Received: 5 September 2022 | Revised: 5 December 2022 | Accepted: 31 December 2022
DOI: 10.1002/lio2.1011

ORIGINAL RESEARCH

Laryngoscope Investigative Otolaryngology

Gravity perception disturbance in patients with unilateral Meniere disease

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Funding information
AMED, Grant/Award Number: 22dk0310117h0001

Abstract

Objective: To investigate gravity perception disturbance (GPD) in patients with Meniere disease (MD), we classified GPD type based on the results of the head-tilt perception gain (HTPG) and the head-upright subjective visual vertical (HU-SVV) evaluated by the head-tilt SVV (HT-SVV) test in patients with unilateral MD.

Methods: We conducted the HT-SVV test on 115 patients with unilateral MD and 115 healthy controls. Among the 115 patients, the period from the first vertigo episode to the examination (PFVE) was known for 91 patients.

Results: The HT-SVV test classified 60.9% and 39.1% of patients with unilateral MD as GPD and non-GPD, respectively. GPD was classified according to HTPG/HU-SVV combinations as follows: Type A GPD (21.7%, normal HTPG/abnormal HU-SVV), Type B GPD (23.5%, abnormal HTPG/normal HU-SVV), and Type C GPD (15.7%, abnormal HTPG/abnormal HU-SVV). As the PFVE became longer, patients with non-GPD and Type A GPD decreased; however, those with Types B and C GPD increased.

Conclusion: This study provides novel information on unilateral MD from the perspective of gravity perception by classifying GPD based on the results of the HT-SVV test. This study's findings suggest that overcompensation for vestibular dysfunction in patients with unilateral MD exhibited by large HTPG abnormalities may be strongly associated with persistent postural-perceptual dizziness.

Level of Evidence: 3b

KEYWORDS
gravity perception disturbance, head tilt, Meniere disease, overcompensation, subjective visual vertical

1 | INTRODUCTION

Patients with vertigo/dizziness observed in clinical practice exhibit a variety of clinical features, including gravity perception disturbance (GPD).[1] GPD occurs when there is an anomaly in the gravity perception mechanism, which consists of the central nervous system,[2–5] that integrates sensory input from the otolith organs;[6–8] somatosensory receptors;[9] and semicircular canals.[10] GPD is diagnosed using the subjective visual vertical (SVV) test,[11,12] which is a simple psychophysical paradigm for measuring the visually perceived direction of the gravitational vertical using a visual line stimulus.[13] The conventional SVV test is conducted in the head upright condition and is referred to as the head upright-SVV (HU-SVV) test. The HU-SVV test assesses the HU-SVV, which is a parameter used to evaluate the left–right difference in gravity perception in the head-upright condition.

To examine GPD in more detail, we established the head-tilt SVV test (HT-SVV test), which is performed with the head upright and statically tilted to the left and right.[14] We have previously reported the results of the HT-SVV test in healthy participants[1] and patients with vertigo/dizziness.[15,16] The HT-SVV test assesses the left and right head-tilt perception gains (HTPGs), which is a parameter used to evaluate the magnitude of gravity perception with the head statically tilted to the left and right, in addition to the HU-SVV. The combination of normal and abnormal results of HU-SVV and HTPG of the HT-SVV tests may reveal new GPD characteristics.

In this study, we focused on patients with unilateral Meniere disease (MD) for the following reasons: (1) MD has been well studied because it is a classic and relatively common vertigo disorder.[17,18] (2) Recent magnetic resonance imaging (MRI)[19,20] and vestibular-evoked myogenic potentials (VEMP)[21] studies showed a high rate of otolithic abnormalities in MD; therefore, MD may cause GPD. (3) Since the affected side is unilateral, it is possible to discuss the effects of the affected side on the direction of the HU-SVV and the magnitude of the HTPG. Therefore, the purpose of this study was to examine unilateral MD, classified according to the results of the HT-SVV test, from a new angle based on the characteristics of GPD types.

2 | MATERIALS AND METHODS

2.1 | Participants

This study was conducted on 115 patients with unilateral MD (72 females and 43 males; age: 21–86 years [mean ± standard deviation, 56.3 ± 14.6, median: 57.0 years]; affected side: 54 right, 61 left), according to the diagnostic guidelines of the International Classification of Vestibular Disorders.[22] The study excluded patients who were assigned another vertigo-associated diagnosis (e.g., stroke, vestibular migraine, benign paroxysmal positional vertigo, and cervical vertigo). The patients were those who had visited and were hospitalized at the Vertigo/Dizziness center in Nara Medical University Hospital to complete the HT-SVV test between July 2014 and December 2020. Among the 115 patients, the period from the first episode of vertigo to the examination (PFVE) was known for 91 patients, with a range of 1–500 months, mean ± SD of 99.5 ± 118.7 months, and median of 51 months. As controls, 115 healthy participants (72 females and 43 males, age: 21–82 years [54.8 ± 15.8, 55.0 years]) of similar age and sex ratio were included in the study.

This study was approved by the Ethics Committee of Nara Medical University Hospital, Japan (identification number: 916) and was conducted in accordance with the principles of the Declaration of Helsinki. All participants provided written informed consent.

2.2 | Examination procedure

The HT-SVV test was performed using a simple examination system (HT-SVV system, UNIMEC, Fuchu, Japan), that we developed as described previously.[1] The participants sat on a chair ~60 cm from a bar-display box and wore goggles to eliminate any visual reference cues outside the bar. At the beginning of each trial, the participant was asked to tilt the head slowly leftward or rightward (approximately −30°, 0°, or 30° head tilt; 0° is upright, that is, in the direction of gravity, and rightward is positive), according to the examiner's instructions, while keeping the participant's trunk upright and their eyes closed. After the head was maintained in a static condition, the participant was asked to open their eyes and answer the SVV by aligning the bar to the subjective gravity axis using a keypad. The SVV was measured 14 times (four times in each of the −30° and 30° conditions and six times in the 0° condition) in pseudo-random order. At the same time, the head-tilt angle (HTA) was monitored using a linear accelerometer attached to a head cap.

Eighty-three (51 females and 32 males, age: 23–86 years [56.4 ± 14.5, 57.0] years) of 115 patients with unilateral MD also underwent the simplified caloric test,[23,24] which is easy and useful for detecting endolymphatic hydrops thought to cause MD, in the same week as the HT-SVV test. The simplified caloric test was performed by irrigating 5 ml of cold water at 20°C into the external auditory ear canal for 15 s. Both ears were stimulated separately with a 5-min interval between tests. The induced nystagmus was recorded using video oculography.

2.3 | Assessment

The HU-SVV was calculated as the average of six measurements of the SVV during the head upright position. Usually, the HU-SVV is expressed in absolute values, but when signing the HU-SVV, a positive value was defined if the HU-SVV deviated to the affected side and vice versa.

The head-tilt perception (HTP) was defined as the value obtained by subtracting the SVV from HTA: HTP = HTA – SVV (Figure 1A). We calculated the slope of the regression lines (thick lines in Figure 1A) fitted to the HTA and HTP data using the fact that HTA and HTP show linearity when HTA is between −30° and 30°.[4] This slope is termed the HTPG. The representative data are shown in Figure 1B. The left HTPG (0.79) was calculated from the data obtained under HTA between −30° and 0°, and the right HTPG (1.37) was calculated from the data obtained under HTP between 0° and 30°. If the gravity perception is completely accurate, namely, HTPG = 1 and HU-SVV = 0°, the result is a straight line with slope 1 through the origin (thin line in Figure 1B).

In addition, we assessed the HTPG asymmetry ratio (AR) for each participant using the following index:

$$\text{HTPG AR}\,(\%) = 100 \times |(\text{left HTPG} - \text{right HTPG})/(\text{left HTPG} + \text{right HTPG}). \quad (1)$$

Also, we evaluated the effect of the affected side using the following index based on (1):

$$\text{Signed HTPG AR}\,(\%) = 100 \times (\text{affected side of HTPG} - \text{unaffected side of HTPG}) / (\text{affected side of HTPG} + \text{unaffected side of HTPG}). \quad (2)$$

If the signed HTPG AR is positive, the HTPG of the affected side is larger than that of the unaffected side and vice versa.

In this study, the reference values were set for HTPG (0.80–1.25), HTPG AR (<10%), and HU-SVV (<2.5°).[1] If any of these values were beyond the reference ranges, the diagnosis of GPD was confirmed. Based on the abnormal result of HTPG (HTPG and/or HTPG AR) and HU-SVV, GPD was classified into the following three types. Type A, in which HTPG was normal but HU-SVV was abnormal, Type B, in which HTPG was abnormal but HU-SVV was normal, and Type C, in which both HTPG and HU-SVV were abnormal.

The simplified caloric test was evaluated using the maximum slow-phase eye velocity (°/s) of nystagmus induced after cold-water irrigation.

2.4 | Statistical analyses

The study results were assessed using the Mann–Whitney *U* test for comparing nonpaired data, Wilcoxon signed-rank test for comparing paired data, Kruskal–Wallis test with a post hoc Steel–Dwass test for multigroup comparisons, and Fisher's exact test for sex distribution between the two groups. Statistical significance was set at $p < .05$. All analyses were performed using Statcel 4 (OMS, Saitama, Japan).

3 | RESULTS

3.1 | Comparison between patients with unilateral MD and healthy participants

The results of the HT-SVV test, HTPG, HTPG AR, and HU-SVV, along with the age and sex ratio in patients with unilateral MD and healthy participants, are summarized in Table 1. Among them, only HU-SVV was significantly larger in patients with unilateral MD (median: 1.7°) than in healthy participants (1.0°).

3.2 | Classification of GPD type

Based on the results of the HT-SVV test, 70 (60.9%) of 115 patients with unilateral MD were diagnosed with GPD and

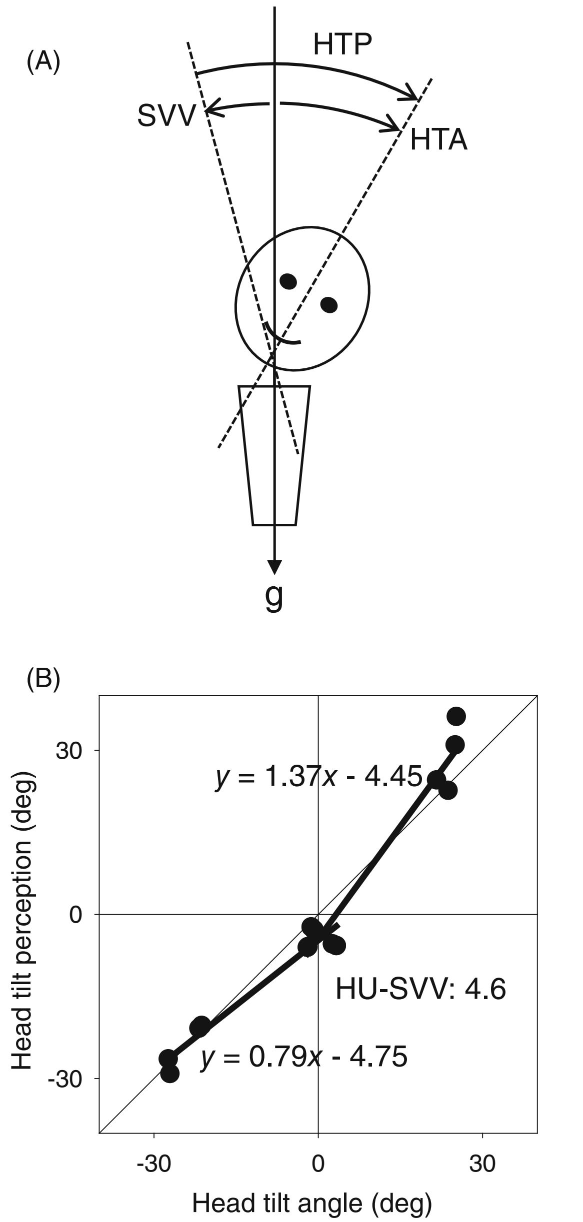

FIGURE 1 Gravity perception assessment. (A) Head-tilt perception (HTP) was defined as the value obtained by subtracting the subjective visual vertical (SVV) from the head-tilt angle (HTA). (B) Head-tilt perception gain (HTPG) was defined as the slope of the regression lines fitted to the HTA and HTP data (thick lines). The left HTPG (0.79) was calculated from the data obtained under HTA between −30° and 0°, and the right HTPG (1.37) was calculated from the data obtained under HTP between 0° and 30°. If the gravity perception was completely accurate, the result was a straight line with slope 1 through the origin (thin line).

the remaining 45 patients (39.1%) were classified as non-GPD. Furthermore, GPD was classified into three types (Types A–C) as shown in Figure 2. Type A GPD was observed in 25 patients (21.7%), Type B in 27 patients (23.5%), and Type C in 18 patients (15.7%). HTPG abnormalities in Types B and C included HTPG AR− (large or small HTPG on both sides) and AR+

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TABLE 1 Comparison between patients with MD and healthy participants.

	Patients with MD ($n = 115$)	Healthy participants ($n = 115$)	p-value
Age, median (range), years	57.0 (21–86)	55.0 (21–82)	.432
F:M ratio	72:43	72:43	1.000
HTPG, median (range)	1.04 (0.48–1.83)	1.02 (0.70–1.34)	.364
HTPG AR, median (range), %	5.3 (0.1–31.2)	3.9 (0.1–18.4)	.115
HU-SVV, median (range), degree	1.7 (0.0–8.2)	1.0 (0.0–3.7)	<.001

Abbreviations: AR, asymmetry ratio; F, female; HTPG, head-tilt perception; HU-SVV, head upright subjective visual vertical; M, male; MD, Meniere disease.

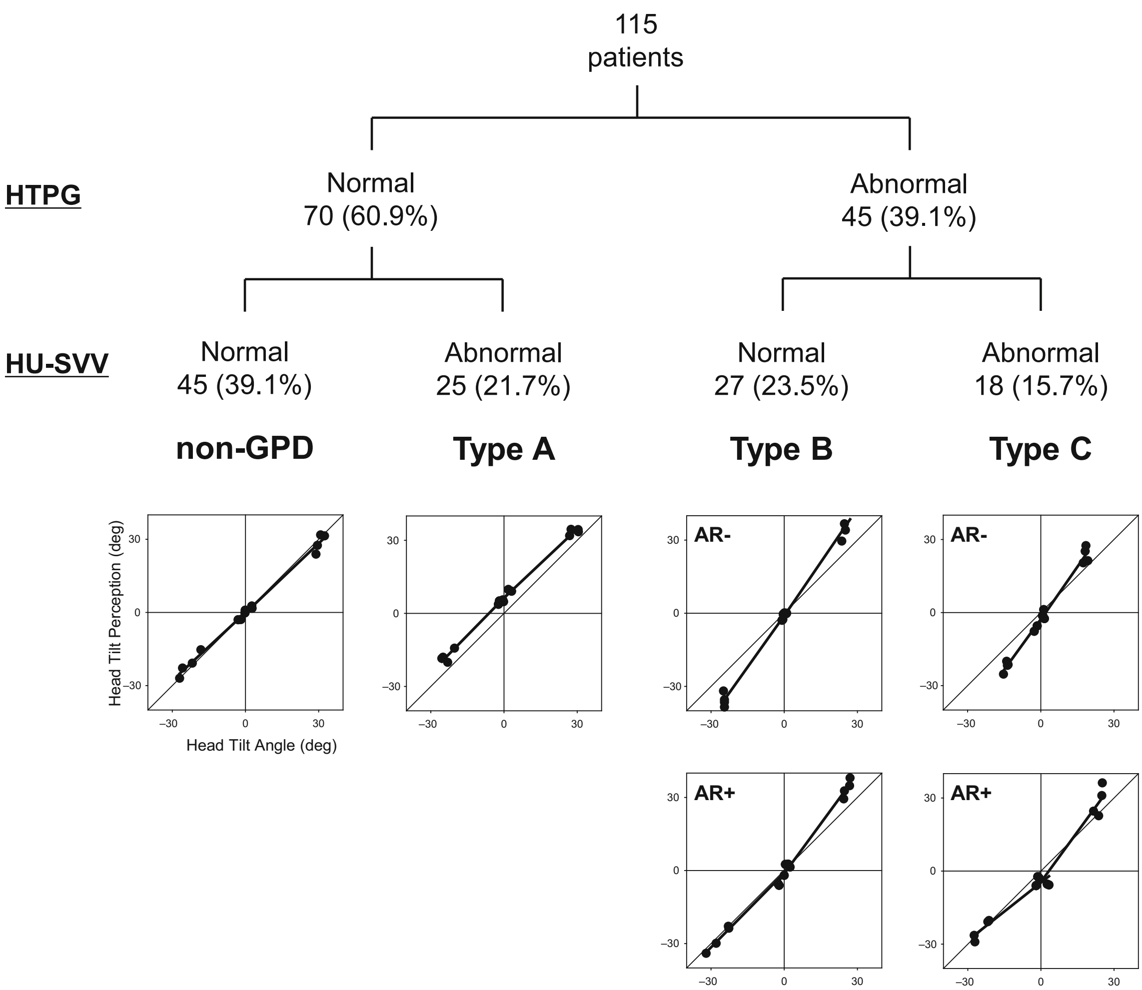

FIGURE 2 Type classification of gravity perception disturbance (GPD). Based on the results of the head tilt-subjective visual vertical (HT-SVV) test, 70 (60.9%) of 115 patients with unilateral Meniere's disease (MD) were diagnosed with GPD. GPD can be classified into three types (Types A–C). Type A GPD, in which the head-tilt perception gain (HTPG) was normal, whereas the head-upright SVV (HU-SVV) was abnormal, was found in 25 patients (21.7%). Type B GPD, in which HTPG was abnormal, whereas the HU-SVV was normal, was observed in 27 patients (23.5%). Type C GPD, in which both HTPG and HU-SVV were abnormal, was observed in 18 patients (15.7%). The remaining 45 patients (39.1%) were classified as non-GPD. AR, asymmetry ratio.

(large or small HTPG on one side and/or abnormal HTPG AR), as shown in Figure 2. AR+ was predominant in both Type B (82.1%) and Type C (83.3%). Of all the HTPG abnormalities, a relatively large HTPG was predominant in both Type B (82.1%) and Type C (66.7%).

3.3 | Comparison of parameters of the HT-SVV test between each GPD type

Figure 3 shows the results of the HTPG, HTPG AR, and HU-SVV of Types A–C, together with that of the control and non-GPD groups.

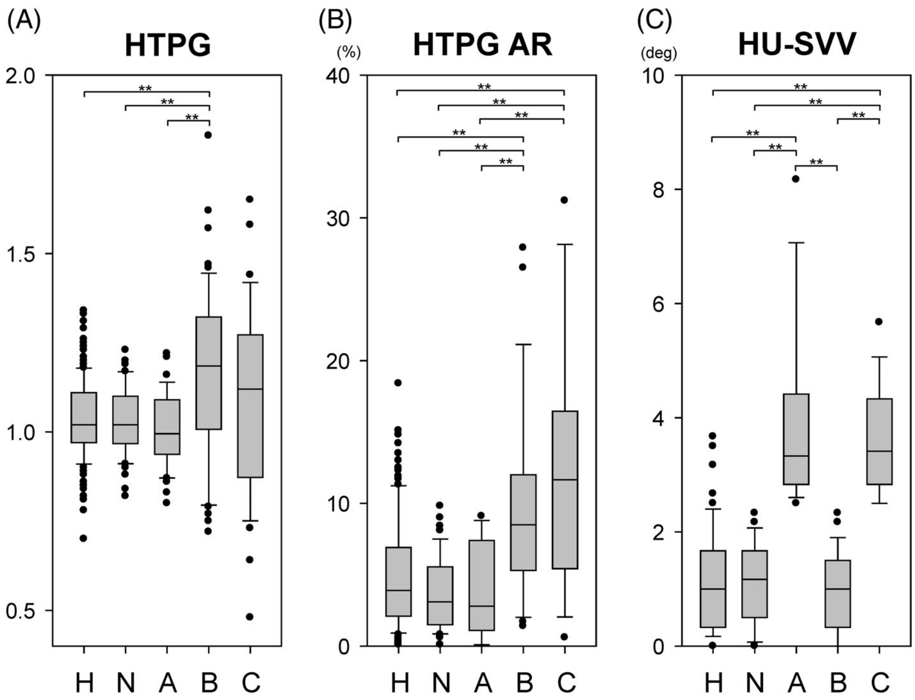

FIGURE 3 Comparison of parameters of the head tilt-subjective visual vertical (HT-SVV) test. (A) Head-tilt perception gain (HTPG) in Type B was significantly larger than that in the control, nonperception disturbance (GPD), and Type A groups; however, Type C showed more variability and no significant difference compared with the other groups. (B) HTPG asymmetry ratio (AR) in both Types B and C was significantly larger than that in the other groups. (C) The head-upright subjective visual vertical (HU-SVV) in both Types A and C was significantly larger than that in the other groups. Whiskers indicate 10th to 90th percentiles, and the horizontal line represents the median. A, Type A; B, Type B; C, Type C; H, healthy participants; N, non-GPD. $^{**}p < .01$ (Steel–Dwass test).

HTPG in Type B was significantly larger than that in the control, non-GPD, and Type A groups; however, Type C exhibited greater variability and no significant difference compared with the other types (Figure 3A). HTPG AR in both B and C Types was significantly larger than that in the other groups (Figure 3B), whereas HU-SVV in both Types A and C was significantly larger than that in the other groups (Figure 3C).

3.4 | Effect of the affected side on gravity perception in each GPD type

Thereafter, we examined the effect of the affected side of the unilateral MD on gravity perception. Regarding the HTPG, only Type C showed a significant difference between the affected and unaffected sides, and the affected side was larger than the unaffected side (Figure 4A).

Based on the HTPG results, only the signed HTPG AR of Type C was significantly positive compared with that of the controls (Figure 4B). Although Types A and C showed a relatively wide distribution, the signed HU-SVV was not significantly different among the control, non-GPD, and other GPD-type groups (Figure 4C).

3.5 | Difference between the affected and unaffected sides in the caloric test

The caloric test showed that the response of the affected side was significantly smaller than that of the unaffected side in the non-GPD and Type A groups; nevertheless, no difference was observed in the Types B and C groups (Figure 4D).

3.6 | Change in the percentage of GPD types according to PFVE

Figure 5 shows the percentages of non-GPD and the three GPD types in each of the three PFVE groups: ≤ 1 year ($n = 18$), >1 year, ≤ 10 years ($n = 48$), and > 10 years ($n = 25$). In PFVE ≤1 year, non-GPD (44.4%) and Type A (33.1%) showed high percentages, which subsequently decreased to 32.0% and 24.0% in PFVE >10 years, respectively. In contrast, the percentages of Types B and C increased from 16.7% and 5.6% in PFVE ≤1 year to 28.0% and 16.0% in PFVE >10 years, respectively.

4 | DISCUSSION

In this study, patients with unilateral MD were diagnosed with GPD or non-GPD using the HT-SVV test, and GPD was further classified into Types A–C. Type A is a GPD in which the SVV deviation is almost constant regardless of whether the head is upright or tilted to the left or right, resulting in a parallel shift in the relationship between the HTP and HTA from non-GPD, as shown in Figure 2; in other words, the gravity axis of the patient is tilted. Type B involves GPD, which has been regarded as non-GPD by the conventional HU-SVV test because the SVV does not deviate in the head-upright condition. However, the SVV deviates when the head is tilted to the left and/or right. Type C is a complex form of GPD in which the SVV deviates with the head upright and the direction and/or magnitude of the deviation varies with a head tilt.

The HU-SVV is measured when the head is upright (condition for the HU-SVV test), that is, gravity acts equally on both sides of the head. In contrast, the HTPG shows the magnitude of gravity

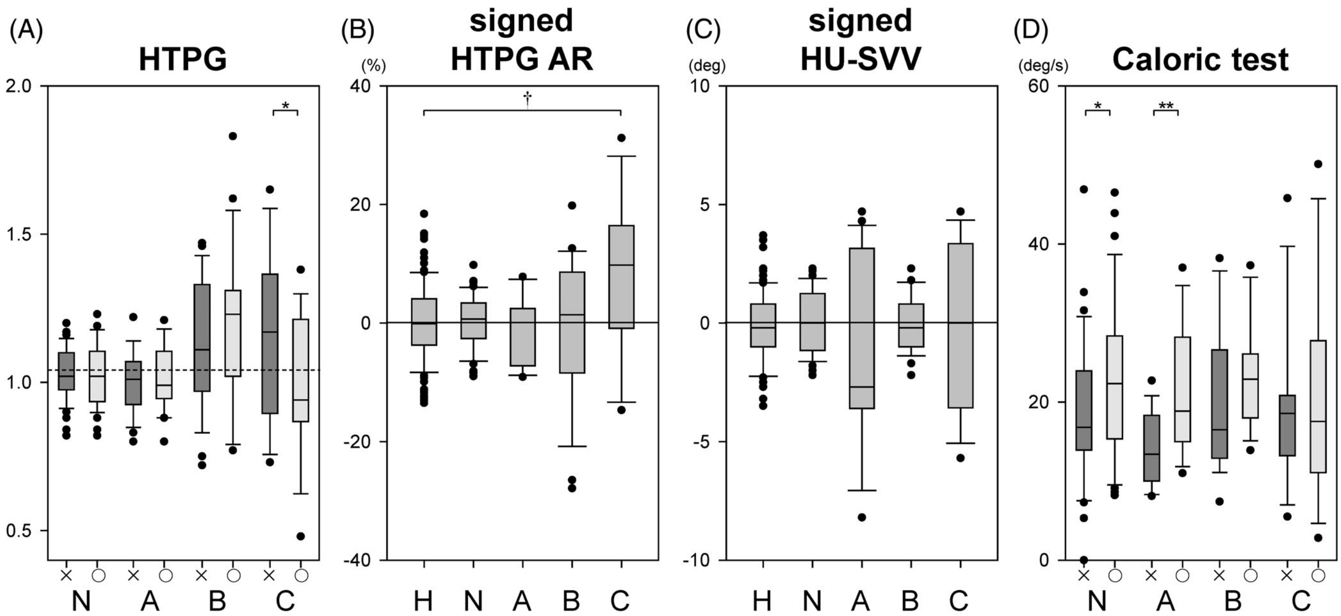

FIGURE 4 Effect of the affected side on gravity perception in each type of gravity perception disturbance (GPD). (A) Head-tilt perception gain (HTPG) in Type C only showed a significant difference between the affected and unaffected sides, and the affected side (1.17 ± 0.27) was larger than the unaffected side (1.00 ± 0.24). The dotted line represents the average of healthy participants. (B) Signed head-tilt perception gain asymmetry ratio (HTPG AR) in Type C only was significantly positive compared with that of the controls. (C) Signed head-upright subjective visual vertical (HU-SVV): although Types A and C showed a relatively wide distribution, the signed HU-SVV was not significantly different among the control, non-GPD, and any GPD-type groups. (D) Caloric test: the response of the affected side was significantly smaller than that of the unaffected side in the non-GPD and Type A groups; nonetheless, no difference was observed in the Types B and C groups. A, Type A; B, Type B; C, Type C; H, healthy participants; N, non-GPD; o, unaffected side; x, affected side. **p* < .05, ***p* < .01 (Wilcoxon signed-rank test). †*p* < .05 (Mann–Whitney U test).

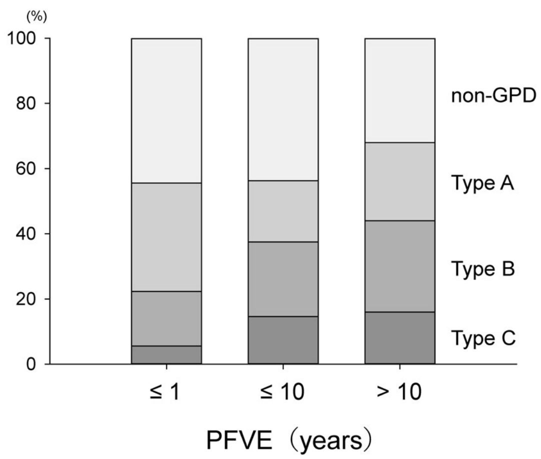

FIGURE 5 The percentage of gravity perception disturbance (GPD) types according to first vertigo to the examination (PFVE). In PFVE ≤1 year, non-GPD (44.4%) and Type A (33.1%) cases were present at high percentages, which subsequently decreased to 32.0% and 24.0% in PFVE >10 years, respectively. In contrast, the percentages of Types B and C increased from 16.7% and 5.6% in PFVE ≤1 year to 28.0% and 16.0% in PFVE >10 years, respectively.

perception when the head is tilted to the left or right (condition for the HT-SVV test), that is, gravity is stimulated asymmetrically to the left or right sides of the head. The otolith organs and gravity sensors are composed of the utriculus and sacculus, and the utriculus responds mainly to head-tilt conditions within 30° to the left and right in the HT-SVV test.[25]

In addition, the utriculus responds predominantly to ipsilateral head roll tilt; for example, the right utriculus responds mainly when the head is tilted to the right.[26] Although McKenna et al.[27] reported that the SVV during head roll tilt was influenced by the somatosensory receptors of neck muscles, the small difference in the SVV between head tilt alone and whole-body roll tilt in normal participants[14] indicates that the effect of the somatosensory receptors of neck muscles is thought to be minor. Accordingly, at least in the acute phase, HTPG is considered to assess ipsilateral utriculus function.

Among the three types of GPD, cases of Types A and C with abnormal HU-SVV were classified as GPD using the conventional HU-SVV test. The combined total was 37.4% cases of unilateral MD. Previous studies using the conventional HU-SVV test have reported a GPD diagnosis rate of 63.3% in acute MD,[28] 46.2% in chronic MD,[29] and 25%–50% in chronic vertigo including MD.[30] As most of the patients in this study had chronic unilateral MD, our results are reasonable.

Kumagami et al.[28] reported that the HU-SVV of patients with unilateral MD usually deviated to the affected side in the acute phase due to otolith dysfunction. As the directions of HU-SVV deviation in Types A and C were not always on the affected side, the reason cannot be explained only by delayed recovery of otolith function or

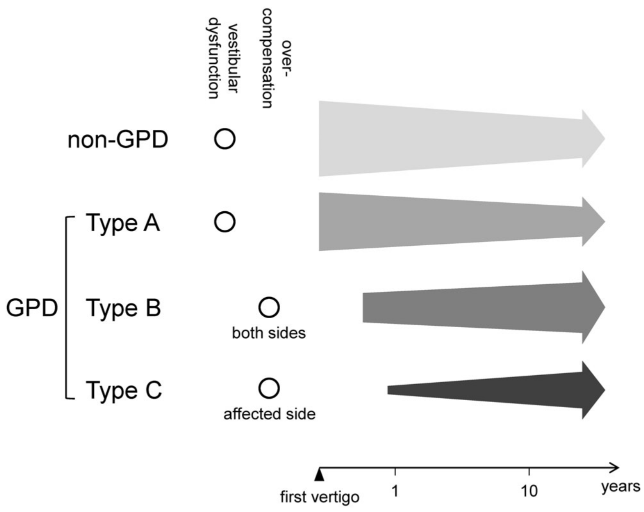

FIGURE 6 Time course of unilateral Meniere's disease by analogy with the characteristics of gravity perception. Peripheral type of gravity perception pattern (nongravity perception disturbance [GPD] and Type A), which is associated with vestibular dysfunction, decreased, and central type of gravity perception pattern (Types B and C), which is associated with overcompensation, increased with prolongation of the period from the first vertigo episode to the examination.

insufficient central compensation. The differences between Types A and C, other than those related to HTPG, are as follows: (1) Type A had a larger percentage of short-term PFVE than long-term PFVE, whereas Type C had the opposite effect. (2) In the caloric test, Type A showed a decreased response on the affected side, whereas Type C showed no difference between the affected and unaffected sides. These differences indicate that those classified as Type C, unlike Type A, have lost the features of peripheral vestibular dysfunction observed in early MD[31] due to prolonged disease.

In Types B and C, where the HTPG was abnormal, large HTPG abnormalities were more common than small HTPG abnormalities. In addition, large HTPG abnormalities were observed on both the affected and unaffected sides in Type B, but only on the affected side in Type C. These large HTPG abnormalities are assumed to be overcompensation for vestibular dysfunction, especially of the utriculus, for several reasons: (1) Even in healthy participants, the HTPG becomes larger in the older population relative to the young and in the standing position relative to the sitting position, suggesting that an unstable posture increases the HTPG to enhance the righting reflex;[1] (2) Eulenburg et al.[32] proposed that the central sensitization of otolith perception in older participants counterbalances age-related functional decline in peripheral vestibular and somatosensory systems based on a functional MRI study; and (3) Theysohn et al.[33] reported that exposure to an ultrahigh-static magnetic field using 7-T MRI causes temporary dysfunction and overcompensation of the vestibular system.

Based on the properties of gravity perception of unilateral MD revealed in this study, unilateral MD can be grouped into a peripheral type of gravity perception pattern (decreased response in caloric test and normal HTPG like non-GPD and Type A), which exhibits vestibular dysfunction, and a central type of gravity perception pattern (large HTPG-like Types B and C), which exhibits overcompensation, as shown in Figure 6. Peripheral type of gravity perception pattern decreased and central type of gravity perception pattern increased with prolonged PFVE, suggesting that the peripheral type of gravity perception pattern recovers or shifts to the central type of gravity perception pattern. In other words, central and peripheral types of gravity perception patterns were widely different pathologies. Thus, in terms of gravity perception, there are various types of unilateral MD, and an appropriate clinical approach is required for each type.

Yagi et al.[34] reported that patients with persistent postural-perceptual dizziness (PPPD) showed significantly bilateral large HTPG (central type of gravity perception pattern), although their HU-SVV, VEMP, and posturography results were normal. Additionally, PPPD is a chronic vestibular syndrome, like Types B and C of unilateral MD, characterized by vestibular symptoms lasting >3 months, typically preceded by acute vestibular disorders.[35] These facts indicate that overcompensation for vestibular dysfunction exhibited by large HTPG abnormalities may be strongly associated with PPPD.

This study had a few limitations. First, the study was conducted in a hospital that treats patients referred from other hospitals and clinics, most of whom have intractable conditions. Therefore, only a few patients with acute phase of unilateral MD were included in this study. Second, this was a retrospective cohort study, and there are limitations to examining the time course of unilateral MD. Third, although the caloric test was performed along with the HT-SVV test in this study, other vestibular-related tests, such as MRI, VEMP, and the video head impulse test, should also be performed, and the results should be compared to clarify the pathogenesis of unilateral MD in more detail.

5 | CONCLUSION

This study provides novel information on unilateral MD from the perspective of gravity perception by classifying GPD based on the results of the HT-SVV test. This study suggested that overcompensation for vestibular dysfunction in patients with unilateral MD exhibited by large HTPG abnormalities may be strongly associated with PPPD. Future studies should be conducted on other diseases involving vertigo/dizziness from this perspective.

ACKNOWLEDGMENTS

We thank Taeko Ito and Masumi Takada for their assistance with data collection. We also thank Editage for English language editing.

FUNDING INFORMATION

This research was partially supported by AMED under GRANT Number 22dk0310117h0001.

CONFLICT OF INTEREST

We declare no competing interests.

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How to cite this article: Wada Y, Shiozaki T, Yamanaka T, Kitahara T. Gravity perception disturbance in patients with unilateral Meniere disease. *Laryngoscope Investigative Otolaryngology*. 2023;8(1):212-219. doi:10.1002/lio2.1011