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Original Article

Electrically Evoked Auditory Brainstem Response over Round Window by Bipolar Stimulation

Noelia Muñoz Fernández, Carlos de Paula Vernetta, Laura Cavallé Garrido, Miguel Díaz Gómez, Constantino Morera Pérez

Department of ENT, La Fe University and Polytechnic Hospital, Valencia, Spain (NMF, CPV, LCG, CMP)
MED-EL GmbH Spain Office, Madrid, Spain (MDG)

ORCID IDs of the authors: N.M.F. 0000-0003-4280-4827; C.P.V. 0000-0002-8747-457X; L.C.G. 0000-0001-8367-8084; M.D.G. 0000-0003-2514-8899; C.M.P. 0000-0002-0996-9227.

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OBJECTIVES: Auditory brainstem potentials can be elicited by electrical stimulation of the round window (RW). In this technique, extracochlear stimulation is objectively used in the selection of cochlear implant (CI) candidates to avoid cochlear damage. However, until now, its use is limited due to the large artifacts generated by electrical stimulation. Our objective was to obtain reliable and reproducible electrically evoked auditory brainstem responses (eEABRs) using a new method of stimulation

MATERIALS and METHODS: This was a prospective study including subjects who underwent electrical stimulation on RW during CI surgery between 2013 and 2016. A "Stimulator Box," which produces electric stimuli identical to those provided by a CI, and an evoked potential recording equipment were used. The results obtained with monopolar and bipolar electrodes were compared.

RESULTS: RW eEABR recordings of 49 subjects (mean age, 34 years) were characterized by their stability and by having wave V between 3 and 5.5 ms. A higher percentage of responses were obtained on increasing the phase duration instead of the pulse amplitude. A significantly greater percentage of positive responses were obtained using bipolar stimulation than using monopolar stimulation ($p<0.001$).

CONCLUSION: Using extracochlear electrical stimulation technique, described herein, and bipolar electrical stimulation probe allows for reliable and reproducible eEABR recordings in CI candidates.

KEYWORDS: Cochlear implant, brainstem auditory evoked potentials, round window, electrical stimulation

INTRODUCTION

Electrically evoked auditory brainstem responses (eEABR) are records of the neural activity of the auditory pathway elicited by extracochlear electrical stimulation, particularly of the round window (RW). Animal studies have shown that these records correlate with the number of surviving cells in the spiral ganglion [1, 2]. Thus, eEABR recordings obtained with the stimulation of RW can be used to preoperatively determine the extent of excitability of the auditory nerve and brainstem of a cochlear implant (CI) candidate [1].

Earlier, for CI candidates, "promontory test" was used to predict functional outcomes through the electrical stimulation of the auditory nerve with an electrode on the promontory. It was a subjective test in which the CI candidates reported when the auditory stimulation at different frequencies was perceived by varying intensities of the stimulus [3]. Lack of response to the electrical stimulation was generally considered a contraindication to cochlear implantation [4]. The promontory test was, however, later found to inaccurately predict CI users' levels of speech performance and was, thus, abandoned as a test for CI candidacy [5].

Performing an objective recording, such as eEABR via a transtympanic electrode placed on the promontory or RW, is a much more reliable technique to preoperatively judge the excitability of the auditory pathway. Chouard et al. [6] and Meyer et al. [7] were some of the first authors to show that eEABR can be elicited by extracochlear electrical stimulation. Later, Pau et al. [8] demonstrated that accurately placing a "golf club"-type electrode within the RW niche allows for a sensitive and reliable stimulation and, therefore, better eEABR recordings than those obtained with promontory stimulation.

Corresponding Address: Noelia Muñoz Fernández E-mail: noeliamufer@gmail.com

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This technique is especially useful in CI candidates in whom the presence of the auditory nerve is doubtful or in CI candidates with other related disorders that cast doubts on the potential effectiveness of CI. Studying the morphology of the wave V can help predict the intact neural population and may even aid in choosing which ear should be implanted if the CI candidate has bilateral deafness. This technique is now widely accepted and used for CI candidates because it can accurately help detect auditory neuropathies [9] and can help predict the postoperative speech understanding of CI candidates [10]. However, the eEABR waves obtained immediately after electrical stimulation have a morphology that is much less defined than that of any other potential [4, 11] because the artifacts originating from the electrical stimulation itself mask and contaminate the morphology of the biological responses. Therefore, identification of the waves may be problematic due to the large variability in their appearance.

This can prevent the detection of eEABR in certain situations. Therefore, despite being a useful procedure, its use in conventional clinical practice is limited by the artifacts. While there is no doubt on the value of these potentials as an objective indicator of the activation of the peripheral auditory pathway, a more reliable technique is necessary.

The aims of this study were to obtain reliable and reproducible evoked auditory brainstem responses elicited by electrical RW stimulation using a new method of stimulation, which provides stimulation identical to that provided through a CI, and to compare the results using monopolar and bipolar configurations.

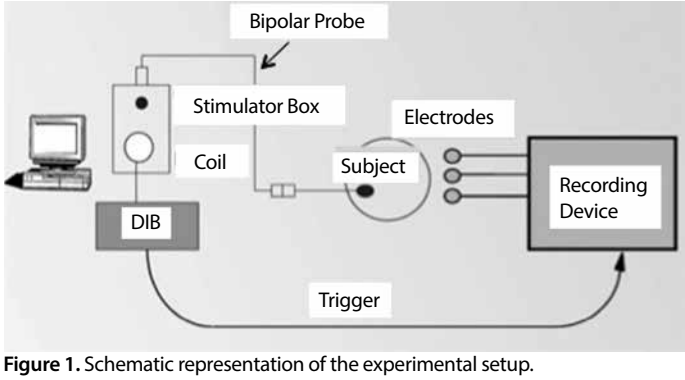

Figure 1. Schematic representation of the experimental setup.

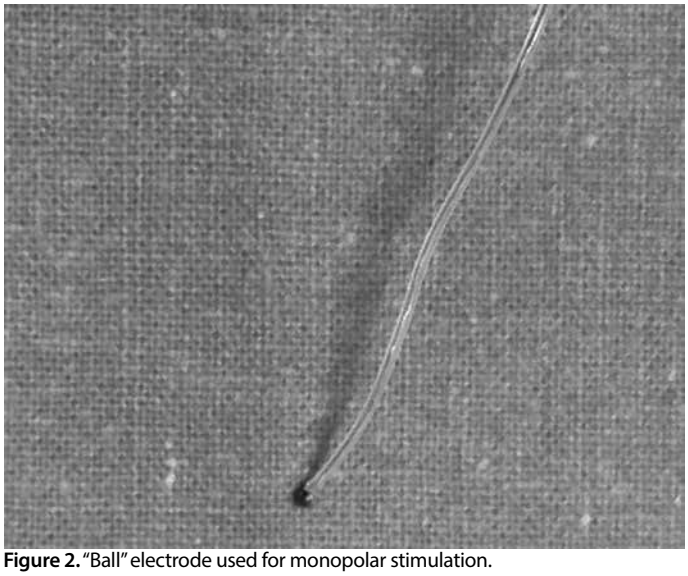

Figure 2. "Ball" electrode used for monopolar stimulation.

MATERIALS and METHODS

Subjects and setting

The subjects in this prospective, descriptive, comparative study included a subset of patients from the CI program at the Otolaryngology Department of University Hospital La Fe. None of the subjects had retrocochlear pathologies, radiological malformations, or otosclerosis. All the subjects provided their written informed consent prior to any study-related procedures. The study was approved by the Clinical Research Committee of the Hospital.

Stimulation Device

The stimulation device provided by MED-EL (MED-EL AG®; Innsbruck, Austria) generated the electrical stimuli. This device included several specific elements: 1) a laptop with the MAESTRO® 4.0.2 programming software (Innsbruck, Austria), 2) a DIB II® [diagnostic interface box, (Innsbruck, Austria)] that controlled the stimulation and synchronization with the recording equipment, 3) a coil to send the stimulation data, and 4) a device called "Stimulator Box" (Innsbruck, Austria) that contains the electronics of a MED-EL COMBI 40+® CI (Figure 1).

The electrical stimulus was a balanced biphasic pulse with negative initial phase. The pulses were defined by their amplitude (range, 1-1700 μA) and their phase duration (range, 53.3-400 μs/phase). Electrical stimuli were adjusted by increasing the amplitude up to the compliance limit, and from there, lengthening the phase duration. The result was expressed in charge units (qu) where 1 qu corresponds to approximately 1 nanocoulomb. The stimulation rate was 34 Hz. To avoid neural adaptation to same charge level stimulation and to confirm the reproducibility of the records, the measurements at the same charge level were non-consecutively recorded.

Recording Device

The Navigator Pro recording device (Natus Medical Incorporated, Pleasanton, CA, USA) was used to collect eEABRs. For each stimulation amplitude, 1500 sweeps were recorded, averaged, and filtered from 30 to 3000 Hz, thereby improving the quality of responses. Needle electrodes were used; they were placed on the subjects' heads: the active electrode at vertex (Cz), the reference electrode on the contralateral mastoid (M), and the ground electrode on the forehead (Fz). An activation (*Trigger*) cable was used to synchronize the recording device with the DIB II® interface. A radiofrequency (RF) filter was used between the subject and the recording device to remove the undesired signals on the RF range emitted by the Stimulator Box. Three jumper cables were used to connect the RF filter to the recording amplifier.

Intraoperative Session

eEABRs were collected during cochlear implantation, for which a posterior tympanotomy approach was used, just before performing the cochleostomy. For each measurement, stimulation was applied in monopolar and bipolar configurations. In the monopolar configuration, a "ball" electrode was placed over RW (Figure 2) with the ground electrode placed on the subject's neck. In the bipolar configuration, a bipolar probe Neurosign® (Whitland, UK) with two parallel electrodes

(100×0.75 mm) was placed (Figure 3) very close to each other. One electrode was placed over RW and the other over the promontory.

To block the activation of myogenic potentials on the eEABR recordings, a muscle relaxant, Esmeron® (Rocuronium bromide; N.V. Organon, Oss, Holland), was administered prior to stimulation [12, 13]. The impedances of the recording electrodes were less than 5 kΩ, and the synchronization between the recording and the stimulation systems was tested before recording. eEABR recording was performed by progressively increasing the stimulation charge: first, the amplitude was increased up to the compliance level while keeping the phase duration constant, and from this level, phase duration was increased until eEABR was obtained.

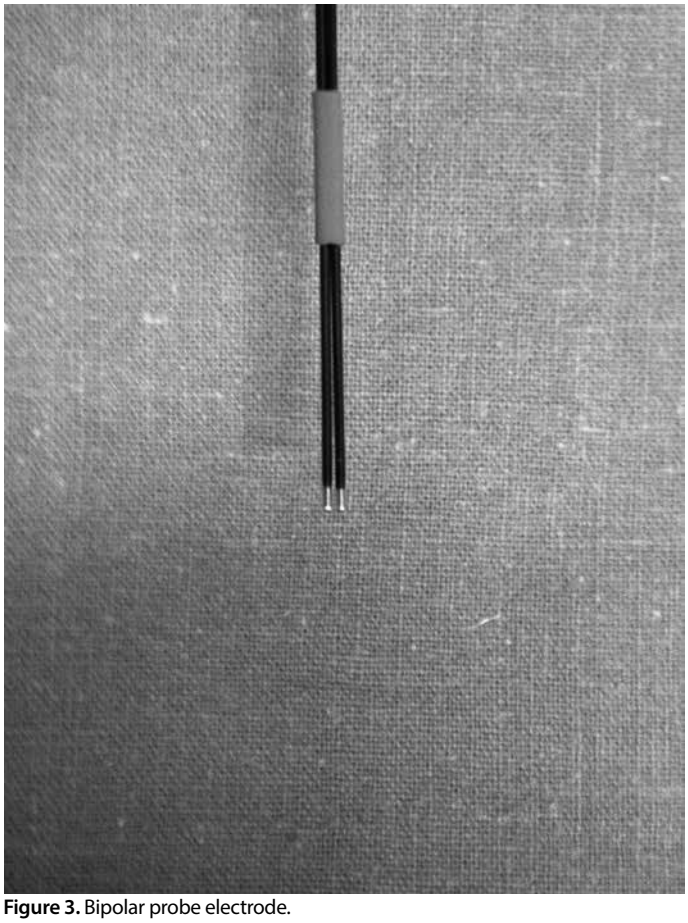

Figure 3. Bipolar probe electrode.

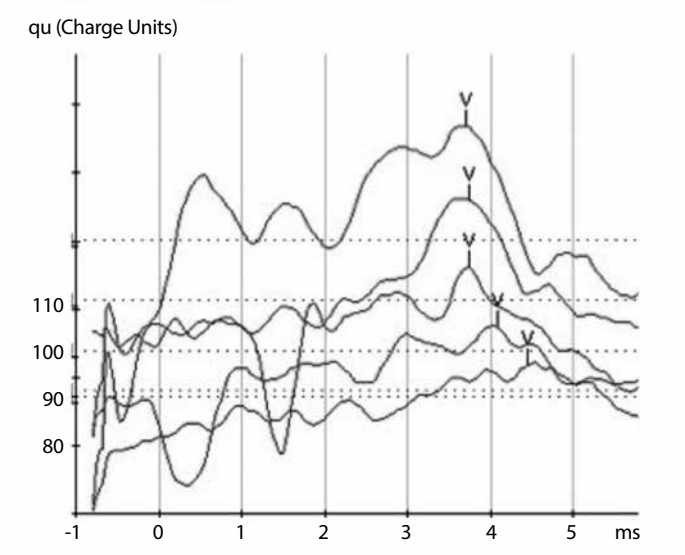

Figure 4. Latency increases as charge unit decreases.

For the comparative analysis, we classified eEABR morphology as "positive," "weak," or "negative":

-"Positive" was defined as the presence of wave V between 3 and 5.5 ms that was reproducible in more than three non-consecutive records with the same electrical charge.
-"Weak" was defined as presence of wave V between 3 and 5.5 ms that was reproducible across less than three non-consecutive records with the same electrical charge.
-"Negative" was defined as the absence of wave V.

Statistical Analysis

Subject demographics, eEABR morphology, latency and amplitude of eEABR, and the stimulation setting (amplitude and phase duration) were analyzed for statistical purposes.

Measures of central tendency were used for the descriptive analysis. χ^2 and Mann–Whitney tests were used for the comparative analysis. The Statistical Package for the Social Sciences (SPSS) version 20.0 software (IBM Corp.; Armonk, NY, USA) was used. $p<0.05$ was regarded as significant.

RESULTS

Subjects

We included 49 subjects (19 females, 30 males; mean age, 34 years) in the study between 2013 and 2016. The most common etiology of hearing impairment was an idiopathic progressive postlingual hearing loss (Table 1). More recordings were performed in the right ear than in the left ear (67% vs 32%).

Bipolar Stimulation Intraoperatively

On analyzing the eEABR responses measured using bipolar stimulation, the following common characteristics were observed:

a) Reproducibility of eEABR was confirmed by replication: repeating eEABR responses with identical electrical charges was essential to confirm their reproducibility.

b) Wave V latency was between 3 and 5.5 ms and was reproducible in three non-consecutive recordings with the same charge level (Figure 4).

c) Latency increased when the charge level was decreased (Table 2).

d) Because the electrical artifacts were applied during the electrical stimulation and recorded at the beginning of the eEABR recording window, the first eEABR component, specifically wave I, was almost entirely masked by the artifact.

The analysis of the percentage of responses depending on the electrical charge showed the rate of response to be 6.5% between 0 and 50 qu, 67.7% between 51 and 100 qu, 77.4% between 101 and 150

Table 1. Etiology of sensorineural hearing losses

Etiology	Percentage (%)
Idiopathic progressive	48.4%
Idiopathic congenital	25.8%
Sudden hearing loss	12.9%
Drug therapy	6.5%
Infection	3.2%
Ménière's Disease	3.2%

Table 2. Stimulation Charge vs Wave V Latency

Stimulation Charge Range (qu)	Average Latency (ms)
0-55	4.78
51-100	4.42
101-150	4.17
151-200	3.89
200-250	3.68

qu: charge units; ms: milliseconds

qu, 61.3% between 151 and 200 qu, and 12.9% between 201 and 250 qu. Thus, it can be observed that the probability of finding wave V was lower when the electrical charge was too high or too low.

On comparing how variables affected both the stimulation and recording, we obtained the following results:

Type of stimulation: positive responses were significantly more ($p<0,001$) likely with bipolar stimulation (100% positive responses) than with monopolar stimulation (60% positive responses, 30% weak responses, and 10% negative responses).

No myogenic action potentials were activated.

DISCUSSION

Cochlear electrical stimulation was a technique initially recommended for the preliminary evaluation of CI candidates [14]. Since Meyer et al. [7] performed 460 electrical stimulations with a 93% recorded positive responses, many other authors found it essential in the preoperative evaluation of the neuronal survival, especially in children [13, 15-18]. Truy et al. [19], however, found that stimulation artifacts made these potentials difficult to record.

Regarding whether RW or promontory is the preferred stimulation location, several groups [4, 14, 20] obtained better results with RW stimulation. We agree with Gibson and Sanli [9] that the electrode should be positioned within RW for a more effective electrical stimulation of the cochlea. Different types of stimulation electrodes have been reported: Shipp and Nedzelski [14] used a 2 mm "ball" electrode; Gibson and Sanli [9] used the "golf club"-type electrode. For monopolar stimulation, we initially used a "ball" electrode over RW, but because it is flexible and light, it moved easily during the registration and, therefore, required fixation with *gelita-Spon*® (Eberbach, Germany). Thus, we used an alternative approach with a bipolar electrode probe, which required higher electrical charges during stimulation. In our results, we obtained 100% positive responses with bipolar stimulation but only 60% positive responses with monopolar stimulation. This means that with monopolar stimulation, 40% of the subjects had an eEABR with possibly small amplitude that could have been masked by an electrical artifact.

In their study on 47 pediatric CI users without radiologic malformations, Nikolopoulus et al. [10] found that there were no significant differences between subjects with preoperative positive responses (n=35) and subjects who had no preoperative responses (n=12), demonstrating that false-negative responses might be obtained when stimulation is performed using a single active electrode. We found only one article that reported using bipolar stimulation [21]; however, unlike our work, two independent electrodes were used in that study, but as per the authors, good results could not be obtained due to the use of high intensities. Although that and the present study both had the similar problem of high intensities used during stimulation, we did obtain responses in all of our subjects. We believe that apart from the type of stimulating electrode, using the "Stimulator Box" favored the registering process in our study. However, despite the good results, detection of responses evoked by the electrical stimulation presented some challenges. The stimulation conditions used play a vital role. In a study by Freeman et al. [22], waves Vs were registered with biphasic pulses of 500 µA amplitude and 200 µs phase duration. We had to use higher intensities. Kileny and Zwolan [23] also used biphasic pulses of 200 µs duration per phase with a variable intensity up to a maximum of 999 µs.

In our study, we observed shorter latencies than those found in previous studies [24, 25], although sometimes only a slight decrease was found between with higher and lower intensities [26]. In a study by Kileny et al. [27], the mean latency was 4.69 ms. We obtained similar latencies in the range of lower charges (4.78 ms in the range of 1–50 qu). However, unlike Kim et al. [28], we did not use amplitude as a comparative measurement as in our experience, it possesses high variability, even when the noise level is controlled. According to another study, eEABR generates a stimulus artifact, which interferes with the electrical recording of waves I and II; therefore, the authors focused only on the analysis of waves V [29]. In the present study, it was observed that eEABR wave V was easily and rapidly recorded despite performing extracochlear stimulation.

Recently, intracochlear stimulation has been proposed to evaluate the auditory nerve [30], but it causes intracochlear damage that can be avoided using our technique. We think that the presence of wave V in our study may reflect the functional integrity of the cochlear nerve and auditory brainstem potentials were evoked in all subjects with a simple and reproducible technique without being aggressive with the cochlea.

CONCLUSION

Careful patient selection and accurate preoperative testing are important in maximizing CI candidates' desired postoperative results. RW eEABR recording is a useful tool for checking the survival of neural elements in the auditory pathway. Using our technique, we obtained reliable and reproducible results with extracochlear electrical stimulation using a bipolar probe. Variations in the phase duration, while maintaining constant high amplitudes, provide more reliable results than other stimulation conditions. Use of muscle relaxants is essential prior to the collection of potentials so that contamination with other types of potentials can be discarded.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of University and Polytechnic Hospital La Fe.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept C.M.P.; Design N.M.F., C.M.P.; Supervision C.M.P.; Resources N.M.F., C.D.V., L.C.G., M.D.G., C.M.P.; Materials by M.G.D.; Data Collection and/or Processing N.M.F, C.D.V., L.C.G.; Analysis and/or Interpretation N.M.F, M.D.G., C.M.P.; Literature Search N.M.F.; Writing Manuscript – N.M.F.; Critical Review - C.M.P.

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