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Contribution of Vestibular-Evoked Myogenic Potential (VEMP) testing in the assessment and the differential diagnosis of otosclerosis

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: The aim of this prospective clinical study was to evaluate the clinical importance of Vestibular-Evoked Myogenic Potentials (VEMPs) in the assessment and differential diagnosis of otosclerosis and otologic diseases characterized by "pseudo-conductive" components. We also investigated the clinical appearance of balance disorders in patients with otosclerosis by correlating VEMP results with the findings of caloric testing and pure tone audiometry(PTA).

Material/Methods: Air-conducted(AC) 4-PTA, bone-conducted(BC) 4-PTA, air-bone Gap(ABG), AC, BC tone burst evoked VEMP, and calorics were measured preoperatively in 126 otosclerotic ears.

Results: The response rate of the AC-VEMPs and BC-VEMPs was 29.36% and 44.03%, respectively. Statistical differences were found between the means of ABG, AC 4-PTA, and BC 4-PTA in the otosclerotic ears in relation to AC-VEMP elicitability. About one-third of patients presented with disequilibrium. A statistically significant interaction was found between calorics and dizziness in relation to PTA thresholds. No relationship was found between calorics and dizziness with VEMPs responses.

Conclusions: AC and BC VEMPs can be elicited in ears with otosclerosis. AC-VEMP is more vulnerable to conductive hearing loss. Evaluation of AC-VEMP thresholds can be added in the diagnostic work-up of otosclerosis in case of doubt, enhancing differential diagnosis in patients with air-bone gaps. Otosclerosis is not a cause of canal paresis or vertigo.

MeSH Keywords: Osteosclerosis • Audiometry, Pure-Tone • Hearing Loss, Conductive • Vestibular Evoked Myogenic Potentials

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Background

Otosclerosis is a primary, hereditary, localized, metabolic bone disease of bone derived only from the bony otic capsule. It is characterized by alternating phases of abnormal removal of mature bone of the otic capsule by osteoclasts, and replacement with new woven bone of greater thickness, cellularity, and vascularity.

The otosclerotic focus may be asymptomatic (**histological** otosclerosis with 10% overall prevalence). Because it has predilection for the fissula ante fenestrum, involvement of the stapedial footplate may result in its fixation and an asymmetric conductive hearing loss (**stapedial** otosclerosis) whereby sounds partly fail to reach the inner ear (cochlea) [1, 2]. Involvement of other parts of the otic capsule (**cochlear** otosclerosis) may result more often in cochlear symptoms (especially a high-frequency sensorineural hearing loss, which usually manifests late in the disease, and 75% tinnitus) and vestibular symptoms (in 25% of cases, most commonly a sense of disequilibrium, occasionally attacks of positional and motion-related vertigo with rotatory nystagmus), or a combination of these 2 symptoms (**combined** otosclerosis with mixed hearing loss) [3].

Diagnosis of otosclerosis is usually based on family history and clinical and audiologic examination [4–6].

Stapedectomy/stapedotomy is the surgery of choice; placing a piston prosthesis into the vestibule through the oval window fenestra provides mobile continuity between the inner ear and ossicular chain.

Testing the vestibular function in patients with otosclerosis is of particular interest. The bithermal caloric test (BCT) is representative physiological test of the function of the lateral semicircular canal (LSCC) and its afferents, and VEMPs mainly reflects the function of the saccule and its afferents.

VEMP testing has gained clinical recognition over the last 2 decades. It is an objective, quick, and non-invasive measure of saccule function that, along with the utricle, primarily respond to linear acceleration in any direction. The saccule, which is the lower of the 2 otolithic organs, is most sensitive to gravity because it is in the vertical plane. It also has a slight sound sensitivity, which is thought to be a remnant from the function of the saccule as an organ of hearing in lower animals [7,8]. The acoustic sensitivity of the saccule has been attributed to its proximity to the footplate of the stapes, which leads to its mechanical stimulation during stapedial motion in response to sound and can be measured. This is the basis of the VEMP test, which is almost entirely saccular in origin. It has been widely used since 1992 after Colebatch and Halmagy described it as it is known in modern days. They selected the SCM as their standard recording site of vestibular and myogenic response to sound [9–11]. VEMP testing utilizes sophisticated computerized equipment to interpret waveforms on a computer screen for each ear, each type of stimulus used, and each intensity level. The purpose of the air-conducted VEMP is to determine if the saccule stimulated by the sound, the activated inferior vestibular nerve (IVN), central connections in the brainstem [lateral vestibular nucleus (Deiters's nucleus), accessory nerve nucleus], the 11th nerve, and the sternocleidomastoid muscle (SCM, mostly ipsilaterally) via the medial vestibulospinal tract (MVST) are intact and working normally [12].

Bone-conducted VEMP is a useful measure of vestibular function, especially in the presence of conductive hearing loss, such as in otosclerosis, where the bone-conducted sound activates the vestibular apparatus more effectively than air-conducted sound [13–17]. The bone-conducted sound can stimulate the saccule and other parts of the vestibular end organs on both sides as the utricle.

The objectives of the current study were to: (a) investigate the audio-vestibular profile of stapedectomy candidates by analyzing the audiogram, VEMP, and calorics results; (b) evaluate the cause of vestibular dysfunction in patients with otosclerosis; and (c) to determine the clinical utility of VEMPs in the differential diagnosis of otosclerosis and otologic diseases that can cause "pseudo-conductive" hearing loss such as SCDS and LVAS.

Material and Methods

Seventy-four Caucasian (51 female, 23male) patients were seen in our academic tertiary referral centre Otolaryngology Department of Hippokration Hospital, University of Athens, and were prospectively assessed as candidates for stapes surgery for otosclerosis (mean age 38.09 years, range 23–60 years).We selected an age range of 23–60 years because there is evidence that the VEMP response rate decreases after age 60 [18–20].

Fifty-two patients had bilateral otosclerosis and 22 had unilateral otosclerosis. Therefore, a total of 126 preoperative otosclerotic ears were included in this study. No patient had a positive history for chronic otitis media [21], skull trauma, superior canal dehiscence syndrome (SCDS), or large vestibular aqueduct syndrome (LVAS) [22,23].

Forty-two (56.7%) patients had positive family history of otosclerosis. Tinnitus was present in 62 (83.7%) subjects, 24 (32.4%) patients reported dizziness, with 1 case of left-sided BPPV treated with Epley manoeuvre, and another 2 presented with first-degree right-beating spontaneous nystagmus.

All the patients enrolled in this study were evaluated prior to stapedectomy using a standard diagnostic protocol that

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included audiological assessment consisting of pure tone and speech audiometry, tympanometry with stapedial reflexes, ENG with bithermal caloric testing (BCT), and VEMP test [24]. Of these patients, 1 underwent high-resolution computed tomography (HRCT) for further evaluation of the disease [25]. In all patients, the mean of 4-frequency pure tone hearing thresholds (4-PTA at 500, 1000, 2000, and 4000 Hz) was measured for both air and bone conduction and consequently the ABG (air-bone gap). VEMPs were recorded with a GN Otometrics (Taastrup, Denmark) ICS CHARTR EP version 5.2 analyser with a 2-channel averaging capacity. VEMPs were recorded while patients were seated in an upright position and instructed to maintain their heads turned contralaterally to the stimulated ear to achieve intense and constant sternocleidomastoid muscular effort during the whole recording period of each trial [26].The skin was scrubbed, and the impedance of the recording electrodes was maintained below 5 KOhms. The 2 active recording electrodes were placed symmetrically at the middle third of each SCM, the reference electrode was placed on the upper forehead, and the ground electrode was placed at the middle of the forehead.

The acoustic stimulus (loud, short tone bursts) [27] intensity range was 95–102 dB HL for AC-VEMPs and 42–65 dB HL for BC-VEMPs [500 Hz tone bursts were given at 95 dB HL for AC-VEMPs and 42 dB HL for BC-VEMPs; 1000Hz tone bursts were given at 102 dB HL for AC-VEMPs and 65 dB HL for BC-VEMPs; rate 5.1/second, ramp 1 millisecond (msec), plateau 0 ms]. Stimuli were delivered monaurally via headphones (TDH-40, Telephonics, New York, USA) for elicitation of VEMPs evoked by air-conducted signal (AC-VEMPs) and the Bone Oscillator B71 placed at the ipsilateral mastoid for evocation of responses by bone-conducted stimuli (BC-VEMPs) with no contralateral masking, and the myogenic potential was recorded ipsilaterally by surface electrodes. There was no difference between VEMP parameters of the right and the left ear. The electromyographic (EMG) activity of the ipsilateral sternocleidomastoid muscle was recorded, and every trial of 150 stimuli was averaged and repeated twice to verify the reproducibility of the waveform, and to provide the final vestibular evoked myogenic potential waveform. The EMG signal from each side was amplified and bandpass-filtered (high-pass 2 Hz, low-pass 500 Hz). The stimulus analysis time for each run was 100 ms [28].

The peak latencies of the first positive-negative component of the vestibular evoked myogenic potential response (P1 and N1) were measured for each patient. The vestibular evoked myogenic potential response was considered to be absent when there were no recognizable or reproducible biphasic waveforms, or when the amplitude of the potential was less than 20 mV.

Electronystagmography recordings (ENG) were performed with a Life-Tech model 3002 electronystagmograph (Houston, Texas, USA). A Hortmann Airmatic (Neurootometrie, GN Otometrics, Taastrup, Denmark) air irrigator was used for the bithermal air caloric tests. The methodology has been reported in detail elsewhere. In our laboratory, any caloric asymmetry of more than 22% was defined as canal paresis [29].

The Statistical Package for the Social Sciences version 11.0 software was used for statistical analysis. Student's T-test, ANOVA and chi square testing were used to compare different values. Results are shown as mean and standard deviation. The criterion for statistical significance was set at a P-value of ≤ 0.05 (2-tailed).

For comparison, 35 healthy volunteers adults (17 men and 18 women; mean age 37.3 years)for AC-VEMPs and 13 healthy adults (6 men and 7 female; mean age 37.76 years) for BC-VEMPs, without previous hearing, vestibular, or neurological disorders, were also enrolled in this study. These control subjects underwent the same neuro-otological test battery. All volunteers had a normal otoscopic examination and a normal pure tone audiometric (PTA) threshold. AC vestibular evoked myogenic potential waveforms were obtained on both sides in all of the 35 healthy volunteers (70 ears) and BC vestibular evoked myogenic potential waveforms in all of the 13 healthy volunteers (26 ears). The mean AC P1 value was 16.26 ms (SD 1.32) and the mean AC N1 value was 24.42 (SD 2.52). The mean BC P1 value was 14.09 (SD 2.70) and the mean BC N1 value was 22.30 (SD 3.91).The P1 and N1 delay was defined as any value greater than the mean plus 2 SDs of the normal population (i.e., any P1 value greater than 18.49 ms and any N1 value greater than 30.12 ms) was considered delayed.

This study was conducted with the understanding and the consent of all subjects, patients, and volunteers before inclusion.

Results

AC-VEMPs and BC-VEMPs *vs.* audiological measurements

Pre-operatively, AC-VEMP was performed in 126 ears and AC-VEMP and BC-VEMP were performed in 109 ears each. AC-VEMP was present in 34 ears, while BC-VEMP was recordable in 48 ears. The mean AC 4-PTA, mean BC 4-PTA, and mean ABG (air-bone gap) were compared between the group of ears with AC-VEMP presence and AC-VEMP absence, respectively [30]. The same was done between the group of ears with BC-VEMP presence and BC-VEMP absence. The results appear in Table 1. Statistically significant differences (Student's t-test) were found in all 3 parameters between the group with AC-VEMP(+) (present) and AC-VEMP(–) (absent). In contrast, the comparisons between the ears with presence and absence of BC-VEMP were not significant.

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Table 1. Comparison of means of ABG, AC 4-PTA, BC 4-PTA in the groups formed by the presence and absence of AC-VEMP and BC-VEMP respectively.

	AC-VEMP (+)	AC-VEMP (–)	p value	BC-VEMP (+)	BC-VEMP (–)	p value
Pre-operative ears	34	92		48	61	
Mean AC 4-PTA (dB)	47.67 (SD 16.09)	57.28 (SD 16.35)	0.004 (S)	53.17 (SD 16.33)	58.46 (SD 16.38)	0.09 (NS)
Mean BC 4-PTA (dB)	25.64 (SD 9.37)	30.01 (SD 11.36)	0.049 (S)	28.02 (SD 12.72)	31.00 (SD 10.48)	0.193 (NS)
Mean ABG (dB)	22.23 (SD 11.50)	27.27 (SD 10.96)	0.026 (S)	25.15 (SD 10.92)	27.45 (SD 11.13)	0.282 (NS)

*SD – standard deviation; S – significant; NS – no significant.

Table 2. Comparison of presence and absence of AC and BC-VEMPs in 109 preoperative otosclerotic ears.

	BC-VEMP (+)		BC-VEMP (–)		Total	
AC-VEMP (+)	27	(24.77%)	5	(4.59%)	32	(29.36%)
AC-VEMP (–)	21	(19.26%)	56	(51.38%)	77	(70.64%)
Total	48	(44.03%)	61	(55.97%)	109	(100.00%)

Table 3. Comparison of mean latencies of peaks P1,N1 between controls and 109 otosclerotic ears.

AC-VEMP (+)	Mean P1 (msec)	p value	Mean N1 (msec)	p value
Controls (n=70)	16.26 (SD 1.32)		24.42 (SD 2.52)	
Otosclerosis (n=32)	15.31 (SD 2.80)	0.102 (NS)	24.03 (SD 2.89)	0.385 (NS)
BC-VEMP (+)				
Controls (n=26)	14.09 (SD 2.70)		22.30 (SD 3.91)	
Otosclerosis (n=48)	15.49 (SD 3.00)	0.02 (S)	24.75 (SD 4.39)	0.022 (S)

Incidence of AC-VEMPs and BC-VEMPs

Table 2 shows the combination of the 2 tests (AC-VEMP and BC-VEMP) in a total of 109 ears. The response rates of present AC-VEMPs and present BC-VEMPs were 29.36% (32 ears) and 44.03% (48 ears) respectively. Chi-square revealed a strong correlation between these 2 investigations; when AC-VEMP was present, it tended to be the BC-VEMP; but when AC-VEMP was absent, so was the BC-VEMP.

Comparison of mean latencies of peaks P1 and N1 between healthy (controls) and otosclerotic ears

The percentage of VEMP presence in healthy subjects was shown to be about 100% in controls without history of ear disease or head trauma. Table 3 shows no significant statistical difference between the means of the latencies P1, (nor of N1) of the normal ears and the ears affected with otosclerosis with recordable AC-VEMP. On the contrary, a significant statistical difference was noted between the means of latencies P1(and N1) of normal ears and ears affected by otosclerosis with elicited BC-VEMP.

Comparison of the mean ABG, AC 4-PTA, and BC 4-PTA among the 4 groups formed by the combination of AC and BC-VEMP

Mean ABG in each 1 of the 4 groups formed by the combination of AC and BC-VEMP appears in Table 4. No significant effect of the factor group was found, meaning that no statistical differences existed among the ABG means (one-way between-subjects ANOVA).

On the contrary, ANOVA showed statistically significant differences among the means of AC 4-PTA between the group

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Table 4. Comparison of the means of ABG, AC 4-PTA and BC 4-PTA among the 4 groups formed by the combination of AC and BC-VEMP in 109 otosclerotic ears.

Groups	AC-VEMP (+)/ BC-VEMP (+)	AC-VEMP (–)/ BC-VEMP (+)	AC-VEMP (+)/ BC-VEMP (–)	AC-VEMP (–)/ BC-VEMP (–)
Pts (n)	27	21	5	56
Mean ABG	23.04 (SD 11.14)	27.86 (SD 10.27)	18.50 (SD 14.77)	28.25 (SD 10.56)
Mean AC 4-PTA	48.55 (SD 15.75)*	59.11 (SD 15.42)	45.00 (SD 19.54)	59.66 (SD 15.72)*
Mean BC 4-PTA	25.76 (SD 10.48)	31.25 (SD14.46)	26.50 (SD 6.51)	31.40 (SD 10.71)

* Statistical significances are shown with asterisk.

Table 5. Caloric responses in relation with VEMP elicitability in 109 otosclerotic ears. Numbers of ears and percentages (in brackets) are shown. No statistical relationship was found (Chi-square).

	AC-VEMP (+)	AC-VEMP (–)	BC-VEMP (+)	BC-VEMP (–)
Calorics				
Normal	23 (71.9%)	50 (64.9%)	29 (60.4%)	43 (70.5%)
CP	9 (28.1%)	27 (35.1%)	19 (39.6%)	18 (29.5%)
p value	0.461		0.366	

of ears with presence and absence of both air- and bone-conducted VEMP. [The mean of the group with both VEMP present (48.55 dB) differs statistically from the mean of the group with both VEMP absent (59.66 dB)].

However, no statistical differences were found among the BC 4-PTA in the same 4 groups.

Caloric responses in otosclerosis

Preoperatively, the results of caloric responses were assessed in relation with the results of AC and BC-VEMP (chi-square) in 109 otosclerotic ears. Table 5 shows no correlation either between canal paresis (CP) occurrence and air-conducted VEMP presence (p=0.461), or with canal paresis and bone-conducted VEMP presence (p=0.366).

Dizziness in patients with otosclerosis

Vestibular symptoms occur in approximately 20–37% of patients affected by otosclerosis, but their pathogenesis remains unclear. In our study, 24 (32.4%) of 74 patients presented with symptoms of dizziness in the form of vertigo or disequilibrium (after carefully completing a medical questionnaire, only patients with symptoms compatible with labyrinthine origin were found in the dizziness group). To study the relationship between dizziness, means of AC 4-PTA, BC 4-PTA, AC-VEMP, BC-VEMP and calorics in patients affected by otosclerosis, preoperatively, the following groups of patients were defined as: group D (patients who complained of dizziness) and group ND (patients with no complaint of dizziness) [31–33]. The D group was composed of 42 ears and the ND group was composed of 84 otosclerotic ears. The mean of AC 4-PTA thresholds in groups D and ND were 57.63(SD 16.81) and 53.22(SD 16.65) dB, respectively (Table 6). There were no significant differences between the 2 groups (Student's T–test, p=0.167). Mean BC 4-PTA thresholds in groups D and ND were 30.78(SD 9.88) and 27.65 (SD 11.36) dB, respectively. No significant difference was observed between the 2 groups (Student's T-test, p=0.131) (Table 6).

For caloric testing, 19 of 42 (45.2%) ears showed abnormal results in D group with 11 unilateral CP (1 presented with left-sided BPPV) and 4 bilateral CP (1 presented with first-degree right-beating spontaneous nystagmus). In the ND group, 24 out of 84 (28.6%) ears showed abnormal calorics, with 16 unilateral and 4 bilateral CP. No statistical relationship was found between the calorics results and the appearance of dizziness (χ^2, p=0.06) (Table 6).

No statistical relationship was found between AC/BC-VEMP presence and dizziness. (χ^2, p=0.06 for AC-VEMP, p=0.598 for BC-VEMP) (Table 6).

To assess the possible relation of the factors of dizziness and caloric results in the measurements of AC 4-PTA, BC 4-PTA and ABG, a 2-way ANOVA was carried out with dizziness having 2 levels [i.e., yes (dizziness present) and no (no dizziness)]

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Table 6. Comparison of results of auditory and vestibular examination between dizziness (D) group and non-dizziness (ND) group formed by 42 and 84 otosclerotic ears respectively.

	D group (42 ears)	ND group (84 ears)	p value
Audiometry			
AC 4-PTA (dB)	57.63 (SD 16.81)	53.22 (SD 16.65)	0.167
BC 4-PTA (dB)	30.78 (SD 9.88)	27.65 (SD 11.36)	0.131
ABG (dB)	26.36 (SD 10.70)	25.68 (SD 11.63)	0.75
Calorics			
Normal	23 (54.8%)	60 (71.4%)	
CP	19 (45.2%)	24 (28.6%)	0.06
BC-VEMP			
Present	17 (40.47%)	38 (45.23%)	0.598
Absent	25 (59.52%)	46 (54.76%)	
AC-VEMP			
Present	7 (16.7%)	27 (32.1%)	0.06
Absent	35 (83.3%)	57 (67.9%)	

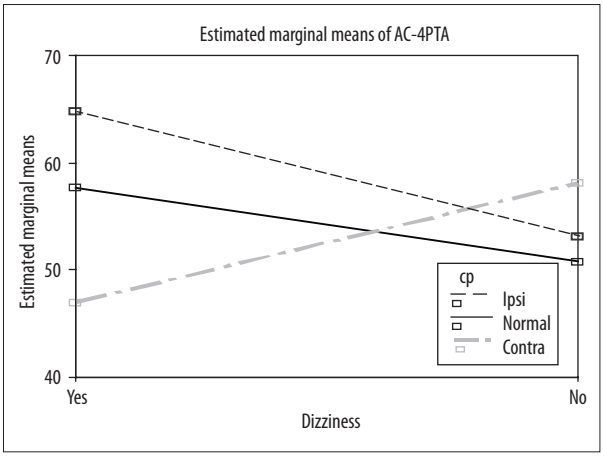

Figure 1. The means of AC 4-PTA (as produced by two way between subjects ANOVA) are displayed for the three groups of ears (CP ipsi, CP contra, normal) in the dizziness (yes) and no dizziness (no) group of patients. The contralateral ear (ear with normal calorics) shows lower PTA thresholds than the ears with CP in the dizziness group, but shows higher thresholds in the no dizziness group. A statistically significant interaction was found for the factors Dizziness*Calorics.

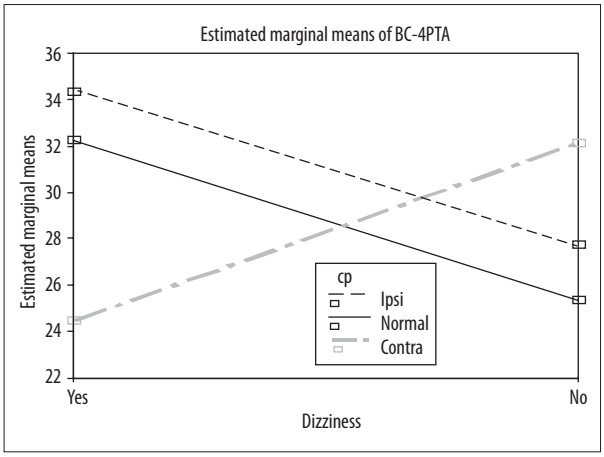

Figure 2. The means of BC-4PTA (as produced by two way between subjects ANOVA) are displayed for the three groups of ears (CP ipsi, CP contra, normal) in the dizziness (yes) and no dizziness (no) group of patients. The contralateral ear with normal calorics shows lower PTA thresholds than the ears with CP in the dizziness group, but shows higher thresholds in the non dizziness group. A statistically significant interaction was found for the factors Dizziness*Calorics.

and caloric results having 3 levels (i.e., CP at the ipsilateral ear [the ear in which PTA and air-bone gap(ABG) are measured and enter the study], CP at the contralateral ear (so the ear measured has normal calorics), and normal calorics (referring to cases with no canal paresis to either ear). For cases with bilateral CP in both ears were counted as ipsilateral CP.

Concerning AC and BC 4-PTA, the ANOVA did not show a significant main effect either for dizziness or for calorics, meaning that there were no significant differences of the means of the above measurements, neither between the dizzy and non-dizzy group, nor between the ears with CP and the ears with normal calorics.

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However, a statistically significant interaction was found between the 2 factors (dizziness and calorics) in relation to AC and BC-PTA thresholds. In the dizziness group (D), ears with CP showed much higher means of AC and BC 4-PTA, whereas in the non dizziness (ND) group the contralateral ear (with normal calorics) showed higher AC and BC 4-PTA means (Figures 1 and 2). Concerning the ABG, no significances were found (p=0.364 for the interactions, p=0.971, p=0.522 for the main effects of dizziness and calorics, respectively).

Discussion

Otosclerosis is one of the most common causes of progressive hearing loss in Caucasians [2]. Nevertheless, few published studies have attempted to investigate inner ear function and impairment of VEMPs in otosclerosis.

Our results, by using AC and BC tone-burst VEMPs in combination with audiologic findings, are in agreement with the fact that AC-VEMP is more vulnerable to conductive hearing loss, whereas BC VEMP is not.

The magnitude of mean ABG, AC 4-PTA, and BC 4-PTA is likely responsible for the pre-operative difference in elicitation of AC-VEMPs, confirmed by the significantly lower pre-operative ABG in patients with recordable AC-VEMPs in comparison to those with absent AC-VEMPs (22.23 *vs.* 27.27 dB HL, Table 1), lower mean of AC 4-PTA (47.67 *vs.* 57.28, Table 1) and BC 4-PTA (25.64 *vs.* 30.01, Table 1). The magnitude of mean ABG, AC, and BC 4-PTA appears to have no effect on the pre-operative difference in elicitability of BC-VEMPs. Complementary to this is the finding that the latencies P1 and N1 of BC-VEMPs in otosclerotic ears are statistically longer than those of normal ears (Table 3), whereas the latencies of AC-VEMP are not. This can be explained by the "persistence" of BC-VEMP appearance in ears with advanced otosclerosis, where AC-VEMP has already vanished [34]. The low presence rate of BC-VEMPs pre-operatively (44.03%) could be caused by inner ear damage due to an ototoxic effect of substances produced by otosclerotic foci of the otic capsule on saccular receptors [40].

The fact that the mean of ABG differs considerably between ears with present and absent AC-VEMP, whereas in ears with BC-VEMP it does not (Table 1), reveals a different "behavior" of the 2 types of VEMPs in relation to ABG values**.** The different trends concerning the ABG means when considering each VEMP measurement separately, can explain the lack of statistical significance in the means of ABG among the 4 groups formed by the combination of AC and BC-VEMP. One trend annuls the other. The same is true for BC 4-PTA and AC 4-PTA, with the exception that the latter shows a statistically significant difference between the group of AC/BC-VEMP both present and AC/BCVEMP both absent (Table 4). The small group of 5 ears with present AC-VEMP and absent BC-VEMP could be explained by the fact that the bone conduction stimulus in the present study was relatively low (65 dB HL), so these could be patients with otolithic organ disease needing a stronger stimulus to produce BC-VEMP, whereas the much stronger air-conducted stimulus could do it. In fact, these are ears with relatively low ABG means (18 dB, Table 4), so the transition of air-conducted stimuli was not severely hindered.

About one-third of patients with otosclerosis presented with vertiginous symptoms. A possible relationship of vertigo and otosclerosis is an understandable assumption, because otosclerosis is a disease affecting structures proximal to the vestibule [35], but until now, sufficient and concrete evidence supporting this has been lacking. Assessment of the functional state of the labyrinth as a total by using a combination of VEMP with calorics provided us with interesting observations.

Firstly, when vertigo/dizziness as a symptom was compared with caloric responses (not taking otosclerosis into account), results were borderline insignificant (p=0.06, Table 6). This is an acceptable finding. Any vertiginous patient can have a normally functioning labyrinth with symptoms due to incomplete central compensation or migrainous vertigo.

No relation could be found between VEMP results and calorics, neither for air- nor for bone-conducted VEMPs (Table 5). This is an interesting finding, supporting the notion that caloric deficiencies are rather irrelevant to VEMP deficiencies in patients with otosclerosis, so it encourages the assumption that VEMP deficiencies are due to otosclerosis and are not caused by a history of vestibular neuritis.

AC and BC-VEMP also did not show any relationship with dizziness either (Table 6), although the percentage of ears with present AC-VEMP in the non-dizziness population (32.1%) was at the borders of statistical significance compared with the percentage of ears with present AC-VEMP in the dizziness population (16.7%).

There are authors who assume that the balance problems associated with otosclerosis are caused by saccular dysfunction originating from endolymphatic or saccular hydrops [36–39] or direct invasion of the otosclerotic focus to the saccular macula or saccular afferents [35,40]. A 2012 study by Saka et al. [33] found that balance problems in otosclerosis were associated with abnormal results for BC-VEMP. Conversely, the present analysis of 74 patients with otosclerosis, relying on the assessment of a higher clinical sample than other prospective studies, could not support this theory based on VEMP only. A possible involvement of otolithic organs in vertiginous symptoms (otolithic vertigo) needs further investigation (subjective visual

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vertical and horizontal) as well as a more detailed questionnaire dealing with the specifics of otolithic vertigo symptoms.

ANOVA assessed the relation of vertigo and caloric results, each separately, as well as a combination, with ABG and PTA measurements (i.e., the severity of otosclerosis). The results showed no main effect of these 2 factors on the severity of otosclerosis (ABG), meaning that the degree of hearing loss was not relevant to either dizziness or caloric results. This is understandable, considering that the semicircular canals are relatively spared from the disease. In fact, only 1 patient presented with BPPV. BPPV could be a clinical entity connecting (not immediately) saccular involvement with a semicircular canal, but just 1 patient is not enough to support any possible attribution of BPPV to otosclerosis.

However, ANOVA showed a significant interaction of vertigo and calorics in relation to PTA, both air-conducted (AC 4-PTA) and bone-conducted (BC 4-PTA). This means that canal paresis (CP) influences PTA means differently in the 2 groups of patients. In the group of vertiginous patients (D), ears with canal paresis showed higher PTA thresholds; whereas in the non-vertiginous group (ND), the ears with canal paresis showed lower PTA thresholds than ears with normal calorics (Figures 1 and 2). One possible explanation is that although otosclerosis is not a cause of canal paresis or vertigo, if vestibular neuritis (or hydrops or any other vestibular cause of canal paresis) affects an ear with advanced otosclerosis, (i.e., high threshold of AC and/or BC-PTA), central compensation is delayed and vertiginous symptoms persist; whereas in cases of less advanced otosclerosis, compensation is expected to be faster.

The principal assumption of the present study is that the mere presence of VEMP does not exclude otosclerosis. Despite the conductive hearing loss, VEMP can still be elicited in a number of preoperative otosclerotic ears. In our study, the response rate of the AC-VEMPs was only 29.36%, but the response rate of BC-VEMPs was 44.03%. Therefore, a possible suggestion is to proceed to VEMP threshold measurements in case of doubt. Specifically, positive AC-VEMP with pathologically decreased thresholds (less than 70 dB to tone-burst testing at 500 Hz, while thresholds for evoking VEMP using air-conducted tone-burst in our study were ranging between 95 and 102 dB) excludes middle ear pathology such as otosclerosis and provides a reference for further imaging examination to exclude the alternative diagnosis of SCDS (superior canal dehiscence syndrome) and LVAS (large vestibular aqueduct syndrome). Therefore, when it is not possible to make an accurate diagnosis based solely on the audiogram and immittance testing results, VEMP testing can be added in the diagnostic work-up of otosclerosis to provide additional confirmation. Thus, VEMP testing outcomes may provide the basis not only for better preoperative counselling, but also for safety issues regarding stapedectomy candidates.

Conclusions

These study findings lead to several conclusions.

The presence of VEMP does not exclude otosclerosis. Despite the conductive hearing loss, VEMP can be elicited in a small number of ears with otosclerosis. The AC-VEMP is more vulnerable to conductive hearing loss, whereas BC-VEMP is not; however, the low presence rate of BC-VEMPs could be caused by inner ear damage [40].

The evaluation of VEMP thresholds, by using air-conducted tone-burst, can be added in the diagnostic work-up of suspected otosclerosis in case of doubt, providing additional confirmation, narrowing down the differential diagnosis in patients with “pseudo-conductive” components, and reducing medical cost by preventing unnecessary radiation exposure and unsuitable middle ear surgery.

Vertiginous symptoms should not be attributed to otosclerosis itself, but to causes affecting the semicircular canals. Perhaps further investigations into otolithic disturbances (such as subjective visual vertical and horizontal) and a questionnaire more oriented to otolithic vertigo symptoms could reveal possible clinical impacts of utricular and saccular involvement in the disease.

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