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RESEARCH ARTICLE

Normative vestibulo-ocular reflex data in yaw and pitch axes using the video head-impulse test

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Abstract

Background and Aim: The video head-impulse test (vHIT) measures the vestibulo-ocular reflex (VOR) driven by each semicircular canal, following high-acceleration head rotations. The main measurable response is the ratio of eye movement velocity to the angular head velocity, which reflects canal function. Although normative data is available for VOR gain, most studies only report horizontal VOR characteristics, ignoring variations in vertical plane VOR gains. The purpose of this study was to establish normative data for future comparisons of vestibulopathy patients.

Methods: Vestibulo-ocular reflex gain and refixation saccades were assessed across 50 healthy individuals between the ages of 20 and 64, without any previous or current vestibular disorders, by applying and measuring horizontal and vertical head impulses.

Results: The mean VOR velocity gain was 0.96 (SD=0.11) and 0.93 (SD=0.17) for the horizontal and vertical canals, respectively. The variation of the gain in right anterior/left posterior and left anterior/right posterior movements appeared to be wider than in the laterals, but the results were not influenced by direction ($p>0.05$). Refixation saccades occurred in 7.2 percent of all impulse trials, with a majority occurring covertly in lateral canals. Unlike saccades (more often observed in subjects older than 50), the VOR velocity gain varied independently of age.

Conclusion: The findings suggest these gain values can be used to determine VOR deficits in patients. vHIT values are affected by different factors, especially in the vertical plane, so further study is needed to confirm normal ranges of vertical vHIT values.

Keywords: Head impulse test; vestibulo-ocular reflex; semicircular canals; eye movement

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Introduction

The video head-impulse test (vHIT) as used in clinical vestibular settings, is a newly available tool for the measurement of the vestibulo-ocular reflex (VOR) to angular acceleration during natural, physiological head movements. As a bedside test (clinical HIT, cHIT) it was first described by Halmagyi and Curthoys [1-4].

The ability of the vHIT to test each semicircular canal (SCC) function separately is achieved by delivering head impulses in the plane of the canal under study, and in analyzing the very early part of the response (<100ms). This has made the test sufficiently specific and sensitive to detect vestibular deficits (unilateral or bilateral). Due to this, it is a non-invasive, quick and very well-tolerated test, one which has gained rapid acceptance in the neurotology community [1,5,6].

High velocity, passive head impulses to one side or other stimulate the semicircular canal (SCC)in the plane of stimulation. In normal subjects, the response to that head thrust (with a latency of <10ms) is for the eyes to move in the opposite direction but at the same velocity. This is in order to maintain their gaze on a target [3,6]. However, in individuals with a vestibular deficit, where the head velocity could not be correctly detected or would be under-detected, the reflex eye movement is not compensatory enough; as such, some corrective eye movements are produced during (i.e. covert saccades) or at the end of the head impulses (i.e. overt saccades) to refocus eyes on the target again [3,5-7]. Overt saccades may be detectable with the naked eye, but detecting covert saccades is too difficult for visual inspection [1,2,4,8,9].

Taking the previous information into account, a video system that allows for the precise and simultaneous recording of head and eye velocity will provide the possibility to calculate the gain of the VOR and to characterize the corrective saccades [10]. When head and eye velocities are compared, in normal subjects they are very similar (when divided, the result, or ‘gain’ should be 1) [11], but in patients with deficits, the eye velocity is lower than the head velocity (gain<1). Considering these saccades in the definition of the response is important, because in some patients with unilateral vestibulopathy, normal VOR gains with refixation saccades have been reported [4,12]. It can also provide important information of isolated semicircular canal dysfunction in evaluating peripheral vestibular disorders [13]. The gain of the VOR is affected by age in different, somewhat unclear ways, as it is not similar for the different SCC receptors, and it is influenced by the head/neck mobility, as well as by the method of delivering the impulses, probably [4,6,14-16].

In the literature, most of the reports on the clinical application of the EyeSeeCam video head-impulse test system are related to yaw axis stimulation, with information on the vertical semicircular canals remaining scarce [1,4,5,17-20]. Considering suggestions from recent studies, it is important to establish normative values for each type of equipment and protocol [1,13,20]. That prompted this study, in which we were interested in achieving data from normal subjects to assess VOR ratings after stimulating the three semicircular canals in both ears. To the best of our knowledge, this is the first study establishing normative vHIT parameters in normal Iranian participants. This will allow progress to be made in future studies on patients with dizziness.

Methods

For this study, we included healthy, normal individuals. To verify normal subjects, air conduction (AC) and bone conduction (BC) pure tone audiometry (PTA) revealed hearing thresholds≤15 dB HL between 250-8000 Hz for AC and 500-4000 Hz for BC respectively. All participants had normal middle ear function as established by immittance acoustic. Subjects reported no previous history of vertigo or dizziness. An eye exam disclosed any major visual impairments or ptosis. They were free of significant symptoms or signs of central nervous system disease.

All participants were previously examined to avoid including subjects with spontaneous nystagmus or a limited range of neck motion. Medications that could have some interaction with the VOR test were discontinued 24-48 hours before testing. Subjects were recommended to avoid alcohol consumption before testing. All of the subjects were informed verbally about the test procedure and gave their written informed consent to participate in the study.

Horizontal and vertical vHIT responses were performed with the EyeSeeCam™ (Interacoustics A/S Denmark™). The subjects were sitting in a well-lit room, 1.5 m directly in front of a target located at eye level [1,4,5,21].

Lightweight goggles were fitted properly and tightly to the subject’s head. The system included a high-speed infrared camera (sampling rate of 220 Hz) on the left side [5,17].

Vestibulo-ocular reflex evaluation

Eye calibration was performed by instructing the subject to keep his/her eyes completely open and fixed on 5 laser dots 8.5 degrees around the central target. The task was to look at the different spots without moving the head. Calibration was repeated if the subject could not perform the task correctly [5,17].

Head mobility was evaluated by rocking the head smoothly to the right and left, and back and forward, so the dynamic range of the subject's head motion was obtained.

Subjects were then instructed to keep their eyes open wide, and to stare at the target until the test was finished; neck muscles were to be kept relaxed, and subjects were told to let their head be freely controlled by the operator's hands (the examiner asked the subject not to move their head by themselves). They were advised not to blink (or to do so as little as possible) and not to touch the goggles during the test procedure [5,17]. The subjects were asked to clench their teeth to minimize slippage during head impulses [5].

The camera was adjusted as precisely as possible to track the pupil continuously. It was readjusted if needed, and particular attention was paid to avoid the image of the pupil touching the edge of the image, as well as avoiding LED reflections in the pupil.

All these steps were carried out on all subjects. Following this, the measurement of the horizontal VOR (hVOR) was started. The examiner stood behind the subject, grasping the top of his/her head, and delivered brief, random, abrupt angular head rotations within a range of 150-300 degrees for horizontal impulses and 100-150 degrees for vertical impulses [5,6].

In a full test, at least 20 head impulses in the yaw axis were delivered with the head positioned at a 30° anterior inclination [22], moving to the lateral axes (right and left) from the center through a small amplitude, and at about a 10-20 degree angle randomly [3,5,6].

The function of the vertical semicircular canals (SCCs) in the pitch axis were evaluated with regard to their position and their functioning in a push-pull fashion [6] (i.e. right anterior-left posterior and left anterior-right posterior, also respectively known as RALP and LARP) [15,23].

To test RALP and LARP function, the head of the subject was turned 30-40 degrees to the right side (for LARP) and 30-40 degrees to the left (for RALP) in such a way that purely vertical eye responses were elicited and recorded after the stimulation of the vertical SCCs. For this, the examiner's right hand was placed on top of the subject's head in such a way that their fingers were pointing at the target. The left hand was placed under his/her chin.

As before, the clinician instructed the subject to hold their gaze on the target from the corner of his/her eyes, before activating each pair by moving their head forwards and backwards. 20 head impulses in each vertical axis were also provided.

As vertical VOR responses are more easily affected by artifacts, causing VOR gains which lead to higher or lower false values, special care was taken to avoid them in each of the impulses used. In particular, we took the following steps:

- Trying not to touch the goggles and camera wire
- Making sure that the goggles were firmly fitted
- Avoiding moving the skin and trying to just move the skull
- Avoiding eyelid dropping

At the end of each study (horizontals, RALP, LARP), the traces were evaluated. The test was repeated after giving the subject a rest whenever responses included an excessive amount of artifacts, or if the subject was not alert during the task. In Fig. 1, we present an example of a, an artifact response.

At the end of each head impulse test, the instantaneous gain was measured at 40, 60, and 80 ms for horizontal canals, and an analysis of velocity regression –a calculation derived by comparing eye and head velocity between 0 and 100 ms (post-impulse onset) to quickly estimate symmetry between vestibular systems– was provided. Besides this, a regression slope

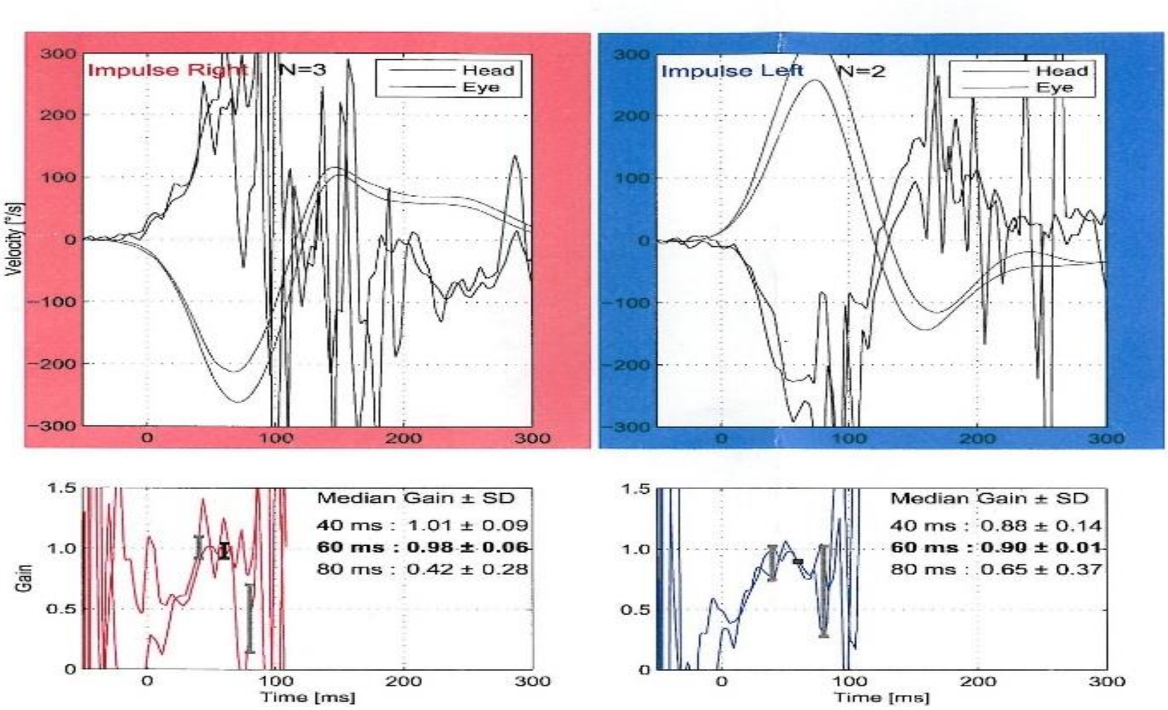

Fig. 1. An example of video head-impulse test results with many artifacts, due to a narrow palpebral fissure and excessive blinking. The test could not be completed by this subject.

calculated as gain and a gain plot in all semicircular canals were also reported. Refixation saccades were recorded in a time window of 700 ms after the head movements. All impulses were performed by a single right-handed examiner during the study.

All data were stored and analyzed in an SPSS 16.0 file, after excluding responses with technical artifacts such as blinking or eyelid movements, without any bias. For the left and right horizontal canals, just a 60 ms mean gain time was used because of the frequent occurrence of covert catch-up saccades seen in some patients in previous studies [5].

A Kolmogorov-Smirnov (K-S) normality test showed that the assumption of normality of the raw data was accepted in all conditions. A descriptive analysis was performed to achieve a mean±SD VOR gain of the horizontal and vertical semicircular canals, a 60 ms mean gain in the lateral plane, mean gain asymmetries and standard deviations. The significant of directional differences was determined by a student's t test.

The incidence of refixation saccades was expressed in terms of frequencies and percentage, as it is a qualitative parameter. A one-way ANOVA was used to find the gain changes by aging and the differences between the horizontal and vertical canals. The student's t test was used to assess the relationship between genders and mean VOR gain in each SCC. The relationship between the occurrence of refixation saccades and age groups was evaluated by using Chi-square data (χ^2) and Fisher's exact test. Level of significance was set at $p<0.05$.

Results

For this study, we included 57 healthy normal individuals; 7 were excluded because of technical problems while performing the test: excessive blinking (n=2), narrowed palpebral fissure (n=2), and excessive artifacts produced by goggle slippage (n=3). As such, the final population was made up of 50 subjects (22 male and 28 female) with a mean age of 32±12 years old, between 20 and 64.

Table 1. Vestibulo-ocular reflex results at 60 ms in the horizontal semicircular canals of normal group (n=50)

SCCs in Yaw axis	n/N	60 ms mG (SD)
Right	50/50	0.92 (0.18)
Left	50/50	0.86 (0.14)
Total	100	0.92 (0.18)

SCCs; semicircular canals, n; number of subjects, N; number of subjects in the population, mG (60 ms); mean VOR gain at 60 ms

In the 50 healthy subjects, overall, 4517 impulses were accepted and available for data analysis: 1686 in the horizontal plane (844 to the right and 842 to the left) and 2831 in the vertical plane. The hVOR mean regression gain was 0.97±0.11 for rightward head impulses and 0.95±0.12 for leftward; differences were not significant (t test, p=0.431), as well as in the instantaneous mean gain at 60 ms (p=0.127). The mean VOR gain at 60 ms for horizontal canals is shown in Table 1.

The mean VOR gain for vertical semicircular canals was 0.93±0.17. As can be seen in the error bars in Fig. 2, there is high variability for VOR gain amounts in the vertical plane, but a comparison of mean VOR gain in anterior and posterior SCC pairs did not indicate any directional dependence (p>0.05).

Interestingly, significant differences within the gain of horizontal and vertical canal pairs were observed by ANOVA (F=2, p<0.037). Tukey HSD revealed the most significant difference between the horizontal and posterior canals (p=0.047).

The mean gain asymmetries for the lateral canals, RALP and LARP were 4%, 9.1% and 7.5% respectively. The summary of mean gain, gain asymmetry and impulse number in each SCC is given in Table 2.

In addition, mean gain changes with age were also not found to be significant in the horizontal and vertical planes (ANOVA, p>0.05). Mean VOR gain and mean gain asymmetries defined by age groups were reported in Table 3. The gains for all six SCCs, also did not differ with respect to either gender (Student's t test, p>0.05).

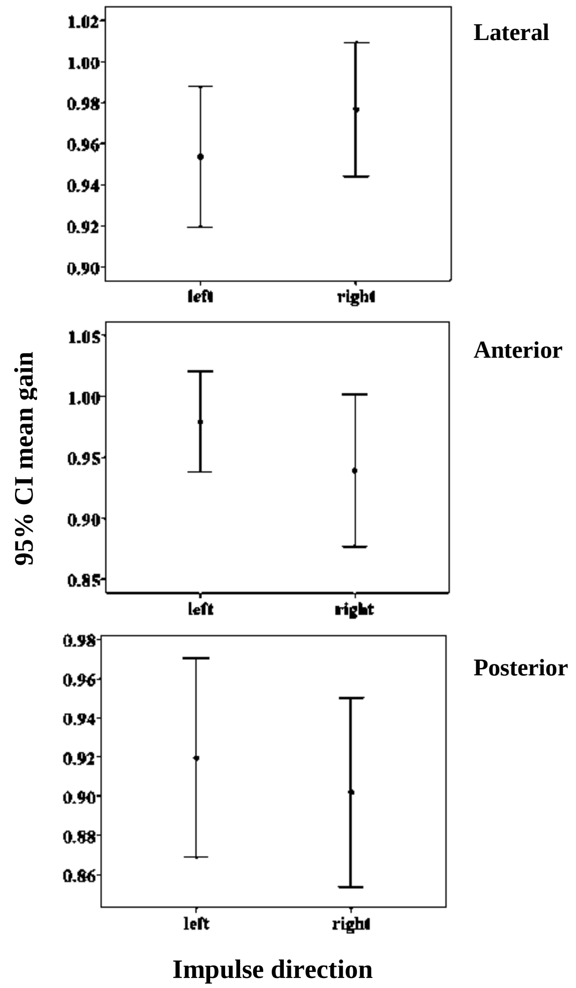

Fig. 2. Mean and 95% confidence intervals of VOR gain as a function of direction for each lateral, anterior and posterior semicircular canal pairs from the top to the bottom. As shown the variation range of mean gain in right anterior canal is larger than left anterior but it is not statically significant.

The distribution of the occurrence of refixation saccades in these 50 normal subjects is shown in Fig. 3. Covert and overt catch-up saccades were observed in 7.2% of all impulse trials, with most of them occurring in the horizontal plane. We compared the mean gain of horizontal canals in subjects with and without refixation saccades. The mean gain of right/left lateral SCCs in

Table 2. Data of the stimulus and results of the video head-impulse test according to each semicircular canal in normal subjects

SCC	RL	LL	RA	LP	LA	RP
n/N	50/50	50/50	50/50	47/50	45/50	48/50
mIN (SD)	16.8 (4)	16.8 (4.5)	16 (5.2)	15 (5.8)	12.9 (4.5)	12.6 (4.8)
mG (SD)	0.97 (0.11)	0.95 (0.12)	0.93 (0.21)	0.91 (0.17)	0.98 (0.14)	0.90 (0.16)
mGas% (SD)	4 (3.2)		9.1 (7.3)		7.5 (7.3)	
Combined mG (SD) of Yaw Axis	0.96 (0.11)					
Combined mG (SD) of Pitch Axis	0.93 (0.17)					

SCC; semicircular canal, RL; right lateral SCC, LL; left lateral SCC, RA; right anterior SCC, LP; left posterior SCC, LA; left anterior SCC, RP; right posterior SCC, n; number of subjects, N; number of subjects in the population, mIN; mean impulse number in each subject, mG; mean VOR gain, mGas; mean gain asymmetry calculated (gain R-gain L)/(gain R+gain L) × 100 between paired SCCs, R; right, L; left

subjects with refixation saccades was slightly lower (0.96±0.12/0.93±0.12) than those without refixation saccades (0.98±0.10/0.97±0.11), but this difference was not significant (p>0.05).

In our sample group, refixation saccades existed in 13.6% and 50% of subjects younger than 50 years and older than 51 years, respectively, as can be seen in Table 4. The χ^2 test and Fisher's exact test indicate that this difference between subjects younger than 50 years and older than 51 years is significant (p=0.03).

Discussion

The new video head-impulse test (vHIT) provides quick information about peripheral vestibular system functioning, according to its unique characteristic of assessing all six SCCs simultaneously, and uncovering catch-up saccades during or after head rotations [24]. The present study used this test to evaluate vestibulo-ocular reflex mannerisms in the horizontal and vertical planes among 50 healthy subjects between the ages of 20 and 64. The

Table 3. Mean vestibulo-ocular reflex gain and mean gain asymmetries, according to age groups in 50 normal participants

	mG (SD) of semicircular canals						mGas%(SD)		
Age groups (year)	**RL**	**LL**	**RA**	**LP**	**LA**	**RP**	**Lateral**	**RALP**	**LARP**
20-30	0.96 (0.12)	0.94 (0.12)	0.91 (0.23)	0.93 (0.17)	0.98 (0.13)	0.92 (0.18)	3.96 (3.50)	10.26 (7.49)	6.70 (7.00)
31-40	0.94 (0.10)	0.90 (0.07)	0.95 (0.19)	0.91 (0.15)	0.93 (0.17)	0.86 (0.06)	3.22 (3.19)	8.00 (7.19)	5.70 (7.00)
41-50	1.04 (0.12)	1.01 (0.12)	0.96 (0.26)	0.90 (0.19)	0.96 (0.11)	0.88 (0.15)	4.14 (2.60)	4.14 (2.19)	10.16 (9.4)
51-60	1.00 (0.08)	0.99 (0.17)	0.99 (0.13)	0.86 (0.23)	1.01 (0.15)	0.82 (0.16)	6.20 (2.04)	12.00 (10.86)	12.25 (11.44)
61-64	0.92	0.94	1.01	0.85	1.11	1.15	1	2	14

mG; mean VOR gain, mGas; mean gain asymmetry calculated (gain R-gain L)/(gain R+gain L) × 100 between paired SCCs, R; right, L; left, RL; right lateral SCC, LL; left lateral SCC, RA; right anterior SCC, LP; left posterior SCC, LA; left anterior SCC, RP; right posterior SCC, RALP; right anterior left posterior, LARP; left anterior right posterior

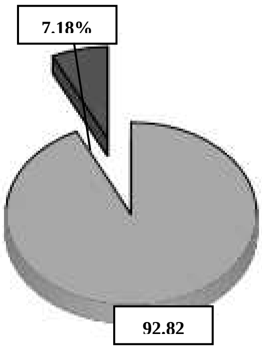

Fig. 3. Catch-up saccade occurrence distribution in 50 normal subjects. light gray: without catch-up saccades, dark gray: with catch-up saccades.

main purpose of this work is to provide statistical data for mean VOR gain variation in a normal field, based on the few available clinical evaluations of pitch axis, using the EyeSeeCam video head-impulse system.

The mean gain of the VOR variation in each SCC was reported separately, along with refixation saccades appearance. The effects of direction, age and gender on them were also investigated. The occurrence of refixation saccades is more likely as age increases, but we found no significant gain reduction in terms of age that was similar to certain earlier studies which reported age-related changes in VOR mean gain and refixation saccades [3,5,16]. Matiño-Soler et al. found a greater occurrence of saccades with increasing age, as well as a decreasing VOR gain in subjects older than 70, with higher velocity impulses [3]. Similarly, the recent study of McGarvie et al. on age-dependent normative values revealed no gain changes until 80-89 [15]. Ulmer et al. did not report any significant age effect over their control population either, [22] and Yang et al. also noted a steady gain value from 20 to 60 [20]. Our results seem to be reasonable, as the population studied was not older than 64 years. The mean VOR gain and gain asymmetries in each age groups did not show any meaningful pattern with increasing age but in the posterior canal of both sides, mean VOR gain values decreased as age increased except for right

Table 4. Occurrence of refixation saccades in subjects by age group (n=50)

Age group (year)	n/N	%
20-30	3/28	10.71
31-40	3/9	33.33
41-50	0/7	0
51-60	3/5	60
61-64	0/1	0

n; number of subjects, N; number of subjects in the population

posterior of 60’s. This is likely due to the presence of only one subject in this age group. Interestingly, Guerra Jiménez and Pérez Fernández reported gain reduction in the posterior canal as age increased which starts from the age of 50 [14].

The mean gain in the yaw axis was 0.96 deg/s. This is approximately in line with the normative data of horizontal VOR gain as obtained by Mossman et al. (from their study on 60 normal subjects among 20-80 years old) [25] and Blödow et al.’s work on 20 healthy controls along with 117 patients using EyeSeeCam vHIT, which showed average results of 0.96/0.97 [4].

It should be mentioned that the data obtained were less favorable in the vertical canals. A high variation in gain values, with high standard deviations, were achieved from the pitch axis – especially from the right anterior, as demonstrated in Fig. 4. This finding can be supported by a higher gain asymmetry percentage in LARP and RALP versus lateral. Even though the gain values had a wide range in the posterior canals, it was nearly symmetrical in pairs. The left anterior canal mean gain was higher than right side in the healthy study group used, but the head impulse direction was not generated with any bias in terms of magnitude. These gains findings showed neither horizontal nor vertical significant differences, in contrast with some studies’, which reported significant gain differences between rightward and leftward thrusts, which were based on hand prominence or camera placement on the goggle [1,3,15].

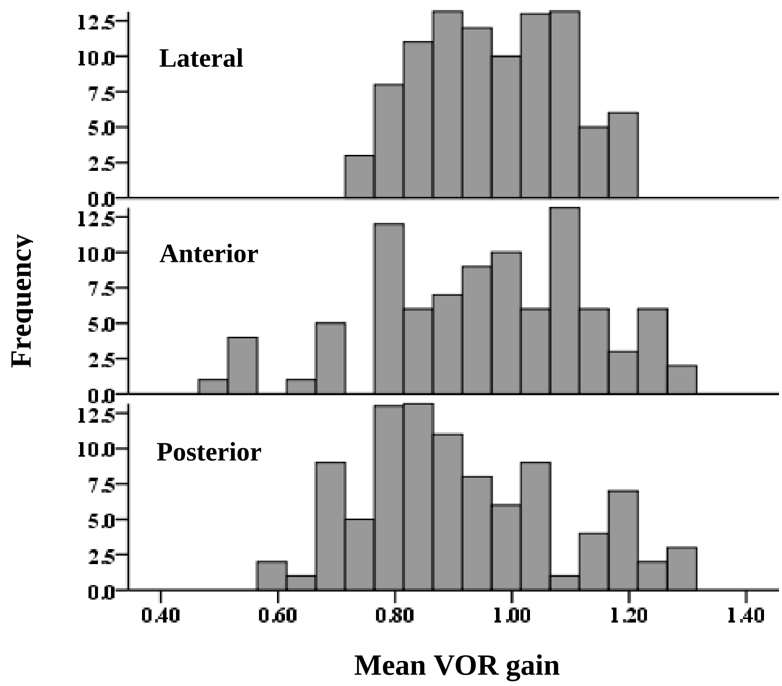

Fig. 4. The distribution of mean vestibulo-ocular reflex velocity gain frequency in 6 semicircular canals across 50 healthy subjects during right and left rotations. The highest variability is observed in the anterior canals.

Also, the extended range of gain in the vertical canals has previously been reported by some authors [15,16].

McGarvie et al.'s study of a wide age range of 91 healthy individuals demonstrated a greater VOR gain variability, with a larger gain from the right anterior than the left, at all velocities. This was because the camera on that system's goggle only measured the right eye [15]. On the contrary, we found a larger mean VOR gain in the left anterior canal than the right, which might be due to either the methodology or the geometry of the test. That is to say, the EyeSeeCam video head-impulse system records just the left eye, or else may suffer from technical problems such as eyelid artifacts or inappropriate pupil tracking. The influence of camera placement could be explained by the reflex latency difference between the abducting and adducting eye when just one eye is evaluated, or by the examiner's stronger hand preferences, as mentioned in other studies [1,3,15,18]. The direction was not clinically important in some studies looking at a normal population, similar to this study [4,5].

These findings are consistent with the explanation regarding the limited mobility of the head during vertical impulses, as well as regarding its rotation for stimulating RALP and LARP. Some subjects, especially those who are elderly or obese, can tend to tighten their neck muscles too much during the test. In our experience, delivering horizontal impulses was easier for the examiner and more tolerable for the subjects, compared with vertical ones. With a closer look one can conclude that head rotation amplitude in posterior canal is more limited. This leads higher horizontal canal gains compared to anterior and higher anterior canal gains compared to posterior as mentioned in

McGarvie et al. and Bansal and Sinha study [15,24] like ours, except for left anterior which was discussed earlier. It seems even with all the consideration given to applying vertical impulses, some artifact elements can still affect the vHIT results, especially in the vertical plane. A very high or very low velocity gain is likely to be due to goggle slippage after hand placement on the goggle band, hair, or eyelid artifacts. Also, Cerchiai et al. claimed that vertical SCCs are susceptible to artifacts, so they did not consider the results for vertical plane in their study on Meniere's disease patients [26]. Accurate calibrations in the case of some less cooperative individuals, as well as goggle slippage were two major limiting factors in this research. One suggestion for future studies would be to examine instantaneous gain results at 40, 60 and 80 ms, and to compare these with the regression average gain. Also, it might be possible to investigate potential directional effects on vHIT results, since the camera can be placed on either the left or right sides in the EyeSeeCam system. Although the test was performed carefully, and suspicious traces were excluded, the high gain variation in verticals suggests that researchers should continue to establish normative data, and to validate these findings in the vertical plane with a more detailed analysis.

Conclusions

The present study shows mean VOR gain variation across six semicircular canals in a normal population. VOR gain seems to be stable with respect to age, so these values may be helpful in peripheral vestibular deficiencies diagnosis across a wide age range. However, refixation saccades should be interpreted with additional considerations. It would be interesting to study a large sample size of the healthy population with an emphasis on VOR characteristics driven from the vertical semicircular canals, and affected by test protocols and related variables, such as head impulse velocity or target distance.

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