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Travelling wave velocity test and Ménière's disease revisited

Gerd M. E. Claes · Michel Wyndaele · Claudia F. J. De Valck · Jos Claes · Paul Govaerts · Floris L. Wuyts · Paul H. Van de Heyning

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Abstract Transtympanic Electrocochleography (TT-ECoG) and the glycerol test can aid in the diagnostic process of Ménière's disease (MD). Measurement of travelling wave velocity (TWV) has been proposed as an alternative to TT-ECoG to detect endolymphatic hydrops. We assessed the feasibility and obtained normative data of the TWV test in the diagnosis of MD, and compared the test results in MD patients with their symptoms and their TT-ECoG results. The TWV test records two runs of auditory brainstem responses to clicks that are ipsilaterally masked with two different high pass filtered noise bands. The resulting latency difference of peak V was used as a measure of the TWV. The 95% confidence interval of this latency difference was defined in a group of 28 normals. Subsequently, the test was performed in nine MD patients. After the TWV test, seven of these patients underwent a TT-ECoG. The symptoms of MD patients at the time of testing and their TT-ECoG results were compared with TWV test results. The 95% confidence interval of the latency difference of peak V in the control group was 0.190–0.668 ms. A latency difference <0.190 ms indicates an increase in TWV, and thus reflects a positive test. In nine MD patients, we found a clear correlation between the result of the TWV test and TT-ECoG. The TWV test result did not significantly correlate with a single symptom. Our findings suggest that the TWV test can be useful to detect endolymphatic hydrops, but further experiments with larger patient groups are needed to confirm the diagnostic value of the TWV test.

G. M. E. Claes (✉) · M. Wyndaele · C. F. J. De Valck · J. Claes · P. Govaerts · F. L. Wuyts · P. H. Van de Heyning
University of Antwerp, University Hospital of Antwerp, ENT Department, Wilrijkstraat 10, 2650 Edegem, Belgium
e-mail: gerdclaes@yahoo.com

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Introduction

Ménière's disease (MD) is defined as the idiopathic syndrome of endolymphatic hydrops [4, 23, 27] which is an abnormal build-up of endolymph fluid in the inner ear. The typical symptoms (recurrent spontaneous episodes of rotatory vertigo, fluctuating sensorineural hearing loss, tinnitus with or without aural fullness) are usually not all present in the early stages of the disease.

In 1995, the diagnostic criteria for MD were published by the American Academy of Otolaryngology (AAO-HNS), together with the Committee on Hearing and Equilibrium [4]. According to these guidelines, diagnosis of MD is based on clinical symptoms and exclusion of identifiable "other causes". Four degrees of diagnostic certainty are defined: certain, definite, probable and possible MD.

It is assumed that permanent cochlear damage correlates with duration of the disease [22]. Pure tone audiometry, Electronystagmography (ENG) and auditory brainstem responses (ABR or BERA) document functional changes of the inner ear of which most are non-specific for MD. Radiological studies of the temporal bone and the posterior fossa are used to exclude other diagnoses.

There are a number of hypotheses concerning how endolymphatic hydrops affects cochlear function. Based on these theories, different techniques have been developed to detect endolymphatic hydrops and to distinguish MD patients from non-MD subjects.

One hypothesis is that hydrops causes a distension of the scala media and alters the position of the cochlear basilar membrane. As a consequence, the measured evoked

cochlear electrical potentials will be of higher amplitude. Transtympanic electrocochleography (TT-ECoG) measures the amplitude of the summating potential (SP), the action potential (AP) and the SP/AP amplitude ratio elicited by acoustic stimulation. Different studies have shown that this SP/AP ratio is increased in patients with MD [9, 10, 14, 19, 29]. Although TT-ECoG can detect endolymphatic hydrops, it is an uncomfortable, invasive and sometimes painful test for the patient [2].

An older diagnostic test is the glycerol test, which also has uncomfortable side effects like headache, nausea and vomiting [2, 21].

Consequently there is a clear need to develop other methods for the diagnosis of MD.

In 1991, Thornton and Farrell [25] published a non-invasive test to diagnose endolymphatic hydrops. The travelling wave velocity test (TWV test) is based on the hypothesis that chronic endolymphatic hydrops causes a stiffening of the basilar membrane [26]. It is assumed that higher rigidity of the basilar membrane increases the speed of the travelling sound wave. Thornton and Farrell measured a significantly higher TWV in 20 MD patients, compared to a control population. The TWV normalised after administration of glycerol, which suggests that the TWV test can indeed detect changes in endolymphatic hydrops and pressure.

Don et al. [6] introduced the CHAMP™ test (Cochlear Hydrops Analysis Masking Procedure), which is based on the same principle as the TWV test. The first report on this test suggested high diagnostic accuracy in differentiating definite MD from normal controls.

We aimed to assess the feasibility and to obtain normative data of the TWV test in the diagnosis of MD, and to compare the test results in MD patients with their symptoms and their TT-ECoG results.

Materials and methods

The TWV test

Travelling wave velocity is the speed at which the amplitude peak of basilar membrane displacements travels apically in the cochlea during sound stimulation. This velocity can be estimated using ABR to clicks in which a high-pass filtered noise is presented to the test ear in free field. This noise masks a part of the cochlea, resulting in derived ABR waveforms. As the cochlea is successively masked with lower cut-off frequencies, the derived ABR waveforms are presumed to reflect the activity of cochlear elements along a restricted segment of the basilar membrane. In TWV testing, two different cut-off frequencies are used. The main outcome of the TWV test is not the wave velocity but a calculated latency shift. Longer ABR latencies are found when using a lower cut-off frequency [24]. A shorter latency shift correlates with a higher TWV.

Stimuli

The derived ABRs were obtained using a Nicolet Viking IV apparatus, generating auditory stimuli and measuring brainstem responses. We used rarefaction clicks at a rate of 11.4 clicks per second, presented to the test ear using a Nicolet TIP 300 insert phone with an open tip to allow free field filtered noise masking. The default intensity of these clicks is 80 dBHL or 60 dB above the hearing threshold in patients with hearing loss. Simultaneously, a white masking noise was presented contralaterally at 40 dBHL, also with insert phones.

Brainstem responses were measured by three Blue Sensor™ electrodes, placed at the vertex (active electrode), the ipsilateral (reference electrode) and contralateral mastoid tip (ground electrode). Impedance measurements never exceeded 4 kΩ and were usually between 1 and 2 kΩ. The impedance difference between two electrodes never exceeded 1 kΩ.

The ipsilateral high-pass filtered noise was generated using FiNo 1.0.0, especially designed software, running on a laptop computer with a standard soundcard. The frequency spectrum of the generated noises showed an attenuation of 90 dB/octave at the different cut-off frequencies. The two cut-off frequencies used are 1,650 and 6,600 Hz. This noise was presented in free field through a Logitech 2-2200 THX Sound System. The speakers were placed at 50 cm away from the test ear. Intensity of the masking noise was calibrated using a Quest™ 2100 Sound Level Meter before each test. Using the free field method eliminates possible impedance problems when clicks are electrically mixed with masking noise.

ABR recordings

Subjects were placed on a chair in a sound proof room. Two runs of ABR recordings were performed: one run with clicks presented with ipsilateral high-pass filtered noise at 1,650 Hz, and a second run with clicks presented with high pass filtered noise at 6,600 Hz. All the recordings were averaged after at least 2,000 clicks. The peak of waves III and V were labelled for each response.

The first recording represents the response from the region of the cochlea below 1,650 Hz. The second recording represents the response from the region of the cochlea below 6,600 Hz, with shorter peak latencies than the first recording.

The latency shift between the two runs was calculated for wave III and V (Fig. 1).

Electrocochleography

The TT-ECoG was carried out using unfiltered click stimuli and tone burst stimuli. The test was performed and interpreted following the test protocol that was published by Wuyts et al. [29, 30]. For click stimuli, we used sweeps of 500 broadband clicks (100 μs duration) at a rate of 11.4 clicks per second and an intensity of 90 dBnHL. For tone burst stimuli, we used sweeps of 700 tone bursts at frequencies 0.5, 1, 2, 4 and 8 kHz with a rate of 37.4/s and an intensity of 100 dBnHL. When the SP response amplitude at 1 kHz tone bursts was more negative than −3 μV, the criterion for endolymphatic hydrops was met. Using click stimuli, the test was suggestive for endolymphatic hydrops when the SP/AP ratio exceeded 0.35.

Patients and setting

The tested patients were recruited from the outpatient clinic of the ENT Dept of the Antwerp University Hospital, which is a tertiary referral centre. The study protocol was approved by the ethical committee of the Antwerp University Hospital.

Each subject/patient underwent otoscopic examination and pure-tone audiometric testing at the time of the TWV test.

Control group

Twenty-eight normal hearing subjects in good general health underwent a bilateral TWV test. The group consisted of 16 male and 12 female subjects with a mean age of 29 years. All subjects had a negative otovestibular history. They specifically had no complaints of hearing loss, vertigo, tinnitus or aural fullness.

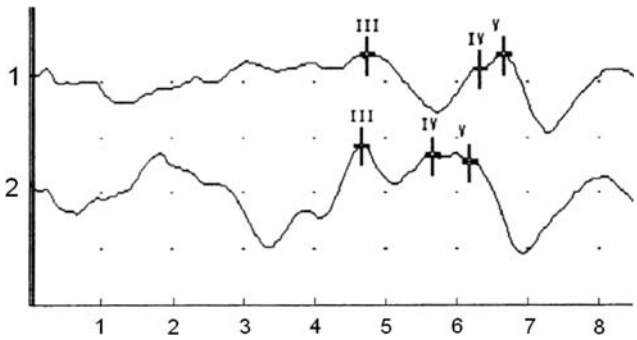

Fig. 1 ABR recordings used to calculate the latency shift: *1* using high pass filtered noise at 1,650 Hz and *2* using high pass filtered noise at 6,600 Hz

Ménière's disease patients

Nine MD patients (five males, four females) were included. Their mean age was 39 years.

Two MD patients underwent bilateral TWV testing without TT-EcoG. They were patients with an established unilateral diagnosis of MD, and were personally invited to participate in this study.

Six patients were sent by the ENT clinician for a bilateral TT-EcoG, and underwent bilateral TWV testing at the same time. One patient with unilateral total deafness was sent for a contralateral TT-ECoG, and underwent TWV testing at the same time.

All 17 ears were divided into 4 categories: Definite MD, Probable MD, Possible MD and asymptomatic contralateral ears. A distinction has to be made between normal ears and symptomatic contralateral ears of a unilateral Ménière's disease patient, since it has been shown that 27% of the latter show signs of endolymphatic hydrops [12].

Table 1 shows the symptoms of the 9 patients at time of testing.

Figure 2a–d show the pure-tone audiogram of each patient. Hearing thresholds were obtained at seven test frequencies: 125 Hz, 250 Hz, 500 Hz, 1 kHz, 2 kHz, 4 kHz and 8 kHz. The audiograms were divided into four categories, based on their configuration: low- and mid-frequency hearing loss (Fig. 2a), high frequency hearing loss (Fig. 2b), flat hearing loss (Fig. 2c) and normal hearing (Fig. 2d).

Statistical analysis

The ABR latencies and latency shift data, collected from the control group were analysed using SPSS 12.0 with the Kolmogorov–Smirnov test. The Student *t* test was performed to compare between the left and right ear the latency shift at wave V within the same person. For comparison with MD patients, only latency shifts measured at the left ears of the normal subjects were used. Statistical difference was considered significant at the $P < 0.05$ level.

Results

Normative data

For the 28 control subjects, the latency shift at wave III and V was calculated. This was done by subtracting the wave latency for the 1,650 Hz high pass masking condition from the wave latency for the 6,600 Hz masking condition.

Table 1 Current symptoms and classification of the Ménière's disease patients at the time of the TWV test

	Vertigo	Hearing loss	Tinnitus	Aural fullness	AAO-HNS
Patient 1 left	0	0	0	0	Asymptomatic contralateral
Patient 1 right	0	0	0	0	Definite MD
Patient 2 left	×	×	×	×	Definite MD
Patient 2 right	0	0	0	0	Asymptomatic contralateral
Patient 3 left	0	×	×	×	Definite MD
Patient 4 left	×	×	×	0	Definite MD
Patient 4 right	×	0	×	0	Probable MD
Patient 5 left	×	0	×	0	Probable MD
Patient 5 right	×	0	×	0	Probable MD
Patient 6 left	0	×	×	0	Probable MD
Patient 6 right	0	0	0	0	Asymptomatic contralateral
Patient 7 left	0	0	0	0	Possible MD
Patient 7 right	0	0	0	0	Asymptomatic contralateral
Patient 8 left	0	0	0	0	Possible MD
Patient 8 right	0	0	0	0	Possible MD
Patient 9 left	0	0	0	0	Asymptomatic contralateral
Patient 9 right	0	×	×	×	Possible MD

× Symptom present, *0* symptom absent

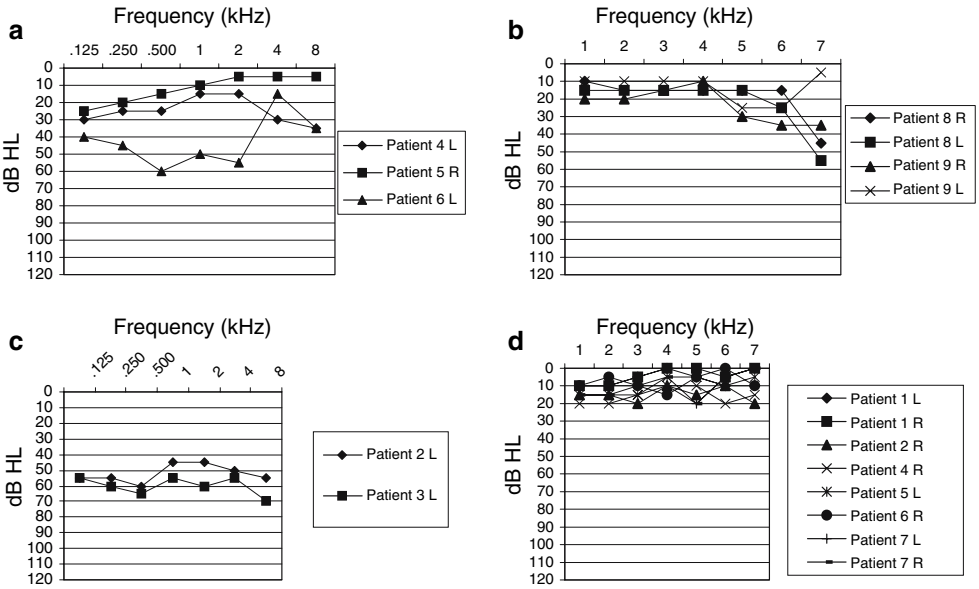

Fig. 2 Pure tone audiograms of each patient, divided into four categories: low- and mid-frequency hearing loss (**a**), high-frequency hearing loss (**b**), flat hearing loss (**c**) and normal hearing (**d**)

Table 2 shows descriptive statistical data for the latency shift at wave III and V. Both measured parameters showed a normal value distribution.

In order to estimate the TWV, we used the latency shift calculated at wave V. Other investigators also use wave V [6, 24, 25], because it is the most prominent and easy to recognize on ABR recording. Furthermore, Table 2 shows that the standard deviation of the latency shift at wave V is smaller than the latency shift calculated at wave III.

The mean latency shift at wave V in the control group is 0.429 ms. The lower 95% confidence limit was 0.19 ms. Therefore, latency shifts <0.19 ms can be considered abnormal and suggestive for endolymphatic hydrops.

Ménière's disease patients

All patients, except patient 3, underwent bilateral TWV testing. Patient 3 was only tested on the left side because of a total deafness on the right side. Table 3 shows the latency shift of wave V, calculated from bilateral TWV testing. Latency shifts <0.19 ms are highlighted, as this represents a positive TWV test. The results of bilateral TT-ECoG testing are also displayed.

Table 2 Descriptive statistical data for the latency shift at wave III and V

	Latency shift at wave III	Latency shift at wave V
N	28	28
Mean (ms)	0.150	0.429
5th percentile (ms)	−0.133	0.289
95th percentile (ms)	0.568	0.673
Standard deviation (ms)	0.195	0.122
Standard error (ms)	0.0368	0.0231
95% confidence interval (ms)	[−0.232; 0.532]	[0.190; 0,668]

Table 3 Summary of the TWV and TT-ECoG testing of the MD patients

Patient	Latency shift wave V (ms)	TT-ECoG clicks	TT-EcoG tone burst
Definite MD			
1 Right	0.58		
2 Left	0.16*	+	+
3 Left	0.28	+	+
4 Left	0.54	−	−
Probable MD			
4 Right	0.54	−	−
5 Left	0.42	+	−
5 Right	0.16*	+	−
6 Left	0.20	−	−
Possible MD			
7 Left	0.18*		
8 Left	0.04*	−	−
8 Right	0.00*	+	−
9 Right	−0.04*	+	+
Contralateral ears			
1 Left	0.24		
2 Right	0.58	−	−
6 Right	0.36	−	−
7 Right	0.50		
9 Left	0.22	−	−

* positive TWV test, + test suggesting MD, − test not suggesting MD

Table 4 shows the correlation between the result of the TWV and the result of the TT-ECoG for the seven patients that underwent both tests.

Table 3 shows that all four "Possible MD" ears have a positive TWV test result, while out of four "Definite MD" ears, only one ear tested positive. The asymptomatic contralateral ears all have normal TWV results.

Six ears have a positive ECoG test, of which four also have a positive TWV test. In total, five cases have a positive TWV test, of which four also have a positive ECoG test. In 10 out of 13 results (77%), the result of the TWV test corresponded to the result of the TT-ECoG using clicks. When using tone burst stimuli, this was the case in 9 out of 13 results (69%). The Odds Ratio (OR) that a TWV test is positive when the TT-ECoG with clicks is positive, is 12. For TT-ECoG with tone bursts, the OR is 4,67.

Table 4 Correlation between TWV test and electrocochleography results

	TWV +	TWV −
TT-ECoG click +	4	2
TT-ECoG click −	1	6
TT-ECoG TB +	2	1
TT-ECoG TB −	3	7

TB tone burst

Table 5 shows the correlation between the symptoms of the patient at the time of the test and the result of the TWV test.

This table illustrates that there is no correlation between a single symptom and the result of the TWV test

The OR that a patient with vertigo has a positive TWV test is 1.33. For hearing loss, the OR also equals 1.33. For tinnitus, the OR of a positive TWV test is 1.2, while for aural fullness this is 2.25.

Discussion

Using the latency shift calculation at wave V of two derived ABR waveforms, we obtained normal travelling wave velocity measures in a group of 28 control subjects.

As displayed in Table 2, measurements of the latency shift of wave V have the smallest standard deviation, and thus wave V must be preferred over wave III. The mean latency shift at wave III is 0.15 ms. At wave V, the mean latency shift has increased to 0.43 ms. Both waves represent retrocochlear responses, and current hypotheses are unable to explain this difference. None of the previous reports [5–8, 17, 24, 25] have mentioned latency shifts at wave III. Ideally one would choose to measure the latency shift at wave I, the only ABR wave of pure cochlear origin. However, this wave is often hard to recognize on an ABR recording, making its latency measurements less reliable.

Thornton and Farrell introduced the TWV test in 1991 [24, 25], and found that the mean normal TWV ranged from 3.1 to 24.8 m/s. Donaldson and Ruth measured the TWV in a normal control population of 24 subjects [7]. They found normal TWV values between 1.2 and 11.1 m/s.

Table 5 Correlation between symptoms at time of the test and the result of the TWV test

	TWV +	TWV −
Vertigo +	2	3
Vertigo −	4	8
Hearing loss +	2	3
Hearing loss −	4	8
Tinnitus +	3	5
Tinnitus −	3	6
Aural fullness +	2	2
Aural fullness −	4	9

This experiment was repeated in MD patients [8], however no increase in TWV was measured. To estimate the TWV, Donaldson and Ruth used Greenwood's scale, a map of the cochlea which shows a frequency specificity for each point along the basilar membrane [15].

Kim et al. [17] measured the TWV in a population of ten normal hearing subjects and seven MD patients. They used Békésy's scale to estimate the TWV [1] and found a higher TWV in MD patients (23.2 m/s at 8 kHz). In our study, when using the Greenwood's scale, the mean TWV in the 1,650–6,600 Hz region of the cochlea is 22.19 m/s in normals. Comparison of the TWV between different auhors is made difficult by the different cut-off freqeuncy of the high pass noise used in these studies.

A problem with developing objective tests for the diagnosis of MD is the lack of a Gold Standard. Endolymphatic hydrops and the composition of the endolymph fluid change over time, explaining the episodic nature of the symptoms [22]. To avoid influence of fluctuating disease, our patients underwent audiometry, TWV test and TT-ECoG at the same time.

The clinical diagnosis of MD is based on a combination of symptoms and clinical findings. The lack of correlation between a single symptom and the TWV test result therefore does not incriminate the value of the latter, but in our opinion illustrates the need for additional objective tests to support this clinical diagnosis.

The result of the TWV test corresponded to the result of the TT-ECoG using clicks in 77% of the cases, where this is 69% when using tone bursts. In our experiment, the odds of a positive TWV test is higher for TT-ECoG with clicks (OR = 12) than for TT-ECoG with tone bursts (OR = 4.67), however this is not a significant difference, because of the small number of cases.

In clinical practice, TT-EcoG is most often chosen as additional test to confirm diagnosis of endolymphatic hydrops [16]. It is, however, not included in the guidelines proposed by the AAO-HNS [4], possibly because there are numerous articles claiming low specificity and sensitivity of TT-ECoG [3, 11, 18, 20]. Extratympanic ECoG has been proposed as a repeatable diagnostic test for endolymphatic hydrops. Because of less favorable signal-to-noise ratio, extratympanic EcoG is possibly even less sensitive than the transtympanic technique [13, 19].

The number of studies based on the work of Thornton and Farrell is rather limited. A possible reason for this is the uncertainty about the pathophysiological hypothesis on which the test is based. According to this hypothesis, endolymphatic hydrops causes distension of the membranous labyrinth. In longstandig cases of ELH, the elasticity of the labyrinth and the basilar membrane decreases, which results in an increased endolymphatic pressure and consequently a displacement of the basilar membrane which affects cochlear function (hearing loss, tinnitus). The stiffening of the basilar membrane also causes the TWV to increase. In the vestibulum, displacement of the cupula gives rise to vertigo.

However, a recent experimental animal study in guinea pigs [28] showed no significantly increased endolymphatic pressure in cases of endolymphatic hydrops. In this experiment, endolymphatic pressure was measured 3 months after induction of endolymphatic hydrops. These findings are not compatible with the above described pathophysiological hypothesis.

In 2005, Don et al. [6] introduced CHAMP™ test (Cochlear Hydrops Analysis Masking Procedure) as a new diagnostic test for MD. This test also studies latency shifts of wave V in derived ABR patterns, but the used cut-off frequencies of the masking noise are different from our study. The CHAMP™ test was conducted in 23 definite MD patients and compared with the results in 38 non-MD normal-hearing subjects. By applying a cut-off value for the latency difference of 0.3 ms, their measures did not demonstrate an overlap between the MD group and the control group and therefore the authors concluded that the test had an extremely high, even 100%, sensitivity and 100% specificity for diagnostic use in individual patients. Don describes a phenomenon of undermasking in non-Meniere subjects resulting in a two-component wave V and a mean shift of 1,024 ms of the undermasked component in the control group versus −0.004 ms in the MD group. However, until now these promising results have not been confirmed by others. In a study by De Valck et al., MD patients could not be differentiated from non-MD subjects with otovestibular symptoms, using the CHAMP™ test [5].

Under the assumption that hydrops leads to higher TWV, the fluctuating character of endolymphatic hydrops may still lead to normal test results in a case where diagnosis based on the clinical picture over a longer timespan still suggests MD. A diagnosis based on an objective and repeatable measure will however still be helpful in the diagnosis of early and atypical cases of MD. A non-invasive

and therefore repeatable test should be preferred over TT-ECoG, provided it is equally or more reliable.

It is theoretically more useful to estimate the TWV over the whole length of the cochlea, as this will result in larger latency shifts, and possibly less overlap between normal subjects and patients. We intend to test a larger population of MD patients who, ideally spoken, present with active symptoms at time of testing.

Conclusions

We obtained TWV measures in 28 normal subjects and in 9 MD patients, who underwent an electrocochleography at the same time. Despite the small sample size, the results of the TWV test correlated to the results of electrocochleography. We found no significant correlation between the TWV test result and symptoms like vertigo, hearing loss, tinnitus and aural fullness evaluated separately. Our findings suggest that the TWV test can be useful to detect endolymphatic hydrops. This non-invasive test can be carried out repeatedly in one patient, which makes it useful in follow-up and evaluation of medical treatment. Further experiments with larger patient groups are needed to confirm the value of the TWV in the diagnosis of endolymphatic hydrops.

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