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Characterizing nystagmus using a portable eye movement recorder in patients with Meniere's disease and MRI-confirmed endolymphatic hydrops

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ABSTRACT

Objective: Meniere's disease (MD) causes episodic vertigo and fluctuating hearing loss. During attacks, nystagmus may appear either toward (i.e., irritative) or away from (i.e., paralytic) the affected ear, but it is difficult to observe these patterns in real-time. This study captured nystagmus using a portable eye movement recorder (PEMR) at the onset of attacks and analyzed its characteristics in patients with endolymphatic hydrops (EH) confirmed on contrast-enhanced magnetic resonance imaging (CE-MRI).

Methods: This study enrolled 54 patients with MD diagnosed using the Japan Society for Equilibrium Research criteria. All patients were provided with a PEMR and instructed to record their eye movements immediately after the onset of a vertigo attack and at designated follow-up time points. Patients were grouped into those with endolymphatic hydrops (EH) (certain MD group, CMD) and without EH (definite MD group, DMD) based on CE-MRI findings. Nystagmus was categorized as either irritative or paralytic based on direction.

Results: Based on CE-MRI, 41 out of 54 patients had EH. In the CMD group, 38 patients had nystagmus, including 33 and 5 with irritative and paralytic nystagmus, respectively. In the DMD group, 10 patients had nystagmus, including 2 and 8 with irritative and paralytic nystagmus, respectively. The distribution of nystagmus types differed significantly between the groups ($\chi^2 = 14.69$, $p = 0.00013$). Reversal of nystagmus direction over 24 h tended to be more frequent in the CMD versus DMD group, although the difference was not significant (15 vs. 2 cases, $\chi^2 = 1.313$, $p = 0.251$). No significant association was found between the direction or directional change of nystagmus and the localization of EH (vestibular, cochlear, or both) or the laterality of EH (unilateral or bilateral).

Conclusion: PEMR enabled the real-time recording and characterization of nystagmus during vertigo attacks. Irritative nystagmus was significantly more common among patients with EH versus those without EH, suggesting that irritative nystagmus reflects active hydropic stimulation of the vestibular apparatus. In contrast, paralytic nystagmus, which was more frequently observed in patients without EH, may indicate relative vestibular hypofunction rather than acute hydropic excitation.

1. Introduction

Meniere's disease (MD) is a chronic inner ear disorder characterized by fluctuating sensorineural hearing loss, tinnitus, and recurrent episodes of vertigo [1]. Although its etiology is not completely understood, the most widely accepted pathological mechanism is endolymphatic hydrops (EH) [2], an excessive accumulation of endolymph in the cochlea and vestibular organs. Postmortem studies of patients with MD have revealed histopathological evidence of EH, supporting its central role in the disease process [3,4]. Recent advancements in contrast-enhanced magnetic resonance imaging (CE-MRI) have enabled the visualization of EH in both the vestibule and cochlea [5,6]. This is because gadolinium diffuses into the perilymphatic space but not into the endolymphatic space, which therefore appears as a dark area. Thus, the evidence of EH on CE-MRI is important for the diagnosis of MD.

In Japan, MD is typically diagnosed based on symptom history and

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audiological examination, based on the Japan Society for Equilibrium Research (JSER) criteria [7]. The JSER criteria are largely based on the criteria from Bárány Society [8], which classifies MD into "definite" and "probable" cases. The Bárány Society diagnoses definite MD (DMD) based on the presence of both low-frequency sensorineural hearing loss and repeated episodes of vertigo, whereas probable MD is diagnosed if there are fewer clinical features. However, these guidelines rely primarily on subjective clinical history without incorporating objective markers such evidence of EH on imaging. In contrast, the JSER criteria include an additional category, certain MD (CMD), which requires the presence of cochlear or vestibular EH on CE-MRI. Thus, CMD is the only category of MD grounded in the anatomical confirmation of EH. Therefore, CE-MRI is currently used in Japan to arrive at a detailed diagnosis.

Despite its diagnostic utility, CE-MRI does not provide real-time information about inner ear function during episodes of vertigo. Nystagmus, which reflects the asymmetry of vestibular input, is a key objective sign of peripheral vestibular dysfunction, notably seen during vertigo attacks [9]. Typically, nystagmus in MD initially beats toward the affected ear, referred to as irritative nystagmus (IN). After the acute vestibular dysfunction, the direction of nystagmus may change direction toward the unaffected ear, referred to as paralytic nystagmus (PN). However, these directional changes are difficult to capture in the clinical setting, because vertigo attacks often occur outside of medical facilities. Accordingly, we developed a portable eye movement recorder (PEMR) that consists of an infrared video camera embedded in a wearable device [10]. The PEMR enables patients to self-record eye movements at the onset of vertigo episodes.

The present study builds upon our previous report (Ueno et al., 2024), which investigated diagnostic stratification based on the presence of endolymphatic hydrops and nystagmus findings. In the current study, we extend this work by addressing a pathophysiological question, examining whether the localization of endolymphatic hydrops is associated with specific nystagmus phenotypes during vertigo attacks. Whereas the previous study focused on diagnostic classification, the present investigation evaluates the relationship between hydrops localization and nystagmus characteristics. To address this question, CE-MRI data were reanalyzed to separately evaluate cochlear and vestibular hydrops, an analytical approach not performed in the prior study.

This study investigated the association between EH confirmed via CE-MRI and the characteristics of nystagmus recorded via PEMR at various timepoints during vertigo attacks among patients with MD, including analyses of the relationship between hydrops localization and nystagmus characteristics.

2. Materials and methods

2.1. Study design

This study was approved by the ethics committee of our hospital (Nos. 22282, 23156) and performed in accordance with the Declaration of Helsinki. This study was registered in the UMIN Clinical Trials Registry (UMIN000020047, UMIN000053728).

2.2. Patient selection

This study included patients diagnosed with DMD based on the JSER criteria at our institution between December 2015 and April 2023 [7]. CE-MRI was performed in all patients, and those with findings of EH were classified as CMD.

The inclusion criteria were as follows: 1) age $\geq$ 20 years, 2) presence of vertigo attacks at least once every 2 weeks, 3) with CE-MRI findings, and 4) successfully recorded nystagmus during vertigo attacks using a PEMR. The exclusion criteria were as follows: 1) did not undergo CE-MRI due to renal dysfunction or refusal, 2) previous endolymphatic sac surgery or intratympanic gentamicin injection, 3) with cochlear implantation prior to recording, and 4) presence of comorbid vestibular or neurological disorders that could affect the diagnosis or interpretation of nystagmus, including conditions other than Meniere's disease. After applying the inclusion and exclusion criteria, 54 patients were enrolled in this study. The study cohort partially overlaps with that reported in Ueno et al. (2024), although it is not identical. The recruitment period of the present study extended one year beyond the previous study. In addition, inclusion criteria were refined to focus on patients with pure Meniere's disease; cases with strong features suggestive of vestibular migraine included in the previous analysis were excluded (n = 4), while seven newly enrolled patients were added. These modifications resulted in a revised cohort analyzed under a different study objective.

2.3. Determining the affected side

The affected side of MD was determined in all patients based on a previous report [10]. The flow diagram is described in Fig. 1. First, the side with cochlear symptoms (e.g., hearing loss, tinnitus, or ear fullness) during vertigo attack was identified as the affected side. Second, if the cochlear symptoms were bilateral, the side with hearing loss was identified as the affected side. Hearing loss was defined using pure-tone audiometry as a difference of 30 dB or more in bone-conduction hearing thresholds at 2 consecutive frequencies below 2000 Hz compared to the other side. Third, if hearing loss was bilateral, then the side with abnormal results upon additional vestibular examinations (e.g., caloric test, electrocochleography [ECochG], and vestibular evoked myogenic potentials [VEMP]) was identified as the affected side. In the bithermal caloric test, canal paresis above 20% was considered a positive result. Asymmetry ratios above 32.7% on cervical VEMP (cVEMP) and above 40.8% on ocular VEMP (oVEMP) were defined as abnormal [11]. On ECochG, a summating potential amplitude (SP) to action potential amplitude (AP) ratio (SP/AP ratio) above 40% was defined as abnormal.

2.4. Portable eye movement recorder (PEMR)

A custom-built PEMR (Biomedica Co., Osaka, Japan) was used; its structural details and other information were described previously [10]. Following closure of Biomedica Co., device production was transferred to oneA Co (Osaka, Japan), beginning in September 2022. Then, a new version of the PEMR was also used in this study (Fig. 2). Both systems were capable of accurately detecting the direction of nystagmus. The device consisted of a head-mounted infrared charge-coupled device camera, embedded in a goggle-type frame and connected to a portable digital recorder. Patients were instructed to wear the PEMR upon experiencing an episode of vertigo. After putting on the goggles and pressing a single button, patients were asked to opened their eyes, and the recording started automatically and stopped after a preset duration. The device provided voice guidance throughout the entire procedure, even when wearing the goggles. Each recording lasted 1 min, and patients were instructed to perform recordings up to 4 times per vertigo episode. Video recordings were scheduled at the following time points: 1) at the onset of the vertigo attack, 2) immediately after symptom resolution, 3) one hour after symptom resolution, and 4) the following day. Two of the authors (H.T. and K.H.S.) independently reviewed all the recordings and discussed their findings to reach a consensus regarding the type of nystagmus observed. IN and PN were defined as nystagmus beating toward and away from the affected ear, respectively. When multiple recordings were obtained from a single patient, the predominant nystagmus direction across recordings was defined as the representative nystagmus type for patient-level analysis.

2.5. CE-MRI protocol and evaluation of EH

All patients underwent CE-MRI using either the MAGNETOM Trio (Siemens Medical Solutions, Erlangen, Germany) or Sigma Excite HD 3 T

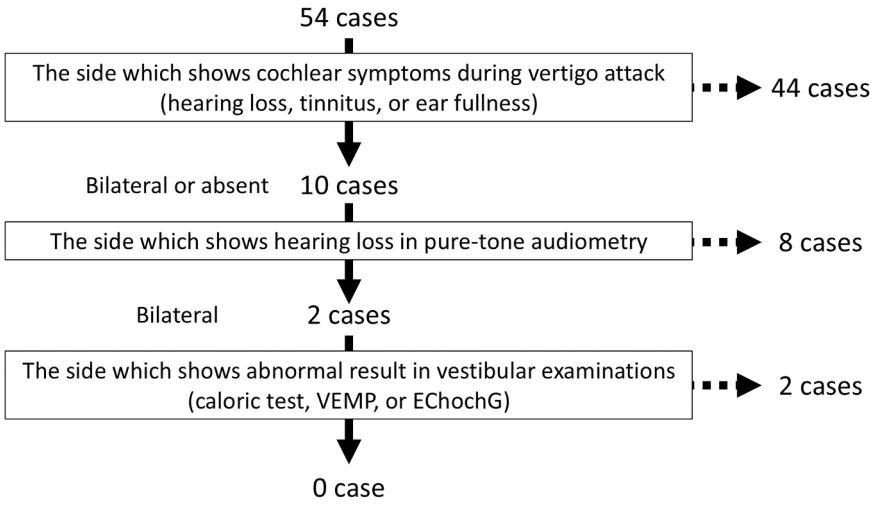

Fig. 1. Flow diagram for determining the affected side. During the vertigo attack, 44 out of 54 patients demonstrated unilateral cochlear symptoms. Out of the remaining 10 patients without cochlear symptoms, 8 had hearing loss on pure-tone audiometry. Two patients with bilateral hearing loss had abnormal results on vestibular examinations.

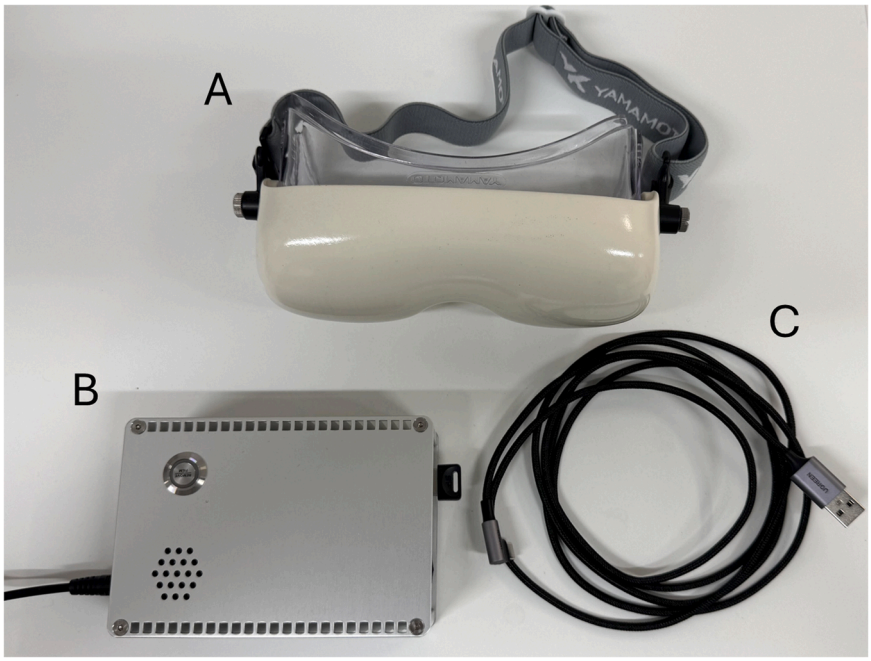

Fig. 2. New version of the portable eye movement recorder. A) A goggle-type frame including a head-mounted infrared charge-coupled camera inside. B) A portable digital recorder. C) A cable which connects the goggle-type frame (A) to the recorder (B).

(GE Healthcare, UK). CE-MRI was performed according to the previous article [5,6]. CE-MRI was performed 4 h after intravenous injection of gadoteridol (ProHance; Bracco Diagnostics, BIPSO GmbH, Singen, Germany). A double dose (0.4 ml/kg) was administered for examinations using GE scanners, whereas a single dose (0.2 ml/kg) was used for Siemens scanners. Two-dimensional fluid-attenuated inversion recovery (2D-FLAIR) images were used to evaluate EH. Two of the authors (Y.U. and T.I.), blinded to the patients' clinical information, independently examined the CE-MRI findings and determined the presence or absence of EH in the cochlea and/or vestibule.

2.6. Statistical analysis

Statistical analyses were performed using JMP version 17 statistical software (IBM Japan, Tokyo, Japan). Categorical variables were compared between groups using the chi-square test or Fisher's exact test (i.e., Fisher–Freeman–Halton exact test), as appropriate. A two-tailed p-value < 0.05 was considered statistically significant.

3. Results

3.1. Patient characteristics

A total of 54 patients with MD were included in the final analysis; their characteristics are described in Table 1. All patients recorded at least one vertigo attack using the PEMR and underwent CE-MRI of the inner ear. Due to the presence of EH in the cochlea or vestibule on CE-MRI, 41 patients (76%) were classified as CMD, whereas 13 patients without identifiable hydrops (24%) were classified as DMD. The overall cohort included 21 males and 33 females with a median age of 53 years

Table 1
Patient characteristics.

	Total	CMD group	DMD group
Number of patients	54	41	13
Age, years, median (range)	57 (20–84)	55 (20–84)	41 (22–74)
Sex, male/female	21/33	18/23	3/10
Laterality, right/left	18/36	13/28	5/8

CMD group, certain Meniere's disease; DMD group, definite Meniere's disease

(range: 20–84). The CMD group included 18 males and 23 females with a median age of 55 years (range: 20–84). The DMD group included 3 males and 10 females with a median age of 41 years (range: 22–74). The right side was affected in 18 cases (CMD group, n = 13; DMD group, n = 5), whereas the left side was affected in 36 cases (CMD group, n = 28; DMD group, n = 8). In the CMD group, there were 35 cases of unilateral EH and 6 cases of bilateral EH. All cases of unilateral EH showed hydrops on the same side as the auditory symptoms.

3.2. Results of PEMR recordings

At the onset of vertigo, 48 out of 54 patients exhibited observable nystagmus, specifically classified as IN in 35 patients (64.8%) and PN in 13 patients (24.0%). Meanwhile, 6 patients (11.1%) did not exhibit any clear nystagmus. Nystagmus was predominantly horizontal or horizontal-torsional. An example is shown in the supplementary movie, which demonstrates IN in a patient with MD affecting the left ear. All evaluations were made in reference to the affected side, as determined by cochlear symptoms and audiological/vestibular testing. Patients in the CMD group were classified as having IN in 33 cases (80.4%), PN in 5 cases (12.1%), and no clear nystagmus in 3 cases (7.3%). In contrast, patients in the DMD group were classified as having IN in 2 cases (15.3%), PN in 8 cases (61.5%), and no clear nystagmus in 3 cases (23.0%) The prevalence of IN was significantly higher in the CMD group versus the DMD group ($\chi^2 = 14.69$, $p = 0.00013$, Table 2), indicating an association between IN and the presence of EH on CE-MRI. Out of all 54 patients, 26 had complete recordings at all 4 designated time points described earlier. Directional reversal of nystagmus (i.e., from IN to PN or vice versa) was observed in 15 patients with CMD and 2 patients with DMD. Although directional reversal was more common in the CMD group, this did not reach statistical significance ($\chi^2 = 1.313$, $p = 0.251$, Table 3). Reversal from IN to PN was observed in 10 patients, whereas reversal from PN to IN was observed in 7 patients.

3.3. Relationship between the localization of EH and direction of nystagmus

This study evaluated the relationship between the localization of EH on CE-MRI and the characteristics of nystagmus recorded on PEMR. Among 41 patients with EH in the affected ear, IN was the predominant pattern across all subgroups of EH localization: vestibular (n = 14), cochlear (n = 5), and both vestibular and cochlear (n = 14). On the other hand, PN was less common (vestibular, n = 2; cochlear, n = 0; both, n = 3). Fisher–Freeman–Halton exact test showed no significant association between EH localization and the direction of nystagmus (p = 1.000; Table 4A).

Supplementary movie. Irritative nystagmus in a patient with Meniere's disease of the left ear.A video clip is available online. Supplementary material related to this article can be found online at doi:10.1016/j.anl.2026.04.005.

Table 2
Direction of nystagmus.

Direction of nystagmus	CMD group	DMD group	Total
Irritative	33*	2	35
Paralytic	5	8	13
Total	38	10	48

CMD group, certain Meniere's disease; DMD group, definite Meniere's disease
* $\chi^2 = 14.69$, $p = 0.00013$

Table 3
Directional reversal of nystagmus.

Directional reversal	CMD group	DMD group	Total
Positive	15	2	17
Negative	23	8	31
Total	38	10	48

No significance, $\chi^2 = 1.313$, $p = 0.251$
CMD group, certain Meniere's disease; DMD group, definite Meniere's disease

No significant association was found between EH localization and directional reversal of nystagmus. Directional reversal was observed in 6, 2, and 7 patients with vestibular EH, cochlear EH, and both vestibular and cochlear EH (p = 1.000; Table 4B).

No significant association was found between bilateral EH and the direction of nystagmus ($\chi^2 = 0.077$, $p = 0.781$; Table 5A). IN was observed in 5 cases with bilateral EH and 28 patients unilateral EH. PN was observed in 1 case of bilateral EH and 4 cases of unilateral EH. Directional reversal was seen in 2 out of 6 patients with EH bilateral EH and in 13 out of 32 patients with unilateral EH, revealing no significant difference ($\chi^2 = 0.112$, $p = 0.737$; Table 5B).

4. Discussion

This study investigated the relationship between EH confirmed via CE-MRI and the direction of spontaneous nystagmus recorded during vertigo attacks among patients with MD. A PEMR device was used to capture nystagmus at the onset of attacks, and the underlying pathology of MD was evaluated based on the EH hypothesis. Although a subset of patients overlapped with our previous report, the present study differs in its hypothesis, analytical framework, and outcome measures. Specifically, this study focuses on the relationship between hydrops localization and dynamic nystagmus characteristics, providing new pathophysiological insight beyond the diagnostic stratification addressed previously. The major findings of this study were as follows. First, EH was confirmed on CE-MRI in 41 out of 54 patients. Second, IN was more frequently observed in patients with CMD versus those with DMD. Third, directional reversal of nystagmus was also more frequent in patients with CMD versus DMD, but this did not reach statistical significance. Fourth, EH localization on CE-MRI (i.e., vestibule, cochlea, or both) was not significantly associated with the occurrence of IN nor with directional reversal of nystagmus. Lastly, the presence of bilateral EH

Table 4A
Relationship between endolymphatic hydrops localization and direction of nystagmus.

Direction of nystagmus	Vestibule	Cochlea	Vestibule and cochlea	total
Irritative	14	5	14	33
Paralytic	2	0	3	5
total	16	5	17	38

No significance, p = 1.000 (Fisher–Freeman–Halton exact test)

Table 4B
Relationship between endolymphatic hydrops localization and directional reversal of nystagmus.

Directional reversal	Vestibule	Cochlea	Vestibule and cochlea	total
Positive	6	2	7	15
Negative	10	3	10	23
total	16	5	17	38

No significance, p = 1.000 (Fisher–Freeman–Halton exact test)

Table 5A
Relationship between endolymphatic hydrops laterality and direction of nystagmus.

Direction of nystagmus	Bilateral EH	Unilateral EH	total
Irritative	5	28	33
Paralytic	1	4	5
total	6	32	38

No significance, $\chi^2 = 0.077$, p = 0.781
EH, endolymphatic hydrops.

Table 5B
Relationship between endolymphatic hydrops laterality and directional reversal of nystagmus.

Directional reversal	Bilateral EH	Unilateral EH	total
Positive	2	13	15
Negative	4	19	23
total	6	32	38

No significance, $\chi^2 = 0.112$, p = 0.737
EH, endolymphatic hydrops.

was not related to either IN or the directional reversal of nystagmus.

Studies are conflicting regarding the direction of initial nystagmus observed at the onset of a vertigo attack, with some reporting this to be IN [12,13], whereas others report PN to be the initial type [14]. The present study used PEMR to capture the initial nystagmus at the onset of a vertigo attack, which reflects the acute pathological change of MD. Notably, IN was significantly more common in the CMD group, whereas PN was more prevalent in the DMD group. This suggests that EH may be associated with altered inner ear pressure dynamics which can initially trigger excitatory vestibular responses. Directional reversal of nystagmus was often seen after the attack [15,16], and this was captured during the PEMR recordings. Although no significant relationship was found between the directional reversal of nystagmus and the presence of EH, directional reversal was common in the CMD group. Given these findings, we hypothesize that the underlying mechanism of directional changes is complex and cannot be explained solely by the severity of EH. Nevertheless, the presence of EH can trigger vestibular excitation and instability of vestibular function.

The localization of EH (i.e., within the cochlea, vestibule, or both) demonstrated no significant relationship with the direction of nystagmus (Table 4A), nor with the directional reversal of nystagmus (Table 4B). Thus, while the presence of EH may predispose a patient toward IN, the precise site of EH within the inner ear does not appear to determine the directionality or temporal evolution of the nystagmus response. A recent study reported a relationship between cochlear EH and vestibular dysfunction among patients with MD [17]. In the present study, all 5 patients with cochlear EH likewise exhibited IN. However, this study did not evaluate the actual volume of EH on CE-MRI, which could reflect the severity of pressure of the endolymphatic space [18]. Future studies should evaluate the volume of EH by measuring the endolymphatic space on CE-MRI.

Bilateral EH demonstrated no significant association with the direction of nystagmus (Table 5A), nor with directional reversal of nystagmus (Table 5B). Thus, bilateral EH does not necessarily indicate severe MD or unstable vestibular function. Nevertheless, the presence of bilateral EH possibly contributes to vestibular imbalance. Further investigation is needed to clarify the functional significance of bilateral EH, such as a quantitative analysis and detailed evaluation of the endolymphatic space, rather than simple dichotomization into positive or negative. This approach could enable a more appropriate assessment of patients with bilateral EH, since qualitative classification alone may be insufficient.

Two different MRI systems (Siemens and GE) were used in this study, which may have introduced variability in image quality. CE-MRI acquired with Siemens scanners was performed using the HYDROPS protocol [5], whereas GE imaging followed a previously reported protocol [6]. Although image quality differed slightly between systems, endolymphatic hydrops could be consistently detected with both protocols. While quantitative evaluation was more challenging in GE images, the primary analyses of this study were based on categorical detection of EH rather than precise quantitative measurements. Therefore, inter-system variability is unlikely to have substantially affected the study conclusions.

This study highlights the diagnostic value of combining CE-MRI findings with PEMR. The strong link between IN and EH confirmed on CE-MRI supports the hypothesis that the initial phase of vertigo in MD is often driven by irritative vestibular responses due to fluctuations in inner ear pressure. Furthermore, the use of PEMR enables patients to record nystagmus during natural attacks, capturing dynamic features that are not typically seen during clinic visits.

5. Conclusion

This study investigated the relationship between the direction and directional change of nystagmus captured via PEMR and EH confirmed via CE-MRI among patients with MD. The strong association between IN and EH supports the role of hydrops as both a functional and anatomical driver of vertigo. While the localization of EH did not show significant associations with direction and directional reversal of nystagmus, this area needs further investigation, particularly a quantitative evaluation of the endolymphatic space. In conclusion, PEMR offers a novel, non-invasive window into the pathophysiology of MD and may become a pivotal tool for its diagnosis, monitoring, and treatment stratification.

Declaration of Generative AI and AI-assisted technologies in the writing process

None declared.

Declaration of Competing Interest

None.

Acknowledgments

The ethics committee of Osaka University Hospital approved the study (Nos. 22282, 23156). This study was registered in the UMIN Clinical Trials Registry (UMIN000020047, UMIN000053728). The authors would like to thank Enago (www.enago.jp) for the English language review.

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Informed consent

Informed consent was obtained from all individual participants included in the study.

Author Contributions

R.O., T.I., K.H.S. and H.I. designed the study. R.O. and K.H.S. wrote the manuscript. H.T. and K.H.S. reviewed the PEMR recordings. Y.U. and T.I. reviewed the CE-MRI and determined the presence of EH. Y.O. and T.S reviewed and revised the manuscript. All authors contributed to the writing of the final manuscript.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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