European Archives of Oto-Rhino-Laryngology (2019) 276:993–1000
https://doi.org/10.1007/s00405-018-05267-7

OTOLOGY

Quantitative evaluation of endolymphatic hydrops with MRI through intravenous gadolinium administration and VEMP in unilateral definite Meniere's disease

Ping Guo[1] · Wenfang Sun[2] · Suming Shi[1] · Fang zhang[3] · Jiali Wang[1] · Wuqing Wang[1]

Received: 16 September 2018 / Accepted: 21 December 2018 / Published online: 29 January 2019

Abstract

Purpose To help clinicians to further understand the significance of vestibular-evoked myogenic potential (VEMP) examinations to diagnose MD and the quantitative relationship between VEMP and MRI in assessing the location and degree of endolymphatic hydrops (EH) in definite Meniere's disease (MD) patients.

Methods Fifty-six patients with unilateral definite MD participated in this study, which used MRIs through intravenous gadolinium administration (IV-Gd), audiometry, caloric tests and VEMP tests. The VEMP results of 26 healthy volunteers were used as a normal reference value.

Results The participants were found through MRI to have differing degrees of vestibular and cochlear EH. Quantitative comparison of MRI and VEMP results found that the response rates of oVEMP decreased with cochlear EH increasing; the asymmetry ratio (AR) of oVEMP can be used to find whether cochlear EH or not, and the P1–N1 amplitude was lower in the extreme cochlear EH group ($P < 0.01$). The AR of cVEMP was larger in severe vestibular EH group than that of the mild or no vestibular EH group ($P < 0.01$). The correlation between the degree of cochlear EH and the mean PTA threshold was statistically significant ($P < 0.05$). The duration of MD correlated positively with vestibular EH ($P < 0.05$). The abnormal rate of caloric tests was higher in severe vestibular EH group than that of the mild or no vestibular EH group ($P < 0.05$).

Conclusions The advantages of MRIs by IV-Gd administration were obvious in assessing the location and degree of EH. oVEMP and PTA can be indirectly used to evaluate the extent of cochlear EH, cVEMP and caloric tests can be used to assess the extent of vestibular EH on the condition of absent MRIs.

Keywords Endolymphatic hydrops · MRI · VEMP · Meniere's disease

Introduction

Meniere's disease (MD) is an intractable inner ear disorder characterized by fluctuating sensorineural hearing loss, spontaneous vertigo attacks, tinnitus, and aural fullness. Endolymphatic hydrops (EH) is considered a characteristic sign of MD. "Definite" and "probable" are the only two categories of MD according to MD's diagnosis criteria created by the Classification Committee of the Bárány Society in 2015 [1].

As we all known, the certain diagnosis of Meniere's disease depends mostly on autopsy to find EH in the past. Three-dimensional fluid-attenuated inversion recovery (3D-FLAIR) magnetic resonance imaging (MRI) was the first direct visualization of EH in vivo, which was done 24 h after the administration of intratympanic gadolinium (IT-Gd) by Nakashima et al. [2]. Shortly thereafter, as technology improved, three-dimensional real inversion recovery (3D-real-IR) MRI and 3D-FLAIR MRI were performed 4 h after the administration of intravenous gadolinium (IV-Gd) to show EH, and it is becoming more popular in clinical practice [3–5].

✉ Wuqing Wang
wwuqing@eent.shmu.edu.cn

1 NHC Key Laboratory of Hearing Medicine, Department of Otolaryngology, Eye Ear Nose & Throat Hospital Shanghai, Fudan University, 83 Fenyang Rd, Shanghai 200031, People's Republic of China

2 Department of Otolaryngology, Chongqing General Hospital, Chongqing 400000, People's Republic of China

3 Department of Radiology, Eye Ear Nose & Throat Hospital Shanghai, Shanghai, People's Republic of China

VEMP has been used conventionally to examine the function of otoliths, based on the hypothesis of efferent specificity proposed by Curthoys [6]. Cervical VEMP (cVEMP) arises from saccular macula and inferior vestibular nerve input pathways, and the sternocleidomastoid muscles are a strong projection of cVEMP [7, 8]. Ocular VEMP (oVEMP), however, originates primarily from the utricular macula and superior vestibular nerve input pathways, and the inferior oblique muscle is a strong projection of oVEMP [8, 9]. Using these tests to evaluate the localization and prevalence of hydrops formation can mimic the declining sequence of hydrops formation in temporal bone studies.

Pure-tone audiometry (PTA), caloric tests and VEMP have been used indirectly to diagnose MD in present clinical study. However, quantitative evaluations of the relationship between the location and degree of EH in vivo, and indirect examinations to help evaluate EH and diagnose MD, are rare. In this study, we quantitatively analyze cVEMP; oVEMP; caloric tests; disease duration; frequency of vertigo attacks; and degrees and locations of EH found by 3D-IR MRI IV-Gd administration in patients with definite MD. The results of this study may help clinicians to better understand the significance of VEMP examinations to diagnose MD.

Materials and methods

This study was conducted from July 2014 to December 2017. We recruited patients with unilateral defined MD who were referred to the Department of Otorhinolaryngology at the Eye and ENT Hospital of Fudan University, China. The study's protocol was approved by the Ethics Committee of Fudan University's review board, and written informed consent forms were obtained from the participants. Participants chosen for this study had two or more definitive episodes of vertigo with hearing loss, tinnitus, and aural fullness, but no history of middle ear, head trauma or neurological disorders such as benign paroxysmal positional vertigo, vestibular migraines, sudden sensorineural hearing loss, and so on. The VEMP results of 26 healthy volunteers (male/female = 16/10, age: 46.4 ± 13.6 years) matched to the recruited patients were used in a reference group.

Locally enhanced MRI

All patients were subjected to a double dose (0.4 mL/kg of body weight) IV injection of Gd-HP-DO3A. MRIs were performed 4 h after the intravenous administrations (Verio; Siemens Healthcare, Erlangen, Germany), using a 32-channel phased-array receive-only coil. T2-space and 3D-real-IR sequence MRIs were applied to collect the images. The parameters for the 3D-real-IR sequence were as follows: voxel size = 0.2 × 0.2 × 0.6 mm; scan time = 15 min and 20 s; repetition time = 6000 ms; echo time = 181 ms; inversion time = 1850 ms; slice thickness = 0.6 mm; field of view = 160 × 160 mm; and matrix size = 768 × 768.

Image evaluation

Gadolinium is absorbed into the perilymph space of the inner ear after its intravenous administration. When EH is present, the endolymph fluid occupies the perilymph fluid area, which is confined to the bony labyrinth. Therefore, the endolymphatic space becomes enlarged and visible as a negative signal, dilating to the contrast-enhanced signal of the perilymph space [10, 11]. Two radiologists with 16 years of experience in otology-radiology and 8 years of experience in radiology, respectively, as well as a senior otology doctor, independently evaluated the images. Cochlea and vestibule were analyzed separately. For cochlear analysis, the respective degrees of EH were graded using a 4-point ordinal scale (0 = no EH, 1 = mild EH, 2 = marked EH, and 3 = extreme EH), according to Sun [12, 13]. For vestibular analysis, EH severity was assessed by determining the vestibular endolymph ratios, which corresponded to the ratios of endolymph space to total vestibular space. Adobe Photoshop CS5 (Adobe Systems Inc., San Jose, CA) was used in the vestibular analyses [14].

VEMP tests

A Bio-logic Navigator PRO auditory brainstem response diagnosis system (Bio-logic Auditory Evoked Potential Version 7.0.0; Natus, Pleasanton, CA) was used for the VEMP tests in a sound-proof examination room. VEMP waveforms were induced through the stimuli of ACS with a 500-Hz short-tone burst (1 ms rise/fall time and 2 ms plateau time) transmitted via inserted headphones. Generally, 120 stimuli were applied to each ear. The initial stimulus intensity was 95 dB nHL, which decreased step by step 5 dB nHL until the VEMP response was not appeared. This process was repeated three times. Before applying the electrodes, the patient's skin was disinfected and coated with a conductive paste. The resistance between the electrodes was controlled at < 5KΩ.

cVEMP tests and observations

An inverting electrode was placed on the middle of the sternocleidomastoid muscle (SCM), a non-inverting electrode was placed on the lower part of the suprasternal fossa, and a common electrode was placed on the middle of the contralateral SCM. The sites of the electrodes did not need to be changed, for the inverting and common electrodes could be switched automatically on both sides of SCM. Patients were asked to lift their heads when they heard a stimulus sound from the headphones. The presence of cVEMP was recognized when the amplitude of the first positive–negative–positive peak (P1–N1–P2) appeared. The absence of cVEMP was recorded in cases in which the waveforms were not recognized or did not repeat. The P1 potential was identified as the first positive peak in the waveform, N1 was identified as the first negative peak in the waveform, and the peak-to-peak amplitude was the P1–N1 amplitude. The asymmetry ratio (AR) between a subject's ears was calculated as follows: AR = (larger amplitude − smaller amplitude)/(larger amplitude + smaller amplitude) × 100[9].

oVEMP tests and observations

An inverting electrode was placed on the orbital margin below the center of the eye, a non-inverting electrode was placed approximately 20 mm below on the cheek, and a common electrode was placed on the contralateral orbital margin below the eye. We needed to move the non-inverting electrode to the contralateral cheek when testing the opposite side because the inverting and common electrodes could be switched automatically on both sides of the orbital margin below the eyes. During this test, patients were asked to gaze at a target about 30° above the visual horizontal line when they heard a stimulus sound from the headphones. The presence of oVEMP was recorded when the peaks of the first negative and positive biphasic waves (N1–P1) appeared. The P1 latency and N1 latency were defined from 0 ms to the corresponding maximum peak of the recorded waveforms.

Pure-tone audiometry (PTA) tests

All patients' hearing thresholds were tested before the IV-Gd administration. PTA thresholds were tested at all frequencies (0.125–8 kHz). With regard to the affected ears, all patients showed varying degrees of sensorineural hearing loss and pure-tone thresholds means the average of the 0.5, 1, 2, and 3 kHz hearing thresholds. The hearing thresholds of the contralateral ears were in the normal range.

Caloric tests

The patients underwent caloric tests in a supine position, and keep the head flexed at 30°. One minute constant flow of air (8 L/min) was irrigated into each ear with a GN Otometrics Type air irrigator (Otometrics, Taastrup, Denmark) for which the air temperature was at 49 °C or 23 °C. The cool temperature was irrigated prior to hot air 5 min, according to Jongkees' formula to determine canal paresis (CP) [15], however, CP > 22% was considered to be an abnormal response with cool and hot air irrigation [16].

Statistical analysis

Statistical analysis was performed using statistical software (SPSS Version 20.0; SPSS, Chicago, IL, USA). A P value < 0.05 was considered statistically significant. ANOVA tests and Kruskal–Wallis tests were used to compare the cVEMP and oVEMP values in the MD-affected ears, unaffected ears, normal reference group's ears and differing EH groups of MD-affected ears, Bonferroni was applied to correct the P value for multiple testing. The Chi-square test was used to compare the abnormal rates of caloric tests in various vestibular EH. Spearman correlation was used to find associations between the degree of EH in either cochlear or vestibular and PTA threshold, the duration of MD, CP and the frequency of vertigo attacks.

Results

Fifty-six participants with unilateral defined MD were included in the final sample. The demographic data of these participants are summarized in Table 1. No adverse effects or complications were observed after the intravenous administration of gadolinium. The participants were found to have differing degrees of EH in either the vestibule or the cochlea after the gadolinium administration (Fig. 1). The grade given according to the degree of the patients' cochlear EH was 0 in 11 of the patients, 1 in 24 of the patients, 2 in 9 of the patients, and 3 in 12 of the patients. The grade of vestibular EH was 0 in 8 of the patients, 1 in 11 of the patients, and 2 in 37 of the patients. There was no significant correlation between cochlear EH and vestibular EH ($P > 0.05$).

The response rates for cVEMP and oVEMP of the affected ears of unilateral MD patients were lower than that of the groups with normal reference ears and unaffected ears. The response thresholds for cVEMP and oVEMP of the affected ears, however, were higher than that of the groups with the normal reference ears ($P < 0.01$). The N1–P1 amplitudes for the oVEMP of the affected ears were lower than that of the groups with normal ears ($P < 0.01$) (Table 2).

Table 1 The clinical characteristics of the patients

Male/female	34/22
Age (years)	50.4 ± 10.2
Disease duration (years)	8.5 (1.2–20)
Degree of cochlear hydrops: 0/1/2/3	11/24/9/12
Degree of vestibular hydrops: 0/1/2	8/11/37
Endolymph/perilymph space ratio (%)	0.63 ± 0.31
The frequency of vertigo attacks	10.5 ± 5.6
Pure-tone average 0.5–3 kHz (dB)	48.5 ± 20.3

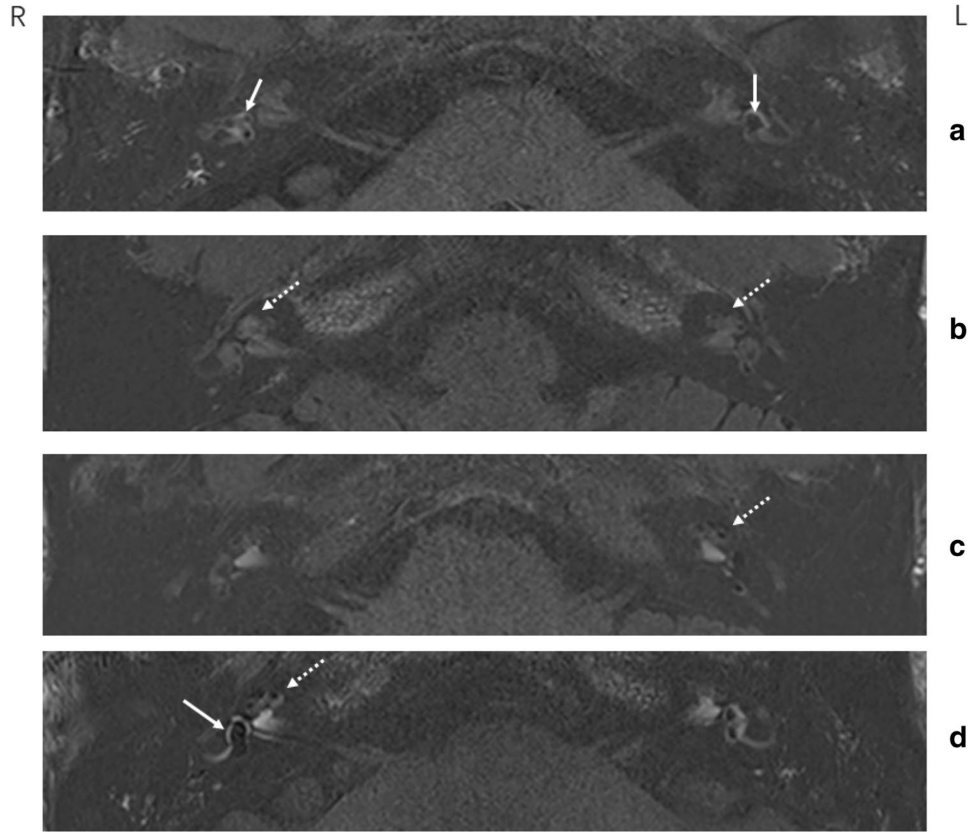

Fig. 1 Differing degrees of cochlear and vestibular endolymphatic hydrops (EH) are shown above. The three-dimensional real inversion recovery magnetic resonance imaging (3D-IR MRIs) examinations detected EH in the cochlea and vestibule 4 h after intravenous Gd injection. **a** The right solid arrow-pointed area was vestibule EH = 0, the left solid arrow-pointed area was vestibule EH = 1; **b** the right dotted arrow-pointed area was cochlea EH = 0, the left dotted arrow-pointed area was cochlea EH = 1; **c** the left dotted arrow-pointed area was cochlea EH = 2; **d** the right dotted arrow-pointed area was cochlea EH = 3, the right solid arrow-pointed area was vestibule EH = 2

Table 2 Comparison VEMP values of affected MD ear, unaffected ear and normal reference ear

	cVEMP					oVEMP				
	Threshold	p1	n1	amp(p1–n1)	R-rate	Threshold	p1	n1	amp(p1–n1)	R-rate
Affected ear	87.5 ± 7.6	16.8 ± 2.1	24.4 ± 2.1	96.4 ± 41	0.68	89.7 ± 5.3	15.9 ± 1.0	11.9 ± 0.9	7.8 ± 2.7	0.52
Unaffected ear	80.8 ± 6.3	17.0 ± 1.9	24.0 ± 2.4	86.3 ± 38.3	0.87	82.2 ± 4.6	16.0 ± 1.3	12.0 ± 1.1	12.3 ± 4.8	0.79
Normal reference	76.0 ± 7.2	15.9 ± 4.9	23.4 ± 5.2	237.6 ± 91.4	0.90	80.0 ± 4.8	15.6 ± 1.3	10.4 ± 1.2	13.8 ± 6.9	0.82
P	0.040*	0.707	0.483	0.249	–	0.042*	0.829	0.579	0.034*	–

p1 P1 latency, *n1* N1 latency, *amp(p1–n1)* P1–N1 amplitude; Kruskal–Wallis test to compare the VEMP amp(p1–n1) of three groups above, ANOVA test to compare the VEMP other values of three groups above

*Mean: $P < 0.05$; the unit of threshold is "dB"nHL, p1/n1 is "ms", amp(p1–n1) is "μV"

In order to analyze the quantitative relationship between the VEMP values and the degrees of EH in both the vestibule and the cochlea, we focused on the EH and VEMP values of the affected ears of unilateral MD. The VEMP values at different degrees of EH in the cochlea and vestibule are shown in Table 3a, b. When tested for threshold stimulation, the response rates of oVEMP decreased with an increase in cochlear EH severity.

The P1–N1 amplitude of oVEMP in extreme cochlear EH was more lower than that of no cochlear EH and mild cochlear EH ($P < 0.01$) (Fig. 2a); the AR of oVEMP in no cochlear EH was more lower than that of various degrees cochlear EH ($P < 0.01$) (Fig. 2b); the AR of cVEMP in severe vestibular EH was larger than those with no or mild vestibular EH ($P < 0.01$) (Fig. 2c). The other values of cVEMP and oVEMP in both cochlear and vestibular EH were not significantly different ($P > 0.05$).

The PTA threshold of the affected ears demonstrated an overall average hearing level of frequency, ranging from 500 Hz to 3 kHz. The correlation between the degree of cochlear EH and the mean PTA threshold was statistically significant ($P < 0.05$), and the vestibular EH did not correlate significantly with the PTA threshold ($P > 0.05$). The abnormal rate of caloric tests was higher in severe vestibular EH group than that of the mild or no vestibular EH

Table 3 (a) VEMP values in various degree vestibular EH, (b) VEMP values in various degree cochlea EH

	cVEMP						oVEMP					
	Threshold	p1	n1	amp(p1–n1)	AR	R-rate	Threshold	p1	n1	amp(p1–n1)	AR	R-rate
(a)												
0	86.9 ± 4.8	16.9 ± 2.1	24.2 ± 1.9	93.8 ± 38.2	0.48 ± 0.28	0.72	90.4 ± 4.1	15.9 ± 0.8	11.7 ± 0.85	9.0 ± 3.5	0.68 ± 0.42	0.56
1	86.3 ± 6.3	16.6 ± 2.1	23.9 ± 3.3	77.3 ± 33.4	0.46 ± 0.22	0.57	89 ± 5.5	15.7 ± 1.6	12.1 ± 1.2	7.5 ± 1.3	0.52 ± 0.45	0.59
2	89 ± 2.2	17.1 ± 2.0	25.7 ± 1.8	112.2 ± 54.6	0.72 ± 0.39	0.69	86.7 ± 2.9	16.7 ± 1.3	12.5 ± 0.62	8.7 ± 5.9	0.61 ± 0.41	0.49
P	0.618	0.925	0.322	0.440	0.045*	–	0.408	0.403	0.356	0.727	0.814	–
(b)												
0	86.8 ± 3.7	16.9 ± 2.6	23.9 ± 1.6	79.8 ± 35.8	0.27 ± 0.28	0.89	90 ± 5.2	15.6 ± 0.6	10.9 ± 0.8	12.6 ± 3.9	0.22 ± 0.16	0.78
1	86 ± 7.4	16.2 ± 1.9	24.0 ± 3.4	120.4 ± 32.7	0.62 ± 0.41	0.63	90 ± 7.1	14.7 ± 2.2	10.9 ± 0.1	10.4 ± 4.8	0.61 ± 0.39	0.56
2	88.2 ± 4.2	17.1 ± 2.2	24.8 ± 2.1	99.2 ± 49.7	0.34 ± 0.32	0.67	89.1 ± 4.9	16.2 ± 0.9	12.6 ± 0.6	7.9 ± 3.2	0.69 ± 0.42	0.49
3	86.9 ± 5.3	16.6 ± 1.7	24.2 ± 1.8	93.6 ± 32.4	0.52 ± 0.45	0.50	90 ± 3.5	16.2 ± 0.8	11.6 ± 0.6	7.5 ± 1.8	0.78 ± 0.37	0.31
P	0.811	0.849	0.745	0.387	0.105	–	0.979	0.244	0.383	0.031*	0.021*	–

p1 P1 latency, *n1* N1 latency, *amp(p1–n1)* P1–N1 amplitude, *AR* The asymmetry ratio, *R-rate* response rates. Kruskal–Wallis test and ANOVA to compare the VEMP in various degree EH of vestibular or cochlea

*Mean: $P < 0.05$; the unit of threshold is "dB"nHL, p1/n1 is "ms", amp(p1–n1) is "μV"

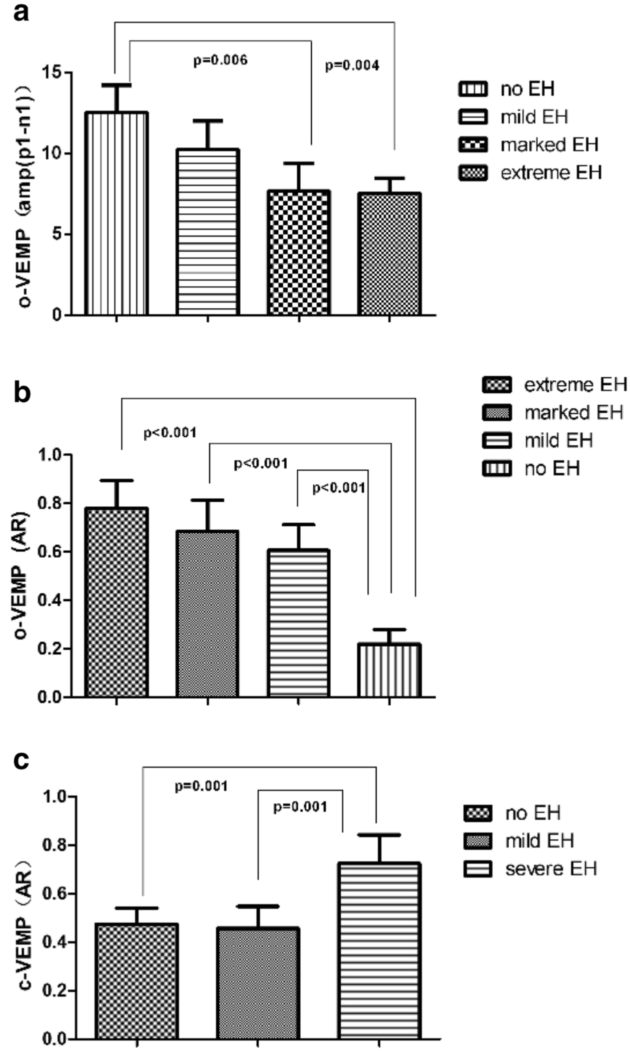

Fig. 2 **a, b** Quantitative comparison of the relationship between oVEMP values (N1–P1 amplitude, AR) and the degree of cochlea EH; **c** quantitative comparison of the relationship between the AR of cVEMP and the degree of vestibular EH. The columns of the histograms represent mean ± SEM, Bonferroni was applied to correct the *P* value for multiple testing, $P < 0.01$

group ($P < 0.05$), however, CP value did not correlated significantly with vestibular EH ratio ($P > 0.05$).

The duration of MD correlated positively with vestibular EH ($P < 0.05$); however, cochlear EH was not correlated with MD duration ($P > 0.05$). There was also no correlation between the frequency of vertigo attacks and vestibular EH ($P > 0.05$) or cochlear EH ($P > 0.05$).

Discussion

Although numerous studies have examined the pathologies of MD, the exact causes of MD are not clear. A number of efforts have been made to produce a consensus for the diagnosis of MD; however, this diagnosis depends mostly on clinical manifestation of MD in patients. Definite MD was diagnosed according to the Bárány Society in 2015 [1] and were found having EH in inner ear using MRI by IV-Gd administration in this study. In previous literature, it has been reported that women are affected slightly more often than men [17]; however, the gender differences of the participants in this study were different. As well known, the diagnosis of MD is mainly based upon clinical symptoms in the past, which are similar to the symptoms of vestibular migraines, and it is difficult to differentiate Meniere's disease and vestibular migraines. Therefore, mixed effects in migraine patients may result in a high proportion of women with MD. In this study, MRI by IV-Gd administration can help distinguish the vestibular migraines from MD [12].

The visualization of EH in patients with MD can provide a basis for further understanding the pathogenesis of MD. 3D-IR and 3D-FLAIR MRI by IV-Gd administration has become increasingly popular in clinical practices due to its examination of invasiveness and independent otologist, which only needs 4 fours to show EH following intravenous administration [3–5]. In this study, the results of MRI using IV-Gd administration revealed that the affected ears of all the MD patients had differing degrees of vestibular and cochlear EH. Severe vestibular EH was observed in 37 of the 56 patients, and mild cochlear EH was observed in 24 of the patients. This indicates that the degree of EH in vestibule and cochlea is not synchronized; there is no significant correlation between vestibular EH and cochlear EH. These results are inconsistent with those of previous reports [18, 19]. However, whether EH initiates from cochlea, the vestibula, or both simultaneously, could not be clarified in this study.

The response rates of cVEMP and oVEMP in the affected ears were lower and the response thresholds were higher than that of normal ears' [20, 21]. Even the amplitude of oVEMP in the affected ears was more lower. These results no doubt indicate that EH in MD can hinder saccular and utricular functions. The response rates of oVEMP were lower than cVEMP, a result that is consistent with a published paper [22] and is supported by the theory that the prevalence of utricular hydrops is lower than that of saccular hydrops in literature, the involvement of the utricle in MD has been reported to be less than that of the saccule [23, 24]. Using this test to indirectly diagnose MD may be useful in clinical practice.

Literature regarding oVEMP in MD characterizes oVEMP as having a reduced response rate, decreased amplitude, and increased threshold [20, 25]. However, quantitative analyses of the relationship with oVEMP values and various EH degrees in vestibule and/or cochlea of MD are rare. This study found that the response rates of oVEMP correlated with cochlear EH, the AR of oVEMP may separate the no cochlear EH from MD, and the P1–N1 amplitude help separate the extreme cochlear EH from other degree cochlear EH. These results indicate that when oVEMP is elicited, the consistency is significant between utricular EH and cochlear EH. The results were different from a previous study that since the saccule is next to the cochlea, the saccule EH frequent site and degree closely followed the cochlear EH [24].

In contrast to the previous results that suggest that sacculus dysfunction is negatively correlated with vestibular EH [26], AR was depicted in this study as a function of vestibular EH [27]. We did not find a significant negative correlation between sacculus dysfunction and vestibular EH; however, we did find that the AR of cVEMP was more higher in severe vestibular EH. That is, if the vestibular EH is severe enough, the sacculus dysfunction was significant. This could result in severe enough vestibular EH to lead to permanent morphological changes of the sensory organs, including the loss of saccular macula associated with the collapse of the saccular wall onto the otolithic membrane, which is consistent with reduced cVEMP [28, 29].

Regarding the association of hearing loss with degree of EH, there have been several different results. Yang et al. considered that both vestibular EH and cochlear EH are correlated with PTA threshold [18], and Wu et al. found that low-tone and mid-tone hearing thresholds are consistent with the extent of EH in all turns of the cochlea [14]. Robert thought that the degree of hearing loss correlates significantly with cochlear EH, but did not mention the hearing loss correlated with vestibule EH [13]. In comparison to those studies, we analyzed the association of mean hearing loss (at 500, 1k, 2k, and 3k frequencies) with the degree of cochlear and vestibular EH. Our result suggest that the correlation between hearing loss and cochlear EH is significant, but the correlation between hearing loss and vestibular EH is not significant.

Caloric test was used to evaluate the function of the horizontal semicircular canal. A few studies had assessed the vestibular function in MD with caloric test [30, 31]. In this study, MRI is not ideal in detecting semicircular canal hydrops. It is not feasible to compare quantitatively the relationship between the degree of semicircular canal hydrops and the results of caloric tests. However, there is an interesting finding that the abnormal rate of caloric tests was higher in severe vestibular EH group than that of the mild or no vestibular EH group, that indicated caloric response would be influenced by hydropic expansion of the vestibular labyrinth. Even in Choi's [32] study, the author found that the abnormal caloric tests were due to severe endolymphatic hydrops rather than vestibular hypofunction.

Conclusion

Advanced MRI technology with Gd intravenous administration offers the advantage of visualizing the degree and location of EH in patients with MD. AR and P1–N1 amplitude of oVEMP can be indirectly used to evaluate the extent of cochlear EH, however, AR of cVEMP can be used to separate the severe vestibular EH. This can help clinicians indirectly evaluate the degree and location of EH and diagnose MD with VEMP examinations under condition of absent MRI by Gd administration.

Funding This work was supported by the National Nature Science Foundation of China (Grant: 81670933 to Wuqing Wang; http://www.nsfc.gov.cn/).

Compliance with ethical standards

Conflict of interest No potential conflict of interest relevant to this article was reported. The study's protocol was approved by the Ethics Committee of Fudan University's review board, and written informed consent forms were obtained from the participants.

References

1. Goebel JA (2016) 2015 Equilibrium Committee Amendment to the 1995 AAO-HNS Guidelines for the Definition of Meniere's Disease. Otolaryngol Head Neck Surg 154:403–404
2. Nakashima T, Naganawa S, Sugiura M, Teranishi M, Sone M, Hayashi H et al (2007) Visualization of endolymphatic hydrops in patients with Meniere's disease. Laryngoscope 117:415–420
3. Homann G, Vieth V, Weiss D, Nikolaou K, Heindel W, Notohamiprodjo M et al (2015) Semi-quantitative vs. volumetric determination of endolymphatic space in Meniere's disease using endolymphatic hydrops 3T-HR-MRI after intravenous gadolinium injection. PLoS One 10:e0120357
4. Imai T, Uno A, Kitahara T, Okumura T, Horii A, Ohta Y et al (2017) Evaluation of endolymphatic hydrops using 3-T MRI after intravenous gadolinium injection. Eur Arch Otorhinolaryngol 274:4103–4111
5. Naganawa S, Kawai H, Taoka T, Sone M (2017) Improved HYDROPS: imaging of endolymphatic hydrops after intravenous administration of gadolinium. Magn Reson Med Sci 16:357–361
6. Curthoys IS (2010) A critical review of the neurophysiological evidence underlying clinical vestibular testing using sound, vibration and galvanic stimuli. Clin Neurophysiol 121:132–144
7. Manzari L, Burgess AM, Curthoys IS (2010) Dissociation between cVEMP and oVEMP responses: different vestibular origins of each VEMP? Eur Arch Otorhinolaryngol 267:1487–1489
8. Kushiro K, Zakir M, Ogawa Y, Sato H, Uchino Y (1999) Saccular and utricular inputs to sternocleidomastoid motoneurons of decerebrate cats. Exp Brain Res 126:410–416
9. Wang SJ, Weng WJ, Jaw FS, Young YH (2010) Ocular and cervical vestibular-evoked myogenic potentials: a study to determine whether air- or bone-conducted stimuli are optimal. Ear Hear 31:283–288
10. Fang ZM, Chen X, Gu X, Liu Y, Zhang R, Cao DR et al (2012) A new magnetic resonance imaging scoring system for perilymphatic space appearance after intratympanic gadolinium injection, and its clinical application. J Laryngol Otol 126:454–459
11. Zou J, Sood R, Zhang Y, Kinnunen PK, Pyykko I (2014) Pathway and morphological transformation of liposome nanocarriers after release from a novel sustained inner-ear delivery system. Nanomedicine (Lond) 9:2143–2155
12. Sun W, Guo P, Ren T, Wang W (2017) Magnetic resonance imaging of intratympanic gadolinium helps differentiate vestibular migraine from Meniere disease. Laryngoscope 127:2382–2388
13. Gürkov RFW, Louza J, Strupp M, Ertl-Wagner B, Krause E (2012) In vivo visualized endolymphatic hydrops and inner ear functions in patients with electrocochleographically confirmed Ménière's disease. Otol Neurotol 33:1040–1045
14. Wu Q, Dai C, Zhao M, Sha Y (2016) The correlation between symptoms of definite Meniere's disease and endolymphatic hydrops visualized by magnetic resonance imaging. Laryngoscope 126:974–979
15. Jongkees LBMJP, Philipszoon AJ (1962) Clinical nystagmography. A detailed study of electronystagmography in 341 patients with vertigo. Pract Otorhinolaryngol 24:65–93
16. Zhou YJ, Wu YZ, Cong N, Wang J, Chi FL (2017) Contrasting results of tests of peripheral vestibular function in patients with bilateral large vestibular aqueduct syndrome. Clin Neurophysiol 128:1513–1518
17. Bruderer SG, Bodmer D, Stohler NA, Jick SS, Meier CR (2017) Population-Based Study on the Epidemiology of Meniere's Disease. Audiol Neuro-otol 22:74–82
18. Yang S, Zhu H, Zhu B, Wang H, Chen Z, Wu Y et al (2018) Correlations between the degree of endolymphatic hydrops and symptoms and audiological test results in patients with Meniere's Disease: a reevaluation. Otol Neurotol 39:351–356
19. Nakada T, Yoshida T, Suga K, Kato M, Otake H, Kato K et al (2014) Endolymphatic space size in patients with vestibular migraine and Meniere's disease. J Neurol 261:2079–2084
20. Winters SMCT, Grolman W, Klis SF (2011) Ocular vestibular evoked myogenic potentials in response to air-conducted sound in Ménière's disease. Otol Neurotol 32:1273–1280
21. Taylor RL, Wijewardene AA, Gibson WP, Black DA, Halmagyi GM, Welgampola MS (2011) The vestibular evoked-potential profile of Meniere's disease. Clin Neurophysiol 122:1256–1263
22. Huang CH, Wang SJ, Young YH (2011) Localization and prevalence of hydrops formation in Meniere's disease using a test battery. Audiol Neuro-otol 16:41–48
23. Merchant SN, Rauch SD, Nadol JB Jr (1995) Meniere's disease. Eur Arch Otorhinolaryngol 252:63–75
24. Okuno T, Sando I (1987) Localization, frequency, and severity of endolymphatic hydrops and the pathology of the labyrinthine membrane in Meniere's disease. Ann Otol Rhinol Laryngol 96:438–445
25. Stephanie M. Winters TC, Wilko Grolman, Sjaak FL, Klis (2011) Ocular vestibular evoked myogenic potentials in response to air-conducted sound in Me´nie`re's disease. Otol Neurotol 32:1273–1280
26. Okumura T, Imai T, Takimoto Y, Takeda N, Kitahara T, Uno A et al (2017) Assessment of endolymphatic hydrops and otolith function in patients with Meniere's disease. Eur Arch Otorhinolaryngol 274:1413–1421
27. Young YH, Huang TW, Cheng PW (2003) Assessing the stage of Meniere's disease using vestibular evoked myogenic potentials. Arch Otolaryngol Head Neck Surg 129:815–818
28. Fraysse BG, Alonso A, House WF (1980) Meniere's disease and endolymphatic hydrops: clinical-histopathological correlations. Ann Otol Rhinol Laryngol Suppl 89:2–22
29. Young YH (2013) Potential application of ocular and cervical vestibular-evoked myogenic potentials in Meniere's disease: a review. Laryngoscope 123:484–491

30. Cordero-Yanza JA, Arrieta Vazquez EV, Hernaiz Leonardo JC, Mancera Sanchez J, Hernandez Palestina MS, Perez-Fernandez N (2017) Comparative study between the caloric vestibular and the video-head impulse tests in unilateral Meniere's disease. Acta Otolaryngol 137:1178–1182
31. Rubin F, Simon F, Verillaud B, Herman P, Kania R, Hautefort C (2018) Comparison of video head impulse test and caloric reflex test in advanced unilateral definite Meniere's disease. Eur Ann Otorhinolaryngol Head Neck Dis 135:167–169
32. Choi JE, Kim YK, Cho YS et al (2017) Morphological correlation between caloric tests and vestibular hydrops in Meniere's disease using intravenous Gd enhanced inner ear MRI. PLoS One 12:e0188301