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ORIGINAL RESEARCH

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Visually enhanced vestibulo-ocular reflex gain in patients with vestibular disease

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Abstract

Objective: Vestibular migraine (VM) is a diagnostic challenge. Visually enhanced vestibulo-ocular reflex (VVOR) gain, a measure of the visual–vestibular interaction, has been proposed as a tool for diagnosing VM. This study seeks to evaluate VVOR gain's diagnostic capability to predict VM and to compare the phenotypes of vestibular patients with elevated versus normal/low VVOR gain.

Methods: A retrospective review of consecutive adult patients at a dizziness clinic from October 2016 and December 2020 was conducted. VVOR gain's diagnostic performance was assessed with the area under the receiver operating characteristic (AUROC) analysis. Demographic factors and clinical presentations were compared between vestibular patients with elevated versus normal/low VVOR gain.

Results: One hundred forty patients (70 with VM) were analyzed. VVOR gain was elevated in 68.6% of patients with VM, compared to 52.9% of patients without VM ($p = .057$). The AUROC of VVOR gain was 0.5902 (95% confidence interval: 0.4958–0.6846). Vestibular patients with elevated VVOR gain were younger than those with normal/low VVOR gain (mean age 50 vs. 62, $p < .0001$). A higher proportion of subjects with elevated VVOR gain had symptoms triggered by certain foods (17.6% vs. 5.5%, $p = .040$) and experienced sound sensitivity (34.1% vs. 18.2%, $p = .040$) and motion sensitivity (23.5% vs. 9.1%, $p = .041$). A greater proportion of VM patients with elevated VVOR gain were triggered by certain foods (27.1% vs. 0%, $p = .006$).

Conclusion: VVOR gain alone has limited ability to discriminate VM from other vestibular conditions and must be interpreted carefully. VVOR gain elevation may be associated with food triggers and motion and sound sensitivity.

Level of Evidence: IV.

KEYWORDS
vestibular migraine, visually enhanced vestibulo-ocular reflex, VVOR

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1 | INTRODUCTION

Vestibular migraine (VM) is one of the most common vestibular disorders, with a prevalence of 2.7% in adults.[1] It is also associated with significant patient morbidity and burden on the health care system. Nearly a quarter of individuals with VM visited the emergency department because of their symptoms, compared to 16.5% of those with any other dizziness problem.[1] Over half of those meeting criteria for VM visited a health professional in nonemergent settings.[1] And yet, despite its substantial disease burden, VM remains underdiagnosed, partly due to its widely variable symptomology.

The Barany Society and the International Headache Society describe the symptoms of VM as spontaneous vertigo, positional vertigo, visually induced vertigo (triggered by a complex visual stimulus), head motion-induced vertigo, and head motion-induced dizziness with nausea.[2] However, VM is not a single, homogeneous disease entity; its phenotypic variability is well known and attributed to the varying degrees of interaction between migraine and the vestibular system and the involvement of both central and peripheral vestibular structures.[3] In light of these diagnostic challenges, Arriaga et al. suggested a diagnostic tool to aid providers in diagnosing VM: elevated visually enhanced vestibulo-ocular reflex (VVOR) gain.[4]

The VVOR mediates the visual–vestibular interaction and is responsible for generating compensatory eye movement in the opposite direction to the head movement, thus stabilizing vision. VVOR testing records the eye movements of the subject in response to a fixed optokinetic stimulus during chair rotations. Arriaga et al. found that VVOR was elevated in 71% of patients with VM compared to only 5% of healthy volunteers ($p < .001$).[4] Noting that elevated VVOR gain was the most common vestibular test abnormality in people with VM, the authors posited that it can serve as a useful diagnostic tool for VM.[4] In another study, Jeong et al. found that the gains and phases of VVOR did not differ between the groups of patients with VM, migrainous dizziness, and only migraines, further complicating the meaningfulness of VVOR results in neurotologic evaluations.[5] A clinically useful diagnostic test would ideally separate those with VM from patients with other vestibular conditions and not just healthy controls. Therefore, we wanted to better understand the performance characteristics of the VVOR in a real-world setting and explore any differences in clinical presentation based on VVOR gain elevation.

Our primary study objective was to assess the diagnostic performance of VVOR gain in predicting VM. As our secondary objectives, we compared the characteristics of all dizzy patients with elevated VVOR gain versus normal/low VVOR gain and compared the phenotypes of VM patients with elevated VVOR gain versus normal/low VVOR gain.

2 | MATERIALS AND METHODS

We conducted a retrospective review of consecutive adults seen at a tertiary dizziness clinic between October 2016 to December 2020. We included only those whose chief complaint was related to dizziness or vertigo and who underwent vestibular testing. We collected demographics, triggers, associated symptoms, past medical history, and vestibular test results (caloric testing, sinusoidal rotary chair, VVOR) from standardized patient questionnaires, clinic notes, and audiology reports and followed Barany Society criteria for diagnosis.[2] This study was approved by the University of California San Francisco Institutional Review Board (18-25365).

Caloric testing was obtained using Interacoustics VisualEyes 525 VNG System and Interacoustics Air Fx Caloric Irrigator. Sinusoidal rotational testing and VVOR data were collected with the Neurolign Dx Neurotologic Test Chair (formerly NeuroKinetics Inc.) using VEST 7.1 I-Portal 3 software and I-Portal NOTC and firewire monocular goggles. Systems were up-to-date on recommended calibrations as specified by the manufacturer. Furthermore, at the beginning of all testing sessions, each individual's eye movements were calibrated for the rotary chair and videonystamography/calorics in accordance with the manufacturer instructions.

For VVOR testing, audiologists collected VVOR gain at two frequencies (0.04 and/or 0.08 Hz) based on provider preference or clinical indication at the time of testing. As per Arriaga et al., VVOR gain above 1.0 was considered elevated.[4] Because individuals with vestibular weakness may not be able to generate appropriate VVOR gain

TABLE 1 Proportion of elevated VVOR gain among the top three most frequent diagnosis groups.

Diagnosis	*n*/*N* with elevated VVOR gain (%)	Mean VVOR gain (standard deviation)
Vestibular migraine	35/46 (76.1)	1.06 (0.11)
Meniere's disease	6/9 (66.7)	1.05 (0.13)
BPPV (unilateral and bilateral)	5/9 (55.6)	0.99 (0.17)

Abbreviations: BPPV, benign paroxysmal positional vertigo; *n*, number of individuals with elevated VVOR gain; *N*, total number of individuals with the diagnosis; VVOR, visually enhanced vestibulo-ocular reflex.

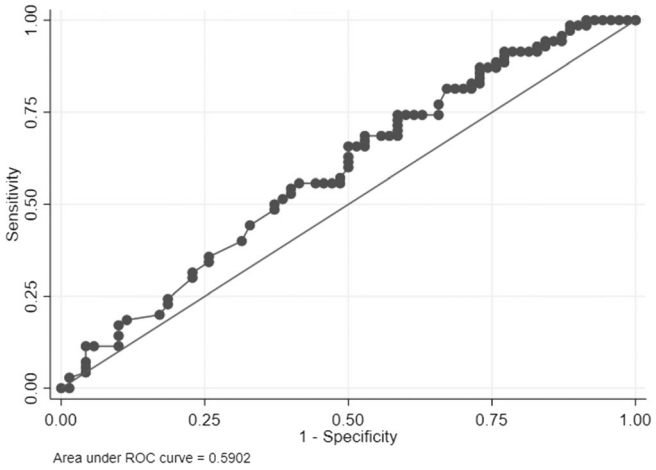

FIGURE 1 Receiver operating characteristic (ROC) analysis with visually enhanced vestibulo-ocular reflex (VVOR) gain to predict for vestibular migraine.

TABLE 2 Comparing phenotypes between subjects with elevated VVOR gain and subjects with normal/low VVOR gain.

	Total ($N = 140$)	Elevated VVOR ($n = 85$)	Normal/low VVOR ($n = 55$)	*p*-value
Age of diagnosis, mean (SD)	**54.7 (15.4)**	**49.9 (15.4)**	**62.1 (12.4)**	**<.0001***
Female sex, *N* (%)	83 (59.3)	54 (63.5)	29 (52.7)	.204
Duration of symptoms, *N* (% of each group)				
Seconds	44 (31.4)	29 (34.1)	15 (27.3)	.394
Minutes	43 (30.7)	25 (29.4)	18 (32.7)	.678
Hours	39 (27.9)	23 (27.1)	16 (29.1)	.793
Days	22 (15.7)	13 (15.3)	9 (16.4)	.865
Constant	39 (27.9)	25 (29.4)	14 (25.5)	.610
Triggers, N (% of each group)				
Loud sounds	21 (15)	10 (11.8)	11 (20)	.183
Sneezing, coughing, straining	**14 (10)**	**12 (14.1)**	**2 (3.6)**	**.048***
Certain foods	**18 (12.9)**	**15 (17.6)**	**3 (5.5)**	**.040***
Riding in a car	17 (12.1)	12 (14.1)	5 (9.1)	.437
Visual stimulation	33 (23.6)	22 (25.9)	11 (20)	.423
Associated symptoms, *N* (% of each group)				
Changes in hearing	23 (16.4)	11 (12.9)	12 (21.8)	.166
Ringing in the ears/tinnitus	46 (32.9)	28 (32.9)	18 (32.7)	.979
Pressure/fullness in the ears	30 (21.4)	21 (24.7)	9 (16.4)	.240
Light sensitivity	53 (37.9)	34 (40)	19 (34.5)	.516
Sound sensitivity	**39 (27.9)**	**29 (34.1)**	**10 (18.2)**	**.040***
Motion sensitivity	**25 (17.9)**	**20 (23.5)**	**5 (9.1)**	**.041***
Headache	49 (35)	31 (36.4)	18 (32.7)	.650
Past medical history, *N* (% of each group)				
Hypertension	33 (23.6)	19 (22.4)	14 (25.5)	.673
Hypercholesterolemia	**19 (13.6)**	**7 (8.2)**	**12 (21.8)**	**.022***
Depression	53 (37.9)	32 (37.6)	21 (38.2)	.949
Anxiety	63 (45)	36 (42.4)	27 (49.1)	.434
Migraine	70 (50)	45 (52.9)	25 (45.5)	.387
Head trauma	54 (38.6)	28 (32.9)	26 (47.3)	.089
Falls	**38 (27.1)**	**18 (21.2)**	**20 (36.4)**	**.048***
Dizziness Handicap Index, mean (SD), $N = 126$ (79 elevated, 47 normal/low)				
Total	39.9 (24.1)	41.2 (22.3)	37.6 (27.1)	.415
Functional	14.5 (9.9)	15.2 (9.6)	13.2 (10.5)	.288
Emotional	13.4 (9.0)	14.2 (8.9)	12.2 (10.3)	.241
Physical	12.0 (7.7)	11.9 (7.5)	12.1 (8.0)	.858

Note: Bolded values signifies statistical significance.
Abbreviations: VM, vestibular migraine; VVOR, visually enhanced vestibulo-oculars reflex.

responses, those with unilateral (caloric asymmetry >25%) or bilateral vestibular weakness and/or rotary chair testing abnormalities (gain asymmetry, low gain, low-frequency phase lead) were excluded from our analysis. For subjects with data at both frequencies, we used the gain data at 0.04 Hz because it was a more conservative measurement and was the testing frequency used in previous studies.[4,5] For subjects who underwent VVOR testing only at 0.08 Hz, we used an age-adjusted linear regression analysis to predict the gain at 0.04 Hz (R^2 .8370).

Using Stata v.16 (StataCorp, College Station, TX, USA), we assessed the diagnostic accuracy of VVOR gain for predicting VM with an area under receiver operating characteristic (AUROC) analysis. The primary endpoint was VVOR gain at 0.04 Hz. Exploratory endpoints included triggers, associated symptoms, and the Dizziness Handicap Inventory (DHI). We compared differences in categorical variables using Pearson's chi-square test and Fisher's exact test and continuous variables using a two-sample *t*-test and analysis of variance (ANOVA) test. *p*-value <.05 was considered statistically significant. Although we performed comparisons between multiple variables, we did not perform Bonferroni adjustments for two reasons. One, the study was not powered for such corrections. Two, because we aimed to explore potential relationships

between certain phenotypes and VVOR gain elevation that could inform our interpretation of a common vestibular test, we sought to minimize Type II errors.

3 | RESULTS

From October 2016 to December 2020, 385 subjects who had seen the senior author and undergone vestibular testing were identified. The mean age was 54.9 (standard deviation: 16.2), and 57.4% were female. The most common diagnoses were: VM ($N = 173$, 44.9%), unilateral or bilateral vestibular hypofunction ($N = 65$, 16.9%), Meniere's disease ($N = 51$, 13.3%), and benign paroxysmal positional vertigo (BPPV) ($N = 42$, 10.9%).

Of the 385 subjects, 230 underwent VVOR testing. Of these 230 subjects, 28 had VVOR gain data at only 0.04 Hz, 96 at only 0.08 Hz, and 106 at both testing frequencies. Among the 106 with gain data at both 0.04 and 0.08 Hz, the mean gain at 0.08 Hz was higher than the mean gain at 0.04 Hz (1.12 vs. 1.07, $p < .0001$). Furthermore, subjects with vestibular weakness as defined by caloric or rotary chair testing abnormalities had a lower mean VVOR gain than those with normal vestibular function at 0.04 Hz (0.93 vs. 1.02, $p = .005$). We retained 140 subjects with normal caloric and rotary chair test results in our final cohort.

3.1 | Diagnostic utility of VVOR gain in predicting VM

Among these 140 subjects, 70 patients were diagnosed with VM. Forty-eight subjects with VM (68.6%) had elevated VVOR gain, whereas 37 subjects without VM had elevated VVOR gain (52.9%, $p = .057$). After excluding subjects with more than one diagnosis (e.g., a patient with BPPV and VM), we also compared rates of VVOR gain elevation in subjects with the three most common conditions: VM ($N = 46$), Meniere's disease ($N = 9$), and benign paroxysmal positional vertigo ($N = 9$) (Table 1). All diagnosis groups had a high rate of VVOR gain elevation with no statistically significant differences. The mean VVOR gain was also similar across diagnoses according to ANOVA. The AUROC was 0.5902 (95% confidence interval: 0.4958–0.6846), with the ROC curve shown in Figure 1.

3.2 | Comparing phenotypes of patients with elevated versus normal/low VVOR gain

Comparisons of demographics and clinical presentation between patients with and without VVOR gain elevation are shown in Table 2. Eighty-five (60.7%) of 140 clinic patients had elevated VVOR gain. Subjects with high VVOR gain were younger (mean age 49.9, standard deviation: 15.4) than subjects with normal/low gain (mean age 62.1, standard deviation: 12.4, $p < .0001$). Figure 2 shows a scattergram graphing age versus VVOR gain at 0.04 Hz with a line of best fit

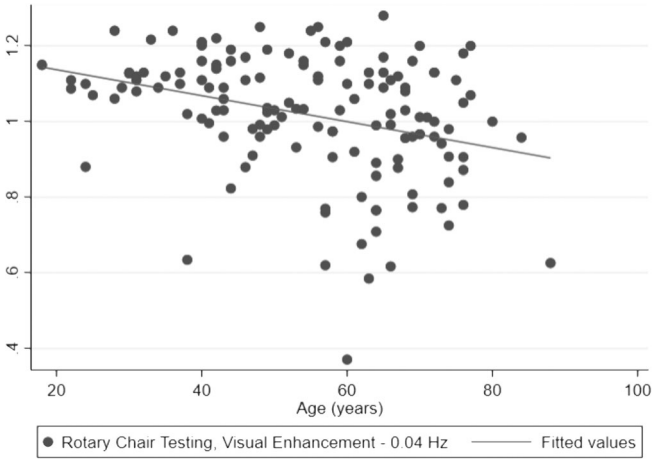

FIGURE 2 Scatterplot of age versus visually enhanced vestibulo-ocular reflex (VVOR) gain.

(correlation = −.3288). There was no difference in sex between groups ($p = .204$).

Higher proportions of subjects with elevated VVOR gain were triggered by certain foods (17.6% vs. 5.5%, $p = .040$) and sneezing/coughing/straining (14.1% vs. 3.6%, $p = .048$) than those with normal/low gain. Both groups were triggered by visual stimulation (watching a movie in a theater, busy intersection, shopping center, scrolling on a computer, busy visual scenes) at similar rates ($p = .423$). A greater proportion of subjects with elevated VVOR gain experienced associated sound sensitivity (34.1% vs. 18.2%; $p = .040$) and motion sensitivity (23.5% vs. 9.1%; $p = .041$) compared to those with normal/low VVOR gain. Subjects with normal/low VVOR gain had higher rates of hypercholesterolemia (21.8% vs. 8.2%; $p = .022$) and falls (36.4% vs. 21.2%; $p = .048$) compared to subjects with elevated gain. There were no differences in either the total or subscale DHI scores ($p > .05$). Rates of migraine history ($p = .387$) and diagnosis of VM ($p = .057$) were similar between the groups.

3.3 | Comparing phenotypes of VM patients with elevated versus normal/low VVOR gain

Comparisons of demographics and clinical presentation between VM patients with and without VVOR gain elevation are shown in Table 3. VM patients with elevated VVOR gain were younger (mean age 46.2, standard deviation: 15.2) than those with normal/low VVOR gain (mean age 60.5, standard deviation: 10.4, $p = .0002$). There was no difference in sex ($p = .360$). Certain foods triggered symptoms in subjects with VM with elevated VVOR gain (27.1%) at a higher rate than VM patients with normal/low VVOR gain (0%, $p = .013$). There were no differences in rates of patients triggered by visual stimulation between the two groups ($p = .939$). VM patients with normal/low VVOR gain had higher rates of hypercholesterolemia (27.3% vs. 4.2%; $p = .010$) and falls (45.5% vs. 16.7%, $p = .011$) compared to subjects

TABLE 3 Comparing phenotypes between VM patients with elevated VVOR gain versus normal/low VVOR gain.

	Total ($N = 70$)	Elevated VVOR VM ($n = 48$)	Normal/low VVOR VM ($n = 22$)	p-value
Age of diagnosis, mean (SD)	**50.7 (15.3)**	**46.2 (15.2)**	**60.5 (10.4)**	**.0002***
Female sex, *N* (%)	54 (68.4)	36 (72.0)	18 (62.1)	.360
Duration of symptoms, *N* (% of each group)				
Seconds	20 (28.6)	15 (31.3)	5 (22.7)	.574
Minutes	25 (35.7)	16 (33.3)	9 (40.9)	.539
Hours	26 (32.9)	14 (28.0)	9 (40.9)	.247
Days	16 (22.9)	10 (20.8)	6 (27.3)	.551
Constant	20 (28.6)	16 (33.3)	4 (18.2)	.259
Triggers, *N* (% of each group)				
Loud sounds	14 (20)	7 (14.6)	7 (31.8)	.094
Sneezing, coughing, straining	8 (11.4)	7 (14.6)	1 (4.5)	.420
Certain foods	**13 (18.6)**	**13 (27.1)**	**0 (0)**	**.006***
Visual stimulation	25 (35.7)	17 (35.4)	8 (36.4)	.939
Associated symptoms, *N* (% of each group)				
Changes in hearing	12 (17.1)	6 (12.5)	6 (27.3)	.128
Ringing in the ears/tinnitus	22 (31.4)	14 (29.2)	8 (36.4)	.547
Pressure/fullness in the ears	14 (20)	10 (20.8)	4 (18.2)	1.000
Light sensitivity	35 (50)	24 (50)	11 (50)	1.000
Sound sensitivity	28 (40)	21 (43.8)	7 (31.8)	.344
Motion sensitivity	20 (28.6)	16 (33.3)	4 (18.2)	.259
Headache	36 (51.4)	25 (52.1)	11 (50)	.871
Past medical history, *N* (% of each group)				
Hypertension	16 (22.9)	11 (22.9)	5 (22.7)	1.000
Hypercholesterolemia	**8 (11.4)**	**2 (4.2)**	**6 (27.3)**	**.010***
Depression	30 (42.9)	19 (39.6)	11 (50)	.414
Anxiety	32 (45.7)	20 (41.7)	12 (54.5)	.807
Migraine	50 (71.4)	33 (68.8)	17 (77.3)	.464
Head trauma	27 (38.6)	16 (33.3)	11 (50)	.184
Falls	**18 (25.7)**	**8 (16.7)**	**10 (45.5)**	**.011***
Dizziness Handicap Index, mean (SD), $N = 67$ (48 high, 19 normal/low)				
Total	44.9 (23.2)	44.3 (22.3)	46.3 (26.0)	.750
Functional	16.8 (9.8)	16.8 (9.6)	16.8 (10.5)	.973
Emotional	15.0 (8.2)	15 (7.8)	15.1 (9.5)	.981
Physical	13.1 (7.8)	12.5 (7.8)	14.4 (7.8)	.377

Note: Bolded values signifies statistical significance.
Abbreviations: VM, vestibular migraine; VVOR, visually enhanced vestibulo-ocular reflex.

with elevated VVOR gain. We did not observe differences in the total or subscale DHI scores ($p > .05$).

4 | DISCUSSION

This study sought to analyze the utility of VVOR gain in predicting VM and compare the phenotypes of vestibular patients based on VVOR gain. We found that VVOR gain alone has limited diagnostic capabilities, as subjects with VM and subjects without VM had similar rates of elevated VVOR gain. In our exploratory analysis, elevated VVOR gain was associated with sound and motion sensitivities with dizziness and food triggers. Among those with VM specifically, patients with elevated VVOR gain were on average younger by 14 years, and a higher proportion of these subjects had food triggers.

Horizontal canal function is evaluated through a battery of different but complementary vestibular tests, including calorics, rotary chair, and video head impulse test (vHIT). Caloric testing is a low-frequency test, rotary chair a mid-frequency test, and vHIT a high-frequency test. Each test provides insight into a different frequency region of the vestibular system, as each frequency region recruits distinct vestibular responses. For example, vHIT responses are driven purely by vestibular reflexes,

whereas rotary chair responses activate both smooth pursuit and vestibular reflexes at lower speeds. To test visual–vestibular interactions, rotary chair testing is utilized because a subject must be able to process visual stimuli, which is not possible at higher testing frequencies of vHIT.

VVOR gain is elevated in the majority of patients with VM, but it is also commonly elevated in those with other conditions. In our cohort, 69% of subjects with VM had elevated VVOR gain, which was similar to Arriaga et al.'s finding of 71%.[4] Although Arriaga et al. found a marked difference in rates of elevated VVOR gain elevation between patients with VM and healthy controls, we did not see a statistically significant difference between vestibular patients with and without VM.[4] Furthermore, after excluding those with more than one diagnosis, we observed similar rates of VVOR gain elevation and similar average VVOR gains between those with VM, Meniere's disease, and BPPV. Our AUROC analysis also revealed that VVOR gain had poor discrimination for VM.[6] These results are in line with Arriaga et al.'s discussion, which states that VVOR gain elevation is not unique to VM and should be used as an adjunct to—not a replacement of—a good history and physical exam to distinguish between various vestibular disorders.[4] Our study quantifies the diagnostic performance of VVOR gain and calls for a nuanced interpretation of VVOR gain data, which should consider a variety of factors.

One of the factors to be accounted for is the rotational frequency used in VVOR testing. The literature on the relationship between rotational frequency and gain varies. Viirre et al. demonstrated that VVOR gain enhancement declines with increasing frequency of rotation.[7] Migliaccio et al. showed that VVOR gain remains the same in healthy subjects at 0.1, 0.3, 0.6, and 1.0 Hz.[8] In our study, the VVOR gain of vestibular patients was higher at 0.08 Hz than at 0.04 Hz, which reveals that the VVOR testing frequency may affect VVOR gain.

Another factor to consider is a patient's age. The mean age of VM patients with elevated VVOR gain matches the findings of epidemiological studies of VM, but the mean age of VM patients with normal/low VVOR gain is significantly older.[1,9] The age difference between those with elevated VVOR gain and those with normal/low VVOR gain may be explained by the age-related decline in the vestibular system, with one longitudinal study demonstrating an age-dependent decrease in the gain of visual–vestibular responses.[10,11] Hence, the reason that subjects with normal/low VVOR gain were older was that the visual–vestibular systems of older subjects may be less able to produce VVOR gain elevation, a finding also illustrated in our data (Figure 2). The older age in the normal/low VVOR gain group likely also explains the higher rate of hyperlipidemia, whose prevalence increases with age.[12] A higher mean age may also explain the higher rate of falls among subjects with normal/low VVOR gain, as the incidence of factors that can contribute to fall risk, such as vision, somatosensory, nervous, and cardiovascular issues, increases with age.[13,14]

Our exploratory analysis revealed that VVOR gain elevation was associated with sound sensitivity, motion sensitivity with dizziness, and food triggers. These phenomena are classically associated with migraine, which have been attributed to aberrant multisensory processing in migraineurs.[5,15–18] The rates of migraine and VM were statistically similar between the elevated-gain group and normal/low-gain group. We therefore wonder whether VVOR gain elevation, which is attributed to a hypersensitivity in the integration of visual and vestibular stimuli, may independently correlate with a broader hypersensitivity in the integration of all senses, including visual, auditory, and gustatory.[4,19] These increased sensitivities to stimuli, however, did not translate to greater self-perceived impairment, as evidenced by the similarity in DHI scores between the two groups. Subjects with elevated VVOR gain were also more often triggered by sneezing/coughing/straining, which is typically associated with superior canal dehiscence syndrome or other third window pathology.[20] Although the significance of this association is unclear, a sneeze may be a form of a rapid head movement that precipitates acute vertiginous symptoms.

Among patients with VM, a higher proportion of those with elevated VVOR gain had food triggers. The association of food triggers with elevated VVOR gain among subjects with VM further supports the idea that VVOR gain elevation may be an independent predictor of sensory hypersensitivities. Notably, only 36% of subjects with VM listed visual stimulation as a trigger, which is lower than reported in the literature and attests to the varied symptomology of VM.[21] Although these aforementioned associations with elevated VVOR gain had *p*-values less than .05, their statistical significance must be interpreted carefully; the purpose of this analysis was to suggest potential links between certain phenotypes and VVOR gain elevation that can inform future research, not to establish definitive relationships.

There were several limitations to the study. First, because of the variability in the VVOR testing protocol, not everyone received VVOR testing at the same frequency. By comparing VVOR gain data at two different frequencies, however, we were able to observe that gain was higher at 0.08 Hz than at 0.04 Hz and realized that the VVOR testing frequency may impact gain. For standardization, we utilized a linear regression to obtain a predicted VVOR gain at 0.04 Hz for those with VVOR data at only 0.08 Hz. Although our decision to analyze VVOR gain data at 0.04 Hz was based on the literature, we recognize that analyzing the gain at 0.08 Hz could yield different results.[4,5] Second, this study was conducted at a single tertiary referral clinic, whose experiences may not be generalizable to other practice settings or geographic locations. Third, our study was likely underpowered to detect differences in VVOR gain elevation between the diagnosis groups, as the numbers of subjects in the Meniere's disease and BPPV groups were low after excluding those with more than one diagnosis.

5 | CONCLUSION

To our knowledge, our study is the largest analysis of VVOR gain results of patients at a dizziness clinic. This retrospective study analyzes the real-world utility and associated characteristics of elevated VVOR gain. VVOR gain alone is a poor predictor of VM and should be carefully interpreted along patient age and other clinical data to make the diagnosis of VM. Younger age, triggers by certain foods, and

sound and motion sensitivities were associated with elevated VVOR gain among vestibular patients. Similarly, younger age and food triggers were associated with elevated VVOR gain among subjects with VM.

CONFLICT OF INTEREST STATEMENT

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REFERENCES

1. Formeister EJ, Rizk HG, Kohn MA, Sharon JD. The epidemiology of vestibular migraine: a population-based survey study. *Otol Neurotol*. 2018;39(8):1037-1044. doi:10.1097/MAO.0000000000001900
2. Lempert T, Olesen J, Furman J, et al. Vestibular migraine: diagnostic criteria. *J Vestib Res*. 2012;22(4):167-172. doi:10.3233/VES-2012-0453
3. von Brevern M, Lempert T. Vestibular migraine. *Handb Clin Neurol*. 2016;137:301-316. doi:10.1016/B978-0-444-63437-5.00022-4
4. Arriaga MA, Chen DA, Hillman TA, Kunschner L, Arriaga RY. Visually enhanced vestibulo-ocular reflex: a diagnostic tool for migraine vestibulopathy. *Laryngoscope*. 2006;116(9):1577-1579. doi:10.1097/01.mlg.0000231308.48145.f6
5. Jeong SH, Oh SY, Kim HJ, Koo JW, Kim JS. Vestibular dysfunction in migraine: effects of associated vertigo and motion sickness. *J Neurol*. 2010;257(6):905-912. doi:10.1007/s00415-009-5435-5
6. Hosmer DW, Lemeshow S, Sturdivant RX. *Applied Logistic Regression*. 3rd ed. John Wiley and Sons; 2013.
7. Viirre ES, Demer JL. The human vertical vestibulo-ocular reflex during combined linear and angular acceleration with near-target fixation. *Exp Brain Res*. 1996;112(2):313-324. doi:10.1007/BF00227649
8. Migliaccio AA, Halmagyi GM, McGarvie LA, Cremer PD. Cerebellar ataxia with bilateral vestibulopathy: description of a syndrome and its characteristic clinical sign. *Brain J Neurol*. 2004;127(Pt 2):280-293. doi:10.1093/brain/awh030
9. Morganti LOG, Salmito MC, Duarte JA, Sumi KC, Simões JC, Ganança FF. Vestibular migraine: clinical and epidemiological aspects. *Braz J Otorhinolaryngol*. 2016;82(4):397-402. doi:10.1016/j.bjorl.2015.06.003
10. Baloh RW, Enrietto J, Jacobson KM, Lin A. Age-related changes in vestibular function. *Ann N Y Acad Sci*. 2001;942(1):210-219. doi:10.1111/j.1749-6632.2001.tb03747.x
11. Iwasaki S, Yamasoba T. Dizziness and imbalance in the elderly: age-related decline in the vestibular system. *Aging Dis*. 2015;6(1):38. doi:10.14336/AD.2014.0128
12. Rosada A, Kassner U, Weidemann F, et al. Hyperlipidemias in elderly patients: results from the Berlin Aging Study II (BASEII), a cross-sectional study. *Lipids Health Dis*. 2020;19(1):92. doi:10.1186/s12944-020-01277-9
13. Peel NM. Epidemiology of falls in older age. *Can J Aging*. 2011;30(1):7-19. doi:10.1017/S071498081000070X
14. Alyono JC. Vertigo and dizziness: understanding and managing fall risk. *Otolaryngol Clin North Am*. 2018;51(4):725-740. doi:10.1016/j.otc.2018.03.003
15. Finocchi C, Sivori G. Food as trigger and aggravating factor of migraine. *Neurol Sci*. 2012;33(suppl 1):S77-S80. doi:10.1007/s10072-012-1046-5
16. Furman JM, Marcus DA. Migraine and motion sensitivity. *Continuum (Minneap Minn)*. 2012;18(5 Neuro-otology):1102-1117. doi:10.1212/01.CON.0000421621.18407.96
17. Schwedt TJ. Multisensory integration in migraine. *Curr Opin Neurol*. 2013;26(3):248. doi:10.1097/WCO.0b013e328360edb1
18. Vingen JV, Pareja JA, Støren O, White LR, Stovner LJ. Phonophobia in migraine. *Cephalalgia*. 1998;18(5):243-249. doi:10.1046/j.1468-2982.1998.1805243.x
19. Mallinson AI, Longridge NS. Motion sickness and vestibular hypersensitivity. *J Otolaryngol*. 2002;31(6):381-385. doi:10.2310/7070.2002.34575
20. Minor LB. Clinical manifestations of superior semicircular canal dehiscence. *Laryngoscope*. 2005;115(10):1717-1727. doi:10.1097/01.mlg.0000178324.55729.b7
21. Vuralli D, Yildirim F, Akcali DT, Ilhan MN, Goksu N, Bolay H. Visual and postural motion-evoked dizziness symptoms are predominant in vestibular migraine patients. *Pain Med*. 2018;19(1):178-183. doi:10.1093/pm/pnx182

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