13, 15]. Therefore, tumor size and the size of the access via the middle cranial fossa may influence location of the measurement electrode. The simultaneous use of TT-ECochG and direct CNAP provides more information concerning the status of the auditory organ (the areas located proximally and distally to the tumor) [3–5, 7, 12, 13]. This approach provides the surgeon with rapid access to information concerning response changes from TT-ECochG and direct CNAP. Earliest awareness of these changes facilitates the possibility of earliest intervention against permanent change to individual fragments of the auditory pathway. The surgeon may then attempt to reduce the risk of postoperative hearing loss.

Colletti et al. [13] and Yamakami et al. [17] described cases of changes of CNAP response morphology during CPAT resection. They emphasized that hearing preservation is the most at risk at the moment of tumor removal. The AP amplitude of TT-ECochG slightly decreased (by 1.0 μV) and the latency extended by 0.07 ms. Similar changes were observed by Morawski et al. [6], who found amplitude was not reduced by more than 25% and the latency did not extend above 0.2 ms. In our study, exemplary Patient #1 presented TT-ECochG and CNAP responses with minor, but transient, morphology changes. This patient’s hearing was preserved.

Changes in TT-ECochG and direct CNAP morphology which occurred as a result of surgical manipulation during tumor resection are common [3–5, 7, 12, 13]. Bleeding from the tumor and the necessity to use bipolar coagulation are the most dangerous moments during surgery [6, 13, 17]. It was also observed that long-lasting drilling of the internal auditory meatus or the stretching of the vestibulocochlear nerve during tumor removal contributed to changes in the morphology of TT-ECochG response [3, 12, 13, 17] followed by the reduction in AP amplitude and/or latency extension [3, 6, 7, 17]. In our study, such a situation was observed in exemplary Patient #2. The vestibulocochlear nerve was also tightened and stretched intraoperatively. Consequently, CNAP responses changed significantly, but temporarily, from triphasic into biphasic responses. Another risk was associated with minor bleeding from the labyrinthine artery, which triggered a marked, but partially reversible, desynchronization of CNAP responses. Furthermore, changes in TT-ECochG response were observed but, at the end of surgery, the amplitude and latency returned to baseline values. As a consequence, surgery-related deterioration of the auditory function occurred in the patient. According to the professional literature [3, 6, 13], even in case of a small tumor, irreversible hearing loss may occur as a result of the drilling of the internal auditory meatus, nerve stretching, and tumor removal. Such observations were made in Patient #3, who had irreversible changes to the morphology of TT-ECochG and direct CNAP response. Nerve stretching and tumor resection resulted in the complete loss of response and postoperative hearing tests confirmed complete deafness in the patient. A similar case was reported by Colletti et al. [13]. A vessel was damaged during drilling, exposing the internal auditory meatus which caused complete hearing loss.

The intraoperative monitoring of hearing is supposed to increase the possibility of hearing preservation in patients via controlling TT-ECochG and CNAP responses throughout tumor resection. Both methods provide almost-real-time information. Therefore, the surgeon can be instantly informed of their patients’ potential risk of hearing loss; this early awareness could be used to reduce the risk of hearing loss.

According to recommendations of the Congress of Neurological Surgeons Systematic Review and Evidence-Based Guidelines on Intraoperative Cranial Nerve Monitoring in Vestibular Schwannoma Surgery issued in 2018 [25] and the European Association of Neuro-Oncology (EANO) [2] in 2020, monitoring the function of the eighth cranial nerve should be performed during vestibular schwannoma resection when attempts are made to preserve hearing. Methods of intraoperative monitoring of hearing are being explored intensively [4, 5, 8–11, 14–16] and are contributing to the reduction of risk of surgery-related hearing loss during removal of tumors of the eighth cranial nerve.

CONCLUSIONS

A combination of TT-ECochG and direct CNAP allows for real-time monitoring of auditory function during vestibular schwannoma resection. Importantly, simultaneous implementation of both these methods provides information from various sites of the auditory pathway: distally to the tumor (the distal segment of the vestibulocochlear nerve – TT-ECochG) and proximally to the tumor (the proximal part of the cochlear nerve – direct CNAP). This combination facilitates rapid assessment of the status of the cochlea and the vestibulocochlear nerve during surgical manipulation, which itself may contribute to the risk of hearing loss in a patient undergoing such an operation. Therefore, the surgeon can be informed instantly about changes observed in TT-ECochG and CNAP, which could increase the possibility of preserving the patient’s hearing.

REFERENCES

The authors declare that they have no competing interests.

Competing interests: The authors declare that they have no competing interests.

Corresponding author: Magdalena Lachowska MD, PhD, Associate Professor, Department of Otorhinolaryngology, Head and Neck Surgery, Medical University of Warsaw; Banacha street 1a, 02-097 Warsaw, Poland; Phone: +48 225992521; E-mail: mlachowska@wum.edu.pl

Some right reserved: Polish Society of Otorhinolaryngologists Head and Neck Surgeons. Published by Index Copernicus Sp. z o.o.