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Analysis of video head impulse test saccades data in patients with vestibular migraine or probable vestibular migraine

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abstract

Objective: Saccades accompanied by normal gain in video head impulse tests (vHIT) are often observed in patients with vestibular migraine (VM). However, they are not considered as an independent indicator, reducing their utility in diagnosing VM. To better understand clinical features of VM, it is necessary to understand raw saccades data.

Methods: Fourteen patients with confirmed VM, 45 patients with probable VM (p-VM) and 14 age-matched healthy volunteers were included in this study. Clinical findings related to spontaneous nystagmus (SN), positional nystagmus (PN), head-shaking nystagmus (HSN), caloric test and vHIT were recorded. Raw saccades data were exported and numbered by their sequences, and their features analyzed.

Results: VM patients showed no SN, PN or HSN, and less than half of them showed unilateral weakness (UW) on caloric test. The first saccades from lateral semicircular canal stimulation were the most predominant for both left and right sides. Neither velocity nor time parameters were significantly different when compared between the two sides. Most VM patients (86%) exhibited small saccades, around 35% of the head peak velocity, with a latency of 200–400 ms. Characteristics of saccades were similar in patients with p-VM. Only four normal subjects showed saccades, all unilateral and seemingly random.

Conclusions: Small saccades involving bilateral semicircular canals with a scattered distribution pattern are common in patients with VM and p-VM.

1. Introduction

Vestibular migraine (VM) is a common episodic vestibular disorder. There is no definitive test for VM, making it challenging to diagnose. The symptoms of this disorder may vary depending on its stage. During the ictal period, spontaneous and persistent positional nystagmus can be observed (von Brevern et al., 2004; Polensek and Tusa, 2010; von Brevern et al., 2005). It has been reported that head-shaking nystagmus occurs during interictal periods (Boldingh et al., 2013; Jeong et al., 2010). Most patients with VM have normal vestibular function tests when in symptom-free stages (Huang et al., 2020; Lempert and von Brevern, 2019).

Although the video head impulse test (vHIT) is routinely used in vertigo clinics worldwide, abnormal vHIT findings in VM are rarely reported. In vHIT, vestibular dysfunction is generally identified by the vestibular-ocular reflex (VOR) gain loss and evident saccades, whereas subtle saccades with normal gain are usually overlooked. As a ratio directly indicates vestibular abnormality, gain is more useful than saccades (Tweed et al., 1994). Nevertheless, this measurement is less sensitive than caloric test, and decreased vHIT gains are reported in only 9–11% of VM patients (Kang et al., 2016; Blodow et al., 2014). Qualitatively, saccades are often characterized as overt, covert or combined based on the latency (Weber et al., 2008). It seems unlikely that such characterization would be able to provide a quantitative evaluation of vestibular function, although saccades are frequently observed in VM patients (Huang et al.,

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2020; Calic et al., 2020). This may be because previous studies only compared VOR gain (Blodow et al., 2014) without analyzing saccadic findings.

PR score, a recently proposed saccade time variation parameter, may indicate vestibular recovery status (Rey-Martinez et al., 2015; Matiñó -Soler et al., 2016). Saccades can be independently measured this way. Despite this, the PR score cannot be used to calculate unapparent saccades (velocities less than 65°/s), which may reduce its sensitivity in identifying VM patients. Therefore, an in-depth analysis of saccades data from VM patients, especially those subtle ones, is needed.

Saccades may provide clinicians with a better understanding of VM, in which vestibular test results may not be as normal as once believed. This study compares saccades data between VM patients (including those with probable VM [p-VM]) and normal controls to see if saccades are more sensitive indicators of VM and should be included in the screening vestibular test battery for episodic vestibular disorders. Saccades included in this study were not filtered by a strict boundary and may reflect raw saccades observed in vHIT reports.

2. Materials and methods

2.1. Subjects

Data from vertigo patients seen at the vertigo clinic, Chinese PLA General Hospital, between July 2020 and November 2021, including 17 that met the diagnostic criteria for VM and 61 for p-VM (Lempert et al., 2012), were retrospectively reviewed. Age-matched healthy volunteers (n = 14) were also recruited. Ethics approval was obtained from the Chinese PLA General Hospital ethics committee. Vestibular test results, including spontaneous nystagmus (SN), positional nystagmus (PN), head-shaking nystagmus (HSN) and caloric test (unilateral weakness, UW), were documented during their initial visit.

2.2. vHIT and saccades recording

vHIT was conducted with a video-oculography device (ICS Impulse, GN Otometrics Inc., Denmark). The patient was asked to fixate on a visual target 1 m in front of them in a sitting position. Approximately ten fast, unpredictable, small-amplitude, passive impulses were applied to each side by a skilled examiner. A separate examiner examined all impulses and deleted the ones containing blinking, lost track, poor calibration or low head velocity (less than 150°/s on lateral impulses). This process excluded 3 VM and 16 p-VM patients due to insufficient qualified samples (less than five impulses per side).

For saccadic data analysis, raw data were exported in XML format (eXtensible Markup Language). Saccades were retrieved using the open-source HitCal v5.3 software (https://github.com/bendermh/HITCal). Saccades in each impulse were numbered according to their sequences (Du et al., 2022). The analysis did not establish a time or velocity boundary for saccades. In order to avoid randomness, the rate of saccade occurrence was set to be greater than 50% for each subgroup. Otherwise, all saccades will be excluded from the analysis.

2.3. Data analysis

The statistical analysis was conducted using the IBM SPSS 20.0 software (SPSS Inc., Chicago, IL, USA). The unpaired student's t-test was used on parameters that were in accordance with normal distribution. In other cases, the Wann-Whitney test was applied. All data were presented as mean ± standard deviation. Non-dimensional parameters, such as absolute saccade velocity, were included in this study to eliminate possible influences caused by peak head velocity.

$$Absolute\ saccade\ velocity = (saccade\ velocity)/ \times (peak\ head\ velocity)$$

Swarm, box and violin plots were combined to illustrate data distribution, statistical characteristics and sample vergence. In the violin plot, peaks showed more samples than valleys. Data visualization was generated using the Python 3.7 software (Python Software Foundation, DE, USA.).

3. Results

3.1. General characters of VM patients

Clinical characteristics of the 14 VM patients are summarized in Table 1. Females outnumbered males by 11 to 3. The average age of these patients was 44.21 ± 11.93 years. They all met the diagnostic criteria for VM (Lempert et al., 2012) and experienced vestibular symptoms including spontaneous vertigo, vision-induced vertigo, positional vertigo, motion-induced vertigo and motion-induced dizziness. PN, HSN and SN were barely noticeable in these patients. Five patients had abnormal UW results.

3.2. Saccades in VM patients

Fig. 1 shows saccades in all six semicircular canals (SCCs) on both sides. Randomly-occurring saccades (less than half of all impulses) were excluded from the analysis. Lateral SCC stimulation

Table 1
Clinical features of VM patients.

Patient	Gender	Age (Year)	SN	PN	HSN	UW	Duration of Vestibular Syndrome Attacks	Course of Disease
#1	Female	52	/	/	/	L(18%)	Hours	3 years
#2	Female	43	/	/	/	L(63%)	Hours	2 years
#3	Female	38	/	/	/	L(51%)	Minutes	5 months
#4	Female	38	/	/	/	L(9%)	Days	10 years
#5	Female	58	/	/	/	L(42%)	Days	1 month
#6	Male	54	/	/	L(13)	L(42%)	Minutes	1 month
#7	Male	46	/	/	/	L(19%)	Hours	3 years
#8	Male	58	/	/	/	R(18%)	Hours	7 years
#9	Female	35	/	/	/	0	Days	2 years
#10	Female	38	/	/	/	R(5)	Hours	3 years
#11	Female	63	/	/	/	L(23%)	Hours	5 years
#12	Female	17	/	/	/	R(17%)	Hours	3 years
#13	Female	47	/	/	/	L(41%)	Hours	3 months
#14	Female	32	/	/	/	R(15%)	Hours	2 years

triggered most saccades, followed by the posterior SCC and anterior SCC. There was a high incidence of saccades for both lateral SCCs in these patients (86%, 12/14). Anterior and posterior SCC saccades appeared to occur randomly. On both sides, the second and third saccades were less frequently observed than the first saccade. Therefore, the first saccade from lateral SCC stimulation appeared to be the most crucial parameter among all saccade parameters to describe clinical features of VM.

Table 2 compares the first saccade on the left and right sides, showing identical interaural velocity and time characteristics. Coefficients of variation (CV) of velocity and time parameters showed no statistically significant differences, suggesting that saccades dispersity was equivalent on both sides. CV of latency indicated a relatively scattered pattern of distribution.

Fig. 2 shows a detailed analysis of the first saccade in each VM patient. A: absolute velocities of small-amplitude saccades vary between 0.2 and 0.5 times the peak head velocity in most patients. B: latency of the first saccade from LSC stimulation varies from 200 ms (head movement ends at 140 ms) to 400 ms (recording ends at 560 ms).

3.3. Saccades in p-VM patients

No interaural differences in saccade characters were found among the 45 patients with p-VM (Table 3 and Fig. 3). Both left and right sides presented small first saccades at approximately 1/3 of the peak head velocity (no more than half of the peak head velocity in general). The latency of the first saccade was 275 ms on left and

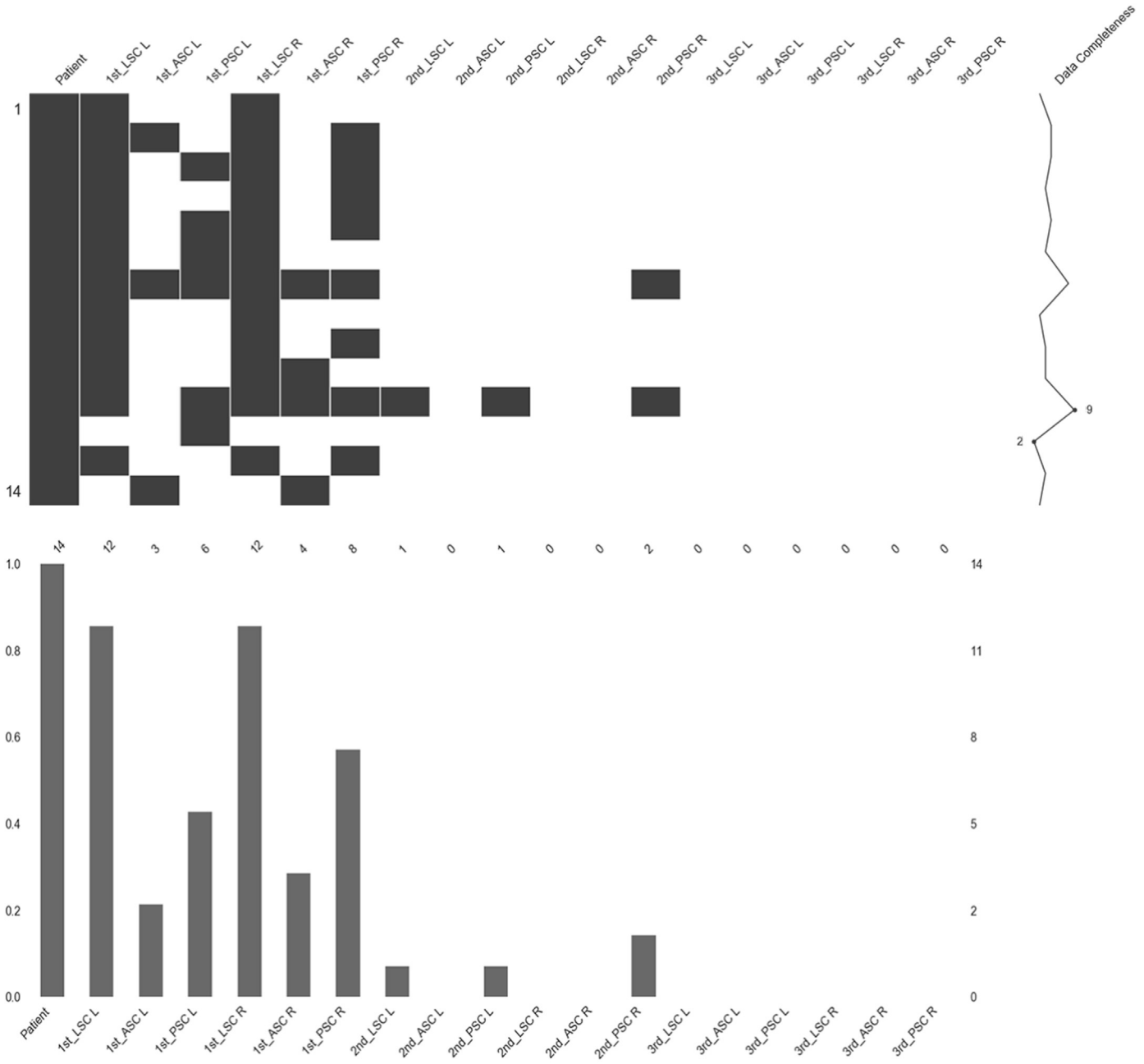

Fig. 1. Completeness of saccades data for the six semicircular canals
ASC: anterior semicircular canal, PSC: posterior semicircular canal, LSC: lateral semicircular canal. 1st, 2nd and 3rd = the 1st, 2nd and 3rd saccade.

Table 2
Comparison of 1st saccade parameters from LSC stimulation between the two sides in VM patients.

Parameters		L	R	P
Gain		0.92 ± 0.07	0.97 ± 0.08	0.066
Velocity	Velocity (°/s)	72.77 ± 32.06	78.74 ± 30.99	0.647
	CV of Velocity	0.37 ± 0.13	0.30 ± 0.11	0.185
	Abs. Velocity	0.34 ± 0.14	0.37 ± 0.13	0.659
	CV of Abs. Velocity	0.39 ± 0.13	0.31 ± 0.11	0.122
Time	Latency (ms)	288.90 ± 61.74	279.65 ± 70.01	0.735
	CV of Latency	0.20 ± 0.12	0.21 ± 0.07	0.796

CV: coefficient of variation (= standard deviation/mean); Abs. Velocity: absolute velocity (a non-dimensional parameter); LSC: lateral semicircular canal.

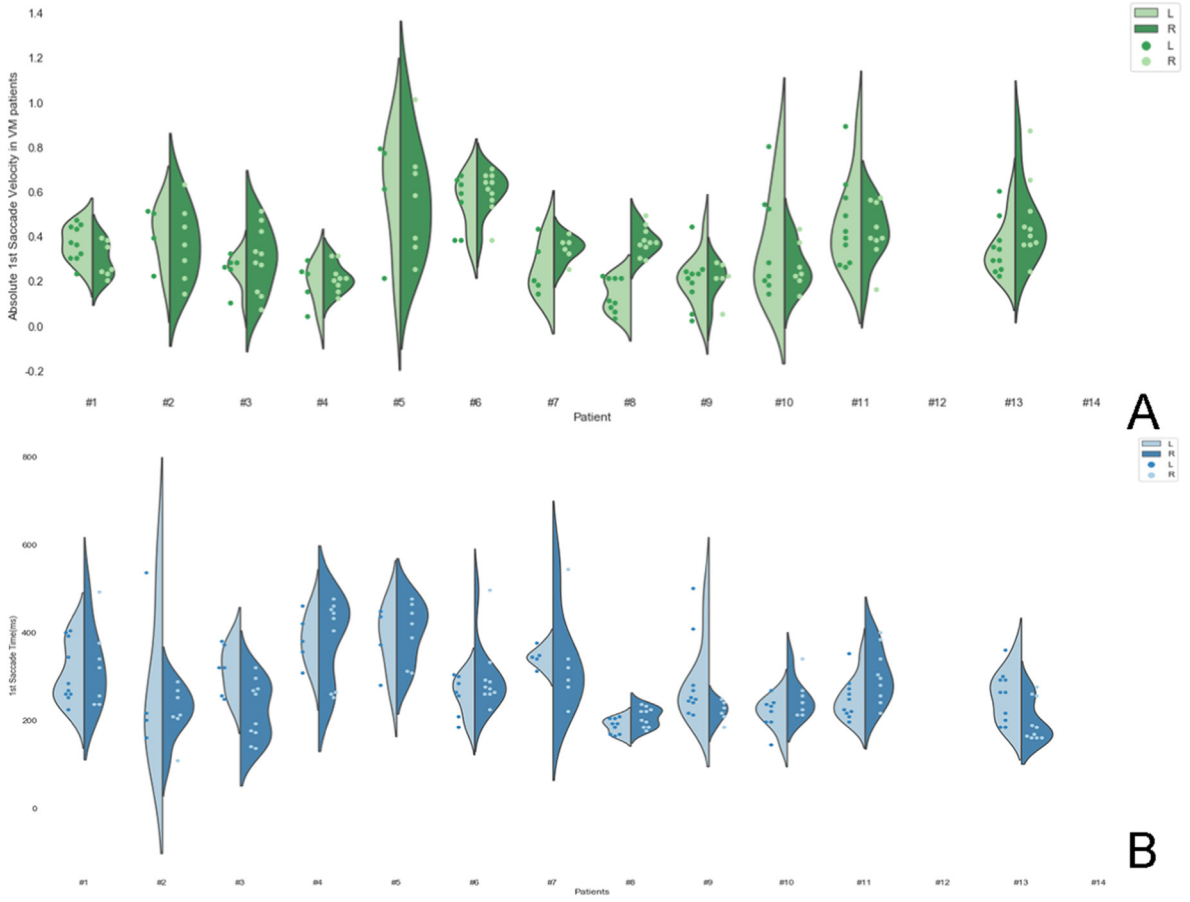

Fig. 2. Analysis of the 1st saccade in individual VM patients. A: absolute velocity; B: saccade latency (ms).

Table 3
Comparison of 1st saccade parameters from lateral SCC stimulation between left and right sides in p-VM patients.

Parameters		L	R	P
Gain		0.96 ± 0.08	0.98 ± 0.09	0.233
Velocity	Velocity(°/s)	61.88 ± 22.33	69.31 ± 33.23	0.279
	CV of Velocity	0.29 ± 0.10	0.31 ± 0.12	0.388
	Abs. Velocity	0.31 ± 0.12	0.34 ± 0.14	0.300
	CV of Abs. Velocity	0.29 ± 0.11	0.31 ± 0.12	0.401
Time	Latency (ms)	275.08 ± 68.12	280.83 ± 73.55	0.736
	CV of Latency	0.25 ± 0.10	0.22 ± 0.12	0.200

281 ms on right for lateral SCC stimulation with head movement ending at 140 ms. CV of latency indicated a scattered distribution pattern.

3.4. Saccades in healthy controls

Among the 14 healthy controls (mean age = 35.36 ± 4.30 years, females to males = 11:3), saccades were triggered in only four

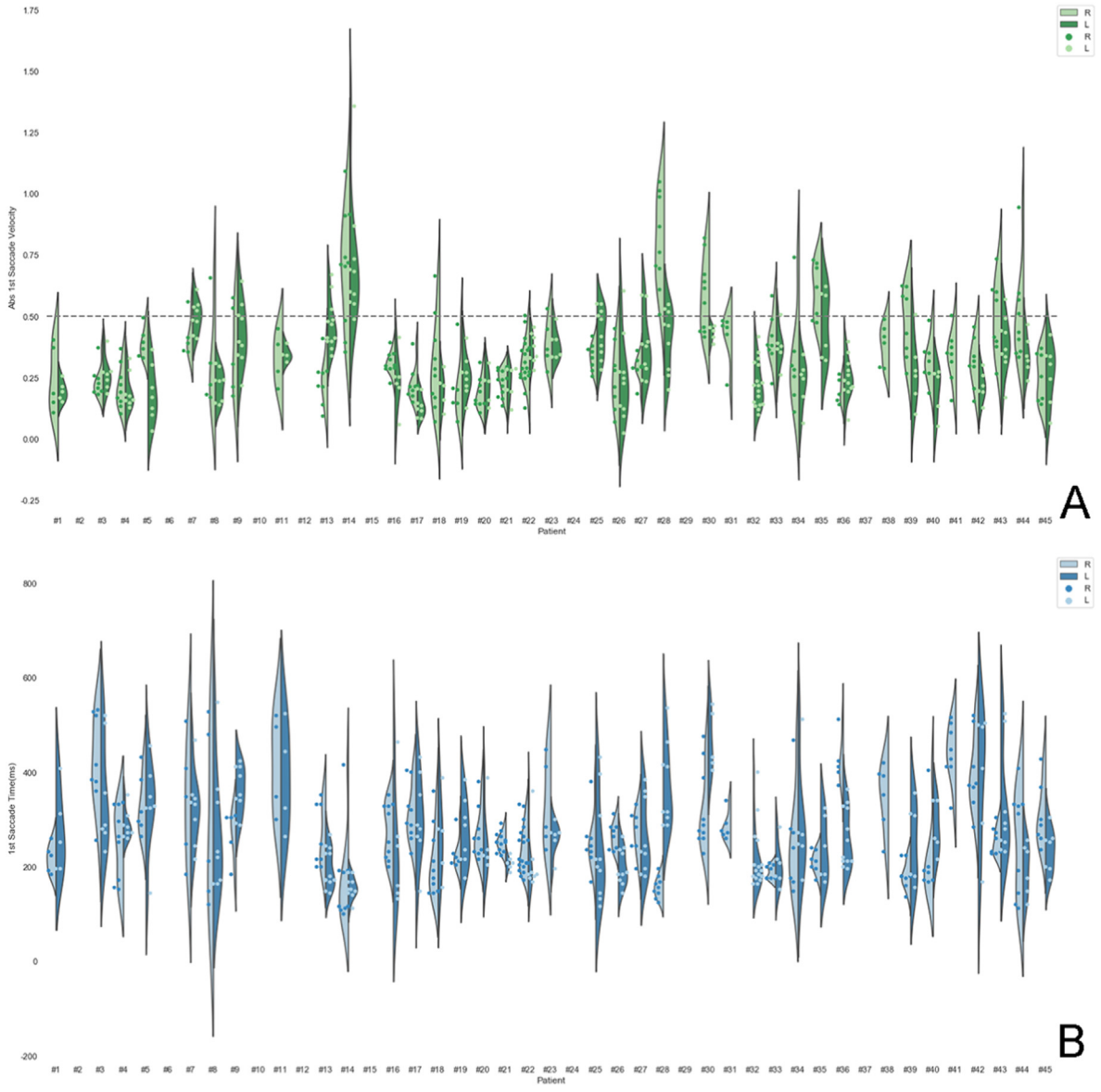

Fig. 3. Analysis of 1st saccades in individual p-VM patients. A: absolute velocity; B: latency (ms).

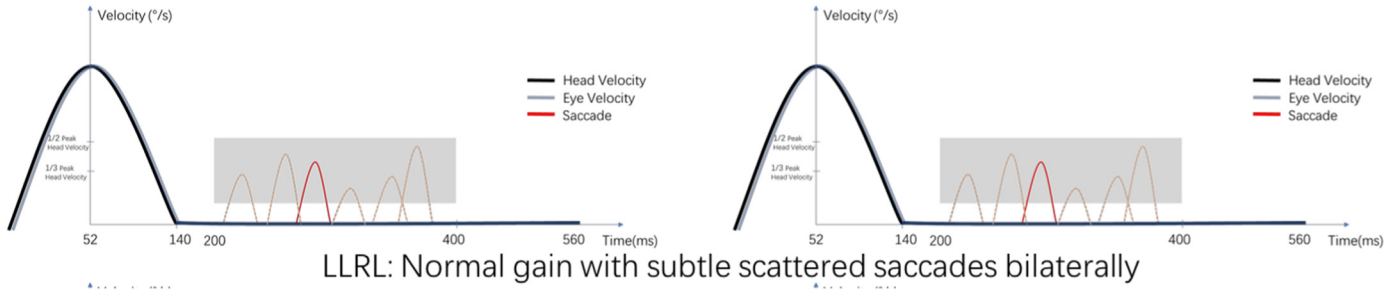

Fig. 4. Saccades in VM patients (including p-VM). LLRL: left and right lateral SCCs.

subjects, all unilateral and seemingly random. The saccade velocities varied from 0.1 to 0.5 times of the maximum head velocity. The interval between saccades ranged from 152 to 524 ms.

4. Discussion

Our findings show that saccades are commonly present in patients with VM and p-VM, usually bilateral from stimulation of

lateral semicircular canals and in the presence of a normal VOR gain. In patients with VM, these saccades are small with a scattered distribution pattern (see Fig. 4). In our study, parameters of saccades were essentially identical between the left and right sides. In healthy subjects, saccades in the presence of normal VOR gain were rare compared to VM patients and only on one side.

Preconceived notions suggest that subtle saccades without gain loss are always considered normal for peripheral and central vestibular systems. Such events have been ignored previously since vHIT gain is always the first concern. However, vHIT includes not only the VOR, but also saccades. VOR is an instant response to a passive head movement. By shifting the gaze, saccades can maintain the image in the fovea to minimize the visual-fovea gap. With vestibular deficits, saccade velocity and eye movement after VOR are related (John and Zee, 2015). During VM attacks, there may be spontaneous nystagmus and persistent positional nystagmus (von Brevern et al., 2004; Polensek and Tusa, 2010; von Brevern et al., 2005), but they do not last long (Calic et al., 2020). Saccades persist when symptoms subside, suggesting that potential dysfunction once existed.

The small amplitude of saccades in VM may suggest that vestibular function is relatively intact in the absence of symptoms. In addition to retinal slip, positional errors can also cause saccades (de Brouwer et al., 2002). This may partially explain why saccades are observed on the healthy side in vestibular neuritis and Meniere's disease (MD) (Du et al., 2021, 2022). On the other hand, based on our findings, saccades appear to be randomly distributed on one side in healthy individuals, which is different from saccades in VM patients.

It is also possible that saccades may indicate some level of perception (Grüsser, 1983). VM patients seem more likely to suffer from imbalance, motion sickness and anxiety (Balci and Akdal, 2020). In addition, patients with VM may experience abnormal spatial orientation integration (Winnick et al., 2018; King et al., 2019). A recent study by Bonaldson suggests that patients with VM are likely to suffer from cognitive dysfunction (Donaldson et al., 2021). Since there are no appropriate indicators of the patient's functional status, designing a rehabilitation program for VM patients is always challenging. Saccades may aid physicians in determining the disease status in patients with VM. Moreover, Saccades, as a sensitive parameter, may be an indicator of VM or p-VM syndrome and should be included in a screening vestibular test battery for evaluation of episodic vestibular disorders.

Further research regarding saccade changes in patients with VM should not be neglected. A proper vestibular function test is essential when it is challenging to differentiate VM from MD (Blodow et al., 2014; Calic et al., 2020). Comparison of saccades between VM and MD patients may be helpful. Similar bilateral saccades may also indicate potential bilateral vestibular dysfunction, for which more thorough investigation is needed.

Declaration of competing interest

This research received no specific grant support. The authors declare that they have no conflicts of interest.

References

Balci, B., Akdal, G., 2020 Oct. Imbalance, motion sensitivity, anxiety and handicap in vestibular migraine and migraine only patients. Auris Nasus Larynx 47 (5), 747–751. https://doi.org/10.1016/j.anl.2020.02.015. PubMed PMID: 32178946.

Blodow, A., Heinze, M., Bloching, M.B., et al., 2014 Dec. Caloric stimulation and video-head impulse testing in Meniere's disease and vestibular migraine. Acta Otolaryngol. 134 (12), 1239–1244. https://doi.org/10.3109/00016489.2014.939300. PubMed PMID: 25399882.

Boldingh, M.I., Ljostad, U., Mygland, A., et al., 2013 Jul-Aug. Comparison of interictal vestibular function in vestibular migraine vs migraine without vertigo. Headache 53 (7), 1123–1133. https://doi.org/10.1111/head.12129. PubMed PMID: 23676003.

von Brevern, M., Radtke, A., Clarke, A.H., et al., 2004 Feb 10. Migrainous vertigo presenting as episodic positional vertigo. Neurology 62 (3), 469–472. https://doi.org/10.1212/01.wnl.0000106949.55346.cd. PubMed PMID: 14872034.

von Brevern, M., Zeise, D., Neuhauser, H., et al., 2005 Feb. Acute migrainous vertigo: clinical and oculographic findings. Brain 128 (Pt 2), 365–374. https://doi.org/10.1093/brain/awh351. PubMed PMID: 15601663.

de Brouwer, S., Yuksel, D., Blohm, G., et al., 2002 Mar. What triggers catch-up saccades during visual tracking? J. Neurophysiol. 87 (3), 1646–1650. https://doi.org/10.1152/jn.00432.2001. PubMed PMID: 11877535.

Calic, Z., Nham, B., Taylor, R.L., et al., 2020. Vestibular migraine presenting with acute peripheral vestibulopathy: clinical, oculographic and vestibular test profiles. Cephalalgia 3 (2), 251581632095817.

Donaldson, L.B., Yan, F., Liu, Y.F., et al., 2021 Nov-Dec. Does cognitive dysfunction correlate with dizziness severity in patients with vestibular migraine? Am. J. Otolaryngol. 42 (6), 103124. https://doi.org/10.1016/j.amjoto.2021.103124. PubMed PMID: 34166962.

Du, Y., Ren, L., Liu, X., et al., 2021 Jan. The characteristics of vHIT Gain and PR score in peripheral vestibular disorders. Acta Otolaryngol. 141 (1), 43–49. https://doi.org/10.1080/00016489.2020.1812715. PubMed PMID: 32930021.

Du, Y., Liu, X., Ren, L., et al., 2022. Exploratory saccades data analysis of video head impulse test in different Meniere's disease stages. J. Vestib. Res. 32 (2), 183–192. https://doi.org/10.3233/VES-201642. PMID: 34366304.

Grüsser, O.J., 1983. Vision and Eye Movements. Springer Berlin Heidelberg.

Huang, T.C., Wang, S.J., Kheradmand, A., 2020 Jan. Vestibular migraine: an update on current understanding and future directions. Cephalalgia 40 (1), 107–121. https://doi.org/10.1177/0333102419869317. PubMed PMID: 31394919.

Jeong, S.H., Oh, S.Y., Kim, H.J., et al., 2010 Jun. Vestibular dysfunction in migraine: effects of associated vertigo and motion sickness. J. Neurol. 257 (6), 905–912. https://doi.org/10.1007/s00415-009-5435-5. PubMed PMID: 20041331.

John, L.R., Zee, D.S., 2015. The Neurology of Eye Movements.

Kang, W.S., Lee, S.H., Yang, C.J., et al., 2016. Vestibular function tests for vestibular migraine: clinical implication of video head impulse and caloric tests. Front. Neurol. 7, 166. https://doi.org/10.3389/fneur.2016.00166. PubMed PMID: 27746761; PubMed Central PMCID: PMCPMC5044462.

King, S., Priesol, A.J., Davidi, S.E., et al., 2019 Oct 4. Self-motion perception is sensitized in vestibular migraine: pathophysiologic and clinical implications. Sci. Rep. 9 (1), 14323. https://doi.org/10.1038/s41598-019-50803-y. PubMed PMID: 31586151; PubMed Central PMCID: PMCPMC6778132.

Lempert, T., von Brevern, M., 2019 Nov. Vestibular migraine. Neurol. Clin. 37 (4), 695–706. https://doi.org/10.1016/j.ncl.2019.06.003. PubMed PMID: 31563227.

Lempert, T., Olesen, J., Furman, J., et al., 2012. Vestibular migraine: diagnostic criteria. J. Vestib. Res. 22 (4), 167–172. https://doi.org/10.3233/VES-2012-0453. PubMed PMID: 23142830.

Matiñó-Soler, E., Rey-Martinez, J., Trinidad-Ruiz, G., et al., 2016. A new method to improve the imbalance in chronic unilateral vestibular loss: the organization of refixation saccades. Acta Otolaryngol. 136 (9), 894–900. https://doi.org/10.3109/00016489.2016.1172730. PubMed PMID: 27109262.

Polensek, S.H., Tusa, R.J., 2010. Nystagmus during attacks of vestibular migraine: an aid in diagnosis. Audiol. Neuro. Otol. 15 (4), 241–246. https://doi.org/10.1159/000255440. PubMed PMID: 19893305.

Rey-Martinez, J., Batuecas-Caletrio, A., Matino, E., et al., 2015 Sep. HITCal: a software tool for analysis of video head impulse test responses. Acta Otolaryngol. 135 (9), 886–894. https://doi.org/10.3109/00016489.2015.1035401. PubMed PMID: 25857220.

Tweed, D., Sievering, D., Misslisch, H., et al., 1994 Nov. Rotational kinematics of the human vestibuloocular reflex. I. Gain matrices. J. Neurophysiol. 72 (5), 2467–2479. https://doi.org/10.1152/jn.1994.72.5.2467. PubMed PMID: 7884472.

Weber, K.P., Aw, S.T., Todd, M.J., et al., 2008 Feb 5. Head impulse test in unilateral vestibular loss: vestibulo-ocular reflex and catch-up saccades. Neurology 70 (6), 454–463. https://doi.org/10.1212/01.wnl.0000299117.48935.2e. PubMed PMID: 18250290.

Winnick, A., Sadeghpour, S., Otero-Millan, J., et al., 2018. Errors of upright perception in patients with vestibular migraine. Front. Neurol. 9, 892. https://doi.org/10.3389/fneur.2018.00892. PubMed PMID: 30425678; PubMed Central PMCID: PMCPMC6218433.