Bithermal caloric test and Video head impulse test in peripheral vestibular pathologies

Abstract

Bithermal caloric test and video head impulse test (vHIT), both evaluate lateral semicircular canal. However vHIT uses natural stimulation and is non-invasive whereas bithermal caloric test can induce vertigo, nausea and other autonomic nervous system related symptoms which makes it less tolerable than vHIT. This initiated a drive for replacing caloric testing with vHIT. However, the main hurdle to this drive is the lack of knowledge whether both these tests assess the same function of the vestibulo-ocular reflex (VOR) pathway. Therefore, present study aimed to find association between the two tests. Fifty individuals with peripheral vestibulopathies (24 Meniere's disease, 19 benign paroxysmal positional vertigo & 7 vestibular neuritis) and 30 healthy individuals underwent lateral canal vHIT and bithermal caloric testing. The results revealed no significant agreement between reduced VOR gain and caloric abnormality, presence of pathological saccades and caloric abnormality and also between vHIT abnormality and caloric abnormality in any of the three clinical conditions ($p > 0.05$). Therefore, using both of them in the test battery is suggested to enhance the chance of identifying vestibulopathies whereas substituting one with the other would reduce the possibility of abnormality detection, at least in Meniere's disease, benign paroxysmal positional vertigo and vestibular neuritis.

Key words: vHIT, Meniere's disease, BPPV, Vestibular neuritis

Introduction

The vestibular system is responsible for identifying head movement and maintaining image stability on the fovea of the retina during motion. Additionally it is also helpful in maintaining postural control of the body when there is a head motion. In a healthy individual with normal vestibular system, the vestibular receptors provide an in-depth and accurate depiction of the head motion in a three-dimensional plane. The information provided by the vestibular receptors is subsequently utilized by the central vestibular pathways for controlling the reflexes and the perceptions that are mediated by the vestibular system. Pathologies within the vestibular system cause abnormalities in these reflexes and translate to sensations of motion when actually there is none (Minor, 1998).

Individuals with a dysfunctional vestibular system (vestibulopathy) regularly complain of balance related deficits like spinning, swaying, or imbalance. All these put together are more generically described by the term ‘dizziness’. In the United States alone, dizziness has been reported to account for nearly ten million doctor visits per year (Kruschinski et al., 2008). Although problems of vision and/or proprioception can be associated with the feeling of dizziness, many frequently found vestibulopathies pivot around peripheral vestibular dysfunction. Benign paroxysmal positional vertigo (BPPV), vestibular neuritis, Meniere’s disease and perilymphatic fistula are among several examples of these vestibulopathies. The vestibulopathy can also result from surgical procedures like labyrinthectomy or neurectomy (Curthoys 2000; Fetter 2000).

Need for the study

The signs and symptoms of vestibular dysfunction, irrespective of the aetiologies, are frequent and most often chronic and disabling. However, the differential diagnosis among these conditions is often tricky, resulting in a label of 'vestibulopathy of unknown cause' rather than a specific condition in several patients (Baloh, 2003). This has lead to several studies whose outcomes hinge around identifying the efficiency of a test by comparing its outcome against two or more tests.

Although there are instances of obtaining hyper-reactive response on several tests of vestibular dysfunction (Ikeda & Watanabe, 1997), the more common finding is that of hypo-reactivity to the stimuli used (Bhansali & Honrubia, 1999) in cases with vestibular pathology. The vestibular hypofunction involving the horizontal semicircular canals can be successfully recognized by the presence of significant canal paresis (asymmetric vestibular responses) during bithermal caloric irrigation (Bhansali & Honrubia, 1999). More recently, the video head-impulse test (vHIT) has also been found useful for identification of vestibular hypofunction involving the horizontal semicircular canal (Weber, MacDougall, Halmagyi, & Curthoys, 2009). While the former test (bithermal caloric irrigation) is a well known test for the measurement of vestibular function, the latter (vHIT) exploits the inherent principles of vestibulo-ocular reflex (eyes move opposite to the head motion with almost exact acceleration as head) to identify a hypofunctional side horizontal canal. During the vHIT testing, high-acceleration small-amplitude head-impulses (head jerks) are applied around an earth-fixed vertical axis while the subject is instructed to maintain gaze fixation at a stationary target. A pathologic response on this test is the one that shows a correcting saccade (eyes move opposite to the head movement but after a delay) because the eyes no longer compensate for the head movement (Weber et al., 2009). Although the video recording version of the head impulse test (HIT) is a more recent development, the horizontal HIT has

been used as a bed-side screening test for assessing the functionality of the horizontal semicircular canals (Beynon, Jani, & Baguley, 1998; Harvey, Wood, & Feroah, 1997). These studies, using HIT without the video recording, had shown moderate sensitivity (35-45%) but high specificity (90%) (Beynon et al., 1998; Harvey et al., 1997). The lower sensitivity was probably because of the examiners' inability to identify the corrective saccades that are made when the head is still in motion (often referred as 'covert saccades').

The video recording version (vHIT) was developed with the aim of improving objectivity when identifying the corrective saccades and also enabling the identification of the covert saccades so that it would help not only in more in-depth analysis of the responses but also commendably improve the sensitivity and specificity in doing so when using the HIT principle (Weber et al., 2009). The outcomes of vHIT have been found to be akin to those of HIT measurements when done using the scleral search coils for improving objectivity (MacDougall, Weber, McGarvie, Halmagyi, & Curthoys, 2009). Perez and Rama-Lopez (2003) reported an increase in the probability of a pathologic HIT (without video recording) with increasing canal paresis on bithermal caloric evaluation. They further reported that a canal paresis of $\geq$ 42.5 % always produced positive results on HIT and the patients with the canal paresis values within normal limits almost never produced a pathologic HIT response. However, such associations have rarely been established when using the vHIT. In fact a recent study showed dissocation between the results of bithermal caloric testing and vHIT (McCaslin, Rivas, Jacobson, & Bennett, 2015). However, McCaslin et al (2015) conducted the study only on individuals with Meniere's disease. They did not include other commonly encountered peripheral vestibular pathologies like benign paroxysmal positional vertigo (BPPV) and vestibular neuritis/labyrinthitis. Therefore, there is a need to investigate the utility of vHIT in identifying vestibular hypofunction and establish the relationship between the outcomes of vHIT and bithermal caloric test in various peripheral vestibular pathologies.

Aim of the study

The present study aimed at investigating the utility of vHIT in identifying peripheral vestibulopathies and comparing its outcome to the well established bithermal caloric test.

Objectives of the study

1. To obtain the outcome of vHIT in healthy individuals.
2. To obtain the outcome of vHIT in vestibular pathologies.
3. To obtain the outcome of bithermal caloric test in healthy individuals.
4. To obtain the outcome of bithermal caloric test in vestibular pathologies.
5. To find the association, if any, between the outcomes of vHIT and bithermal caloric test in healthy individuals and individuals with vestibular pathologies.

Method

Participants

The study included 50 consecutive individuals with peripheral vestibular dys/hypofunction in the clinical group and 30 healthy individuals with normal audio-vestibular function in the comparison group. The age range of participants in clinical group was 10 to 70 years (mean age = 45.7 years) and the comparison group was 18 to 29 years (mean age = 21.83 years). The participants were included in the study after obtaining the written informed consent. The clinical group included individuals with Meniere's disease (n = 24; 7 bilateral & 17 unilateral), vestibular neuritis/labyrinthitis (n = 7; all unilateral) and benign paroxysmal positional vertigo (BPPV) (n = 19; all unilateral). The presence of peripheral pathology was ensured through the diagnosis of the above mentioned conditions, through a battery of tests. The diagnosis was performed according to the standardized cited criteria for definite Meniere's disease (American Academy of Otolaryngology- Head & Neck Surgery, 1995), vestibular neuritis/labyrinthitis (Brandt, 2003) and BPPV (Bhattacharya et

al., 2008). The horizontal canal BPPV was ruled out by negative results on the supine roll test. Further, the presence of middle ear effusion and/or other neurological deficits also resulted in non-inclusion of the participant in the study which was ensured through normal results on immittance evaluation ('A' type tympanogram & presence of acoustic reflexes at 100 dB HL) and a neurological screening (case history & clinical examination) by an experienced neurologist, respectively. Although the presence/absence of sensorineural hearing loss was not a subject selection criterion, it was useful for differentiation between vestibular neuritis and labyrinthitis and ensuring definite Meniere's disease. The audio-vestibular well being of the participants in the comparison group was also ensured through a case history that showed no history of auditory, vestibular or neural pathology and normal results on pure-tone audiometry (pure-tone average $\leq$ 15 dBHL), speech audiometry (speech recognition threshold within $\pm$ 12 dB of pure-tone average & speech identification scores of $\geq$ 90%), immittance evaluation ('A' type tympanograms with presence of ispsilateral & contralateral acoustic reflex at 100 dBHL), Romberg test (no evident sway), Fukuda stepping test (deviation < 45^{o} & distance < 1m from the starting point), tandem gait test (no imbalance or raising of either hand during heel-to-toe walking) and past pointing (finger-to-nose) test (no under/overshooting of the target & no evident tremors during the task).

Instrumentation

Air- and bone-conduction thresholds were obtained using Inventis Piano clinical audiometer with TDH-39 supra-aural headphones and Radioear B-71 bone vibrator, respectively. Immittance evaluation was carried out using Grasson-Staddler Incorporated (GSI) Tympstar diagnostic middle ear analyzer. Nystagmus during bithermal caloric test was recorded using a commercially available BioMed eVNG system with binocular Frenzel's glasses. vHIT was performed using the 'lateral canal' test module of ICS Impulse equipment.

Test environment

Bithermal caloric test was performed in a dark room whereas vHIT was performed in a well illuminated room. Pure-tone audiometry, speech audiometry and immittance evaluations were performed in well illuminated sound treated rooms with ambient noise levels within the permissible limits (ANSI S3.1 1991). All test rooms were air-conditioned.

Procedure

A detailed structured case history was obtained using the Oto-neurological proforma (unpublished) developed at the Dept. of Otorhinolaryngology, All India Institute of Speech and Hearing, Mysore. This was followed by pure-tone audiometry, speech audiometry, immittance evaluation, Romberg test, Fukuda stepping test, tandem gait test and past pointing test for fulfilment of subject selection criteria. Upon fulfilment of subject selection criteria, participants underwent vHIT and bithermal caloric test. Both vHIT and bithermal caloric test were performed on the same day, with vHIT being administered first and ensuring a gap of 1 hour between the two tests. It has long been established that bithermal caloric test should be the last performed test in a test sequence performed in the same session. This is because the caloric test is performed using a very strong non-physiologic stimuli (temperature gradient) which is capable of leaving behind significant order effect on tests that follow it. This was the reason behind always performing vHIT before caloric test. In order to ensure no reminiscent residual impact of vHIT on caloric test, a gap of 1 hour between vHIT and caloric test was used. This order and gap therefore were meant to ensure that the outcomes of bithermal caloric test and vHIT were independent of each other.

Video head impulse testing.

The lateral canal module of video-head-impulse test was used to test the lateral (horizontal) semicircular canals' functions. For this, the participant was seated at a distance

of 1 meter from a wall mounted dot at eye level's height. Laser beam projector located on the monocular goggle wore by the subject projected two laser dots (separated by 20^o) in such a way that the wall mounted dot fell right in between the two laser dots. Participant was asked to alternately look at the two dots. This step ensured calibration of the system. After calibration, laser was switched-off and the participant was asked to maintain gaze on the wall mounted dot at all times. Short lasting head impulses, each ranging between 10^o to 20^o with peak velocity of 150-200^o/s, were made around an earth-fixed imaginary vertical axis. This range of values is similar to that used previously (Lehnen, Aw, Todd, & Halmagyi, 2004; MacDougall et al., 2009). Head impulses were made by the examiner standing behind the participant and randomised in terms of numbers in each direction in order to avoid anticipatory eye movements to compensate for head movements. The recordings corresponding to 20 head impulses each in either direction of head movement were analyzed. vHIT was deemed pathological if the VOR gain (eye velocity divided by head velocity) was < 0.8 (Curthoys et al., 2010). Both overt (saccadic movement performed after a particular head impulse is completed) and/or covert (saccadic movement performed during a particular head impulse) refixation saccades, when present, were recorded and their presence was considered for presence of vestibular pathology (MacDougall et al., 2009). Difference of the right- and left-sided VOR gain was quantified as asymmetry ratio which was calculated using the following formula:

$$\text{Asymmetry ratio} = (R-L)/(R+L)$$

where 'R' and 'L' stand for the absolute average VOR gain values for stimulation towards the right and left side, respectively.

Bithermal caloric test.

Eye movements (nystagmus) were recorded using a commercially available binocular video oculography (video nystagmography) system BioMed eVNG. Prior to caloric testing,

the system was calibrated for each participant by asking the participant to follow a dot which appeared at different known angles on the screen while the participant was seated straight in front of the screen at a distance of 1 meter. Bithermal caloric irrigation was performed by placing the subject in a supine position and keeping head at an angle of 30^{o} above the horizontal in order to achieve a vertical orientation of horizontal semicircular canal. Two temperatures used were 44^{o}C (warm) and 30^{o}C (cold). Irrigation was done for one ear at a time with right ear and warm temperature preceding the left ear and cold temperature. For each ear at each temperature, the ear irrigation was performed for 30 seconds using 30 ml of water from a syringe. Nystagmus were recorded for a total duration of 2 minutes following the completion of irrigation and a gap of 5 minutes was provided before shifting to the opposite ear. During the recording of nystagmus, participant was asked to perform a mental alertness task like reverse counting, simple arithmetic calculations or narration etc., depending on their ability (educational background), in order to ensure alertness. Average slow phase velocity and culmination frequency were calculated for each irrigation. These values were used in the following formula in order to obtain unilateral weakness (canal paresis):

$$\text{Unilateral weakness} = [\{(RW+RC) - (LW+LC)\}/\{(RW+RC) + (LW+LC)]\}]x100$$

where ‘RW’, ‘LW’, ‘RC’ and ‘LC’ stand for average slow phase velocities or culmination frequency for right warm, left warm, right cold and left cold irrigations, respectively. Culmination frequency (number of nystagmus beats appearing in a 30 seconds window of most populated nystagmus activity) of less than 23 was also considered an abnormal result on bithermal caloric testing.

Statistical analyses

Shapiro Wilk's test of normality was performed on the obtained data for bithermal caloric evaluation and vHIT and the results revealed non-normal distribution of the data ($p < 0.05$). Therefore non-parametric statistics were followed for subsequent analyses. Descriptive statistics included reporting mean, median, standard deviation and range. Spearman's rank correlation and Kappa coefficient analyses were performed for finding association between the two tests.

Results

The participants in the study were divided into clinical and comparison group. The clinical group consisted of 50 individuals with peripheral vestibular pathologies and the comparison group consisted of 30 individuals with normal auditory and vestibular system. All the participants underwent vHIT and bithermal caloric test. Findings of vHIT and bithermal caloric test are described below separately for clinical and control groups.

vHIT in comparison group (healthy individuals)

The study included 30 participants having normal auditory and vestibular systems. All of them underwent vHIT for lateral canal on both sides. Figure 1 shows representative vHIT responses obtained from both sides (right & left lateral semicircular canals) from a participant in the comparison group.

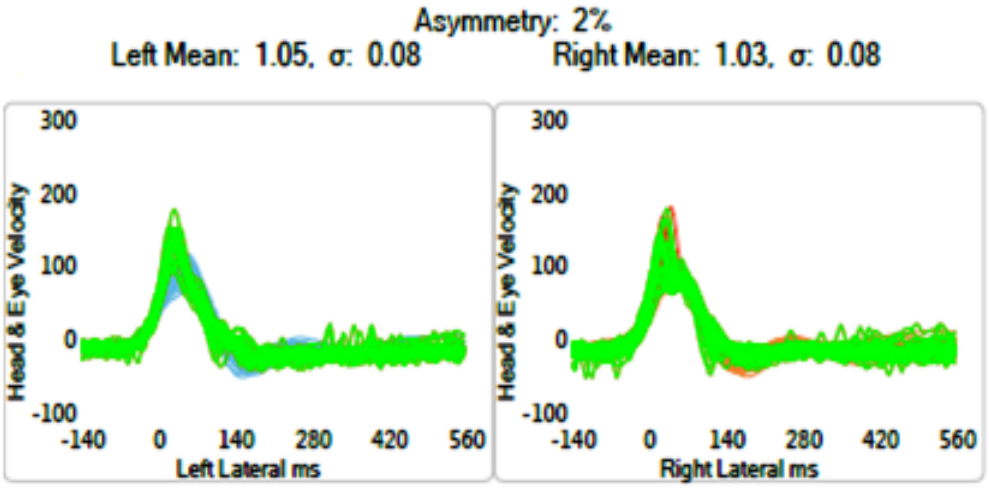


Figure 1: Representative vHIT responses from a participant in the comparison group.

Descriptive statistics were performed to obtain mean, standard deviation, median and range of VOR gain. Table 1 shows the outcome of descriptive statistics for VOR gain of both sides from participants in the comparison group.

Table 1.

Mean, standard deviation, median and range of VOR gain in the comparison group (healthy individuals)

Parameter	Mean	Standard deviation	Median	Range	
				Minimum	Maximum
VOR gain for right side	0.98	0. 10	0.97	0.85	1.41
VOR gain for left side	0.93	0.09	0.91	0.83	1.19
Asymmetry ratio (in %)	6.23	5.95	3.00	0.00	22.0

There was reduced VOR gain (< 0.80), as per the normative data for lateral canal vHIT used else where in the literature (Curthoys et al., 2010), on one side of 1 participant and increased VOR gain (> 1.20) on one side of 1 participant, thereby amounting for abnormal results in 6.66% participants (3.33% ears) in the comparison group when using VOR gain.

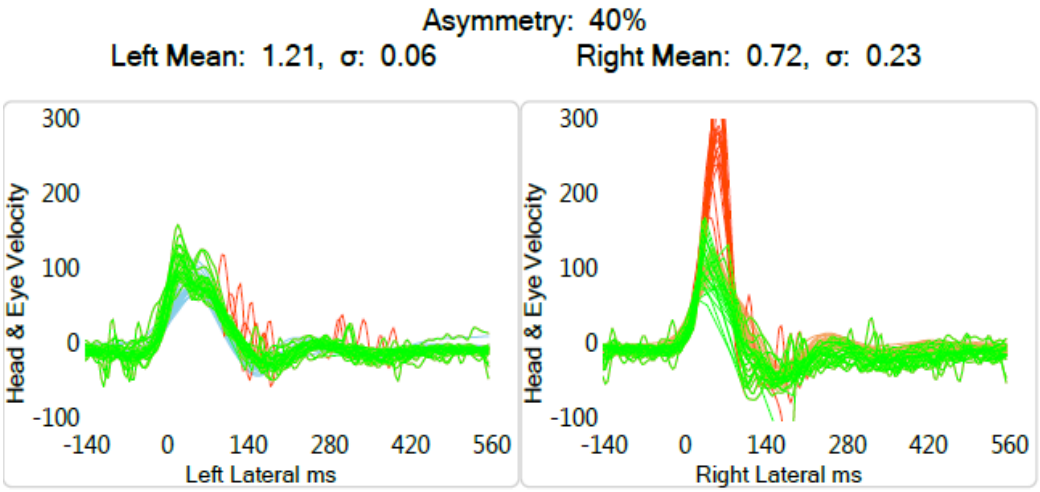
The presence of refixation saccades was operationally defined as pathological when it was present on more than 50% of the impulses (>10 impulses) on one side. In the comparison group, 2 participants had refixation saccades which amounted to pathological results in 6.66% of the participants.

vHIT in clinical group

The study included 50 participants diagnosed with peripheral vestibular pathologies. Of these, 24 participants had definite Meniere's disease (17 unilateral & 7 bilateral), 19 had unilateral posterior canal BPPV and 7 had unilateral vestibular neuritis (all in left ear). The outcome of vHIT in these clinical sub-groups is elaborated separately below.

vHIT in Meniere's disease.

The study had 17 individuals with unilateral and 7 individuals with bilateral Meniere's disease. Figure 2 shows the representative vHIT responses from an individual each with unilateral and bilateral Meniere's disease.



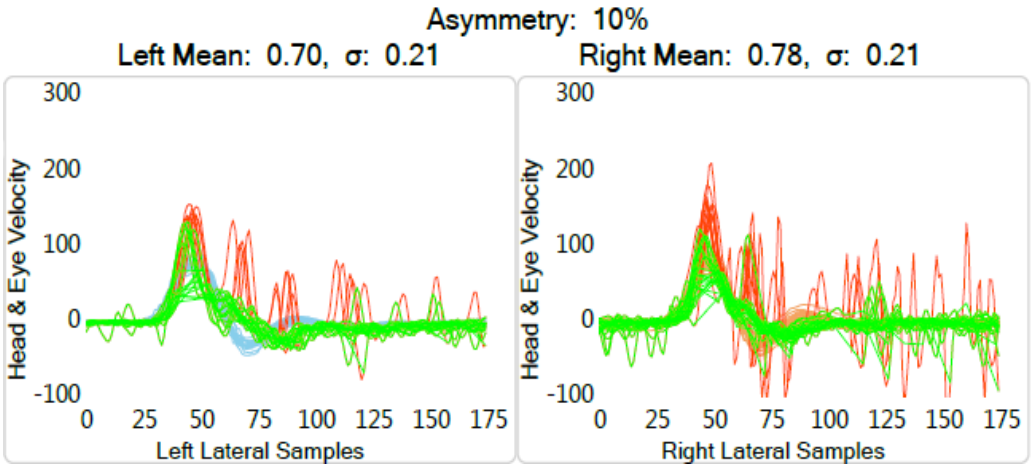


Figure 2: Representative vHIT responses from both sides of an individual with unilateral Meniere's disease (top panel; right ear was pathological) and bilateral Meniere's disease (bottom panel).

Present study had 17 individuals with unilateral and 7 individuals with bilateral Meniere's disease which resulted in 31 ears affected with Meniere's disease and 17 unaffected ears. Mean, standard deviation, median and range of VOR gain in individuals with Meniere's disease are shown in Table 2.

Table 2.

Mean, standard deviation and median VOR gain in affected and unaffected ears of individuals with Meniere's disease

Parameter	N	Mean	SD	Median	Range	
					Minimum	Maximum
VOR gain affected ears	31	0.95	0.16	0.95	0.58	1.21
VOR gain in unaffected ears	17	0.94	0.10	0.94	0.76	1.14

Note: 'SD'- standard deviation

In individuals with unilateral Meniere's disease, mean VOR gain was 0.95 (standard deviation = 0.14, median = 0.95) in affected ears and 0.94 (standard deviation = 0.10, median = 0.94) for unaffected ear. The VOR gain ranged from 0.58 to 1.16 for the affected ears and

0.76 to 1.14 for the unaffected ears. VOR gain was reduced (< 0.80) in 1 (5.88%) affected ear and 2 (11.76%) unaffected ears. Further, pathological saccades were seen in 6 (35.29%) affected ears and 5 (29.41%) unaffected ears. Mean asymmetry ratio was 8.82% (standard deviation = 8.18, median = 6.0) with individual asymmetry ratio ranging from 0 to 28%.

In the present study, 7 participants had bilateral Meniere's disease which was diagnosed based on the audiogram and the presence of tinnitus and blocking sensation. The mean VOR gain was 0.96 (standard deviation = 0.17, median = 0.93) in right and 0.96 (standard deviation = 0.22, median =0.96) in left ears. VOR gain in this group varied from 0.72 to 1.21 in right ears and 0.66 to 1.21 in left ears. The VOR gain was reduced in 3 (21.42%) ears and pathological saccades present in 5 (35.71%) ears. Mean asymmetry ratio was 14.00% (standard deviation = 14.37, median =14.0) with a minimum value of 0% and maximum of 40%.

vHIT in vestibular neuritis.

Out of 50 participants, 7 participants in the present study were diagnosed as having vestibular neuritis, all of them in left ear. Each participant underwent vHIT testing. Figure 3 shows representative vHIT responses obtained from both ears of a participant with vestibular neuritis.

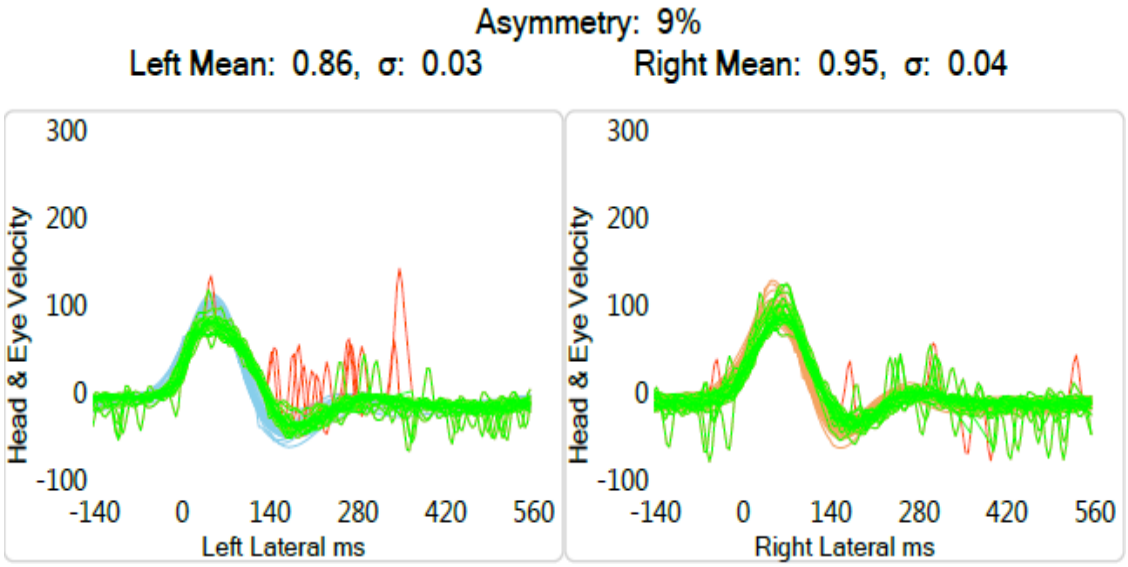


Figure 3: Representative vHIT responses from left and right sides of a participant with vestibular neuritis in left ear.

The obtained VOR gain and asymmetry ratio data were subjected to descriptive statistical analyses. Table 3 shows mean, standard deviation, median and range of VOR gain in cases of vestibular neuritis. The analyses of individual responses showed that VOR gain was reduced in 1 (14.28%) affected ear and 1 (14.28%) unaffected ear in this group. Further, pathological saccades could be observed in 4 (57.14%) affected ears and 1 (14.28%) unaffected ear. Mean asymmetry ratio was 10.0% (standard deviation = 7.02, median = 8.0) with a minimum value of 4% and maximum of 23%.

Table 3.

Mean, standard deviation and median and range of VOR gain in both ears of individuals with vestibular neuritis

Parameter	Mean	Standard deviation	Median	Range	
				Minimum	Maximum
VOR gain left (affected) ears	0.90	0.21	0.91	0.49	1.11
VOR gain in right (unaffected) ears	0.96	0.17	0.96	0.64	1.15

Asymmetry ratio (in %)	10.00	7.02	8.00	4.00	23.00

vHIT in BPPV.

In the present study, 19 participants were diagnosed as having posterior canal BPPV on one side. All 19 participants underwent vHIT recording from both sides. Figure 4 shows representative vHIT responses obtained from both sides of a participant diagnosed with posterior canal BPPV.

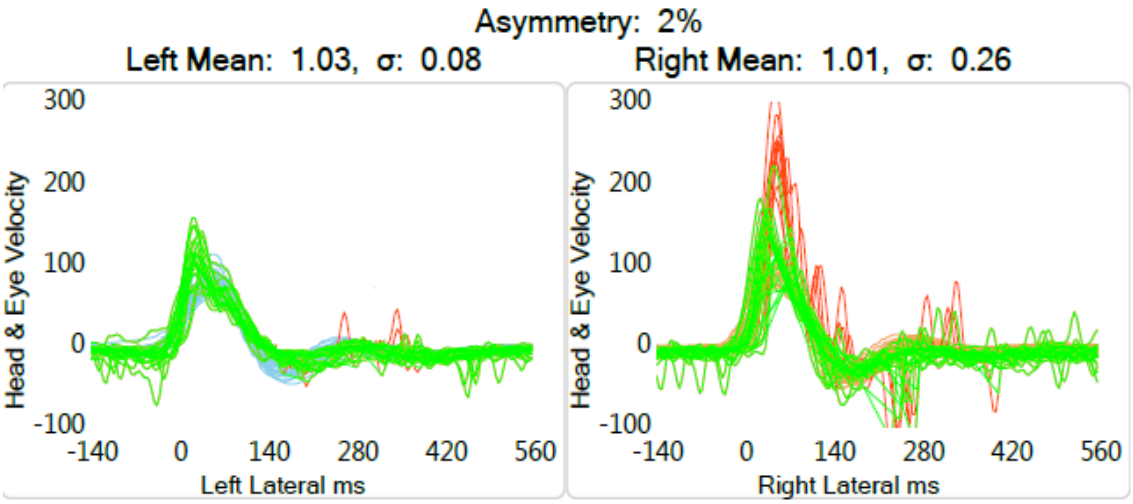


Figure 4: Representative vHIT responses obtained from both sides of a participant with posterior canal BPPV on right side.

The obtained VOR again and asymmetry ratio data were analyzed using descriptive statistics to obtain mean, standard deviation, median and range. Table 4 shows the outcomes of descriptive statistics in the group of individuals with posterior canal BPPV. VOR gain was found to be reduced in 3 (15.78%) affected ears and in 3 (15.78%) unaffected ears. Further, abnormally high VOR gain (>1.20) was observed in 2 (10.52%) affected ears 4 (21.05%) unaffected ears. Therefore, abnormality (reduced or enhanced) in VOR gain was observed in 5 (13.15%) affected ears and 7 (18.42%) unaffected ears in BPPV group. Furthermore,

presence of pathological refixation saccades was evident in 12 (63.15%) affected ears and 7 (36.84%) unaffected ears.

Table 3.

Mean, standard deviation, median and range of VOR gain in both ears of individuals with posterior canal BPPV

Parameter	Mean	Standard deviation	Median	Range	
				Minimum	Maximum
VOR gain in affected ears	0.95	0.22	0.99	0.22	1.26
VOR gain in unaffected ears	0.98	0.24	1.01	0.26	1.31
Asymmetry ratio (in %)	8.39	5.54	6.00	2.00	20.00

Bithermal caloric test in comparison group (healthy individuals)

All 30 participants in the comparison group of the present study, in addition to vHIT, also underwent bithermal caloric test. Figure 5 shows the representative bithermal caloric responses from a participant in the comparison group.

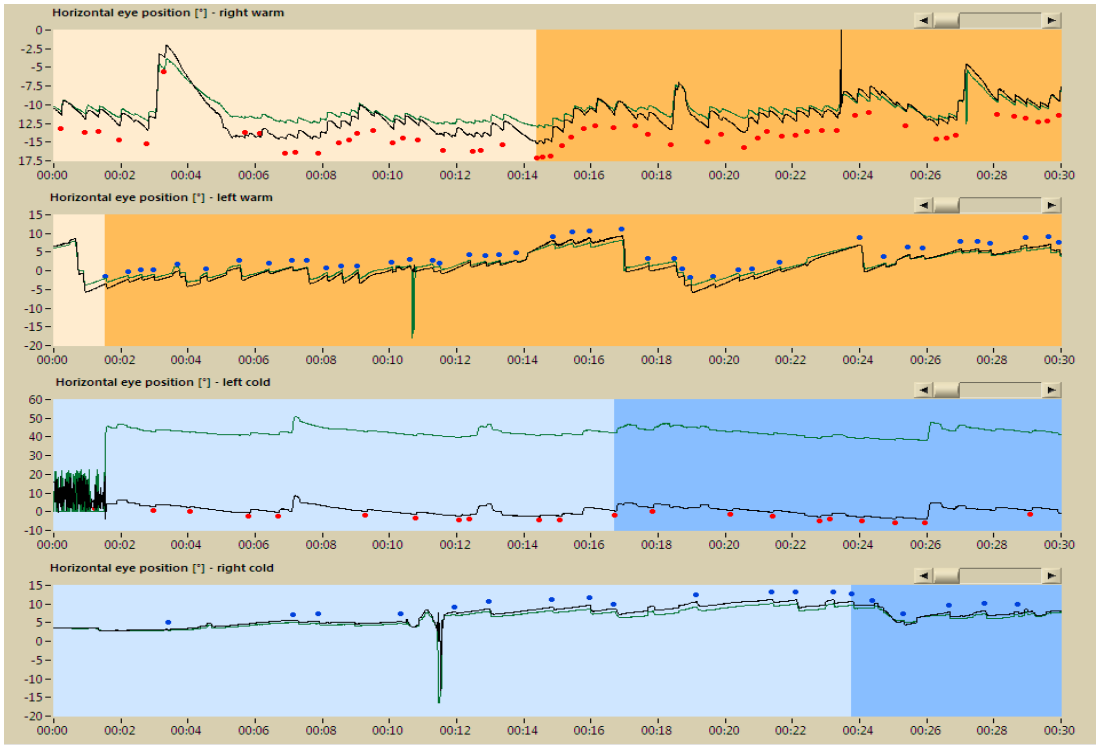


Figure 5: Representative traces of bithermal caloric test obtained from right and left ears for warm and cold temperatures from a participant in the comparison group.

Culmination frequency, which was defined as the number of nystagmus beats appearing in a 30 seconds window of most populated nystagmus activity, was obtained for each irrigation (2 warm & 2 cold; 1 from each ear). The obtained values were utilized to obtain unilateral weakness for each individual. Unilateral weakness was deemed abnormal if the value exceeded 20%. Out of 30 participants in this group, 3 (10%) had abnormal unilateral weakness.

Bithermal caloric test in pathological group

The clinical group included 50 participants diagnosed with vestibular pathologies. All the participants underwent caloric test. The outcomes of the bithermal caloric test in various pathologies are discussed separately below:

Bithermal caloric test in Meniere's disease.

The study had 17 individuals with unilateral and 7 individuals with bilateral Meniere's disease. Figure 6 shows the representative bithermal caloric recordings from an individual each with unilateral and bilateral Meniere's disease.

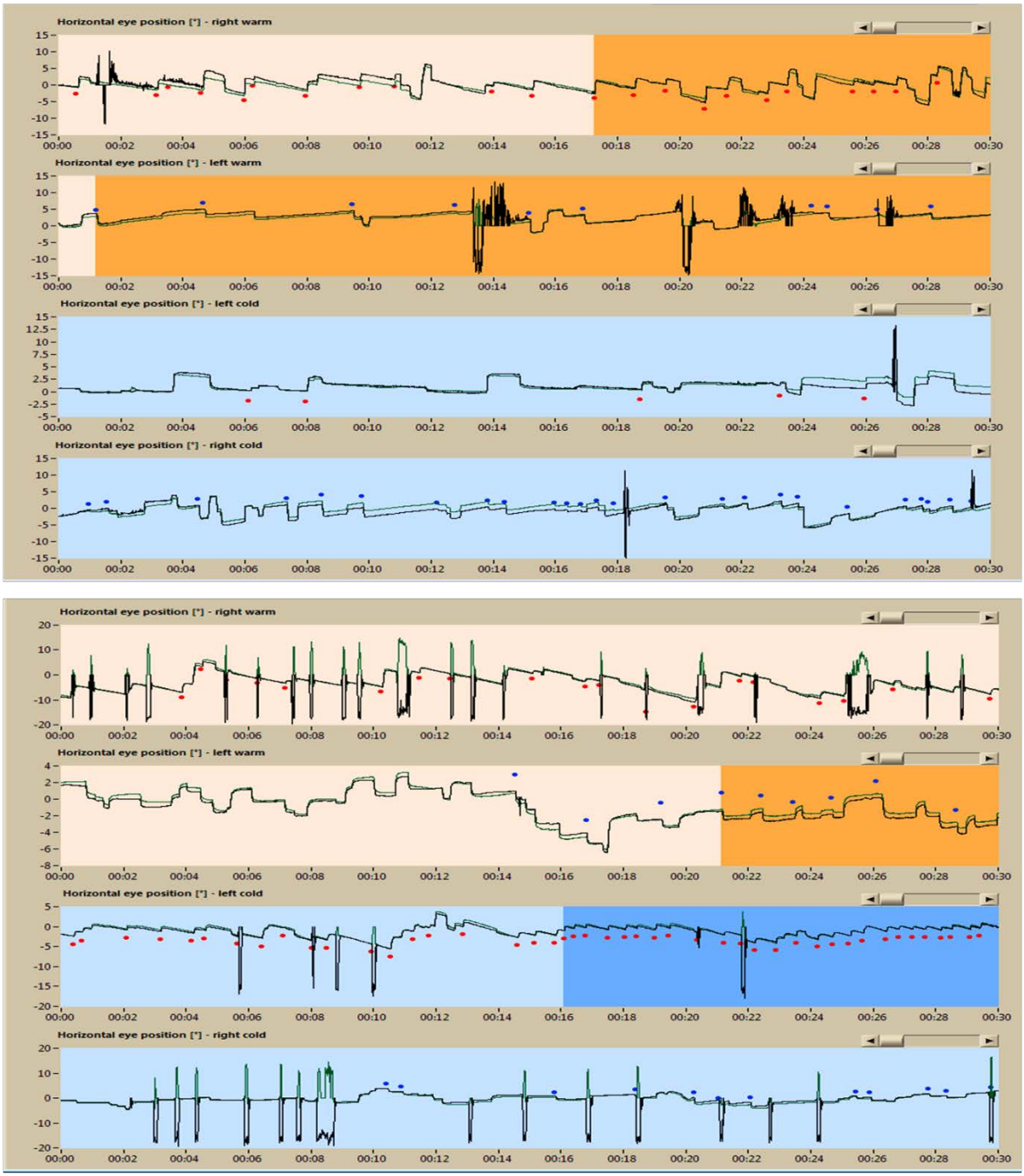


Figure 6: Representative bithermal caloric traces from both sides of an individual with unilateral Meniere's disease (top panel; left ear was pathological) and bilateral Meniere's disease (bottom panel).

Descriptive statistics were done on the obtained data of unilateral weakness from cases with unilateral and bilateral Meniere's disease. Table 4 shows mean, standard deviation, median and range of unilateral weakness on bithermal caloric test in participants with unilateral and bilateral Meniere's disease.

Table 4.

Mean, standard deviation, median and range of unilateral weakness (in %) in Meniere's disease, vestibular neuritis and BPPV

Group	Mean	Standard deviation	Median	Range	
				Minimum	Maximum
Unilateral Meniere's disease	21.00	15.78	18.38	0.00	58.9
Bilateral Meniere's disease	9.93	9.98	5.55	0.64	27.54
Vestibular neuritis	11.95	10.61	7.36	0.53	28.97
BPPV	16.41	13.46	15.66	0.00	47.37

In cases with unilateral Meniere's disease, significant unilateral weakness (>20%) was found in 8 (47.05%) participants. In bilateral Meniere's disease, significant unilateral weakness was evidenced in only 1 (14.28%) participant. However, 3 (42.85%) participants with bilateral Meniere's disease had reduced culmination frequency (< 23 nystagmus beats) on both sides, thereby showing reduced function bilaterally in these individuals.

Bithermal caloric test in vestibular neuritis.

In the present study, 7 participants had vestibular neuritis, all on left side. All of them underwent bithermal caloric test. Figure 7 shows representative bithermal caloric traces obtained from an individual with vestibular neuritis.

Figure 7: Representative bithermal caloric traces obtained from an individual with vestibular neuritis on left side.

Descriptive statistics were done on the obtained data of unilateral weakness. Table 4 shows mean, standard deviation, median and range of unilateral weakness in individuals with vestibular neuritis. Out of seven, 2 (28.57%) participants had significant unilateral weakness.

Bithermal caloric test in BPPV.

The present study included 19 participants diagnosed with posterior canal BPPV. Bithermal caloric test was administered on all of them. Figure 8 shows the representative bithermal caloric traces obtained from an individual with posterior canal BPPV.

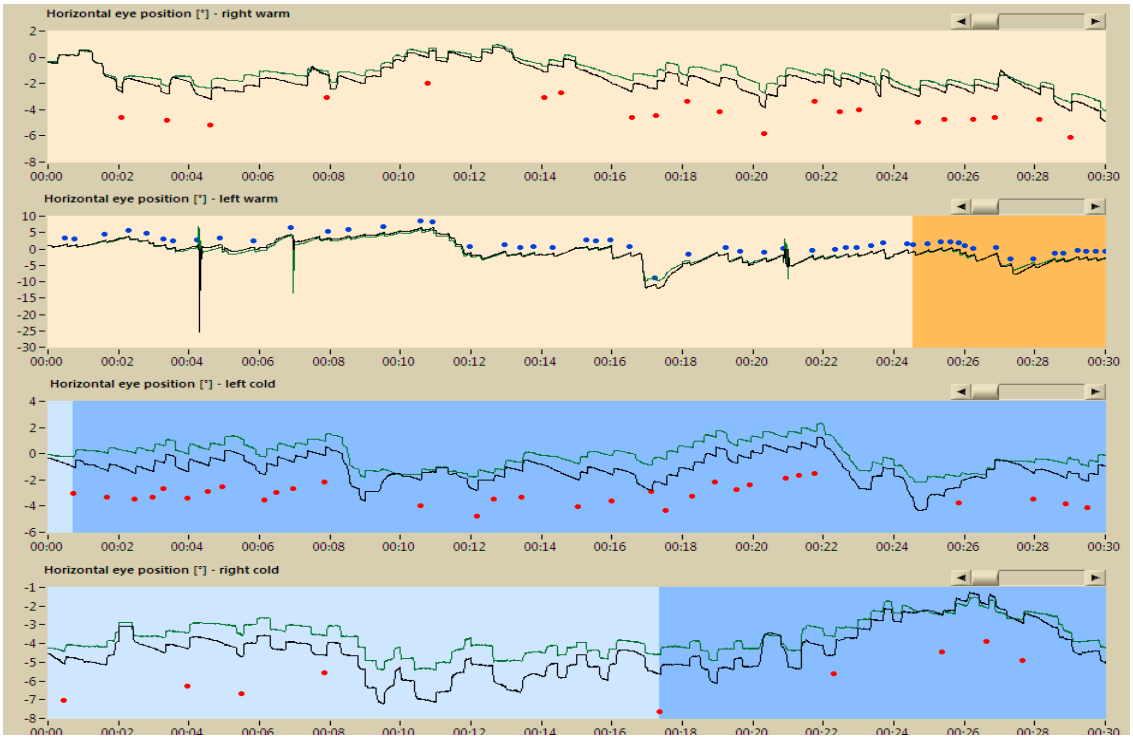


Figure 8: Representative bithermal caloric traces obtained from an individual with posterior canal BPPV on left side.

Descriptive statistics were done on the obtained data to find out mean, standard deviation, median and range of unilateral weakness in individuals with unilateral posterior canal BPPV. Table 4 shows the outcome of descriptive statistics for unilateral weakness observed on bithermal caloric test in individuals with unilateral posterior canal BPPV. Out of 19 participants with posterior canal BPPV, 8 (42.10%) had significantly high unilateral weakness on bithermal caloric test.

Correlation between vHIT and bithermal caloric test

The obtained data for asymmetry ratio on vHIT and unilateral weakness on bithermal caloric test were analyzed for normality of distribution using Shapiro-Wilk's test of normality and the results revealed non-normal distribution ($p < 0.05$). Therefore, correlation between asymmetry ratio and unilateral weakness was investigated using Spearman's rank correlation analysis. The results revealed no significant correlation between asymmetry ratio on vHIT

and unilateral weakness on bithermal caloric test in any of the groups and also overall. The outcomes of Spearman's rank correlation analyses are shown in Table 5.

Table 5.

The outcomes of Spearman's rank correlation analyses in clinical groups and comparison group

Group	*r*-value	*p*-value
Unilateral Meniere's disease	0.48	0.05
Bilateral Meniere's disease	0.41	0.35
Vestibular neuritis	0.27	0.55
BPPV	-0.32	0.18
Clinical group (all three together)	0.23	0.96
Comparison group	-0.10	0.96
Overall (clinical & comparison groups together)	0.15	0.16

Kappa coefficient analyses were done for investigating the statistical significance of agreement between vHIT and bithermal caloric test. In case of comparison group, there was a significant agreement between vHIT and caloric results ($p < 0.05$). In case of clinical group, there was no significant agreement between the two tests overall ($p > 0.05$). Further group-wise analyses for agreement between the two tests are elaborated below:

Agreement between vHIT and bithermal caloric test in Meniere's disease

Among individuals with Meniere's disease, 31 ears were affected including unilateral and bilateral). Of these, 17 (54.83%) ears had agreement between the tests (either both were showing normal results or both were affected) whereas 14 (45.16%) ears had disagreement (one of the two was normal). The BPPV group had 19 ears with pathology. Agreement between the tests was observed in 8 (42.10%) ears and disagreement in 11 (57.89%) ears in

this group. As far as vestibular neuritis is concerned, 4 (57.14%) out of 7 ears represented agreement as against disagreement in 3 (42.85%) ears. Overall, the study included 57 ears with vestibulopathy of which 29 (50.87%) ears demonstrated agreement between vHIT and bithermal caloric test whereas 28 (49.12%) ears showed disagreement between the two tests.

The parameters of vHIT and caloric were tested for agreement between them using Kappa coefficient analyses in unilateral Meniere's disease. There was no significant agreement between reduced VOR gain and abnormal unilateral weakness [K = 0.00, $p > 0.05$], presence of refixation saccades and abnormal unilateral weakness [K = 0.22, $p > 0.05$], abnormal vHIT (presence of refixation saccades or reduced VOR gain or both) and unilateral weakness [K = 0.22, $p > 0.05$] and also between abnormal vHIT and abnormal bithermal caloric test (presence of high unilateral weakness or reduced culmination frequency or both) [K = 0.16, $p > 0.05$]. Hence, the results of Kappa analyses indicate no significant agreement between the results obtained on vHIT and bithermal caloric test.

Kappa analyses in cases of bilateral Meniere's disease revealed no significant agreement between reduced VOR gain and abnormal unilateral weakness [K = 0.30, $p > 0.05$], presence of refixation saccades and abnormal unilateral weakness [K = -0.07, $p > 0.05$], abnormal vHIT and abnormal unilateral weakness [K = -0.07, $p > 0.05$] and also between abnormal vHIT and abnormal bithermal caloric test [K = -0.16, $p > 0.05$]. Hence, there was no significant agreement between vHIT and bithermal caloric test results in bilateral Meniere's disease.

Agreement between vHIT and bithermal caloric test in vestibular neuritis.

The Kappa coefficient analyses were performed to investigate the agreement between the results of vHIT and bithermal caloric test. The results revealed no significant agreement between reduced VOR gain and abnormal unilateral weakness [K = -0.23, $p > 0.05$], presence

of refixation saccades and abnormal unilateral weakness [K = -0.07, $p > 0.05$], abnormal vHIT and abnormal unilateral weakness [K = -0.07, $p > 0.05$] and also between abnormal vHIT and abnormal bithermal caloric test [K = -0.40, $p > 0.05$]. Therefore, like Meniere's disease, there was no significant agreement between the results of vHIT and bithermal caloric test in cases of vestibular neuritis.

Agreement between vHIT and bithermal caloric test in BPPV.

The agreement between vHIT and caloric test in participants with BPPV was evaluated using Kappa coefficient analyses. The results showed no significant agreement between reduced VOR gain and abnormal unilateral weakness [K = -0.10, $p > 0.05$], presence of refixation saccades and abnormal unilateral weakness [K = -0.21, $p > 0.05$], abnormal vHIT and abnormal unilateral weakness [K = -0.21, $p > 0.05$] and abnormal vHIT and abnormal bithermal caloric test [K = 0.01, $p > 0.05$]. Hence, the group of participants with BPPV also demonstrated no significant agreement between the outcomes of vHIT and bithermal caloric test.

Discussion

vHIT in comparison group (healthy individuals)

In the present study, mean asymmetry ratio of 6.23% was obtained in these individuals. These results are in congruence with the previous studies of vHIT in healthy individuals for asymmetry ratio (Murnane et al., 2014; Ulmer et al., 2011). The function of vestibulo ocular reflex is to maintain the image on the most sensitive portion of retina called fovea during rapid head movements. When head rotates with a certain speed and direction, the VOR ensures that eye rotates in the same speed but in opposite direction which helps the object to stay stable on the fovea. This is accomplished because of the activation and inhibition in the semicircular canals. Further, the movement in one direction excites one side

canal and inhibits the other side of the pair, and vice versa (Wuyts, 2008). Hence in healthy individual, an optimal VOR is generated to maintain the image stable in the visual field. This is almost symmetric between the sides, and therefore low asymmetry ratios are obtained (Murnane et al., 2014; Ulmer et al., 2011). The same mechanism is tested in vHIT and therefore the findings are in accordance.

Further, mean VOR gain was 0.93 and 0.98 in left and right ears respectively in healthy individuals (comparison group) and these results of VOR gain when using vHIT are also in agreement with those reported previously (Bansal & Sinha, 2016; Jimenez & Fernandez., 2016; Li et al., 2015; MacDougall et al., 2009; McGarvie et al., 2015; Mossman et al., 2015). Values close to 1 indicate a normal functioning VOR and its pathway (Murnane et al., 2014). This is because, in a healthy individual with nor vestibular or visual abnormality, eye movements are of similar velocities and accelerations as head movement. This is the basis behind vestibule-ocular reflex. Since VOR gain is calculated as the ratio of eye velocity to head velocity and the two of them are similar in a healthy individual, the resultant is close to 1, which was the case in comparison group in the present study.

vHIT in Meniere's disease

The findings in cases with Meniere's disease revealed that only about 13% affected ears had abnormality of VOR gain which represents a minority of ears that were affected with Meniere's disease. The literature of vHIT in cases of Meniere's disease is laced with findings of no abnormality of VOR gain (McCaslin et al., 2015; McGarvie et al., 2015) to abnormality of VOR gain in very few ears with Meniere's disease (Albernaz & Maia., 2014;Blodow et al., 2013, 2014). Further, only about 35% ears with Meniere's disease showed presence of pathological saccades which also similar to those reported previously (Albernaz & Maia., 2014;Blodow et al., 2013, 2014; McCaslin et al., 2015; McGarvie et al., 2015). Thus the

findings regarding VOR gain and presence of pathological refixation saccades in Meniere's disease in the present study are in consonance with those reported previously. The possible reason behind abnormal results on vHIT in only a small minority of ears affected with Meniere's disease could be the preferential damage of type II cells in Meniere's disease. vHIT is a high frequency response and type I cells are responsible for high frequency responses recorded during vHIT (Albernaz, Pedro, & Cusin, 2014; Goldberg, 2000; Park et al., 2005). Further, type I cells are intact in most of the cases of acute Meniere's disease which is why vHIT responses are often normal in these cases (Albernaz et al., 2014; Goldberg, 2000; Park et al., 2005). Another factor that might have contributed to such a finding in the present study could be the gap between the last attack and the vHIT testing. Mahringer and Rambold (2014) reported that the chance of obtaining an abnormal result on vHIT increases in case it is administered within 5 days of the attack of Meniere's disease and subsequently the chances of abnormal results on vHIT reduces with increasing duration since the last attack. All the participants were tested during the asymptomatic period of the disease, although the data of gap between vHIT administration and last attack of Meniere's disease is not available. This might be one of the contributing factors to the finding of normal results on VOR gain and refixation saccades on vHIT in individuals with Meniere's disease.

An intriguing finding in cases of unilateral Meniere's disease was presence of VOR gain abnormality and presence of refixation saccades when evaluating lateral semicircular canal's function on the unaffected side. Nearly 12% of unaffected ears had reduced VOR gain and about 29% had refixation saccades. Previous studies using oto-acoustic emissions (Magliulo et al., 2004), electrocohleography (Visu & Singh, 2012) and cVEMP (Fouly, Minawi, & Dessouki, 2012; Lin et al., 2006; Ribeiro, Almeida, Cavoilla, Gananca, 2005) have shown abnormal results in upto 40% of the asymptomatic ears in individuals with unilateral Meniere's disease. They attributed this kind of a finding to the presence of

'latent'/'occult' Meniere's disease. 'Occult' or 'latent' Meniere's disease refers to a future bilateral involvement possibility despite the asymptomatic nature in one of the ears in cases with unilateral Meniere's disease (Morita et al., 2009; Tsuji, Velazquez-Villasenor, Rauch, Glynn, Wall, & Merchant, 2000). The evidence for this has even been shown in post-mortem studies that demonstrated presence of hydrops in nearly 35-38% of the asymptomatic ears in individuals with unilateral Meniere's disease (Tsuji et al., 2000). Thus, the above mentioned studies regarding 'latent' / 'occult' Meniere's disease substantiates the findings of the present study.

vHIT in vestibular neuritis

The results of present study demonstrated positive findings (presence of refixation saccades / reduced VOR gain) in only 57% of vestibular neuritis ears. This is in dissonance with the findings of previous studies which reported 94.2% sensitivity of vHIT in detecting vestibular neuritis (Bartolomeo et al., 2014; Blodow et al., 2013; Walther et al., 2013). The difference could be attributed to two major factors. First, the studies reporting high sensitivity of vHIT for detecting the presence of pathology in cases of vestibular neuritis have used all the three modules, lateral, LARP (left anterior-right posterior) and RALP (right anterior-left posterior). This enabled them to find pathology in superior as well as inferior nerve ganglions as vestibular neuritis can affect the ganglion cells of superior or inferior vestibular nerve specifically while sparing the other (Moon et al., 2012). However in the present study, the assessment was done using only the lateral canal module which meant that the results would be affected only if vestibular neuritis affected the superior vestibular nerve. The second factor, a more minor one, could be the sample size. Small sample size of 7 in the present study could have drastically affected the percentage of correct identification. A larger sample size might have yielded a higher percentage of correct identification of pathology in ears with

vestibular neuritis, however any degree of certainty can only be applied to it only after doing it in a larger sample size.

vHIT in BPPV

In the present study, VOR gains were found to be essentially normal in majority of individuals with posterior canal BPPV. This is in accordance with the findings of previous studies in this regard (Albernaz & Maia, 2014; Nunez et al., 2014), who also found no abnormalities of VOR gain on vHIT in individuals with BPPV. This also explains the lack of significantly high asymmetry ratio between the ears, as VOR gains were normal on both sides.

Presence of refixation saccades was observed in 63% of the BPPV ears. There are no previous reports as both the above mentioned studies (Albernaz & Maia, 2014; Nunez et al., 2014) did not talk about the presence or absence of refixation saccades in individuals with BPPV. This is a surprising finding since vHIT in the present study was done using the lateral canal module which involved movements in the horizontal plane (along the yaw plane-rotation around the vertical axis) whereas pathology was in the posterior semicircular and not in the lateral canal (which was confirmed using the supine roll test). A possible explanation might arise from the symptomatology of these patients. Despite the presence of BPPV in only posterior canal, a number of these patients describe vertigo induced by head turn towards the affected ear. This might mean that yaw plane movements could be causing some movements of fluid even in the vertical canals, in this case the posterior canal. There is a case report which showed presence of tinnitus for head movements in yaw plane (along the horizontal canal) in a person who had superior semicircular canal dehiscence (Nam, Lewis, Nakajima, Merchant & Levine, 2010). This provides evidence of vertical canal stimulation in case of

horizontal plane head movements which might explain the finding of refixation saccades in posterior canal BPPV in the present study.

In the present study, some of the unaffected ears (36%) of individuals with BPPV also showed vHIT abnormality. In a previous study, Nunez et al (2014) observed presence of refixation saccades on both side impulses in some of the unilateral vestibular dysfunction cases. They observed that this occurrence was more often associated with individuals in whom the "vestibular deficiency was in the middle or normal range" and reported this because of ongoing vestibular compensation (MacDougall & Cuthoys, 2012). This might explain the findings of refixation saccades even in the other ear in some of the individuals with BPPV.

Bithermal caloric test in comparison group

The present study had 30 healthy individuals who underwent bithermal caloric test. Out of them, 27 of them had unilateral weakness <20% (within normal range). Henry (1999) reported that majority of the healthy individuals in their study had unilateral weakness ≤25% and hence there appears to be agreement between the findings of the present study and Henry (1999). The three participants with higher UW could possibly have been outliers.

Bithermal caloric test in Meniere's disease

In the present study, 8 individuals showed abnormally large unilateral weakness and 3 bilateral weakness which amounts to caloric abnormalities in 50% of the participants with Meniere's disease. This value appears deflated when compared to the results of Bergman and Stahle (1967) who observed caloric abnormalities, especially large unilateral weakness in 83% participants with Meniere's disease. Palomar et al (2006) also reported caloric abnormality in 73% participants with Meniere's disease. The differences might be attributed

the difference in the use of the attributes. While culmination frequency was used in the present study for calculating unilateral weakness, Bergman & Stahle (1967) and Palomar et al (2006) used slow phase velocity. When compared against a study using culmination frequency itself, the results were quite similar. Singh, Sinha and Govindaswamy (2012) reported caloric abnormality in nearly 60% participants with Meniere's disease when using culmination frequency as the parameter for calculating unilateral weakness. The reason behind abnormal results is well accepted to the hair-cell damage caused by excessive accumulation of endolymph in the labyrinth (Murofushi, Nakahara, Yoshimura, & Tsuda, 2011).

Bithermal caloric test in vestibular neuritis

Among the 7 particpants with vestibular neuritis, only 2 (29%) had significant unilateral weakness. In a recent study using bithermal caloric test in individuals with vestibular neuritis, Yoo et al (2016) observed abnormally high unilateral weakness in nearly 82% participants in the acute stage, which makes the findings of the present study in dissonance with their study. However, Kim et al (2016) reported recovery in several of the participants who had earlier shown high unilateral weakness and majority of them later showed normal results (<25% unilateral weakness) on caloric test after the initial acute attack. In the present study, none of the participants were evaluated during the acute phase which might explain the normal results in 5 out the 7 individuals with vestibular neuritis in the present study. Further, bithermal caloric test assesses only the nerve fibers arising from the lateral semicircular canal which is a part of the superior vestibular nerve (Mehra., 1964; MacClure., 1964). However, vestibular neuritis could also be confined to Scarpa's ganglion fibers contributing to the inferior vestibular nerve (Moon et al., 2012). It might be a possibility that in 5 participants with normal caloric responses, the inferior vestibular nerve was affected. This could have been confirmed by administering cervical vestibular evoked

myogenic potentials in these participants (cVEMP), however cVEMP was administered as it was not required to fulfil the objectives of the present study.

Bithermal caloric test in BPPV

In the present study, there was abnormal unilateral weakness in 8 of the 19 (42%) participants with BPPV. This value falls well within the range of abnormal unilateral weakness reported in the previously published studies which reported presence of unilateral weakness in 13-50% of individuals with BPPV (Blessing, Strutz, & Beck, 1986; Strupp et al., 1995; Hughes et al., 1997; Karlberg, Hall, Quickert, Hinson, & Halmagyi, 2000; Pollak, Davies, & Luxon, 2002; Molina et al., 2007). This broad range might be a reflection of the variability among individuals with BPPV or variability in the method of these studies.

Association between vHIT and bithermal caloric test in comparison group

There was a significant agreement between the results of vHIT and bithermal caloric test in healthy individuals. This might be primarily because of normal results on both these tests. None of the individuals in this group had vestibular abnormalities and it was confirmed through appropriate test battery. Since the system was normal, so were the results of both these tests. However, in terms of the correlation between asymmetry ratio of vHIT, which is a measure comparing the two ears, and unilateral weakness of bithermal caloric test, which is also a measure comparing the two ears, there was significant correlation. This indicates that possibly these two tests do not assess the same function of the lateral (horizontal) semicircular canal.

Association between vHIT and bithermal caloric test in Meniere's disease

The findings of the present study showed no significant correlation or association between the results of vHIT and bithermal caloric test in individuals with Meniere's disease.

Recently, similar results were reported in studies using vHIT and bithermal caloric test in Meniere's disease (Bell et al., 2015; McGarvie et al., 2015). This might be attributed to the discrepancy in frequency to which each of these two tests correspond. Bithermal caloric test is believed to assess in low frequencies whereas vHIT is reported to assess high frequencies (McCaslin et al., 2014). Some viewpoints believe that selective damage to only type II cells, cells responsible for low frequency responses, in case of Meniere's disease is the reason behind the finding of affected bithermal caloric responses even though vHIT remains intact (McCaslin et al., 2014; Tsuji et al., 2000). However, a more recent study found that the both type I and II cells are affected in cases with Meniere's disease (McCall et al., 2009) and therefore, selective damage to type II cells alone cannot explain the dissociation between vHIT and bithermal caloric test. Some researchers believe that hydropic expansion of the lateral membranous labyrinth can explain the dissociated responses between bithermal caloric test and vHIT in cases with Meniere's disease (McGarvie et al., 2015). According to this theory, endolymphatic hydrops would dissipate the hydrostatic force across the cupula by generating local convective flow and the responses to caloric stimulation would be diminished. However, because the radius of curvature of the entire canal would not increase, its dynamic responses during vHITs would be largely unaffected (McGarvie et al., 2015). Another factor that contribute to this dissociation is the stage of the disease. During the initial days of the disease stage, vHIT results are pathological only during the symptomatic phase (Lopez, Huarte & Fernandez, 2015). In fact, in a study assessing VOR gain, the authors reported reduced VOR gain in 63% of individuals in the acute stages (within 5 days) of the pathology (Mahringer & Rambold, 2014). During or soon after an attack of vertigo in cases with Meniere's disease, the value of canal paresis remains high whereas the VOR gain could be reduced, increased or remain normal (Lee et al., 2016). These variations in VOR gain, especially when there is no active attack, depend on the stage of Meniere's disease. In stages

1 and 2 of the disease, VOR gains are found to be normal or even increase occasionally due to active central compensation. However, stage 3 of the disease is almost always associated with reduced VOR gains when assessed using vHIT. Factors like the type of cell lost, duration and severity of the disease and the time of testing (during or in vicinity of attacks or in the asymptomatic period) all contribute to the variability of the VOR response which differ from individual to individual. Hence all of these reasons support the finding of dissociation in results between bithermal caloric test and vHIT in Meniere's disease in the present study.

Association between vHIT and bithermal caloric test in vestibular neuritis

The outcomes of present study revealed no significant correlation or agreement between the results of vHIT and bithermal caloric test in vestibular neuritis. These results are in dissonance with those reported previously in this regard (Espitia, Garcia, Martan & Plaza, 2014; Lundberg, 2014; McCaslin et al.2014). The major factor that might have contributed to this difference in findings between the present study and those reported previously could be the severity of vestibular neuritis. McCaslin et al (2014) reported high sensitivity and high specificity for vHIT when the caloric asymmetry was severe with values of canal paresis in the order of 39.50%. In the present study, the largest value of canal paresis was 28.97%. This represents lesser severity and therefore normal results on vHIT despite caloric abnormality. This is further supported by Mahringer et al (2014), who reported increase in association between vHIT and bithermal caloric test with increasing severity of the disease. It has also been reported that long duration since the onset of the disease aids central compensation which might affect the results of vHIT (normal results in larger proportion) (Zellhuber, Mahringer & Rambold., 2014) but not so much the results of bithermal caloric test (Zellhuber et al., 2014). This might also contribute to the finding of dissociation between the test results in the present study to some extent.

Association between vHIT and bithermal caloric test in BPPV

The results of correlation as well as agreement between bithermal caloric test and vHIT revealed no significant association between the two tests in individuals with posterior canal BPPV. There is no previous study in this regard. The reason behind dissociation could be the differences in the stimulation. Bithermal caloric test is known to assess lateral canal alone as the stimulus is thermal energy that has access to only this canal. However, in case of vHIT, the stimuli are head jerks delivered primarily in one plane, in this case the plane of the lateral semicircular canal. Although these movements cause excitation or inhibition in only lateral canal when vHIT is done using the 'Lateral' module, the fluids or otoconia particles in posterior canal might also move to some extent. This is supported by the symptomatology of these patients. Despite the presence of BPPV in only posterior canal, a number of these patients describe vertigo induced by head turn towards the affected ear. This might mean that yaw plane movements could be causing some movements of fluid even in the vertical canals, in this case the posterior canal. This assumption is supported by the findings of a recent case report in which presence of tinnitus for head movements in yaw plane (along the horizontal canal) was reported in a person who had superior semicircular canal dehiscence (Nam et al., 2010). This provides evidence of some vertical canal stimulation in case of horizontal plane head movements which might explain the finding of refixation saccades in posterior canal BPPV in the present study despite normal results on bithermal caloric test.

Conclusions

The present study aimed at investigating the association in results of vHIT and bithermal caloric test in healthy individuals and individuals with vestibular pathologies. The results revealed no significant association between the two tests in Meniere's disease, posterior canal BPPV and vestibular neuritis. Further, both of these tests assess the same

lateral canal but both give equally important information about the functioning of the canal in two different frequency ranges. This means that although bithermal caloric test uses a non physiological stimulus which is difficult to tolerate for some and leads to autonomic nervous system stimulation, vHIT cannot replace it in the diagnostic value. Therefore, vHIT and bithermal caloric test should both remain an integral part of the test battery to assess individuals with vestibulopathies, at least in cases with Meniere's disease, BPPV and vestibular neuritis/labyrinthitis. Furthermore, future studies in this area could find whether or not the dissociation between bithermal caloric test and vHIT be generalized to the central pathologies and other peripheral vestibular pathologies too.

Acknowledgements

The investigators would like to thank the Ministry of Health and Family Welfare, Government of India for funding this project. We would also like to thank the Director AIISH, and HODs of Dept. of Audiology and Dept. of ENT for permitting to carry out the project work. Lastly, but not the least, we thank all the participants for participating in the project.

References

Albernaz, P. L. M., & Cusin, F. S. (2016). The Video Head Impulse Test in a Case of Suspected Bilateral Loss of Vestibular Function. *International archives of otorhinolaryngology*, 20(01), 084-086.

American Academy of Otolaryngology-Head and Neck Surgery Committee on Hearing and Equilibrium. (1995). Committee on hearing and equilibrium guidelines for the diagnosis and evaluation of therapy in Meniere's disease. *Otolaryngology-Head and Neck Surgery*, 113, 181-185.

American National Standards Institute. (1991). *Maximum permissible ambient noise levels for audiometric test rooms.* ANSI S3.1. (1991). New York: American national Standards Institute.

Baloh, R. W. (2003). Vestibular neuritis. *New England Journal of Medicine, 348*(11), 1027-1032.

Bansal, S., & Sinha, S. K. (2016). Assessment of VOR gain function and its test–retest reliability in normal hearing individuals. *European Archives of Oto-Rhino-Laryngology*, 1-7.

Bartolomeo, M., Biboulet, R., Pierre, G., Mondain, M., Uziel, A., & Venail, F. (2014). Value of the video head impulse test in assessing vestibular deficits following vestibular neuritis. *European Archives of Oto-Rhino-Laryngology*,271(4), 681-688.

Bell, S. L., Barker, F., Heselton, H., MacKenzie, E., Dewhurst, D., & Sanderson, A. (2015). A study of the relationship between the video head impulse test and air calorics. *European Archives of Oto-Rhino-Laryngology*,272(5), 1287-1294.

Beynon, G. J., Jani, P., & Baguley, D. M. (1998). A clinical evaluation of head impulse testing. *Clinical Otolaryngology and Allied Sciences*, 23(2), 117-122.

Bhansali, S. A., & Honrubia, V. (1999). Current status of Electronystagmography testing. *Otolaryngology- Head and Neck Surgery*, 120(3), 419-426.

Bhattacharyya, N., Baugh, R. F., Orvidas, L., Barrs, D., Bronston, L. J., Cass, S., & Fuller, D. C. (2008). Clinical practice guideline: benign paroxysmal positional vertigo. *Otolaryngology-Head and Neck Surgery*, *139*(5), S47-S81.

Blessing, R., Strutz, J., & Beck, C. (1986). Epidemiology of benign paroxysmal positional vertigo. *Laryngologie, Rhinologie, Otologie*, *65*(8), 455-458.

Blodow, A., Heinze, M., Bloching, M. B., von Brevern, M., Radtke, A., & Lempert, T. (2014). Caloric stimulation and video-head impulse testing in Ménière's disease and vestibular migraine. *Acta oto-laryngologica*, 134(12), 1239-1244.

Blodow, A., Pannasch, S., & Walther, L. E. (2013). Detection of isolated covert saccades with the video head impulse test in peripheral vestibular disorders. *Auris Nasus Larynx*, 40(4), 348-351.

Brandt, T. (2003). Vertigo: its multisensory syndromes. 2 edn., London: Springer.

Curthoys, I. S. (2000). Vestibular compensation and substitution. *Current opinion in neurology*, *13*(1), 27-30.

Espitia, E. A., García, E. H., Parez-Martan, N., & Plaza, G. (2014). Caloric Test and Video-Head-Impulse (v-HIT): Usefulness as Screening Tool of Vestibular Pathology. *Otolaryngology--Head and Neck Surgery*, 151(1 suppl), P80-P80.

Eza-Nunez, P., Farinas-Alvarez, C., & Perez-Fernandez, N. (2014). The Caloric Test and the Video Head-Impulse Test in Patients with Vertigo. *Int Adv Otol*, 10(2), 144-9.

Fetter, M. (2000). Vestibular system disorders. *eLS*.

Fouly, H., Minawi, M. E., & Dessouki, T. E. (2012). Value of VEMP in Detecting Saccular Affection in the Asymptomatic Ear in the Patients with Meniere's disease. *Medical Journal of Cario University*, 80(1), 397-403.

Goldberg, J. M. (2000). Afferent diversity and the organization of central vestibular pathways. *Experimental Brain Research*, *130*(3), 277-297.

Harvey, S. A., Wood, D. J., & Feroah, T. R. (1997). Relationship of the head impulse test and head-shake nystagmus in reference to caloric testing. *American Journal of Otology*, 18(2), 207-213.

Henry, D.F. (1999). Test retest reliability of open loop bithermal caloric irrigation responses from healthy young adults. *The American Journal of Otology*, 20, 220-222.

Hughes, C. A., & Proctor, L. (1997). Benign paroxysmal positional vertigo. *The Laryngoscope*, 107(5), 607-613.

Ikeda, M., & Watanabe, I. (1997). Evaluation of hyperactive caloric responses in patients with inner ear diseases. *ORL Journal of Otorhinolaryngology and Related Specialities*, 59(6), 326-331.

Jimenez, G. G., & Fernandez, N. P. (2016). Reduction in posterior semicircular canal gain by age in video head impulse testing. Observational study. *Acta Otorrinolaringologica (English Edition)*, *67*(1), 15-22.

Karlberg, M., Hall, K., Quickert, N., Hinson, J., & Halmagyi, G. M. (2000). What inner ear diseases cause benign paroxysmal positional vertigo?. *Acta oto-laryngologica*, *120*(3), 380-385.

Kim, M., & Hong, K. M. (2016). Influence of Diazepam on Video Head Impulse Test in Patients with Acute Vestibular Neuritis: Preliminary Study. *Korean Journal of Otorhinolaryngology-Head and Neck Surgery*, 59(1), 15-18.

Kruschinski, C., & Hummers-Pradier, E. (2008, November). Diagnosing dizziness in the emergency and primary care settings. In *Mayo Clinic Proceedings* (Vol. 83, No. 11, pp. 1297-1298). Elsevier.

Lee, S. U., Kim, H. J., Koo, J. W., & Kim, J. S. (2016). Comparison of caloric and head-impulse tests during the attacks of Meniere's disease. *The Laryngoscope*.

Lehnen, N., Aw, S. T., Todd, M. J., & Halmagyi, G. M. (2004). Head impulse test reveals residual semicircular canal function after vestibular neurectomy. Neurology. 62(12), 2294 - 2296.

Li, C., Layman, A. J., Geary, R., Anson, E., Carey, J. P., Ferrucci, L., & Agrawal, Y. (2015). Epidemiology of vestibulo-ocular reflex function: data from the Baltimore longitudinal study of aging. *Otology & neurotology: official publication of the*

American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology, *36*(2), 267.

Lin, M. Y., Timmer, F. C., Oriel, B. S., Zhou, G., Guinan, J., Kujawa, S.G. et al. (2006). Vestibular evoked myogenic potentials (VEMP) can detect asymptomatic saccular hydrops. *The Laryngoscope*, 116(6), 987-992.

Lundberg, J. (2014). Assessment and Dynamics of Vestibular Testing in Vestibular Neuritis– a Retrospective study using Caloric Irrigation and Video Head Impulse Test.

MacDougall, H. G., & Curthoys, I. S. (2012). Plasticity during vestibular compensation: the role of saccades. *Frontiers in neurology*, *3*, 21.

MacDougall, H. G., Weber, K. P., McGarvie, L. A., Halmagyi, G. M., & Curthoys, I. S. (2009). The video head impulse test: diagnostic accuracy in peripheral vestibulopathy. *Neurology*, 73(14), 1134-1141.

MacDougall, H. G., Weber, K. P., McGarvie, L. A., Halmagyi, G. M., & Curthoys, I. S. (2009). The video head impulse test Diagnostic accuracy in peripheral vestibulopathy. *Neurology*, 73(14), 1134-1141.

Magliulo, G., Cianfrone, G., Cuiuli, G., Gagliardi, M., & D'amico, R. (2004). Vestibular evoked myogenic potentials and distortion-product otoacoustic emissions combined with glycerol testing in endolymphatic hydrops: their value in early diagnosis. *Annals of Otology, Rhinology & Laryngology*, *113*(12), 1000-1005.

Mahringer, A., & Rambold, H. A. (2014). Caloric test and video-head-impulse: a study of vertigo/dizziness patients in a community hospital.*European Archives of Oto-Rhino-Laryngology*, 271(3), 463-472.

Mangabeira Albernaz, P. L., & Zuma e Maia, F. C. (2014). The video head impulse test. *Acta oto-laryngologica*, 134(12), 1245-1250.

Martinez-Lopez, M., Manrique-Huarte, R., & Perez-Fernandez, N. (2015). A puzzle of vestibular physiology in a Meniere's disease acute attack. *Case reports in otolaryngology*.

McCall, A. A., Ishiyama, G. P., Lopez, I. A., Bhuta, S., Vetter, S., & Ishiyama, A. (2009). Histopathological and ultrastructural analysis of vestibular endorgans in Meniere's disease reveals basement membrane pathology. *BMC Ear, Nose and Throat Disorders*, *9*(1), 1.

McCaslin, D. L., Jacobson, G. P., Bennett, M. L., Gruenwald, J. M., & Green, A. P. (2014). Predictive properties of the video head impulse test: Measures of caloric symmetry and self-report dizziness handicap. *Ear and hearing*, 35(5), e185-e191.

McCaslin, D. L., Rivas, A., Jacobson, G. P., & Bennett, M. L. (2015). The dissociation of video head impulse test (vHIT) and bithermal caloric test results provide topological

localization of vestibular system impairment in patients with “Definite” Meniere's disease. *American Journal of Audiology*, 24, 1-10, doi:10.1044/2014_AJA-14-0040.

McGarvie, L. A., Curthoys, I. S., MacDougall, H. G., & Halmagyi, G. M. (2015). What does the dissociation between the results of video head impulse versus caloric testing reveal about the vestibular dysfunction in Ménière’s disease?. *Acta oto-laryngologica*, 135(9), 859-865.

McGarvie, L. A., Curthoys, I. S., MacDougall, H. G., & Halmagyi, G. M. (2015). What does the head impulse test versus caloric dissociation reveal about vestibular dysfunction in Ménière's disease?. *Annals of the New York Academy of Sciences*, *1343*(1), 58-62.

McGarvie, L. A., MacDougall, H. G., Halmagyi, G. M., Burgess, A. M., Weber, K. P., & Curthoys, I. S. (2015). The video head impulse test (vHIT) of semicircular canal function–age-dependent normative values of VOR gain in healthy subjects. *Frontiers in neurology*, *6*.

Mehra, Y. N. (1964). Electronystagmography: a study of caloric tests in normal subjects. *The Journal of Laryngology & Otology*, *78*(05), 520-529.

Minor, L. B. (1998). Physiological principles of vestibular function on earth and in space. *Otolaryngology- Head and Neck Surgery*, 118(3 Pt 2), S5–S15.

Molina, M. I., López-Escámez, J. A., Zapata, C., & Vergara, L. (2007). Monitoring of caloric response and outcome in patients with benign paroxysmal positional vertigo. *Otology & Neurotology*, *28*(6), 798-802.

Moon, I. H., Lee, C. G., Park, M. K., Lee, J. D. (2012a). Acute Viral Labyrinthitis. *Research in Vestibular Science, 11(3)*, 92-96.

Morita, N., Kariya, S., Deroee, A. F., Cureoglu, S., Nomiya, S., Nomiya, R. et al. (2009). Membranous labyrinth volumes in normal ears and Meniere’s disease: a three dimensional reconstruction study. *The Laryngoscope*, 119, 2216-2220.

Mossman, B., Mossman, S., Purdie, G., & Schneider, E. (2015). Age dependent normal horizontal VOR gain of head impulse test as measured with video-oculography. *Journal of Otolaryngology-Head & Neck Surgery*,44(1), 1.

Murnane, O., Mabrey, H., Pearson, A., Byrd, S., & Akin, F. (2014). Normative data and test-retest reliability of the SYNAPSYS video head impulse test. *Journal of the American Academy of Audiology*, 25(3), 244-252.

Murofushi, T., Nakahara, H., Yoshimura, E., & Tsuda, Y. (2011). Association of air-conducted sound oVEMP findings with cVEMP and caloric test findings in patients with unilateral peripheral vestibular disorders. *Acta oto-laryngologica*, *131*(9), 945-950.

Nam, E. C., Lewis, R., Nakajima, H. H., Merchant, S. N., & Levine, R. A. (2010). Head rotation evoked tinnitus due to superior semicircular canal dehiscence. *The Journal of Laryngology & Otology*, *124*(03), 333-335.

Palomar-Asenjo, V., Boleas-Aguirre, S., Sanchez-Ferrandiz, N., & Fernandez, N.P. (2006). Caloric and Rotatory Chair test results in patients with Meniere's disease. *Otology & Neurotology*, 27, 945-950.

Park, H. J., Migliaccio, A. A., Della Santina, C. C., Minor, L. B., & Carey, J. P. (2005). Search-coil head-thrust and caloric tests in Meniere's disease. *Acta oto-laryngologica*, *125*(8), 852-857.

Perez, N., & Rama-Lopez, J. (2003). Head-impulse and caloric tests in patients with dizziness. *Otology and Neurotology*, 24(6), 913-917.

Pollak, L., Davies, R. A., & Luxon, L. L. (2002). Effectiveness of the particle repositioning maneuver in benign paroxysmal positional vertigo with and without additional vestibular pathology. *Otology & neurotology*, *23*(1), 79-83.

Ribeiro, S., Almeida, R. D., Cavoilla, H., & Gananca, M. (2005). Vestibular evoked myogenic potentials in affected and asymptomatic ears in unilateral Meniere's disease. *Revista Brasileira de otorrinolaringologia*, 71(1), 60-66.

Riesco-Mac-Clure, J. S. (1964). LXIX Caloric Tests: Methods and Interpretation. *Annals of Otology, Rhinology & Laryngology*, *73*(3), 829-837.

Singh, N.K., Sinha, S.K., & Govindaswamy, R. (2011). Protocol for vestibular assessment and its efficacy in differential diagnosis of some balance disorders. (ARF-AIISH Research Fund) AIISH funded project done at AIISH.

Stahle, J., & Bergman, B. (1967). The caloric reaction in meniere's disease: An electronystagmographical study in 300 patients. *The Laryngoscope*, *77*(9), 1629-1643.

Strupp, M., Brandt, T., & Steddin, S. (1995). Horizontal canal benign paroxysmal positioning vertigo Reversible ipsilateral caloric hypoexcitability caused by canalolithiasis?. *Neurology*, *45*(11), 2072-2076.

Tsuji, K., Velazquez-Villasenor, L., Rauch, S. D., Glynn, R.J., Wall, C., & Merchant, S. N. (2000). Temporal bone studies of the human peripheral vestibular system. Meniere's disease. *Annals of Otology, Rhinology and Laryngology*, 181, 26-31.

Ulmer, E., Bernard-Demanze, L., & Lacour, M. (2011). Statistical study of normal canal deficit variation range. Measurement using the Head Impulse Test video system. *European annals of otorhinolaryngology, head and neck diseases*, 128(5), 278-282.

Visu, D., & Singh, N. K. (2012). Action potential latency in individuals with endolymphatic hydrops. *Student Research at A.I.I.S.H. Mysore (Articles Based on Dissertations Done at AIISH)*, 10, 89-99.

Walther, L. E., & Blodow, A. (2013). Ocular vestibular evoked myogenic potential to air conducted sound stimulation and video head impulse test in acute vestibular neuritis. *Otology & Neurotology*, 34(6), 1084-1089.

Weber, K. P., MacDougall, H. G., Halmagyi, G. M., & Curthoys, I. S. (2009). Impulsive testing of semicircular-canal function using videooculography. *Annals of New York Academy of Science*, 1164, 486-491.

Wuyts, F. (2008). Principle of the head impulse (thrust) test or Halmagyi head thrust test (HHTT). *B ENT*, 3, 23-26.

Yoo, M. H., Kim, S. H., Lee, J. Y., Yang, C. J., Lee, H. S., & Park, H. J. (2016). Results of video head impulse and caloric tests in 36 patients with vestibular migraine and 23 patients with vestibular neuritis: a preliminary report. *Clinical Otolaryngology*.

Zellhuber, S., Mahringer, A., & Rambold, H. A. (2014). Relation of video-head-impulse test and caloric irrigation: a study on the recovery in unilateral vestibular neuritis. *European Archives of Oto-Rhino-Laryngology*, *271*(9), 2375-2383.