

Functional Evaluation of Auditory System in Patients with Cochlear Implant Using Electrically Evoked Auditory Brainstem Responses¹

L. Wang^a, Q. Zhang^b, Q. Wang^c, M. Dong^a, and Y. Zeng^b

^a Department of Otorhinolaryngology Head and Neck Surgery, the First Affiliated Hospital of Zhengzhou University, Republic of China

^b Biomedical Engineering Center, Beijing University of Technology, Beijing, 100124, People's Republic of China

^c Department of Rehabilitation Sciences, The Hong Kong Polytechnic University, Hong Kong, People's Republic of China

e-mail: yjzeng@bjut.edu.cn

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Abstract—Aim: The objective of this study is to evaluate the recovery of hearing function of auditory pathway after cochlear implantation by extracting the characterizations of electrically evoked auditory brainstem responses (EABR). The purpose of this study was to explore a reality and possible EABR test mode in clinical applications, rather than strict animal research.

Methods: 53 patients received Nucleus 24 cochlear implant. The EABR tests were performed with a stimulus frequency of 100 Hz or less and a pulse width of 25, 50, and 75 μ s/phase. The EABR signals were recorded from three electrodes (electrode 3, 10, and 20), simultaneously. The latency of the EABR wave III and V, the EABR threshold and the positive appearance rate of the EABR waves were measured.

Results: This study found that during EABR tests, the artifacts under the alternate polarity stimulus were smaller than those under the monopolarity stimulus. A similar result was found that the artifacts collected on the contra lateral side were smaller than that on the same lateral side. The latency of the EABR waves prolonged with the increase of the stimulus frequency. When the high cut-off frequency of the band-pass filter altered from 1.5 kHz to 3 kHz, the latency of the EABR wave V shortened, but the latency maintained constant from 3 kHz to 25 kHz. When the low cut-off frequency was changed from 100 Hz to 0.002 Hz, the latency of the EABR wave V maintained constant. In addition, it was found that the EABR threshold lowered with increasing the pulse width of the stimulus. This study indicated that the EABR threshold of the signals collected from the electrode 20 were significantly ($p < 0.01$) lower than those obtained from the electrode 3 and 10. However, no statistically significant difference in the EABR threshold existed between the signals collected from the electrode 3 and 10 ($p > 0.05$). Moreover, the latency of the EABR wave III and V at the electrode 3 was significantly ($p < 0.01$) longer than that at the electrode 10 and 20, and the latency of the wave III and V at the electrode 10 was significantly ($p < 0.01$) longer than that at the electrode 20. The positive appearance rate of the EABR waves was 96.22%.

Conclusion: The EABR tests with proper parameters were designed in this study. The characterizations of the EABR waves including amplitude, latency and threshold were extracted at different electrodes. The EABR test provides an effective method to evaluate the functions of the auditory pathway in patients after cochlear implantation.

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INTRODUCTION

Cochlear implantation has been widely applied in the clinic to recover or obtain audition for patients who suffer from severe, extremely severe or total hearing loss. Cochlea implant translates voice into electrical signal to stimulate acoustic nerves [1–4]. Because of electrical stimulation rather than sound stimulation [5, 6], the approach to evaluate the auditory function after cochlear implantation should be different from the traditional methods. However, the postoperative

evaluation on the auditory pathway after cochlear implantation is limited.

The auditory brainstem response (ABR) is a measure of neural synchrony along the auditory pathway through the brainstem. Since the acoustically evoked ABR is absent, ABR can be performed by electrical stimulation through the cochlear implant, which is so called electrically evoked ABR (EABR). The EABRs objectively reflect a series of neural responses from acoustic nerve, cochlear nucleus, superior olivary nucleus, lateral lemniscus, inferior colliculus, medial geniculate body and acoustic radiation. Therefore, the EABR test can be used in the functional evaluation of

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Table 1. The age distribution of the subjects, the number of children and adults, and the onset of deafness

| Age distribution, year | Pre-lingual deafness | Post-lingual deafness | Total |
|------------------------|----------------------|-----------------------|-------|
| 6–11 | 7 | 2 | 9 |
| 12–18 | 25 | 6 | 31 |
| >18 | 9 | 4 | 13 |
| Total | 41 | 12 | 53 |

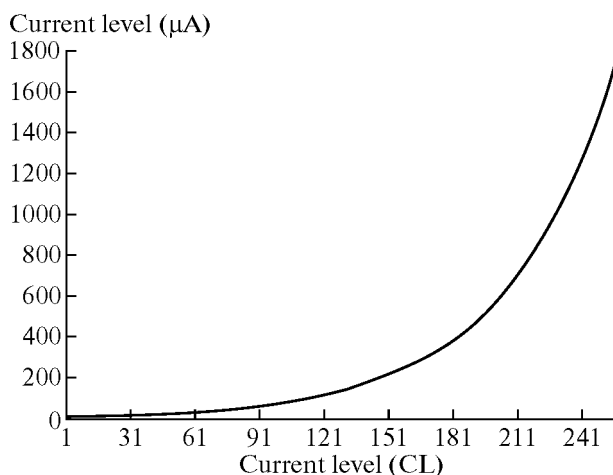
auditory system in patients after cochlear implantation.

In this study, 53 patients received cochlear implant as subjects were chosen, given a code using the advanced confined encoding (ACE) strategy, which is a relatively new encoding strategy used by an artificial cochlear voice processor, and then underwent the EABR test. The objectives of this study are (1) to investigate the effects of different test conditions on the EABR waves and sequentially to obtain a stable and accurate EABR waves for future tests, (2) to extract the characterizations and parameters of the EABR waves, and (3) to evaluate the functions of auditory pathway after cochlear implantation using EABR.

1. METHODS

1.1. Subjects

In this study, 53 patients received Nucleus 24 cochlear implant (Nucleus CI24, Australia). Table 1 shows the age distribution of the patients, the number of children and adult patients and the onset of deafness. All the subjects used unilateral cochlear implants, 32 cases: left ear; and 21 cases: right ear. Of the 53 patients, 16 patients were implanted with Nucleus 24RCS cochlear implant and 37 patients with

**Fig. 1.** Schematic of the EABR testing system.

Nucleus 24M cochlear implant. The age of the subjects ranged from 6 to 57. All the subjects with normal intelligence are able to make a subjective judgment. The main reasons of hearing loss were incorrect medical treatment for 17 cases, congenital disorder for 14 cases, and Mondini inner ear malformation for 2 cases. For the other 20 cases, the reasons were unknown. In this study, the Sprint voice processor and ACE coding strategy were adopted. Before testing, the contents and the purpose of the EABR test were explained to the subjects. With their consents, the examinations were performed from six months to one year after cochlear implantation in the treatment room of First Affiliated Hospital of Zhengzhou University, China.

1.2. EABR Testing System

Figure 1 shows the schematic of the EABR testing system used in this study. The system consists of Nucleus 24 cochlea (Nucleus CI24, Australia), transmission coil and stimulation acceptor, speech processor, amplifier, evoked potential instrument (model ICS, USA), external trigger, portable programming system (PPS), and neural response telemetry (NRT) software (Version 3.0, cochlear company, Australia). Nucleus 24 Cochlea includes 22 inner cochlear electrodes and two external electrodes. The inner electrodes are numbered from 1 to 22 starting from the trough to the peak of the cochlea. The external electrodes are named as MP1 and MP2 and connected to the ground. MP1 is a ball-typed electrode and placed under the temporal muscle; MP2 is a flat-typed electrode and located in the implanted part. The stimulating signal generated by the NRT software reached to the cochlear electrodes through PPS, speech processor, transmission coil and stimulation acceptor (Fig. 2). In this study, biphasic square-waved current and monopolarity stimulus were adopted. Three stimulating electrodes (electrode 3, 10, and 20) were selected as stimulating and recording electrode. MP1 was used as reference electrode. The guiding electrodes were skin surface-typed electrode. The active electrode was placed on the forehead of the subject while the reference electrode was placed at the ipsilateral or contralateral mastoid and the ground electrode was placed between the eyebrows. Resistance between electrodes should be less than 5 k Ω . The external trigger cable connected PPS and evoked potential equipment.

The main difficulties met in this study were electromagnetic interference and stimulus artifacts induced by the surrounding environment [3]. These noises were eliminated using the standard electromagnetic shielding room and the special ground wire with little resistance (less than 3 ohms), and excluding the interference of 50 Hz alternate current (AC).

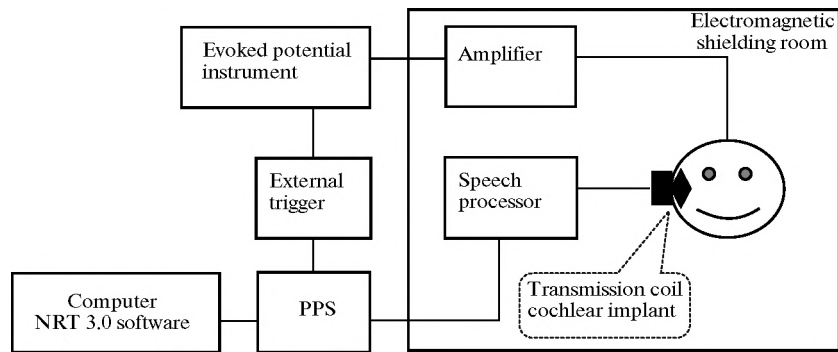


Fig. 2. The logarithmic relationship between current level and current intensity.

1.3. EABR Testing Parameters

The related stimulation parameters of the EABR test were provided by the NRT software and set as follows. The stimulus frequency was generally set less than 100 Hz, and the pulse width was set at 25, 50, 75 $\mu\text{s}/\text{phase}$, respectively. The gain of the amplifier was set between 30000 and 100000. The high cut-off frequency of the band-pass filter was between 1.5 kHz and 25 kHz, and the low cut-off frequency was between 0.002 Hz and 100 Hz. The recording time was approximately 10 ms, and the number of superposition was 1000. During EABR testing, these parameters were modified. Two types of stimulation are provided by the software, i.e. basic stimulation and alternating stimulation.

The unit of the stimulus current was current level (CL). A logarithm relationship was found between current level and current intensity. The scale of current level was set from 1 to 255 CL, i.e. from 10.2 to 1750 μA (Fig. 2).

1.4. EABR Examination

The adult subjects were asked to keep a calm situation during the test. For the children who did not cooperate with the researchers, 10% chloral hydrate aldehydes was given to insure them sleep quietly.

The initial value of stimulus intensity was 150 CL. The intensity would be adjusted lower if the EABR waves could be observed. Otherwise, the intensity would increase gradually with a step of 10 CL until the EABR waves appeared. Then, the intensity reduced with a step of 5 CL. When approaching to the EABR threshold, the stimulus intensity was adjusted with a step of 2 CL. The intensity at the moment when the wave V disappeared was defined as the EABR threshold. This adjustment procedure was performed at least twice to obtain the same result. Then the EABR threshold was obtained.

Two doctors with professional auditory training experiences designed and performed the examination,

and analyzed the EABR waves. The test results were accepted based on their consensus.

1.5. Statistical Analysis

In this study, the latency of the EABR wave III and V, the EABR threshold and the positive appearance rate of the EABR wave were measured. The data were statistically analyzed by our colleagues from Department of Medical Statistics of Zhengzhou University using SPSS 10.0 software. Paired t-test was used, and there was a significantly difference when $p < 0.05$.

2. RESULTS

2.1. Characterizations of EABR Wave

The recorded EABR waves consist of I, II, III, IV, and V waves. However, wave I is easy to be interfered by the artifacts, wave II and IV are unstable. Only wave III and V are more stable. Therefore, this study focused on the analysis of wave III and V. Figures 3 and 4 show the EABR waves III and V obtained from two subjects under different current intensities. One is an 18-year-old male patient with pre-lingual deafness implanted the cochlea for 10 months; the other is a 13-year-old male patient with pre-lingual deafness implanted the cochlea for 11 months. It was found that the amplitudes of the EABR waves gradually reduced and the latencies of the EABR waves prolonged with the decrease of the stimulus intensity. In addition, the latencies of the EABR waves were all shorter than those of the corresponding ABR waves. In Figs. 3 and 4, the abscissa axis represents stimulus intensity with a unit of CL and the vertical axis represents the strength of the evoked potential with a unit of μV .

2.2. Effects of Different Parameters on EABR Wave

As shown in Fig. 5, the artifacts of the EABR waves under the alternate polarity stimulus were smaller than those obtained under the monopolarity stimulus. In Fig. 6, it was observed that the baseline

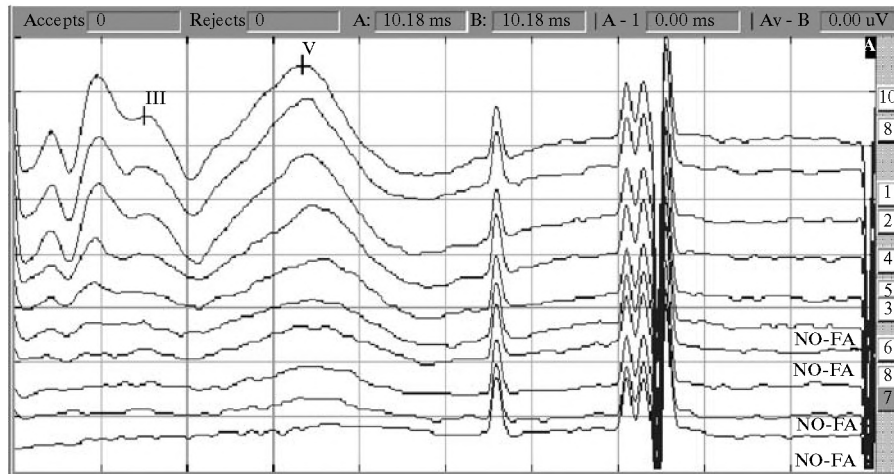


Fig. 3. The EABR waves III and V are recorded from the electrode 20 under the alternating stimuli (pulse width: 50 μ s/phase; stimulus frequency: 48 Hz) with different current intensities of 180, 175, 170, 165, 160, 155, 150, 145, 140, and 135 CL (from top to bottom). The recording time is 10.2 ms. 1.02 ms per grid is set in the abscissa axis and 0.6 μ V per grid in the vertical axis.

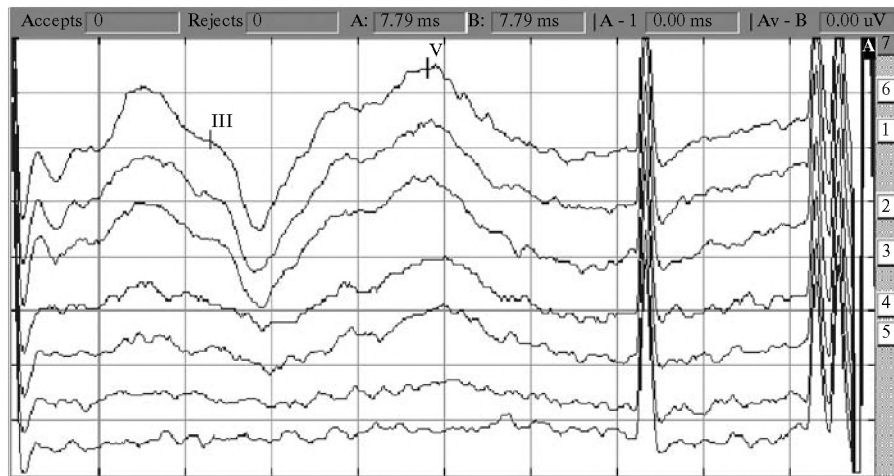


Fig. 4. The EABR waves III and V are recorded from the electrode 20 under the alternating stimuli (pulse width: 50 μ s/phase; stimulus frequency: 48 Hz) with different stimulus intensities, 180, 175, 170, 160, 155, 150, and 145 CL (from top to bottom). The recording time is 7.8 ms. 0.78 ms per grid is set in the abscissa axis and 0.3 μ V per grid in the ordinate axis.

of the EABR waves recorded on the same lateral side shifted and the artifacts of the EABR waves were much larger than those obtained on the contra lateral side, where the waves appeared stable and the baseline shifted little.

In the case of the low cut-off frequency at 100 Hz, Fig. 7 shows that the latency of the wave V became shorter when the high cut-off frequency of the band-pass filter increased from 1.5 kHz to 3 kHz but maintained constant when the high cut-off frequency increased from 3 kHz to 25 kHz. When the high cut-off frequency approached to 25 kHz, an obvious high-frequency noise appeared. On the other hand, in the case of the high cut-off frequency at 3 kHz, the latency of the wave V maintained stable when the low

cut-off frequency changed from 100 Hz to 0.002 Hz (Fig. 8).

2.3. EABR Threshold and Latency of Wave III and V

Table 2 lists the values of the EABR threshold measured at the electrode 3, 10, and 20 under different stimuli with different pulse widths (25, 50, and 75 μ s/phase). It was found that the values measured at the electrode 20 were significantly ($p < 0.01$) lower than those obtained at the electrode 3 and 10. However, there was no significant difference between the values measured at the electrode 3 and 10 ($p > 0.05$). Figure 9 shows the EABR waves recorded from the electrode 3, 10, and 20 while the stimulus intensity

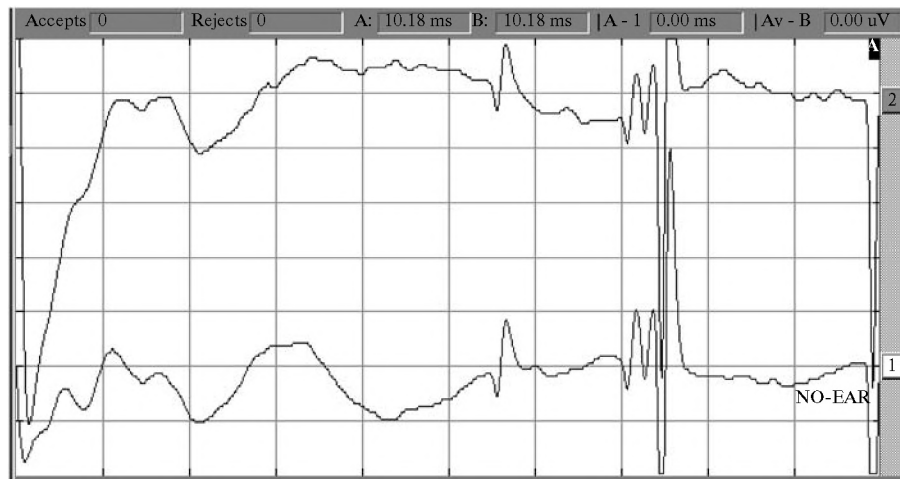


Fig. 5. The EABR waves are recorded from the electrode 20 under the monopolarity stimulus (upper) and the alternate polarity stimulus (lower). The stimuli are set with a 50 μs/phase pulse width, a 48 Hz stimulus frequency, and 175 CL stimulus intensity. The subject is a female 7-year-old patient with post-lingual deafness, implanted the cochlea for 7 months. The recording time is 10.2 ms. 1.02 ms per grid is set in the abscissa axis and 0.4 μV per grid in the ordinate axis.

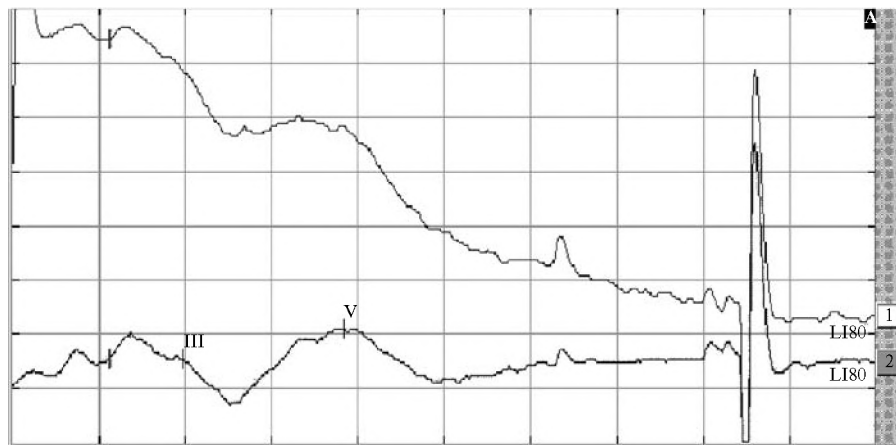


Fig. 6. The EABR waves are recorded on the same lateral side (upper) and the contra lateral side (lower). The subject is a 42-year-old male patient with post-lingual deafness, implanted the cochlea for 10 months. The parameters are set as same as in Fig. 5.

reached to 20 CL higher than the threshold. The latencies of the EABR wave III and V measured at the electrode 3 were significantly ($p < 0.01$) longer than those measured at the electrode 10 and 20 (Table 3). Further, the latencies of the EABR wave III and V at the electrode 10 were significantly ($p < 0.01$) longer than those measured at the electrode 20.

2.4. Appearance Rate of EABR Wave

The EABR waves were tracked from 51 of the 53 subjects. Therefore, the appearance rate of the EABR wave reached up to 96.22%. One of the patients who failed to track the response waves suffered from the dysfunction of auditory pathway.

Table 2. The threshold values (mean ± SD, unit: CL) of the EABR waves obtained at the electrode 3, 10, and 20 under the stimuli with different pulse widths

| Pulse width | Threshold | | | Average |
|--------------|----------------|----------------|----------------|----------------|
| | Electrode 3 | Electrode 10 | Electrode 20 | |
| 25 μs/phrase | 187.63 ± 11.69 | 188.32 ± 11.26 | 183.08 ± 10.40 | 186.34 ± 11.61 |
| 50 μs/phrase | 158.63 ± 10.86 | 159.71 ± 11.17 | 152.92 ± 10.82 | 157.09 ± 11.26 |
| 75 μs/phrase | 144.37 ± 11.52 | 145.71 ± 11.38 | 139.00 ± 10.40 | 143.03 ± 11.72 |

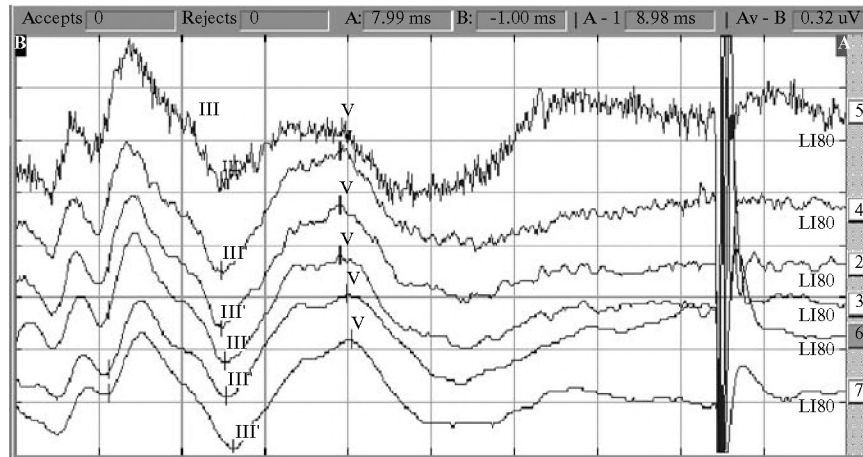


Fig. 7. The EABR waves are recorded from the electrode 20 under the stimulus (pulse width: 50 μ s/phase; stimulus frequency: 48 Hz; and stimulus intensity: 175 CL). The low cut-off frequency of the band-pass filter is set at 100 Hz and the high cut-off frequency is respectively set at 25, 10, 5, 3, 2, and 1.5 kHz (from top to bottom). The subject is a 21-year-old male patient with post-lingual deafness, implanted the cochlea for 12 months. The recording time is 9 ms. 0.9 ms per grid is set in the abscissa axis and 0.4 μ V per grid in the ordinate axis.

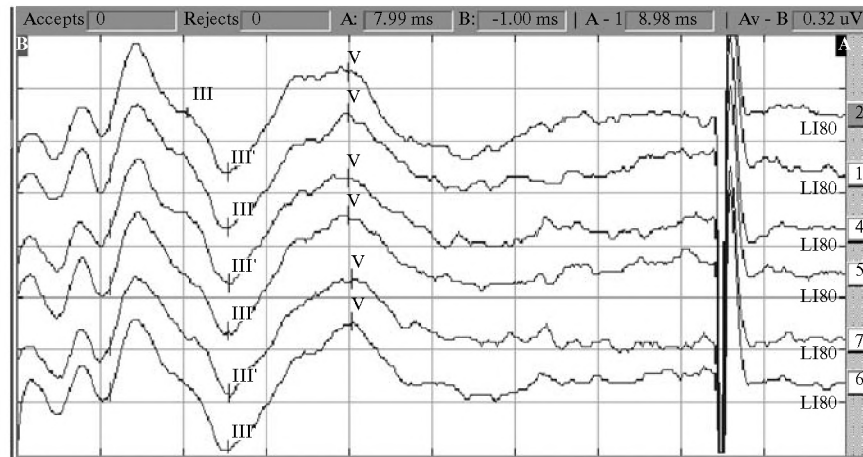


Fig. 8. The EABR waves are recorded from the electrode 20 under the same stimulus as Fig. 7. The high cut-off frequency of the band-pass filter maintains constant at 3 kHz and the low cut-off frequency is respectively set at 100, 10, 1, 0.2, 0.01, and 0.002 Hz (from top to bottom). The subject is a 21-year-old male patient with post-lingual deafness, implanted the cochlea for 11 months. The recording time and the unit of the abscissa and ordinate axis are as same as in Fig. 7.

3. DISCUSSION

3.1. Effects of Different Test Parameters on EABR Wave

Stimulus polarity. In the previous studies on the artificial cochlea with a type of Nucleus 22 and

Nucleus 24, the most common problem encountered was excessive artifacts since only the single polarity stimulation could be performed due to the limitation of the stimulus parameters [7, 8]. A method of blanking out the waves during the first period of 1.2–1.5 ms

Table 3. The values (mean \pm SD, unit: ms) of wave latency and interwave latency of the EABR wave III and V obtained at the electrode 3, 10, and 20 under the stimulus with a 50 μ s/phase pulse width, a 48 Hz stimulus frequency and a stimulus intensity of 20 CL over the threshold

| | Electrode 3 | Electrode 10 | Electrode 20 | Average |
|---------------------|-----------------|-----------------|-----------------|-----------------|
| Latency of wave III | 1.82 \pm 0.16 | 1.75 \pm 0.14 | 1.67 \pm 0.16 | 1.75 \pm 0.16 |
| Latency of wave V | 3.70 \pm 0.25 | 3.58 \pm 0.21 | 3.42 \pm 0.18 | 3.57 \pm 0.24 |
| Interwave latency | 1.98 \pm 0.16 | 1.83 \pm 0.13 | 1.74 \pm 0.17 | 1.82 \pm 0.18 |

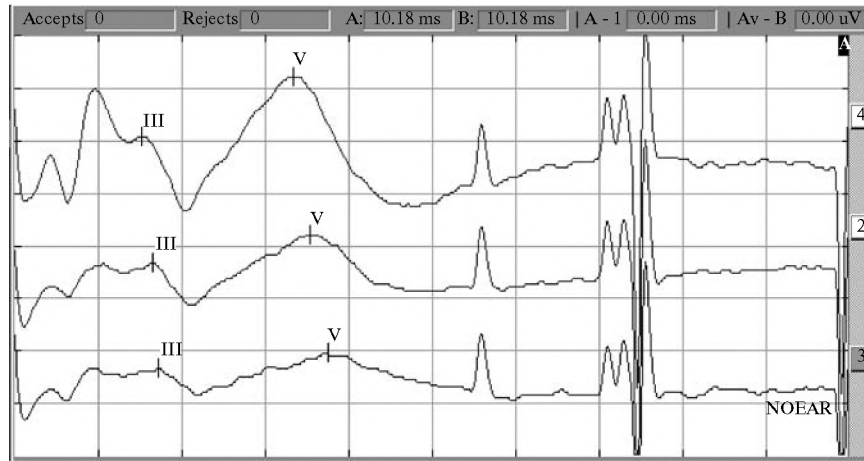


Fig. 9. The EABR waves (from top to bottom) are recorded from the electrode 20, 10, and 3, respectively, under the stimulus with a 50 μ s/phase pulse width, a 48 Hz stimulus frequency, and a stimulus intensity of 20 CL over the threshold. The subject is an 18-year-old female patient with pre-lingual deafness, implanted the cochlea for 8 months. The recording time is 10.2 ms. 1.02 ms per grid is set in the abscissa axis and 0.5 μ V per grid in the ordinate axis.

was used to hide the stimulus artifacts. However, this method does not really solve the problem. This study found that the single polarity stimulus gave rise to tremendous stimulus artifacts, which overlapped the EABR waves during the latency period of 1.2 ms. With the application of the alternate polarity stimulus in this study, the artifacts reduced obviously. Alternating is a basic technique to cancel the stimulus artifacts. A similar result obtained using the technique of neural response telemetry (NRT) was reported by Miller and Abbas [29] in animals and by Dillier et al. [30] in human, although the studies were mainly on early responses.

Band-pass filter. This study also found that the cut-off frequency of the band-pass filter affected the wave latency. First, the low cut-off frequency maintained 100 Hz and the high cut-off frequency was set at 1.5 kHz, 2 kHz, and 3 kHz. It was found that the latency of the wave shortened. While the high cut-off frequency was set at 3 kHz, 5 kHz, 10 kHz, and 25 kHz, the latency of the wave kept steady. The results showed that 3 kHz was a critical frequency. The stimulus frequency below 3 kHz affected the latency of the EABR wave. The appearance of more obvious noises when the high cut-off frequency changed from 10 kHz to 25 kHz showed that large high-frequency noise would be induced if high cut-off frequency was too high. In the ABR test, 3 kHz was usually adopted as high cut-off frequency. It is consistent with our results. Secondly, the high cut-off frequency maintained 3 kHz and the low cut-off frequency was set at 100, 10, 1, 0.2, 0.01, and 0.002 Hz. It was found that the latency of the wave V remained stable.

Test mode. The test mode, testing on the same lateral side or on the contra lateral side, affected the signal collection. On the same lateral side, the collected EABR waves appeared a baseline excursion with obvi-

ous artifacts. However, on the contra lateral side, the EABR waves appeared smooth with slight artifacts. The possible reason might be the distance between the stimulation site and the signal record site. The closer the distance was, the more obvious noise affected the recorded signals. Therefore, the same lateral measurement was liable to be impacted by the stimulus artifacts.

3.2. Characterizations of EABR Wave after Cochlear Implantation

Significantly shorter latency of EABR wave in comparison with ABR wave. This study found that the five EABR waves I, II, III, IV, and V showed a preferable repeatability, which was similar to the ABR waves. However, the latency of the EABR waves was significantly shorter than that of the ABR waves. A previous study reported that the latency of the ABR wave III and V for Chinese people was 3.65 ± 0.25 ms and 5.58 ± 0.26 ms, respectively, under a stimulus of 75 dBHL [10]. In this study, when the stimulus intensity was 20 CL higher than the threshold, the average latency of the wave III and V was 1.75 ± 0.16 ms and 3.57 ± 0.24 ms, respectively, which were shorter than those of the ABR waves. The two results indicate that the difference in the latency of the wave III and V was 1.93 ms and 2.01 ms, respectively. The reason why the latency of the EABR waves shortened might be the

Table 4. The amplitude ratio of wave III and V

| | Elec-trode 3 | Elec-trode 10 | Elec-trode 20 | Average |
|---------------------------------|--------------|---------------|---------------|---------|
| Ratio of wave amplitude (III/V) | 0.37 | 0.34 | 0.41 | 0.35 |

direct impaction of current on the acoustic neuronal spiral ganglion resulting in the omission of some normal voice during perception procedure. In other studies using EABR, the average value of the latency of the EABR wave V was 4.09 ms reported by Truy et al. [11], 4.39 ms by Aubert and Clarke [12], and 4.08 ms by Kubo et al. [13]. These values were different from the result obtained in this study. However, in comparison of the difference in the latency of the wave V between EABR and ABR, the result of a 2 ms discrepancy was basically consistent with this study. Different races, testing environments, equipments and methods might contribute to the difference in latency measurement [9, 14–16].

Differences in EABR threshold and latency measured at different stimulation sites. Nucleus 24 cochlear device has 22 electrodes implanted. The stimuli at the electrode 3, 10, and 20 were used in this study. These electrodes were located near the bottom, central and top of the cochlea. Under a stimulus with a stimulus intensity of 20 CL higher than the threshold, the latency of the EABR wave III and V at the electrode 3 was significantly ($p < 0.01$) longer than those at the electrode 10 and 20. However, there was no significant difference between the values recorded at the electrode 3 and 10 ($p > 0.05$). This might be related to (1) the high survival rate of the spiral ganglion near the top of cochlea in patients with the sensorineural hearing loss, (2) the close distance between the spiral ganglion and the electrodes implanted on the top of the cochlea, and (3) the thicker acoustic neuronal fibers near the top of cochlea [17–19]. In this study, the electrode 20 was implanted on the top of cochlea while the electrode 3 was implanted at the bottom. The difference between the latency values measured at these two electrodes was 0.28 ms. In Allum's study, the difference between the latency values measured on the top and at the bottom of cochlea was 0.4 ms [20].

3.3. Significance of Using EABR to Evaluate Auditory Functions after Cochlear Implantation

The results showed a relatively high appearance rate of the EABR waves, 96.22% for the 53 subjects. The EABR waves were not extracted from two patients. The possible reasons might be the failure in cooperation with the doctors for the one patient with a good subjective hearing response, and the invalid cochlear implantation for the other patient. For the later case, although the position of the implanted electrodes was correct and the cochlear devices worked normally, the patient still had no response to sound after the operation 12 months later. In current, the electrically evoked compound action potential (ECAP) test has been widely used. However, the positive appearance rate of ECAP was less than 90% [21–23]. In addition, the anatomical malformation of the inner ear might induce the disorder of the electric field around the auditory nerve and consequently nerve

cells at different locations induced opposite nerve polarities. They counteracted each other. Therefore, it was difficult to extract ECAP [24, 25]. This study showed that the appearance rate of EABR was higher than that of ECAP. The possible reason is that the EABR [26–28] is recorded in a far field mode, and thus is little affected by the deformity of the inner ear. The results of this study found that the EABR waves recorded a series of neural responses from acoustic nerve, cochlear nucleus, superior olivary nucleus, lateral lemniscus, inferior colliculus, medial geniculate body, and acoustic radiation. Thus, the EABR waves objectively reflected the functions of auditory pathway after cochlear implantation. This method has potentials with a great clinical value.

The purpose of this study was to explore a reality and possible EABR test mode in clinical applications, rather than strict animal research. In a summary, this study determined more appropriate parameters including stimulus polarity, stimulus intensity, stimulus frequency, and cut-off frequency of band-pass filter to stably extract the EABR waves. Our EABR test provides a high positive appearance rate of the EABR waves and more comprehensively evaluates the functions of auditory pathway after cochlear implantation.

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