Table 1. Tone bursts used in the experiments: I, intensity; F, frequency; RF, rise-fall time; and D, duration.

I (dBSPL)	F (kHz)	RF (ms)	D (ms)
40, 60, 80	5	1, 5, 10, 20	300
60	5	5	200, 300, 500
80	5, 20, 40	5	300

contralateral to the exposed cortex, delivered acoustic stimuli with a repetition rate of 0.5–0.9/s. The stimuli delivered were monitored by a microphone placed near the auricle and presented in dBSPL (sound pressure level in dB re 20 μPa). Tone bursts were used as test stimuli, and frequency, intensity, rise and fall time, and duration served as parameters (Table 1). In addition, an 80 dBSPL click was used for reference. All the data presented are the average of 150 trials.

All experiments were conducted within the guidelines of the Animal Experiments Committee of the University of Tokyo.

Data analyses: The cortical AEP of a rat has typical fast positive/negative biphasic onset waves (P1/N1) followed by slow biphasic waves (P2/N2), thereby forming the P1-N1-P2-N2 complex. Under particular conditions, this complex is then followed by relatively fast biphasic offset waves (P_{OFF}/N_{OFF}). We first digitally filtered the measured AEP and separated the fast P1/N1 and P_{OFF}/N_{OFF} waves from the slow P2/N2 waves. We routinely used a zero-phase finite impulse response filter with a 129th order and passband of 10–80 Hz. The passband was sometimes readjusted depending on the predominant frequency range of the measured AEP.

We identified the overall characteristics of offset responses by taking the root mean square (RMS) values within 100 ms after the stimulus termination and averaging RMS values across recording sites. This averaged RMS value refers to an offset cortical activity level (CAL) in this work. Likewise, average RMS values within 100 ms after the onset of stimuli and without stimuli were also defined as onset and spontaneous CAL, respectively, and measured for reference. The time range of CAL was changed depending on filter passband.

We obtained the distribution of onset (P1-N1) and offset (P_{OFF}-N_{OFF}) amplitude and estimated the location of local maximum. To pool the peak location across animals, all the peak locations were plotted in the coordinate, in which the locations of the click-evoked P1 maximums were taken as a common origin. We also explored the onset tonotopic representation for reference by extracting the local maximum of P1 of a faint 40 dBSPL tone. This local maximum is expediently called the characteristic frequency (CF) location according to the test frequency. We finally characterized the amplitude and latency of maximally responsive onset and offset potentials as a function of test frequencies.

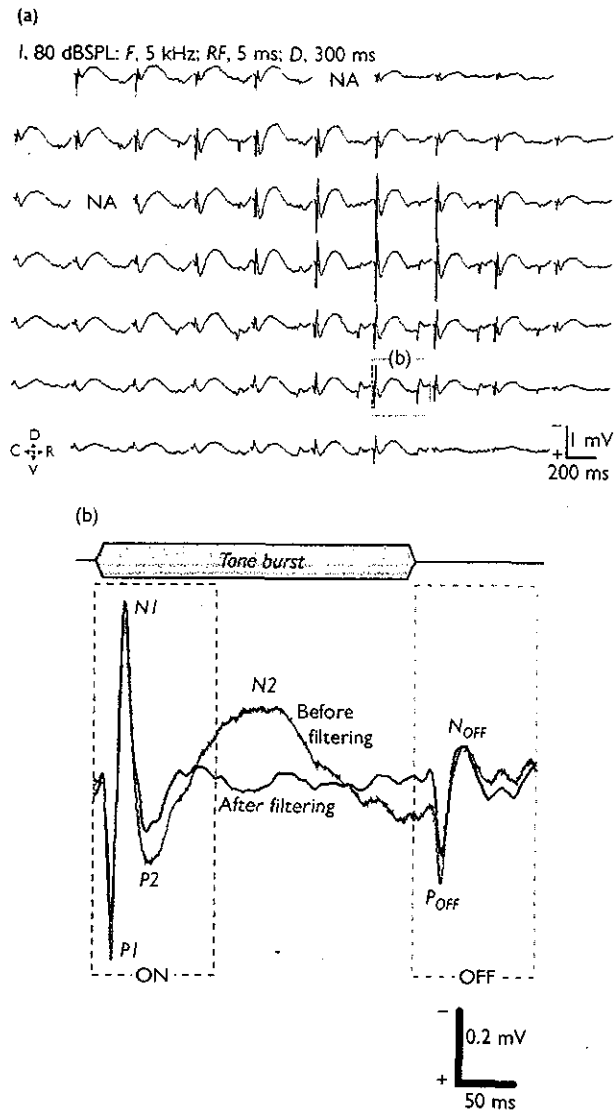

Fig. 1. Experimental data analyzed. (a) Cortical map of tone-burst-evoked potentials. An experimental condition is indicated in each inset here and hereafter. R, rostral; C, caudal; D dorsal; and V, ventral. (b) Definition of the evoked potential waves (P1, N1, P2, N2, P_{OFF}, N_{OFF}) and filtering of the waveform.

RESULTS

Figure 1a shows the typical AEP patterns mapped over the auditory cortex, and Fig. 1b defines the AEP waves (P1, N1, P2, N2, P_{OFF}, and N_{OFF}) and shows how the filtering separated onset and offset components from the measured AEP.

Offset CAL was as low as the spontaneous CAL under 40 and 60 dBSPL, but was significantly higher than the spontaneous CAL under 80 dBSPL (two-side *t*-test here and hereafter for statistical analyses, $p<0.01$), suggesting that distinct offset responses were produced (Fig. 2a,i). Shortening a fall time induced a high offset CAL (20 ms *vs* 1 ms, $p<0.01$). Nevertheless, tones with an intensity of 80 dBSPL and a fall time of 10 ms resulted in a significantly larger offset CAL than tones with 60 dBSPL and 1 ms fall time ($p<0.01$), despite the same decreasing rate. In contrast, onset CAL was generally determined only by the increasing rate of pressure change at a stimulus onset, and CAL at the same increasing rate but different intensities were not statistically significantly different ($p<0.1$). Offset responses

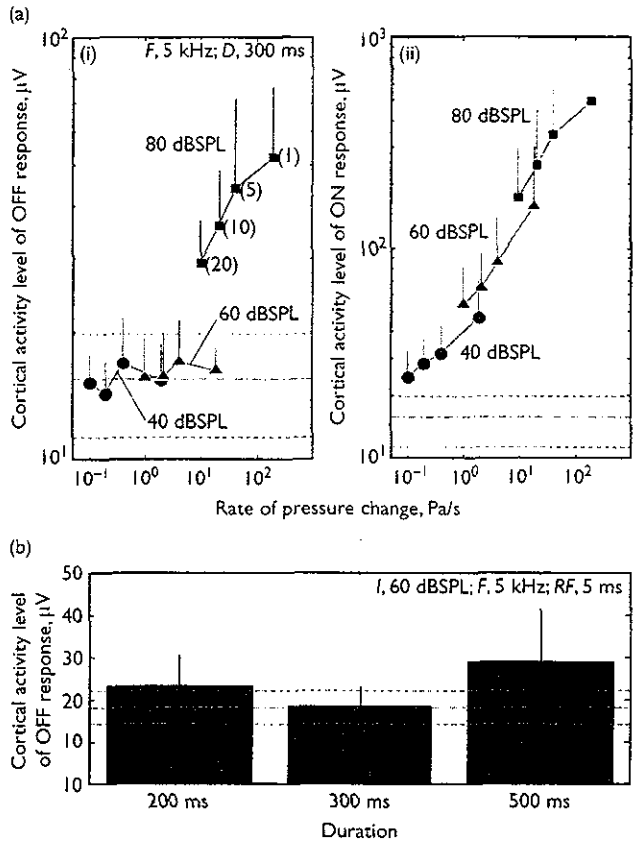

Fig. 2. Cortical activity level. **(a)** Offset (i) and onset (ii) CAL as a function of rate of pressure change (Pa/s). Digits in parentheses indicate rise-fall times. A bar on each marker indicates s.d. here and hereafter. Dashed and broken lines indicate the mean and s.d. of a spontaneous CAL, respectively. **(b)** Offset CAL as a function of duration. Because offset responses of 500 ms duration tones contained frequencies lower than 10 Hz, we used a 5–80 Hz filter and obtained 200 ms RMS values for CAL.

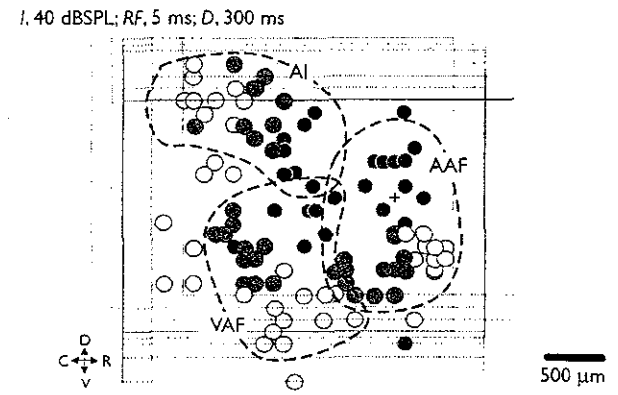

Fig. 3. Tonotopic representation obtained from 12 rat auditory cortices and tonotopicity-based identification of AI, AAF, and VAF. Test frequencies: white, 5 kHz; half tone, 20 kHz; and dark, 40 kHz. PI local maximums of 40 dBSPL tones were plotted with respect to 80-dBSPL-click-evoked PI (+). Squares indicate sensing areas of individual cortices.

were also sensitive to sound duration (Fig. 2b), and long-duration stimuli generally produced large offset responses (e.g. 500 ms duration *vs* 300 ms duration tones, $p<0.05$). However, 200 ms duration tones also evoked larger offset responses than 300 ms duration tones ($p<0.1$), suggesting that offset responses have more complicated duration-tuning characteristics.

AI, AAF and VAF of a rat showed different tonotopic organizations (Fig. 3). AI had a clear posterior-to-anterior tonotopic gradient from low to high frequencies, while AAF and VAF forms a C-shaped tonotopic organization with low- and high-frequencies rostrally and dorsocaudally, respectively. On the other hand, offset responses had a poor tonotopic distribution, but generally appeared at the fringe of their onset responses, resulting in spatial segregation between the onset and offset responses (Fig. 4). Both offset and onset responses appeared over the entire auditory cortex, and the largest responses were usually obtained from AAF. Compared with the tonotopic map (Fig. 3), offset responses were commonly distributed in different CF locations with respect to a test frequency: e.g., the offset responses to 5 kHz tones were elicited in 40 kHz CF location in AI, and 20 kHz CF locations in AAF and VAF.

The amplitude of offset responses (P_{OFF}-N_{OFF}) at a maximally responsive location was sensitive to the test frequencies, and high frequency tones produced large offset responses (5 kHz *vs* 40 kHz, $p<0.01$), while onset responses (P1-N1) were independent of test frequencies (Fig. 5). Likewise, high frequency tones resulted in short latencies in offset responses (P_{OFF}, N_{OFF}; 5 kHz *vs* 40 kHz, $p<0.01$), while no significant difference was observed in onset responses (P1, N1).

DISCUSSION

Tones with high frequency, short fall time, and long duration generally elicited large offset responses. High-frequency selectivity was not reported previously, but this could be species-specific, given that a frequency domain conveying important information is likely different across animals (e.g., ultrasonic communication for rats, sonic communication for human, and specific frequency range for bat echolocation). A similar fall time tuning was found in a human ABR [2], and the duration tuning was also consistent with several animal unit studies from the midbrain [6,11,14] to auditory cortex [15].

Offset responses showed poor tonotopicity and generally appeared at the fringe of their onset responses. Our results directly verified the previous human MEG studies of the auditory cortex, which inferred that the sources of offset responses slightly differed from onset sources [3], and that the high-frequency offset sources were located close to the low-frequency onset sources [4]. Such distributions may be associated with the complementary tuning characteristics of onset and offset responses, which were found by ABR studies [1], and unit studies in the thalamus [13] and cortex [17]; the tuning curves of offset components had two peaks: one at a frequency lower than and the other at a frequency higher than the onset tuning frequency.

Previous patch-clamp recording and pharmacological studies showed evidence that duration-tuned neurons and off neurons probably receive inhibitory inputs prior to the excitation at the stimulus onset and that inhibition is strongest at its onset and is sustained throughout the duration of a sound [7–9]. Taken together with our results, an offset response may be formed by a rebound after an inhibitory input [10,12,19], and the rebound can mainly explain our results as well as previous findings. First, sound

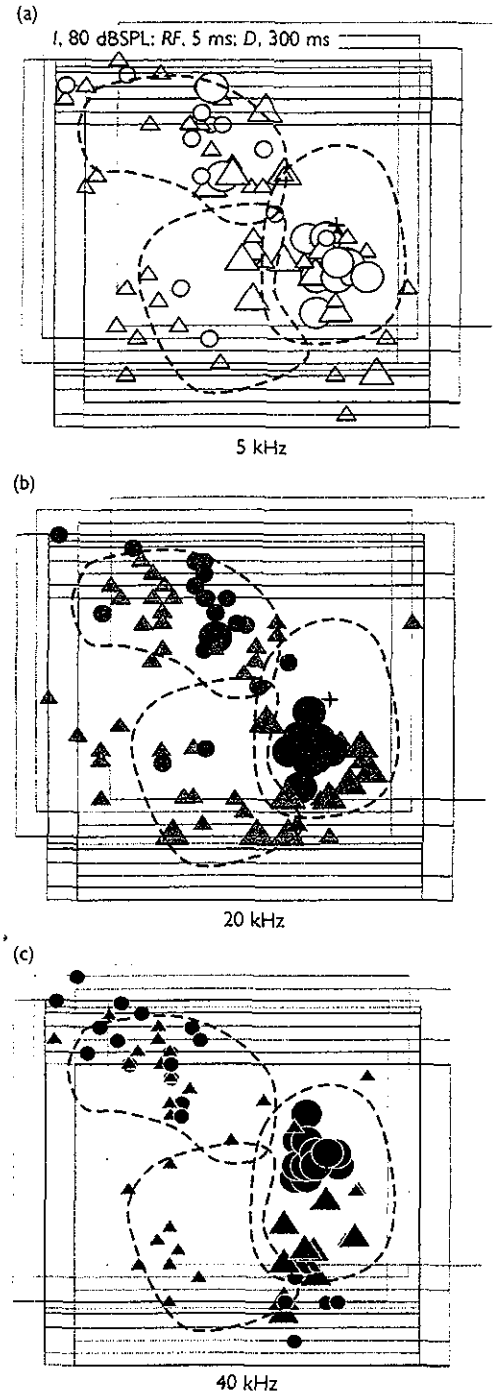

Fig. 4. Local maximums of onset (circles) and offset (triangles) responses recorded from 12 rat auditory cortices. Test frequencies: (a) 5 kHz; (b) 20 kHz; and (c) 40 kHz. Large symbols indicate the maximally responsive locations. See Fig. 3 for the presentation conventions.

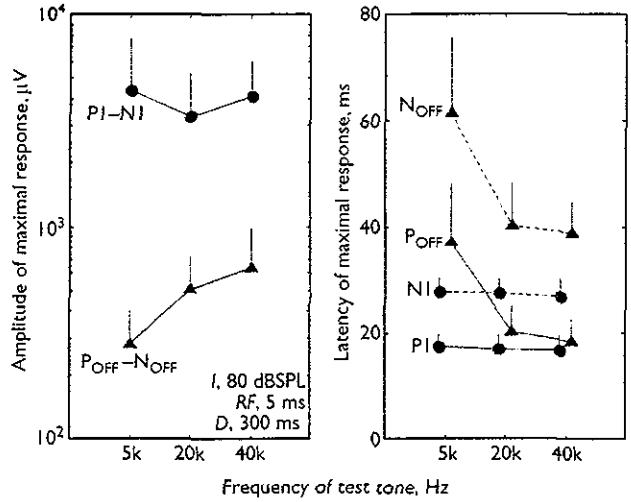

Fig. 5. Amplitude and latency of maximal onset (circles) and offset (triangles) responses as a function of test frequency.

intensity and duration may have relevance to inhibitory strength and period, thereby causing a stronger resumption when intensity and duration increase. Second, a short fall time may make the rebound more synchronous, thereby enhancing responses. Third, the spatial patterns of onset and offset responses may reflect the excitatory and inhibitory response areas of the common tune curves of cortical neurons, in which the inhibitory response areas, known as inhibitory sidebands, usually flank the excitatory response areas [19]. The extrinsic optical recording in the guinea pig auditory cortex also demonstrated that the excitatory response areas were sandwiched or surrounded by inhibitory areas [20], and this may explain the poor *tonotopicity of offset responses*.

The dominant recruitment of inhibition and the complicated interaction of excitatory inputs could endow offset responses with more ambiguous characteristics than onset responses. Difference in binaurality, amplitude, or spectral bandwidth can influence the temporal interaction [8,10] and the integration of this interaction can induce context-dependent changes in the response properties of neurons. Many neurons commonly show changes in their general duration-tuning characteristics and sometimes their response type (i.e., on, on/off, and off), depending on sound intensity, stimulus repetition rate, and stimulus type [11,13,14,16].

CONCLUSION

The present study characterized the auditory-evoked offset responses of the rat auditory cortices by multiple-site surface microelectrode recording. Offset responses were facilitated when the intensity of test tones was high, the fall time was short, and the duration was long. Offset responses did not appear tonotopically, but at the fringe of tonotopic onset distributions. A rebound after the inhibition in the presence of a stimulus may best explain our results, and yet some complicated interactions with other inputs should be taken into account for a unified view of duration-tuned offset responses.

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Vestibular-evoked myogenic potentials in three patients with large vestibular aqueduct

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Abstract

An enlarged vestibular aqueduct (LVA) is a common congenital inner ear anomaly responsible for some unusual vestibular and audiological symptoms. Most of the cases show bilateral early onset and progressive hearing loss in children. The gross appearance on CT scan of the inner ear is generally normal. However, precise measurements of the inner ear components reveal abnormal dimensions, which may account for the accompanying auditory and vestibular dysfunction. Despite extensive studies on hearing and the vestibular apparatus, saccular function is not studied. To our knowledge this is the first report of saccular malfunction in three patients with LVA by means of vestibular evoked myogenic potentials. Conventional audiograms revealed bilateral severe sensorineural hearing loss in two patients and mixed type hearing loss in one patient. Two of the patients complained about vertigo and dizziness but vestibular assessments of the patients showed normal results. The diagnosis had been made by high-resolution CT scans and MR images of the skull that showed LVA in the absence of other anomalies. The VEMP threshold measured from the ear with LVA in two patients with unilateral enlargement of the vestibular aqueduct was 75–80 dB nHL whereas the threshold from normal ears was 95 dB nHL. The third patient with mixed type hearing loss and bilateral LVA had VEMP responses despite a big air–bone gap in the low frequency range. The VEMP in this patient was greater in amplitude and lower in threshold in the operated ear (the patient had a tympanoplasty which did not improve her hearing). These findings and results of other patients with Tullio phenomenon and superior semicircular canal dehiscence, who also showed lower VEMP threshold, confirmed the theory of a 'third window' that allows volume and pressure displacements, and thus larger deflection of the vestibular sensors, which would cause the vestibular organ to be more responsive to sound and pressure changes.

Key words: Large vestibular aqueduct; Vestibular-evoked myogenic potential; Vestibular; Myogenic potential; Sacculus end-organ hypersensitivity; Vestibulocollic reflex

1. Introduction

Although the vestibular end-organs are primarily responsive to head movement and acceleration, non-physiological stimuli, including sound, have been shown to be capable of activating populations of vestibular afferents. Behavioral and physiological studies indicate that the sacculus functions in part as a hearing organ in several non-mammalian species (fish, Popper and Fay, 1973; rays, Löwenstein and Roberts, 1951; toads, Moffat and Capranica, 1976; and birds, Wit et al., 1984) as well as in mammals. For example, sensitivity of the sacculus to sound has been demonstrated among mammals, including guinea pigs (Cazals et al., 1983), cats (MacCue and Guinan, 1995), and squirrel monkeys (Young et al., 1977). In humans, intense sound and vibration can produce vestibular reflexes and illusions of movement (Von Békésy, 1935; Lackner and Graybeil, 1974; Parker et al., 1975). Evidence of this kind suggests that the mammalian sacculus has retained sensitivity to sound. In a series of reports, Bickford et al. (1964) reported an 'inion response' to loud sound and

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Abbreviations: LVA, large vestibular aqueduct; LVAS, large vestibular aqueduct syndrome; VA, vestibular aqueduct; VEMP, vestibular-evoked myogenic potential; SCM, sternocleidomastoid muscle; STB, short tone burst

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speculated that those potentials arise from vestibular afferents, specially the saccule. The effect of loud clicks was further investigated by Colebatch et al. (1994), who, using a different recording site, revealed a biphasic response which was called vestibular-evoked myogenic potential (VEMP). VEMP are muscle reflexes recorded by surface electrodes following repeated high-intensity auditory stimulation. Averaging techniques, similar to those used to record auditory brainstem potentials, are used to capture the VEMP. VEMP evoked by air- and bone-conducted sound, head tapping and DC currents are regarded as a clinical test of the vestibulocollic reflex, especially the sacculocollic reflex.

The vestibular aqueduct (VA) is a bony canal in the otic capsule originating on the medial wall of the vestibule and extending toward the cerebellar face of the petrus pyramid (Arcand et al., 1991). It contains a vein, an artery and the endolymphatic duct. Large vestibular aqueduct syndrome (LVAS) is one of the most common congenital inner ear deformities. Enlargement of the VA is considered to be a minor dysmorphology belonging to the family of Mondini dysplasias. It is clinically important because various types of hearing impairment or vestibular disturbance usually accompany the inner ear malformation (Bauman et al., 1993; Elverland and Mair, 1983). The cause of this functional anomaly is still unknown; it probably results from arrested or aberrant embryologic development of the endolymphatic duct. Identification and clinical detection of the enlarged VA was described by Valvassori and Clemis (1978). The LVA can be recognized on CT scan. Magnetic resonance images (T2-weighted gradient echo) are thin sections able to provide contrast between intralabyrinthine fluid and bone so that all details of the malformation become visible such as its extension into the posterior fossa. The VA is regarded as enlarged if the diameter of the midpoint of the aqueduct or endolymphatic duct on axial images is greater than 1.5 mm. Involvement is bilateral twice as often as unilateral and often associated with radiographically identifiable inner ear anomalies. These anomalies include enlargements of the vestibule, dilation of the ampullated portions of the horizontal and superior semicircular canals, and cochlear abnormalities (Schuknecht, 1980). The enlarged VA comprises abnormalities not only in the structure of the inner ear, but also in the physiology of the auditory and vestibular systems. The clinical picture is variable. Hearing loss ranges from mild to profound, varying from fluctuating to stepwise progressive or sudden. Vestibular disturbances range from mild imbalance to episodic vertigo. While there are many reports on clinical and histopathological findings in LVAS, only a few studies on the vestibular function in patients with LVA have been published. The exact status of the functional structures, degree of abnormality in critical tissue and organs and how they are affected over time by the defective pattern are not known. This study was designed to investigate the vestibular function especially saccular function and sacculocollic reflex in patients with LVA by means of VEMP.

2. Materials and methods

2.1. Patients

Three patients took part in the study. The primary complaint of patients was difficulty in hearing. Patients underwent routine laboratory testing in addition to neurological and neuro-otological evaluation. At direct otoscopic examination patients had normal tympanic membranes and were free of anomaly in the external auditory canal. On high-resolution CT they had normal middle ear, cochlea, and semicircular canals but enlarged VA.

2.2. Audiometry

Pure tone air- and bone-conducted audiometric thresholds were obtained from each patient over the frequency range of 125–8000 Hz.

2.3. Clinical tests of stability

The Romberg and Mann tests with eyes open and closed and the Unterberger stepping test were scored for each patient.

2.4. Caloric testing

Water (20 cc) was used to irrigate the external auditory meatus to induce a thermal gradient across the lateral semicircular canal. The provoked nystagmus was recorded on a Rion ENG recorder. The slow phase velocity of a number of nystagmus beats at response culmination were averaged and recorded. Paresis and directional preponderance were calculated by the Jonkee formula.

2.5. VEMP

VEMP recording techniques have been previously described in detail (Sheykholeslami et al., 2001a,b). Patients were placed in the supine position on a gurney within a sound-treated room. They were instructed to turn and hold their heads as far as possible toward the side contralateral to the stimulated ear (thereby activating the ipsilateral SCM). At that point, the overall electromyogenic (EMG) activity of the SCM was set as the reference level of the tonic contraction (usually 100–400

μV). Patients were asked to maintain contraction at this level throughout the test session (approximately 30 s). Surface EMG activity was recorded by means of Ag/AgCl electrodes. The active electrode was placed over the middle portion of the ipsilateral SCM muscle body as this location appears to generate the most reliable and consistent responses (Sheykholeslami et al., 2001b). The reference and the ground electrodes were placed over the upper sternum and on the midline forehead, respectively. Impedance was less than 20 kΩ. EMG responses were averaged over a series of 128 stimuli and each series was repeated. Auditory stimuli consisted of short tone bursts (STBs) (500 Hz, rise/fall time = 1 ms, plateau = 2 ms), presented to the ear ipsilateral to the contracted SCM muscle. The intensities used were within the range 60–95 dB nHL. The other ear was masked with white noise at 40 dB less than contralateral STB intensities. EMG responses from each side were amplified, bandpass-filtered (20 Hz to 2 kHz) and averaged by a Neuropack evoked potential recorder (Nihon Kohden, Japan). Analysis time was 100 ms. The two recordings were averaged, thus being the average response of 256 sound presentations. Thereafter, the mean peak latency (in milliseconds) and the peak-to-peak amplitude (in microvolts) of each peak (p13 and n23) were measured. These potentials (p13–n23) are known to be of vestibular origin [Colebatch et al., 1994].

3. Case reports

3.1. Patient 1

This 31-year-old female is suffering from hearing loss more pronounced in the right side. She had noticed the problem since she was 6 years old. The right ear was diagnosed off the audiogram scale and the left ear with severe hearing loss. Since then she had been using a hearing aid on the left ear with small benefit. The left ear had fluctuated and worsened over the last 3 years. She had also suffered from tinnitus in the left ear since 6 years old. Although her balance was not severely impaired, she did have sensation of giddiness and dizzi-

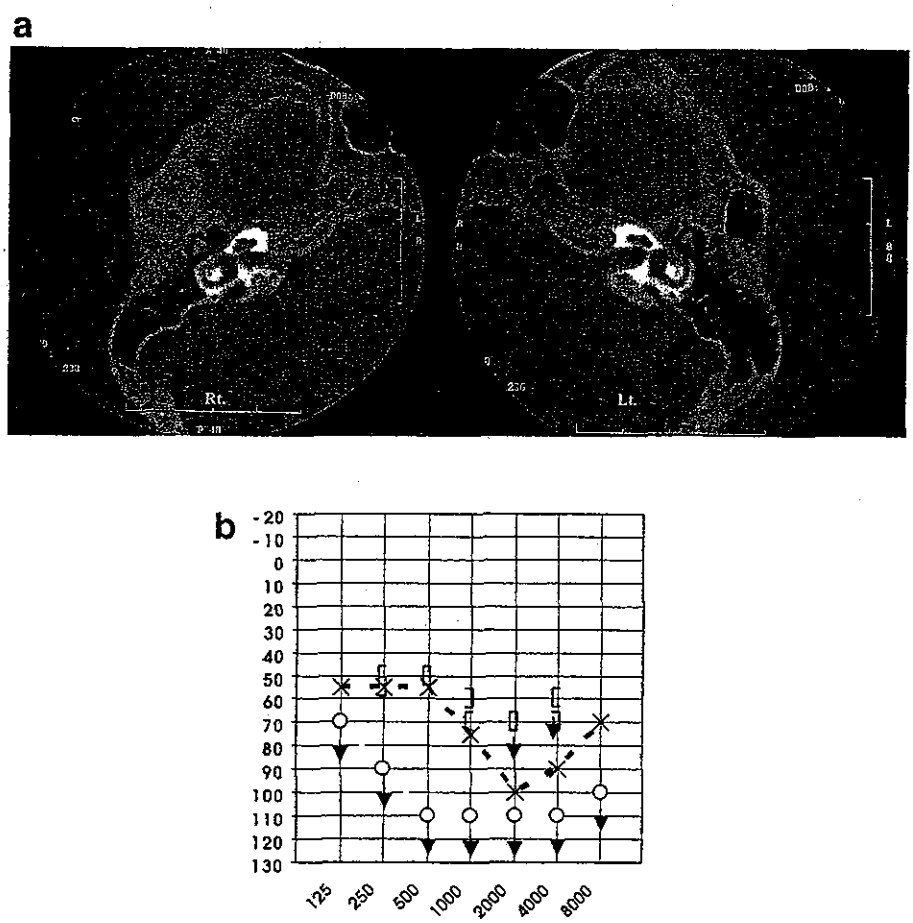

Fig. 1. (a,b) Computed tomograms of the temporal bone of patient 1 (31-year-old female) which revealed unilateral enlargement of the VA. Pure-tone audiogram of the same patient revealed severe hearing loss in the left ear and off the audiogram scale in the right ear. O = right air-conduction hearing level; × = left air-conduction hearing level; [= right bone-conduction hearing level;] = left bone-conduction level.

ness for the last 21 years. Past medical history indicate renal tubular acidosis and allergic rhinitis.

Examination revealed an asymmetrical hearing loss, severe in the left ear (threshold 78.8 dB), more pronounced in the high-frequency range and off the audiogram scale in the right ear (Fig. 1a). Speech and auditory brainstem response threshold was also elevated in both ears (data are not shown).

Neurological and motor system evaluations were normal. Romberg, Mann and stepping tests showed normal results with eyes open and closed. Neither spontaneous nor pressure- or sound-induced nystagmus was found. On high-resolution CT scans, she had an enlarged right VA (Fig. 1b).

Direct otoscopic observation revealed a normal pattern in both ears. Caloric stimulation with 20 cm^3 cold water provoked over 2 min horizontal nystagmus and vertigo in both ears. However, her VEMP were asymmetrical (Fig. 2). The threshold for the right ear was 75 dB nHL; it was higher for the left ear, being 95 dB nHL. Her VEMP on the right side also had a larger amplitude (140 μV) in comparison to the left ear (80 μV).

3.2. Patient 2

She is a 9-year-old with complaint of hearing loss and delayed speech. Primary evaluation at age 5 showed a mixed type hearing loss with an air–bone gap in the low-frequency range. She underwent a tympanoplasty and ossicular chain reconstruction in the left ear 2 years ago, which did not result in hearing improvement.

Neurological and motor system evaluations were normal. Examination revealed no obvious nystagmus or unsteadiness. Romberg, Mann and stepping tests showed normal results with eyes open and closed. Air-conducted pure-tone audiometry showed a severe hearing loss in both ears (threshold of 70 dB for right and 100 dB for left), and air–bone gap in the frequencies lower than 1000 Hz in both ears (Fig. 3a). High-resolution CT scans and magnetic resonance images showed bilaterally enlarged VAs (Fig. 3b).

VEMP showed asymmetrical response threshold and amplitude. The threshold was lower in the operated left ear (85 dB nHL) compared to the right ear (95 dB nHL). Amplitude measurement revealed a much higher response amplitude in the operated left ear (200 μV) in comparison to the right ear (100 μV) (Fig. 4).

3.3. Patient 3

The patient is a 6-year-old female with bilateral profound sensorineural hearing loss.

She is a product of natural vaginal delivery without particular prenatal or postnatal problems. Hearing loss

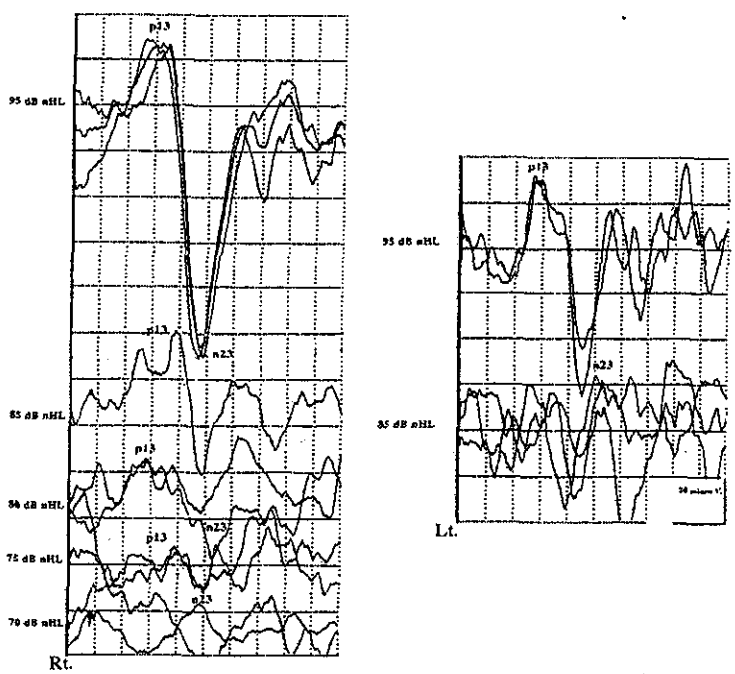

Fig. 2. Air-conducted vestibular evoked myogenic potentials in a 31-year-old female (patient 1) with unilateral (right) enlarged VA. Two responses have been superimposed for each condition to demonstrate reproducibility of VEMP in each individual recording. Lt. indicates electromyographic responses of the left SCM muscle to left ear stimulation and Rt. indicates electromyographic responses of the right SCM to right ear stimulation. Positive (p13) and negative (n23) peak VEMP were recorded in each ipsilateral SCM to unilaterally presented STBs. Note that response threshold and amplitude differs in the ear with enlarged VA (right ear) in comparison to the intact ear (left ear).

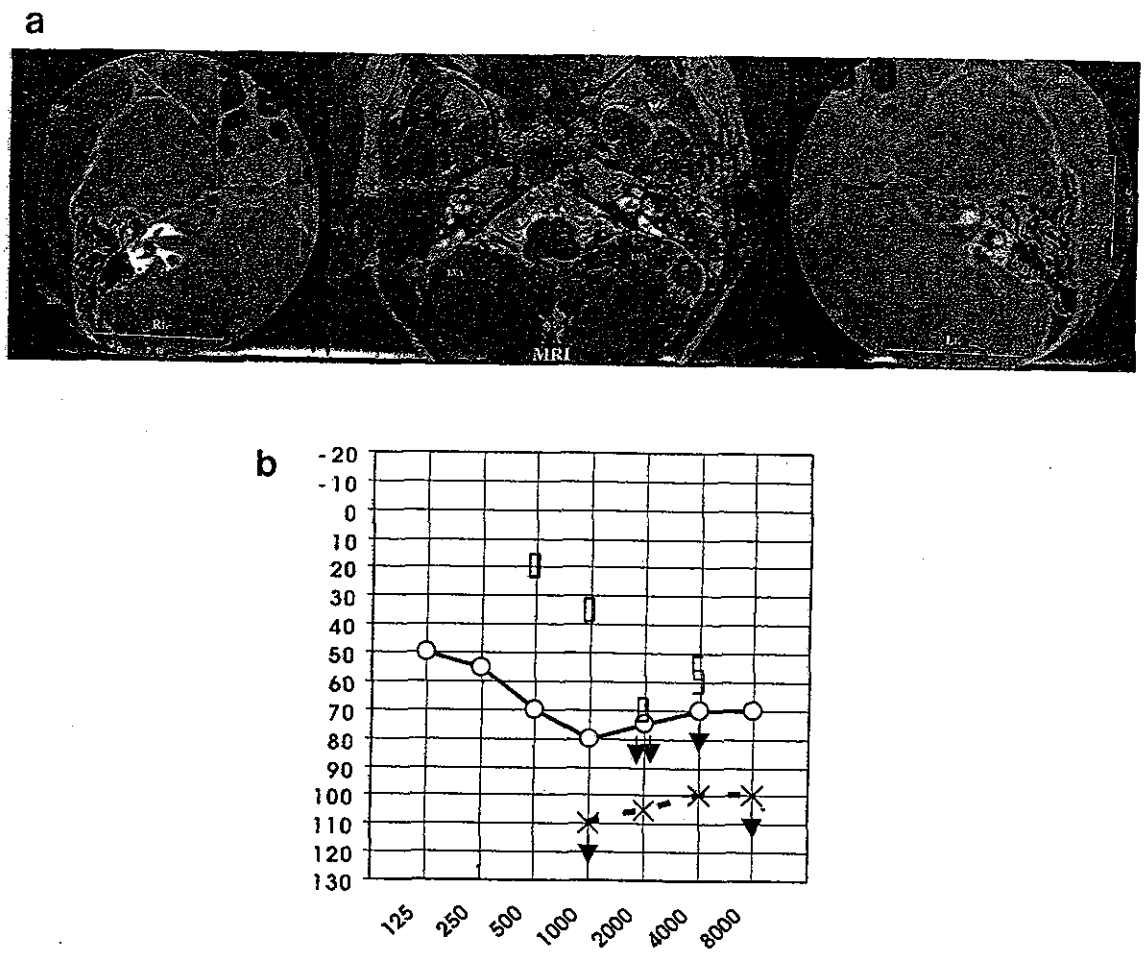

Fig. 3. (a,b) Computed tomograms of the temporal bone of patient 2 (9-year-old female) which revealed bilateral enlargement of VAs. Pure-tone audiogram of the same patient revealed severe hearing loss in the both ears and air–bone gap in the low-frequency range. O = right air-conduction hearing level; × = left air-conduction hearing level; [= right bone-conduction hearing level;] = left bone-conduction level.

was first noticed at the age of 3. She underwent bilateral tympanostomy with ventilation tube placement. High-frequency hearing loss progressively got worse over the last 3 years. The patient also has suffered from frequent episodes of vertigo and nausea. Primary evaluation raised the suspicion of LVH, which was confirmed by CT scan studies.

Clinical neurological and motor system evaluations including Romberg, Mann and stepping tests showed normal results with eyes opened and closed. Neither spontaneous nor pressure- or sound-induced nystagmus was found. On high-resolution CT scans, she had an enlarged right VA (images are not shown). Conventional pure-tone audiometry showed profound sensorineural hearing loss in both ears (threshold of 84 dB for right and 108 dB for left) (Fig. 5).

VEMP were recorded and showed amplitude and threshold asymmetry between ears. Recorded VEMP from the affected (right) ear were greater in amplitude and lower in threshold (85 dB nHL) compared to the left ear without apparent anomaly on the CT scans that showed smaller amplitude and higher threshold of 95 dB nHL (Fig. 5).

4. Discussion

It has been shown that the saccule retains the ability to trigger acoustic reflexes, the vestibular evoked myogenic potentials or VEMP, in certain neck muscles (Townsend and Cody, 1971; Colebatch and Halmagyi, 1992; Colebatch et al., 1994). VEMP are generated by micro-contractions of the SCM induced by high-intensity acoustic stimuli. VEMP are thought to be of vestibular origin as they disappear after vestibular neurectomy and are still present in deaf patients with preserved vestibular function (Colebatch et al., 1994; Colebatch and Halmagyi, 1992).

In this study, vestibular hypersensitivity to sound was demonstrated in patients with LVA. The LVA appears

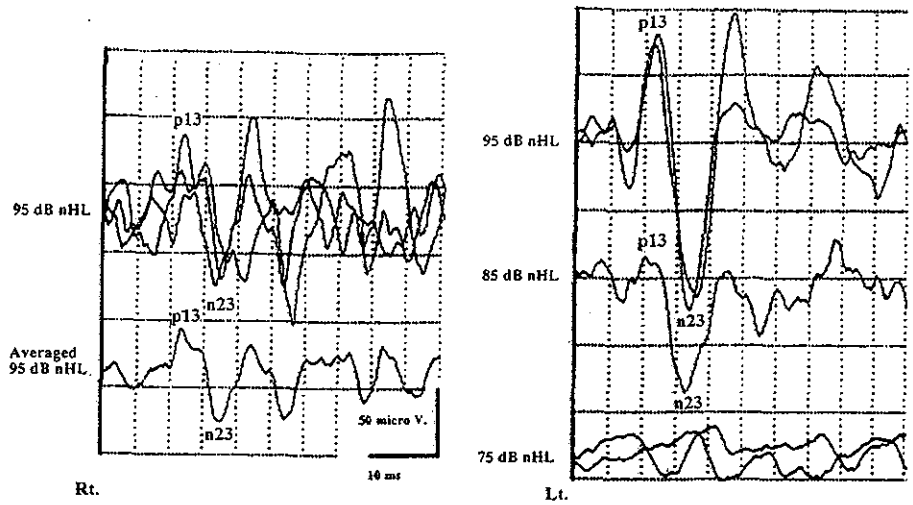

Fig. 4. Air-conducted evoked myogenic potentials recorded from the SCM of a 9-year-old patient with bilateral mixed type hearing loss and bilaterally enlarged VAs. Two responses have been superimposed for each condition to demonstrate reproducibility of VEMP in each individual recording. Lt. indicates electromyographic responses of the left SCM muscle to left ear stimulation and Rt. indicates electromyographic responses of the right SCM to right ear stimulation. Positive (p13) and negative (n23) peak VEMP were recorded in each ipsilateral SCM to unilaterally presented STBs. Despite bilateral mixed type hearing loss with air–bone gap over the low-frequency range, VEMP was recorded, a finding that would not have been expected based upon a middle ear cause of conductive hearing loss. VEMP had higher amplitude and lower threshold in the operated ear.

to affect the responses of the vestibular receptors to loud sounds. Thresholds were lower and amplitudes higher for VEMP recorded from ears with LVA than those recorded both for normal subjects (Sheykholeslami et al., 2001b) and for the non-affected ears in two patients with unilateral LVA.

VEMP thresholds were 75 and 85 dB nHL in the affected ears of the first and third patients with a threshold of 95 dB nHL in the unaffected ears (Figs. 4 and 5). Patient 2 with bilaterally enlarged VA had a bilateral conductive hearing loss. The patient underwent a tympanoplasty and ossicular chain reconstruction on the left ear 2 years ago, which did not result in any hearing improvement. VEMP recorded from the left ear, with a large air–bone gap in low frequencies shown by conventional audiometry, revealed a lower threshold in comparison to the non-operated right ear and also in comparison to normal hearing subjects (Fig. 4). In the absence of LVA, VEMP responses would not have been expected from the affected ears with large air–bone gap to air-conducted stimuli.

In addition to a lowered threshold for VEMP responses in patients with LVA, we also found larger amplitudes of these responses for comparable stimulus intensities on the side of the LVA (Figs. 2 and 4). The VEMP amplitude for the ear with LVA was much higher (140 μV for the right ear of patient 1, 200 μV for the left ear of patient 2, and 700 μV for the right ear of patient 3) than ears with normal VA (80 μV for the left ear of patient 1, 200 μV for the right ear of patient 2, and 450 μV for the left ear of patient 3). These data are interpreted as a vestibular hypersensitivity to sound stimuli.

Otological pathologies other than LVA may lead to a lowered VEMP threshold or a higher amplitude of VEMP. Recent reports have demonstrated enlarged sound-evoked VEMP in patients with sound-induced vertigo and patients with dehiscence of the superior semicircular canal with a pathologically reduced threshold (Colebatch et al., 1994, 1998; Brantberg et al., 1999; Streubel et al., 2001).

VA enlargement is a distinct clinical syndrome in the spectrum of congenital inner ear anomalies. It seems that the bony anomaly of the large VA leaves the membranous labyrinth vulnerable to sudden fluctuations in pressure. Vestibular enlargement usually accompanies LVA whereas semicircular canal deformity is uncommon. It is possible that vestibular complaints like instability and vertigo result from an underdeveloped vestibular system (Okumura et al., 1995). Despite the absence of evidence in favor of intracochlear endolymphatic hydrops in LVAS, impressive erosion of the bone surrounding the duct and sac is highly suggestive of chronic pressure effects (Gussen, 1985). It is conceivable that endolymphatic hydrops in LVAS manifests itself by progressive distension of the sac and duct rather than by intracochlear distension in those patients (Jackler and De La Cruz, 1989). Moreover, vestibular dysfunction in patients with LVAS, some of them with normal hearing, may be due to vestibular end-organ pathology (Yetiser et al., 1999).

It is interesting to speculate on the cause of VEMP

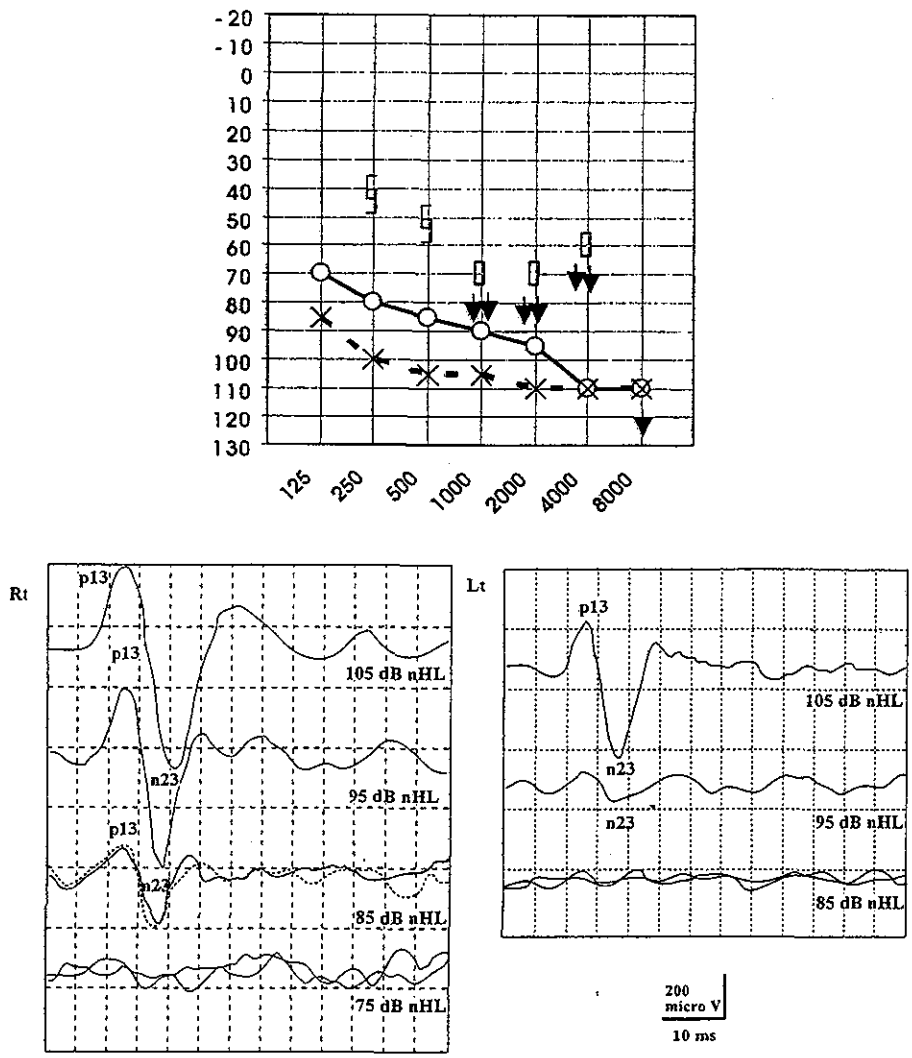

Fig. 5. Top figure shows pure-tone audiogram of patient 3 (6-year-old girl), revealing bilateral profound hearing loss which is worse in the left ear. O = right air-conduction hearing level; × = left air-conduction hearing level; [= right bone-conduction hearing level;] = left bone-conduction level. Bottom figures show vestibular evoked myogenic potentials in a patient with unilateral LVA (right side). Lt. indicates electromyographic responses of the left SCM to the left ear stimulation; Rt. indicates electromyographic of the right SCM to the right ear stimulation. Positive (p13) and negative (n23) peak VEMP were recorded from each ipsilateral SCM to unilaterally presented STBs. Note that response threshold and amplitude differ in the ear with enlarged VA (right ear) compared to the intact left ear.

abnormalities in patients with LVA. The theory of labyrinthine fluid pressure dynamics – the theory of pressure balance – suggested by Allen (1983) postulated that the endolymphatic sac transmitted cerebrospinal fluid (CSF) pressure changes to the endolymph to equalize pressure changes in the perilymph transmitted from the CSF via the cochlear aqueduct. Gussen (1985) observed that the endolymphatic sac and duct in ears with Mondini's dysplasia, an anomaly where the enlarged VA is probably analogous to that of LVAS, were thin-walled and cyst-like, lined by flattened epithelium with no rugal or papillary foldings, devoid of perisaccular loose vascular tissue. Such a sac is expected to be dysfunctional. In normal, one would expect only minimal volume displacement within the vestibular apparatus in response to stapes movements. However, a thin-walled sac in patients with LVA that might be the most distensible portion of the inner ear can act as a third window that allows volume and pressure displacements, and thus larger deflection of the vestibular sensors within the membranous labyrinth, in response to stapes movements. This would cause the vestibular organ to be more responsive to sound and pressure changes.

In conclusion, we speculate that abnormal transmission of the inner ear volume and pressure to the CSF space via the widely patent VA and larger deflection of the vestibular sensors within the membranous labyrinth in response to stapes movements may be a possible contributor to the high amplitude with low threshold VEMP in patients with LVA.

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