[原著] Study on the Origin of Acoustically Evoked Short Latency Negative Response

Study on the Origin of Acoustically Evoked Short Latency Negative Response

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ABSTRACT

The authors previously reported a peculiar V-shaped acoustically evoked short latency negative response (ASNR) at approximately 3-4 msec in auditory brainstem response (ABR) data. ASNR was present only in profound hearing loss ears under intense stimulation. It has already been excluded from any kind of artifacts. Since the peculiar V-shaped waveform of ASNR obviously differed from ABR, ASNR was not interpreted as a potential generated from the conventional auditory pathway. The ASNR individuals were of good vestibular function in spite of profound hearing loss, suggesting the relationship between the ASNR and the vestibular system. The saccule and vestibular nuclei were hypothesized to be the sense organ and the generator of the response respectively. In this paper, the cochlear origin of ASNR was excluded, for the recordings were done by sound stimulation to unaided cochlear implant ears, a cochlear functionless model. Furthermore, vestibular evoked myogenic potential (VEMP), a potential of saccular origin, was used to investigate the saccular function for the ASNR ears. The results revealed normal saccular function for all the ASNR ears and hypofunction or afunction for the profound hearing loss ears with absent ASNR. It is clear that the presence of ASNR is dependent on normal saccular function. Based on the results, we believe that ASNR is of saccular origin. *Ryukyu Med. J., 21(1) 35～40, 2002*

Key words: acoustically evoked short latency negative response, vestibular evoked myogenic potential, profound hearing loss, cochlear implant, saccular function

INTRODUCTION

It is known that in the inner ear it is not only the cochlea that can to be activated by sound energy, but also the otolith organs, especially the saccule, responds to intense sounds[1-5]. Vestibular evoked myogenic potential (VEMP) is the muscle activity in response to vestibular stimulation by intense sounds or skull taps. This response has been verified to be of saccular origin[6-9]. Actually, VEMP is one type of vestibular evoked potential (VsEP), however, VsEP usually refers to shorter neurogenic potentials on the level of the brainstem. VsEP is acquired with acceleration stimulation, which is difficult to control[10]. Application of sound stimulation is much easier than applying acceleration stimulation. For this reason, VEMP in the past decade has become a new clinical means for assessing functions of the saccule and inferior vestibular nerve[11-14].

Recently, we reported a peculiar V-shaped acoustically evoked short latency negative response (ASNR), at approximately 3-4 msec, encountered during auditory brainstem response (ABR) tests[15]. ASNR was present only in profound hearing loss ears under intense stimulation (appearance rate, 11.9%). It was excluded from an artifact by its reproducibility over time, equipment and institutes. Moreover, it became absent after external auditory canal occlusion, which simply blocked the air conduction without any influence upon scalp potentials or equipment. It has neural response characteristics that the latency and amplitude shorten and increase respectively when the stimulus intensity is increased. Since the peculiar V-shaped ASNR waveform obviously differs from ABR, ASNR was not interpreted as a potential generated from the conventional auditory pathway. On the other hand, ASNR morphologically resembles VsEP evoked by electrical stimulation at the vestibular nerve[16]. The ASNR ears were of good vestibular functions in sharp contrast to their profoundly impaired hearings. These suggest a probable relation between ASNR and the vestibular system. Both ASNR and VEMP are acoustically evoked non-auditory responses, therefore, they possibly reflect different neuronal activities along the same neural pathway. According to the short latency of 3-4 msec, we speculated that ASNR is virtually one type of VsEPs from the second order neurons at lower part of the brainstem. The saccule and vestibular nuclei are hypothesized to be the sense organ and the generator of the response respectively. This hypothesis explains why ASNR

appears exclusively in ears with unaffected air conduction, normal vestibular function and profoundly impaired hearing, which is free from the superimposition of ABR waves I-V.

In our previous study the vestibular function of ASNR patients were mainly evaluated based on the results of the caloric and rotation tests, which reflect functions of the lateral semicircular canals. The saccular function remains unknown. The present study conducted VEMP test in these ASNR patients in order to reveal their saccular functions. On the other hand, the impossibility of the cochlear origin of ASNR was further studied. ABR was retested postoperatively in part of the ASNR patients receiving cochlear implant, because these implanted ears provide an appropriate model for excluding the cochlear origin of ASNR.

MATERIALS AND METHODS

Twelve healthy normal-hearing subjects (7 males, 5 females, age range 23-30 years) served as the control group. All of them were free from auditory and vestibular symptoms or history and showed bilateral normal pure tone audiograms. The patient group consisted of 20 bilateral profound hearing loss subjects (14 males, 6 females, age range 6-62 years) including some previously reported ASNR patients. There were 16 cochlear implant users in the patient group wearing a Nucleus-22, Nucleus-24 or Clarion implant. They had been using the devices between 6 months and 7 years at the time of investigation. All these patients were free from retrolabyrinthine lesions. During each test session for the cochlear implant users, the power of the speech processor was turned off and the headset was taken off. Prior to the test sessions, type A tympanogram was confirmed in every ear to exclude conductive hearing disorders.

VEMP Recordings

An evoked potential system, Neuropack Λ (Nihon Koden Corp. Tokyo), was employed to collect VEMP and ABR in a magnetically shielded and sound proof room. Monaural sound stimulation of clicks generated by 0.1 msec electrical pulses were presented to the subjects at a rate of 5/sec through shielded THD-39 headphones. The highest intensity used was 105 dB nHL (normal hearing level). Surface electromyographic activity was collected with Ag/AgCl disc electrodes placed on symmetric sites over the upper half of each sternomastoid muscle with the reference electrode over the upper edge of the sternum and the ground electrode over the forehead. During the recording, the subjects were instructed to rotate their heads to the opposite site of the stimulated ear in order to activate the sternomastoid muscle. Analysis time was 50 msec. The response was amplified and bandpass filtered (20-2000 Hz). Responses to 200 stimuli were averaged for each intensity.

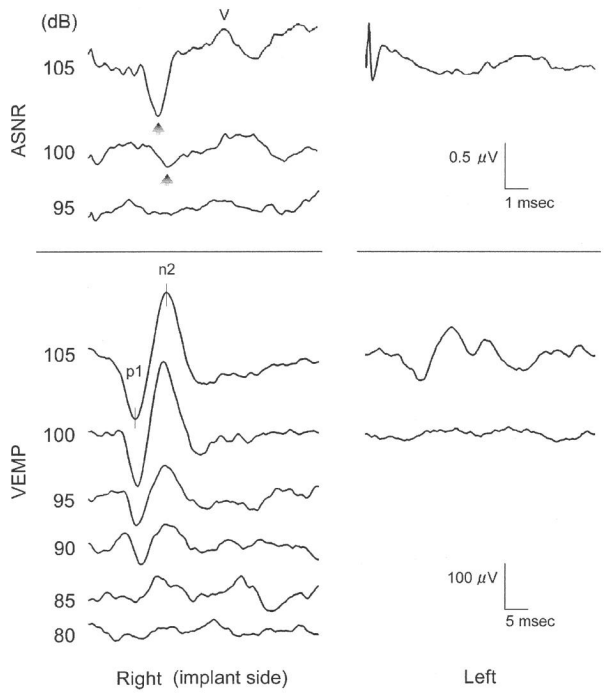

Fig. 1 The ASNR and VEMP waveforms of a 6-year-old boy whose right ear was cochlear implanted. ASNR is a negative deflection at around 3 msec (arrows). VEMP is a biphasic deflection consisting of a positive peak (p1) at around 13 msce and a negative peak (n2) at around 23 msec. ASNRs were present on the right side, the implanted side. At stimulation of 105 dB, the later small upward peak was considered as wave V. VEMPs on this side were clearly recorded with normal threshold. For the left side, ASNR was absent, and VEMP could not be elicited without the maximum stimulus intensity.

ABR Recordings

The ABR recording technique has been described in detail in a previous report[15]. Briefly, click stimuli were presented at a rate of 10/sec, the non-stimulated ear was masked with continuous white noise 40 dB lower than the stimulus sound. The active, reference and ground electrodes were respectively placed on the mastoid (stimulated side), vertex and forehead. Analysis time used was 20 msec. Bandpass filter was set between 100-2000 Hz. Responses were averaged over 1000 sweeps.

Data Analysis

Parameters of the threshold, latencies and peak-to-peak amplitude for the VEMP p1-n2 wave were measured. Depending on the presence/absence of ASNR in ABR data, the ears in the patient group were further divided into two groups, the ASNR group and non-ASNR group. Paired t test, chi-square test, and one-way ANOVA test were performed for statistical analysis with SPSS 10.07 package for Windows (SPSS Inc. Chicago). The differences or changes under $p=0.05$ were considered statistically significant.

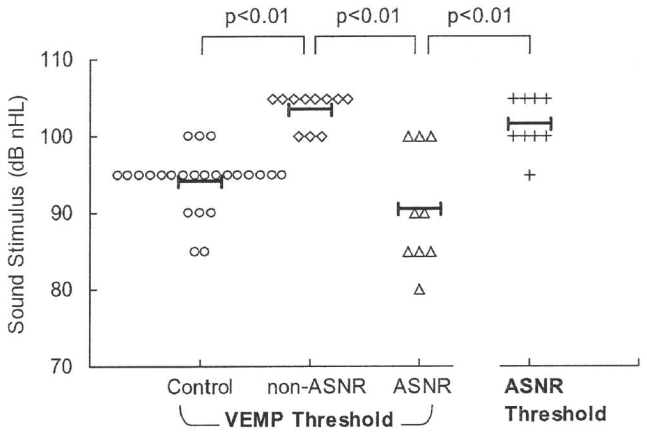

Fig. 2 Summary of the VEMP thresholds for all the groups in conjunction with the ASNR thresholds. In comparison with the other two groups, statistically significant higher VEMP threshold of the non-ASNR group was noted. Additionally, for the ASNR group, the ASNR threshold is significantly higher than the VEMP threshold. Short bars symbolize means.

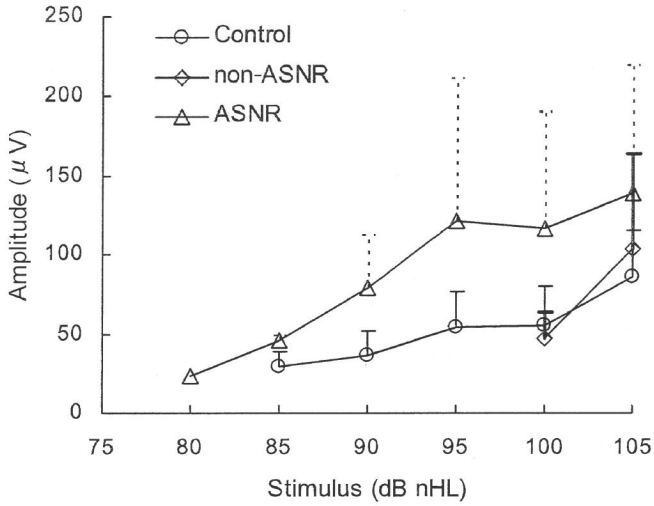

Fig. 3 The Amplitude of VEMP (means and standard deviations) for each group as a function of stimulus intensity. The amplitude was magnified by increased stimuli. The response size was much larger in the ASNR group than in the other two groups. Moreover, it is noted that the amplitude of the ASNR group greatly varied.

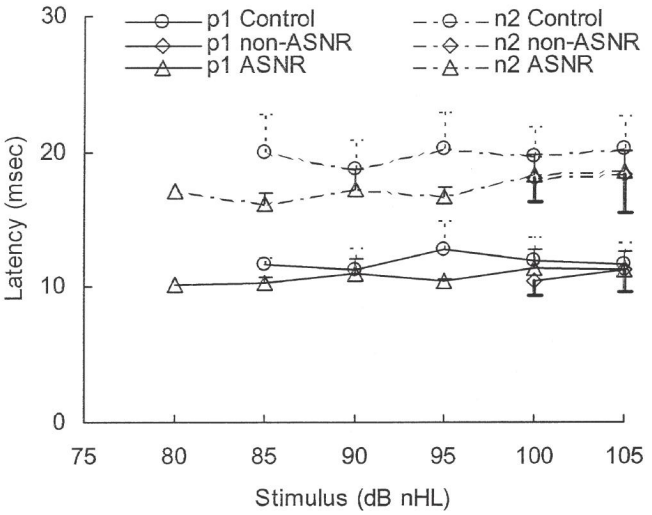

Fig. 4 The Latencies of the p1 and n2 peaks (means and standard deviations) for each group as a function of stimulus intensity. The latencies keep unchanged at any levels of stimulation. Although both the latencies of p1 and n2 for the control group were slightly longer, the three groups were not obviously distinguished from each other.

RESULTS

VEMP, the biphasic wave p1-n2, was present bilaterally in all the subjects in the control group with a threshold range of 85-100 dB nHL (mean, 94.2 dB). ASNR was present in 9 ears (8 subjects), the ASNR group, in which three were cochlear implant ears (Fig. 1). On the other hand, 4 cochlear implant ears showing pre-implant ASNRs were allotted to the non-ASNR group due to the absence of ASNR after implantation. The ASNR threshold was in the range of 95 to 105 dB nHL (mean, 101.7 dB). VEMPs were obtained from each ear in the ASNR group. The threshold was in the range of 80 to 100 dB nHL (mean, 90.6 dB) (Fig. 1). A paired t test revealed that the VEMP threshold is significantly lower than the ASNR threshold in this group ($p<0.01$) (Fig. 2). The threshold difference between the two types of responses ranged from 0 to 20 dB (mean, 11.1 dB). Although two ears demonstrated similar thresholds for the two types of responses at 100 dB nHL, ears with VEMP threshold higher than ASNR threshold were not found.

In 11 ears of the non-ASNR group (31 ears), VEMPs were elicited (threshold range, 100-105 dB nHL; mean, 103.6 dB), This resulted in a significantly lower appearance rate in comparison with the ASNR group ($p<0.01$, chi-square test). A comparison among the VEMP thresholds of all the groups was executed by one way ANOVA test. Higher values were found in the non-ASNR group compared with the control and ASNR groups ($p<0.01$), while there was no statistically significant difference between the control and ASNR groups ($p>0.05$) (Fig. 2).

The amplitude of VEMP was magnified by increased stimuli. The response size was much larger in the ASNR group than in the other two groups, particularly at high stimulus levels (Fig. 3).

The latencies of the p1 and n2 peaks of VEMP did not vary with the stimulus intensity. Although both the latencies of p1 and n2 for the control group were slightly longer, the three groups were not obviously distinguished from each other (Fig. 4).

DISCUSSION

The acoustically evoked short latency negative re-

Table 1 Saccular function in all groups

Group (ears)	Saccular function	
	VEMP (ears)	Absent VEMP (ears)
Control (40)	Normal (40, normal thresholds)	− (0)
ASNR (9)	Normal (9, normal thresholds)	− (0)
non-ASNR (31)	Hypofunction (11, raised thredsholds)	Afunction (20)

sponse at approximately 3 msec, which appeared during ABR recordings in child candidates for cochlear implant, was first reported by Mason[17]. Shiraisi and Kato et al. termed this response "N3" according to its polarity and latency[18,19]. Unfortunately, for such an isolated response, the name N3 is inappropriate and confusing, because N3 terminologically represents the third negative potential in consecutive responses. In addition, N3 is sometimes unable to represent the response latency accurately due to prolonged latency (4 msec) under stimulation of tone pips[15]. In a previous study, from ABR data over 18 years, we found 117 ears with such a response, and termed it ASNR. Many of its physiological behaviors clarified the impossibility of an artifact. Although the neurological origin of ASNR is still not clear, its peculiar waveform unlike ABR and the profoundly impaired hearings of ASNR ears lend support to its non-cochlear origin[15].

Nevertheless, with regard to the residual hearing of profound hearing loss ears, the possibility of cochlear origin could not be completely ruled out. For this reason, we investigated whether ASNR is present in ears without residual cochlear function, cochlear implant ears. Boggess *et al.* assessed post-implant pure tone threshold responses in cochlear implant recipients who had some measurable residual hearing before implantation[20]. The results revealed significantly deteriorated hearings in all implanted ears, while hearings in non-implanted ears remained stable. Other researches have demonstrated that the structure and neural elements in the cochlea may be damaged by both traumatic prosthesis insertions during surgery and long-term electrical stimulation[21-23]. Even if an experienced surgeon can insert an intracochlear electrode array without any trauma to the membrane labyrinth, being a space-occupying foreign body in the scala tympani the prosthesis interferes with the natural mechanism of the cochlea. To our experiences, an intracochlear electrode array influences hearing but usually it does not erase hearing, residual hearing is seen in many implant recipients.

In the present study, there were 3 cochlear implant ears with almost unaltered pre- and post-implant ASNR thresholds. Among them, only one ear became totally deaf after implantation, the other two ears deteriorated but still showed residual hearings with pure tone averages (PTA) of 105 and 110 dB nHL respectively. As shown in Figure 1, under stimulation of 105 dB, posterior to ASNR an upward peak is detected at 6 msec. The peak is considered to be wave V of ABR, which reflects the residual hearing (PTA 105 dB nHL) in this ear. These three cochlear implant ears clarified the non-cochlear origin of ASNR; otherwise, the post-implant ASNR should have been absent or should have been with raised threshold. The only possible origin of ASNR is vestibular. In contrast to the deterioration of residual cochlear function posterior to intracochlear implantation, the post-implant vestibular function is uncertain. It may either remain unaffected or decline[24,25]. The vestibular function is considered normal in the implanted ears with ASNR, while it may deteriorate to various degrees in others, in which the ASNR disappears after implantation.

It has been proved that among the vestibular organs only the otolith organs, especially the saccule, responds to sound stimulation, while the semicircular canals do not[2,4]. Based on this theory, ASNR is thought to be of saccular origin[15]. If so, the presence/absence of ASNR and VEMP should be parallel, since VEMP is also of saccular origin[9]. In this study, as summarized in Table 1, VEMP threshold in the ASNR group was found to be in the normal range. This implies normal saccular function. In the non-ASNR group, about two thirds demonstrated absence of VEMP, suggesting saccular afunction. The remaining one third showed raised VEMP thresholds in comparison with the control and ASNR groups, suggesting saccular hypofunction. It is clear that the presence of ASNR is dependent on normal saccular function. In other words, ASNR is of saccular origin. The mean VEMP size in the ASNR group was much larger than other groups. This fact dose not lead to a conclusion of saccular hyperfunction, because sound or pressure induced vertigo and abnormally low threshold for VEMP were not seen, which are notable signs for vestibular hyperfunction disorders, for example, the Tullio phenomenon[12-14]. The VEMP size varies to a great extent even in the ASNR group (Fig. 3). Extremely large responses were found in only two subjects. This deviation is due to inter-individual variance.

Although ASNR and VEMP are of similar origin, their thresholds differ from each other. In the ASNR group, the threshold of VEMP was significantly lower than that of ASNR. This may be due to the differences in their recording techniques. In accordance with the 3-4 msec

short latency of ASNR, its recording acquires volume-conducted potentials generated from some nuclei located in the brainstem (scalp far-field neurogenic potentials). "Far-field" describes the position of the recording electrodes as being far from the active tissue itself on the outside of the skull. Electricity is conducted by the volume-conductor, the brain and other tissues within the skull. Far-field potentials attenuate with the increase of the distance between the potential generator and recording site. The neural activities near threshold are usually beyond measurement of scalp electrode recording[26]. For VEMP, a near-field myogenic potential with the recording electrode adjacent to the active muscle, its threshold is lower and close to the threshold of neural and muscular activities. Comprehensible examples are available from responses having cochlear origin, ABR and post-auricular myogenic response (PAR)[27], which are also far- and near-field potentials respectively. Except for the strong wave V of ABR, other responses from the brainstem nuclei are undetectable unless the stimuli are 40-50 dB above the subjective auditory threshold. Contrarily, the sound-evoked PAR can be detected at levels only 10-20 dB above the subjective threshold[28].

In conclusion, this study substantiates that the receptor organs of ASNR and VEMP, the saccule, are identical. The short latency of 3-4 msec indicates that the generator site of ASNR is the second order neurons at lower part of the brainstem. The most possible generator is the vestibular nuclei.

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