Refining the video head-impulse test diagnostic accuracy - a retrospective case-control study.

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Abstract

Abstract Objective: To appraise the added benefit of refixation saccades (RS) towards the improvement of the video head-impulse test (vHIT) diagnostic accuracy in cases of suspected left horizontal semicircular canal dysfunction. Study Design: Case-control. Setting: Tertiary referral center. Participants: Twenty patients with a final diagnosis of left horizontal semicircular canal dysfunction and 20 patients for whom vestibular dysfunction was ruled out. Intervention: vHIT recordings of 40 patients with left horizontal semicircular canal (LHSCC) vestibulo-ocular reflex (VOR) gain <0.8. Main outcome measures: LHSCC VOR gain; Presence of RS and their frequency, latency, and velocity characteristics. Results: Gain values > 0.72 were found in all patients with no vestibular disease and in 4 (20%) patients having vestibulopathy. Significantly higher average left-sided RS velocity and frequency were found among the vestibular patients. VOR gain < 0.72 was found to be highly specific for the diagnosis of vestibular dysfunction. However, for gain values in the range of 0.72-0.79 the presence of RS with frequency > 80% largely improved vHIT diagnostic accuracy. CONCLUSIONS: Although VOR gain<0.8 is considered to reflect dysfunction a significant false positive rate for left-sided horizontal vHIT was found for gains in the range of 0.72-0.79. The presence of RS with frequency >80% could improve vHIT diagnostic ability in these patients. Key words: video head impulse test, re-fixation saccades, peripheral vestibular pathology, gain asymmetry in vHIT, lateral semicircular canal hypofunction, saccadic frequency, corrective saccade velocity

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CONCLUSIONS: Although VOR gain<0.8 is considered to reflect dysfunction a significant false positive rate for left-sided horizontal vHIT was found for gains in the range of 0.72-0.79. The presence of RS with frequency >80% could improve vHIT diagnostic ability in these patients.

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Key points

1. The video head impulse test (vHIT) is widely employed for the evaluation of the semicircular canals (SCC) function in velocities and frequencies relevant to daily activities.
2. Current clinical practice considers the vHIT registered vestibulo-ocular reflex (VOR) gain, as the primary measure for SCC function while the role of the recorded re-fixation saccades (RS) is still under evaluation.
3. Difficulty in the interpretation of borderline vHIT gain results stems from the inherited differences in gain values being larger for the adductive eye.
4. Employing the widely used Otometrics - Natus ICS Impulse device (Taastrup, Denmark), in which the camera captures the right eye movements alone, we found that when borderline gain values of 0.72-0.8 are recorded for the left-word impulses raising the possibility of left canal dysfunction, the presence of RS with frequency >80% largely improve the diagnostic accuracy of vestibular pathology.
5. Based on our results we recommend careful re-consideration of the vHIT test results implications when left-sided VOR gain values < 0.8 are recorded. Gain < 0.72 is highly specific for the diagnosis of vestibular dysfunction. However, for gain values in the range of 0.72-0.79 the presence of RS with frequency > 80% would largely improve the diagnostic accuracy

Introduction

The bed-side head impulse test was formulated in 1988 as a measure of the lateral semicircular canal function (1). For this test pathological response is based on the detection of re-fixation saccades (RS) that compensate for the low gain of the failing vestibulo-ocular reflex (VOR). In 2009 the video head impulse test (vHIT) was introduced (2). This technology, which is based on the capturing of eye-movements at a frequency of around 250 Hz, enables the quantification of the VOR gain and the recording of RS both during the head movement and following it ("covert" and "overt" RS respectively). The RS parameters of latency, frequency, and velocity are provided by the commercially available vHIT systems (3). However, current clinical practice considers the VOR gain, for which norms and pathological values have been published, as the primary measure for semicircular canal function while the role of the registered RS is still under evaluation (4-7).

It was found that the RS velocity increases with decreasing gain (8,9). Also, in a group of dizzy patients with normal VOR gains the frequency of the RS was reported to increase with age (8). Several previous studies have examined the possible role of RS parameters in addition to the VOR gain towards the diagnosis of canal dysfunction. High velocity RS were demonstrated together with improved gain values among patients recovering from vestibular neuritis supporting the possible diagnostic value of RS in addition to the gain criterion (10). Overt but not covert RS were frequently recorded in asymptomatic older patients (9,11) differentiated from those found in unilateral semicircular canal dysfunction by their lower frequency and slower peak velocity. The combination of gain values <0.78 and RS frequency > 82% was recently suggested to improve diagnostic accuracy over the low gain parameter alone (9). Others even assert that the interpretation of vHIT results should first rely on the occurrence of RS and only second on the gain values (12). Another study proposed that the presence of RS albeit normal gain values indicate the existence of peripheral vestibulopathy and localizes the side of the lesion (13). For the recently introduced protocol of suppressive head impulse (SHIMP), the amplitude of anti-compensatory saccades was suggested as an indicator of residual semicircular canal function (14).

When mono-ocular eye movements registration is employed, the horizontal vHIT gain values were found to vary according to the side of the eye against which the recording camera is placed. Higher gains and longer saccade latencies were found for rightward impulses when the right eye movements only were captured (4,6,9,11,15).

Study Objectives

The purpose of the study was to appraise the added benefit of RS parameters alongside the VOR gain values towards the improvement of the vHIT diagnostic accuracy. Specifically, the horizontal vHIT (hvHIT) results of patients with leftward VOR gain values <0.8, currently defined as pathological (2,4,5,6,7,16), which was registered by right eye position of the testing system camera, were retrospectively evaluated for the presence of RS. The contribution of low VOR gain values with and without the addition of RS findings to the patients' final diagnosis of left vestibular dysfunction was analyzed. The focus of our study was on the diagnosis of left horizontal canal dysfunction as the mono-ocular right eye placement of the recording camera, might introduce potential bias of lower leftwards VOR gain values (4,6,9,11,15).

Materials and Methods

Study subjects and ethics statement

The hvHIT recordings of 40 dizzy patients with left sided horizontal canal VOR gains <0.8 were retrospectively re-evaluated for the presence of RS. The study groups included 20 patients with a final diagnosis of left horizontal semicircular canal vestibular dysfunction (VD) secondary to vestibular neuritis, vestibular schwannoma and unilateral intra-tympanic gentamicin-induced vestibulopathy and 20 patients for whom vestibular disease was ruled out (NVD). The diagnosis of left vestibular disease was based on the cumulative data of the patient's history, bedside otoneurological examination findings, videonystagmography caloric test results, vHIT findings and imaging results. The NVD subjects had non-specific complaint of dizziness, history that was not typical for vestibular disease, normal bed-side otoneurological examination as well as videonystagmography and imaging studies results. Also, no persistent postural perceptual dizziness (PPPD) nor vestibular migraine cases were included in the NVD group. The contribution of the VOR gain values, RS latency, frequency, and velocity parameters towards the prediction of left vestibular dysfunction was assessed. The study protocol was approved, and an exempt was granted from informed consent procedure by the institutional committee for human experiments (identifying data removed to comply with the instruction to authors)

Study set-up and paradigm

All hvHIT examinations were carried out by the same experienced right-handed examiner (M.K.) employing the Otometrics - Natus ICS Impulse device (Taastrup, Denmark) in which the camera captures the right eye movements alone. For the vHIT system used the VOR gain is calculated as the whole area under the curve of the velocity over time recordings of the eye movement divided by that of the head. Physiologically occurring microsaccades characterized by eye movements smaller than 15 minutes of arch with velocity < 50 deg/sec are screened out by the vHIT system (17). The vHIT test was carried out as has been previously described for the Otometrics - Natus ICS Impulse system (16). For each participant 20 repetitions of the head impulse were randomly carried out to the left and right sides.

The outcome measures for the hvHIT were the horizontal canal VOR gain; percentage of gain asymmetry ((rightward gain – leftward gain / rightward gain + leftward gain)*100), head velocity (degrees/sec), RS velocity (degrees/sec), RS latency (msec), and RS frequency ((number of corrective saccades / number of eligible head thrusts) * 100).

Establishing our laboratory norms for the horizontal vHIT gains.

42 healthy subjects with no vestibular complaints and normal otoneurological examination had vHIT testing of the horizontal semicircular canals employing the Otometrics - Natus ICS Impulse device (Taastrup, Denmark). All the examinations were carried out by the same experienced right-handed examiner (M.K.).

The gain values obtained had normal distribution averaging 0.88+ 0.08 (mean + standard deviation) for the left horizontal semicircular canal and 1+ 0.14 (mean + standard deviation) for the right semicircular canal. Taking into consideration normal range within mean + 2 standard deviations, the calculated normal ranges for the hvHIT gains are 0.72 – 1.04 and 0.72 – 1.28 for the left and right side respectively.

Statistical analysis

Leftward hvHIT gain values, percentage of gain asymmetry, head velocity, RS velocity, latency, and frequency were compared between the VD and NVD groups by the Student unpaired two-tailed test or the non-parametric Mann–Whitney test. Within subjects rightward and leftward head velocities and VOR gains were compared by the Student paired two-tailed test or the non-parametric Wilcoxon matched-pairs signed-ranks test. Data sets were tested for normal distribution by the Shapiro–Wilk normality test and the appropriate statistical tests were accordingly used. Proportions of the cut-off gain values, presence of RS, detection of RS with specific velocity and frequency characteristics, and their combinations were compared between the groups employing the Fisher's exact test. Sensitivity, specificity, positive and negative predictive values towards the prediction of VD were calculated for the various outcome measures and their combinations. P-values <0.05 were considered statistically significant. Statistical analysis was performed using the GraphPad InStat version 3.06 software (San Diego, CA, USA).

Results

The VD and NVD groups each included 11 men and 9 women. The mean subjects' age of the VD group participants was 56.45+ 16.64 years (mean + standard deviation) and did not significantly differ from that of the NVD group which was 50.75+ 14.58 years (unpaired t-test). The final diagnosis of the 20 patients included in the VD group was vestibular neuritis in 17, vestibular schwannoma in 2 and intra-tympanic gentamicin- induced vestibulopathy in 1 patient. The diagnosis of vestibular neuritis was reached only if all the following symptoms and signs were present: acute onset of prolonged severe rotatory vertigo, the presence of spontaneous nystagmus and postural imbalance, and documentation of unilateral reduced caloric response (caloric lateralization > 25%) on the caloric study of videonystagmography.

For the NVD group the average rightward hvHIT gain was 0.93+ 0.1 (95% CI 0.88-0.98) and the leftward gain 0.75+ 0.02 (95% CI 0.74-0.77). The difference was of statistical significance (p<0.0001; Wilcoxon matched-pairs signed-ranks test).

The rightward and leftward head velocity values did not significantly differ reaching 210+ 31.3 (95% CI 195.7-224.9) and 213.9+33.8 (95% CI 198.1-229.7) deg/sec respectively (Paired t-test).

No significant difference was found between the leftward head velocities of the VD and NVD groups registered as 207.3+ 33.2 (95% CI 191.8-222.8) and 213.9+ 33.8 (95% CI 198.1-229.7) respectively (Unpaired t-test).

The average left hvHIT gain of the VD group was significantly lower as compared to the NVD group (0.445+ 0.23 vs. 0.757+ 0.024; p<0.0001, unpaired t-test; Fig. 1) and the gain asymmetry average, where higher gains were recorded for the rightward stimuli, was significantly larger (39.2+ 24.11% vs. 18.12+ 9.05%; p<0.002, unpaired t-test; Fig. 2).

As detailed in section *2.3* the calculated normal range in our laboratory for the right hvHIT gain is 0.72-1.28 and 0.72-1.04 for the left hvHIT gain.

Gain values > 0.72 were found in all NVD patients and in 4 (20%) patients of the VD group (p<0.0001; Fisher's exact test).

Significantly higher left-sided RS velocity and frequency were found in the VD group (221.35+ 89.18 vs. 131+ 42.93 degrees/sec; p<0.0002 and 83.2+ 33.2% vs. 24.15+ 29.8%; p<0.0001, Mann–Whitney test respectively; Fig. 3, Fig. 4). No differences between the groups were found in the RS latency (196.71+ 52.13 vs. 250.82+ 114.78 msec for the VD and NVD groups respectively. Not significant by unpaired t-test, Welch corrected for different standard deviations).

RS were detected in 19 (95%) of the VD patients and 12 (60%) of the NVD group ($p<0.02$; Fisher's exact test).

Among the 19 VD patients in whom RS were detected 17 (89%) had RS frequency > 80%, while in all the 12 NVD patients having RS the frequency value was < 80% ($p<0.0001$ Fisher's exact test).

RS velocity was higher than 150 deg/sec in 17 of the 19 VD patients (89%) and in only 3 of the 12 NVD patients (25%) having RS ($p<0.0004$ Fisher's exact test).

17 of the VD group out of 19 (89%) and 1 of the NVD group out of 12 (8%) had RS with both frequency > 80% and velocity > 150 deg/sec ($p<0.0001$ Fisher's exact test).

15 of the VD group participants (75%) had gain values < 0.72 and RS frequency > 80% while in none of the NVD group such association was recorded ($p<0.0001$ Fisher's exact test).

15 of the VD group (75%) and 3 NVD group participants (15%) presented with gain values < 0.72 and saccade velocity > 150 deg/sec ($p<0.0004$ Fisher's exact test).

The combination of gain values < 0.72, saccade frequency > 80% and saccade velocity > 150 deg/se was found in 15 (75%) of the VD group and none of the NVD group ($p<0.0001$ Fisher's exact test).

The sensitivity, specificity, positive predictive value and negative predictive value of the following outcome measures towards the prediction of VD are detailed in Table 1.

Discussion

vHIT systems employing mono-ocular eye movements recording have an inherited right-left imbalance regarding the horizontal semicircular canal gain values depending on the location of the camera. A study including 212 healthy subjects from all ages showed a mean 9.1% gain value difference in favor of the right side in all age groups while using right eye recording system (6). Another recent study of commercially available vHIT systems reported on 5% rightward gain bias when the right eye movements only were captured (18). While using scleral search coils for accurate binocular eye movements recording it was found that the horizontal VOR gain for the adducting eye exceeded the gain of the abducting eye by an average of 15.3% (19). Several explanations have been offered for this right-left imbalance; a longer neural pathways (trisynaptic) for the adducting medial rectus, compared to the shorter (disynaptic) pathway of the abducting lateral rectus when the system camera captures the right eye movements alone (6,19). Alternatively, the higher gain might stem from the relative decrease in head velocity while a right-handed examiner uses his weaker left hand for the conduction of the rightward head thrust. Others have attributed the rightward higher gain to asymmetry in the maximal active force of the medial rectus when compared to the lateral rectus muscle which is about 26% greater for the adducting muscle (4,20).

Although we have found in the NVD group a significant gain difference in favour of the rightward head impulse which was conducted by a right-handed examiner, the head velocities to both sides were comparable. Thus, for our study the higher right-sided gain is not explained by possible examiner-related factors.

The reported bias in favour of lower left hvHIT gain when right eye movements alone are recorded, that is also supported by our results in the NVD group, might introduce false-positive results of left sided vestibulopathy especially when the VOR gain is used as the sole diagnostic criterion. In the current study we evaluated the added benefit of RS in reaching a final diagnosis of left horizontal semicircular canal hypofunction in using the right mono-ocular ICS impulse vHIT system.

The recommended published VOR gain cut-off value discriminating normal and pathological horizontal semicircular canal function is 0.8 (2,4-7,16). Based on our laboratory norms we have looked at a cut-off value of 0.72. Significantly lower average left-side VOR gain and higher gain asymmetry were found for the VD group, and all the NVD group participants had left hvHIT gain > 0.72. Still the sensitivity of gain <0.72 alone towards the diagnosis of VD was only 80%.

The existence of RS has been previously reported in healthy subjects, with increased frequency and velocity with higher age and lower gain values (6,21). In our study the mere presence of RS had 100% sensitivity but only 40% towards the diagnosis of VD. A recent research has suggested RS frequency of 80% as a parameter for their consistency (13). Adding the restriction parameter of RS frequency>80% increased the hvHIT specificity to 100% with 89% sensitivity.

Various RS velocity criteria have been proposed to distinguish normal vs pathological vestibular function. These include critical RS velocity of 50 (13), 100 (21), 133 (22) and 135 deg/sec (9).

Although RS average velocity was significantly higher in the VD group and significantly higher proportion of VD patients demonstrated RS with velocity > 150 degrees/sec, this RS velocity criterion alone or adding it to the RS frequency >80% parameter did not improve the vHIT prediction values.

Based on our results we recommend careful re-consideration of the hvHIT test results implications when left-sided VOR gain values < 0.8 are recorded. Gain < 0.72 is highly specific for the diagnosis of vestibular dysfunction. However, for gain values in the range of 0.72-0.79 the presence of RS with frequency > 80% would largely improve the hvHIT diagnostic accuracy (Fig. 5).

Our study limitations include its retrospective nature and the relatively small size of the cohort included. Although vestibular disease was ruled out in our NVD subjects, the ideal control group should have been comprised of healthy subjects with no complaint of dizziness, which we found difficult to recruit. Most (85%) of the VD group have suffered from vestibular neuritis. Still, the inclusion of other diagnoses might have introduced some disparity in our results.

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Figure legends

Fig. 1

Box plot of the VOR gain values of patients with a final diagnosis of vestibular dysfunction and those with no vestibular disease. The boundary of the box closest to zero indicates the 25th percentile, the solid line within the box marks the median, the dashed line marks the mean, and the boundary of the box farthest from zero indicates the 75th percentile. Whiskers above and below the box indicate the 90th and 10th percentiles. Circles above and below the 90th and 10th percentiles mark outlying data points.

Fig. 2

Box plot of the VOR gain values left-right asymmetry of patients with a final diagnosis of vestibular dysfunction and those with no vestibular disease.

Fig. 3

Box plot of re-fixation saccades velocity of patients with a final diagnosis of vestibular dysfunction and those with no vestibular disease.

Fig. 4

Box plot of re-fixation saccades frequency of patients with a final diagnosis of vestibular dysfunction and those with no vestibular disease.

Fig. 5

Decision algorithm for horizontal semicircular dysfunction incorporating vHIT gain and re-fixating saccades parameters.

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