

Higher Asymmetry Ratio and Refixation Saccades in Individuals with Motion Sickness

DOI: 10.3766/jaaa.16175

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Abstract

Background: Motion sickness is a complex autonomic phenomenon caused by the intersensory conflict among the balancing systems, resulting in a mismatch of signals between static physical conditions of the susceptible individual exposed to dynamic environment.

Purpose: The present study was done to assess the sacculocollic reflex pathway and six semicircular canals in individuals susceptible to motion sickness.

Research Design: Standard group comparison was used.

Study Sample: A total of 60 participants with an age range of 17–25 yr were included, where group I comprised 30 participants with motion sickness and group II comprised 30 participants without motion sickness. The Motion Sickness Susceptibility Questionnaire–Short was administered to classify the participants into groups with or without motion sickness.

Data Collection and Analysis: The cervical vestibular-evoked myogenic potential (cVEMP) test and video head impulse test (vHIT) were administered to all participants. The Shapiro–Wilk test revealed normal distribution of the data ($p > 0.05$). Hence a parametric independent sample *t* test was done to check significant difference in cVEMP and vHIT parameters between the two groups.

Results: The present study revealed no significant difference for cVEMP latencies and amplitude in individuals with motion sickness. However, significantly higher cVEMP asymmetry ratio was observed in individuals with motion sickness. Though the vestibulo-ocular reflex (VOR) gain values showed no significant difference between the two groups except for the right anterior left posterior plane, the asymmetry in VOR gain values revealed significant difference between the groups, suggesting asymmetry as a better parameter than absolute VOR gain values. Also, the presence of refixation saccades in 100% of the individuals with motion sickness accorded with various studies reported earlier with vestibular-related pathologies.

Conclusions: Presence of higher asymmetry ratio in cVEMP and vHIT test results plus refixation saccades to stabilize the gaze in vHIT can suggest some amount of vestibular anomalies in individuals with motion sickness.

Key Words: asymmetry, cVEMP, motion sickness, refixation saccades, VOR gains

Abbreviations: CNS = central nervous system; cVEMP = cervical vestibular-evoked myogenic potential; LA = left anterior; LARP = left anterior right posterior; LL = left lateral; LP = left posterior; RA = right anterior; RALP = right anterior left posterior; RL = right lateral; RP = right posterior; vHIT = video head impulse test; VOR = vestibulo-ocular reflex

INTRODUCTION

Motion sickness is an autonomic phenomenon resulting in discomforts due to the conflict among the balancing systems (vestibular, somatosensory, and visual systems) where there is a mis-

match signal between static physical conditions of the susceptible individual exposed to a dynamic environment (Reason, 1978; Owen et al, 1998; Yates and Miller, 1998; Tal et al, 2006). Different varieties of motion sickness may include traveling sickness (Turner and Griffin, 1999; Turner et al, 2000), space sickness (Bacal et al, 2003; Paule

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et al, 2004; Heer and Paloski, 2006), seasickness (Tal et al, 2007; Golding and Gresty, 2015), and sickness induced in tilting and nontilting trains (Bromberger, 1996; Persson, 2008), featuring nausea, emesis, vomiting, paleness, cold sweats, headache, drowsiness, malaise, poor forward visibility, distress, and affected psychomotor functioning. However, the strength of these symptoms may vary across individuals, depending on the exposure of type of stimuli, their intensity, and individualistic motion sickness susceptibility variance (Buyuklu et al, 2009).

Even though there are many published studies and theories on motion sickness, none have been able to describe the complete physiological basis of it. Most familiar of all, sensory rearrangement theory by Reason (1978) has tried describing the incongruity of sensory, somatosensory, and vestibular systems for maintaining balance, resulting in features such as vomiting and nausea, as the brain assumes the discordance created due to intoxication, resulting in vomiting to flush out the problem (Treisman, 1977). Similarly, the subjective vertical conflict theory (Bos and Bles, 1998) has attempted to explain motion sickness as the by-product of otolith asymmetry or canal-otolith conflict (Yates et al, 1998; Tal et al, 2006) due to the variation in otoconial masses across two labyrinths (Scherer et al, 2001; Helling et al, 2003). Likewise, the postulates by Guedry and Benson (1978) on intersensory conflict between vestibular and proprioceptive systems, visual and vestibular systems, or intrasensory conflict of functional otoliths and semicircular canals (Yates et al, 1998; Dai et al, 2007) do not explain motion sickness generated in some conditions, such as passive low-frequency vertical acceleration (Yates et al, 1998), which emphasizes the fact that there is presence of motion sickness even when visual and vestibular systems deliver the same information to the central nervous system (CNS).

All the mentioned studies are in agreement with the notion that there is an involvement of the vestibular system in individuals with motion sickness. Therefore, the conflicts among the motion-sensing peripheral vestibular structures of the inner ear are to be assessed well in understanding the phenomenon of motion sickness. Earlier studies were done to measure canals' functionality via electronystagmography in individuals with motion sickness where the incidence of faster slow-phase velocity has been suggestive of a hyperactive vestibular system (Lidvall, 1962), which is the converse of the study by Mallinson and Longridge (2002). Also the study by Buyuklu et al (2009) reported no significant difference for canal paresis between individuals with motion sickness and without motion sickness, concluding the caloric test to be an insensitive tool in detecting individuals with motion sickness. Also, cervical vestibular-evoked myogenic potentials (cVEMPs) have been reported with affected amplitude

and thresholds of cVEMP response in individuals with seasickness in comparison to normal individuals (Tal et al, 2006). However, other studies have come across with no significant statistical difference between the two groups (Tal et al, 2006; Buyuklu et al, 2009). Also the presence of a higher interaural asymmetry ratio in the motion-sickness population was reported in a few studies (Singh et al, 2014), but other studies assert the converse (Buyuklu et al, 2009; Fowler et al, 2014). Furthermore, a recent study on ocular VEMP revealed the presence of higher interaural asymmetry ratio and no difference across latency and amplitude in the motion-sickness population (Xie et al, 2012).

Even though these vestibular test batteries were performed previously on individuals with motion sickness, lacunae still persist. The well-known caloric test gives us an overview of vestibular functioning, but it lags with assessment of only two lateral semicircular canals in the frequency range of $\sim 0.002\text{--}0.004$ Hz, which is beyond the daily exposure (Perez and Rama-Lopez, 2003). Hence the other two planes of semicircular canals—that is, the right anterior left posterior (RALP) and left anterior right posterior (LARP)—still remain unexamined. This urgent requirement of the objective tests in examining dynamic functions of all six semicircular canals has been possible with the recent advancement of the noninvasive instrument known as the video head impulse test (vHIT) (Halmagyi and Curthoys, 1988), based on the principle of the head impulse test (Baloh et al, 1977; Böhmer et al, 1985).

The vHIT is a software-based test with lightweight goggles, consisting of a gyroscope to measure the refixation saccades and vestibulo-ocular reflex (VOR) gain function (MacDougall et al, 2009). Also it is found to have good sensitivity and specificity across both the healthy and the pathological vestibular population. The presence of refixation saccades as an indicator of compensatory mechanism was observed in individuals with vestibular migraine (McGarvie et al, 2015), benign paroxysmal positional vertigo (Blödow et al, 2014), vestibular neuritis (Bartolomeo et al, 2014), and also in the case of Ménière's disease (McCaslin et al, 2014).

There is a dearth of studies in the assessment of all six semicircular canals in individuals with motion sickness. Also no other reports are present in the literature regarding examination of all six semicircular canals and the sacculocollic reflex pathway in the same set of motion-sickness population. Therefore, there is a need to understand the functioning of these organs of the vestibular system in individuals with motion sickness. Hence, the aim of the present study is to evaluate the functioning of the sacculocollic reflex pathway and all six semicircular canals in individuals susceptible to motion sickness and compare with normal individuals, checking for any difference in vestibular functioning in the motion-sickness group.

METHOD

Participants

A total of 60 participants in the age range of 17–25 yr, with a mean age of 22 yr, were included in the study and divided into two groups. Group I had 30 participants with motion sickness, and group II consisted of 30 participants without motion sickness. The

Motion Sickness Susceptibility Questionnaire–Short form was administered to classify the participants into groups with or without motion sickness. The questionnaire is designed to find out susceptibility to motion sickness and the most effective motion (transport/swings/amusement rides) resulting in sickness. It has two parts: part A for any experience of motion sickness during childhood and part B for a period lasting >10 yr. It has a 4-point rating scale, ranging

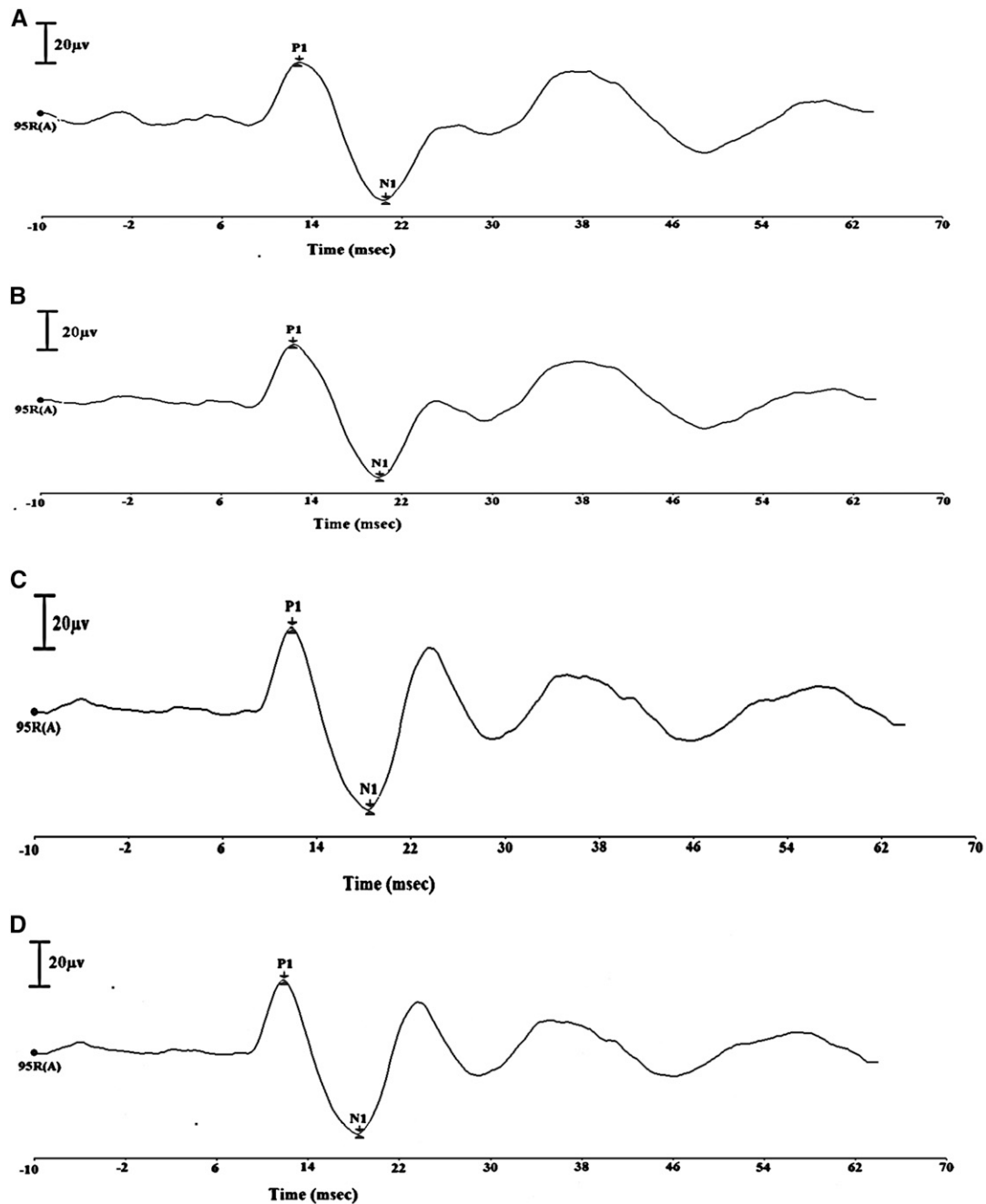


Figure 1. cVEMP grand average waveform of individuals respectively with and without motion sickness. (A) and (B) are the respective right and left ear cVEMP response of an individual with motion sickness. (C) and (D) are the respective right and left ear cVEMP response of an individual without motion sickness.

from 0 (never felt sick) to 3 (frequently felt sick). A cutoff score of 3.0 was used as the indication criterion for presence of motion sickness. Similar criteria have been adapted in other studies (Simmons et al, 2010; Singh et al, 2014). All the participants were informed initially about the study in detail, and a written consent form was obtained from all the participants.

Instrumentation

A calibrated GSI-61 audiometer (GSI VIASYS Healthcare, Madison, WI) with TDH-39 headphones (Telephonics, Farmingdale, NY) encased in an MX-41/AR supra-aural cushion was used for estimation of air-conduction pure-tone thresholds. Bone-conduction threshold was estimated using a RadioEar B-71 bone vibrator (Radioear, KIMMETRICS, Smithsburg, MD). Middle ear status was evaluated by using a calibrated Grason-Stadler Tympanometer middle ear analyzer. cVEMP was recorded using the intelligent hearing system version 4.3.02 (Intelligent Hearing System, Miami, FL) with ER-3A insert earphone (Etymotic Research, Inc., Elk Grove Village, IL). vHITs were carried out with prototype ICS Impulse video goggles (GN Otometrics, Taastrup, Denmark), with a camera speed of 250 frames/s, recording motion of the right eye. All the measurements were carried out in an acoustically treated double-room situation.

Procedure

Case history was initially taken from all the participants, and the Motion Sickness Susceptibility Questionnaire–Short was administered to place the participants into one of the two groups (either with motion sickness or without). Informed consent was taken from all the participants before the testing procedure. Pure-tone thresholds were obtained for all the participants using modified version of the Hughson and Westlake procedure (Carhart and Jerger, 1959) at octave frequencies between 250 and 8000 Hz for air conduction and between 250 and 4000 Hz for bone conduction. Immittance audiometry was carried out in both ears using a probe tone frequency of 226 Hz. Later ipsilateral and contralateral acoustic reflex threshold was measured for 500, 1000, 2000, and 4000 Hz stimuli.

Recording of cVEMP

The cVEMP was recorded for both groups of participants, who were seated in an upright position in a reclining chair. Surface electrodes were placed as follows: active electrode to the upper third of the ipsilateral sternocleidomastoid muscle, reference electrode to the ipsilateral sternoclavicular joint, and the ground electrode to the midline of the forehead after scrubbing the skin surface with an abrasive gel to obtain both absolute and interelectrode impedance of 5 and 2 kΩ, respectively. Electromyogenic potential was monitored through the electromyography monitoring device to ensure an equal amount of muscle contraction from all the participants. Intelligent hearing system electromyography monitoring device averaged the cVEMP response only when the sufficient amount of muscle contraction was achieved. The 500 Hz short-tone bursts with 2-0-2 cycle were used as stimulus. A total of 200 stimuli were presented at 95 dB nHL (equivalent to 125 dB SPL) at a repetition rate of 5.1 Hz. The responses were band-pass filtered between 30 and 1500 Hz. Analysis time was kept at 70 msec with a prestimulus baseline recording of 10 msec.

Video Head Impulse Test

Using the Otosuite vestibular software (GN Otometrics, Taastrup, Denmark), vHIT was administered in a well-lit room. A Frenzel glass with a clean attached face cushion was tightened appropriately to avoid slippage, such that the camera could track participants’ pupil movement. Calibration was performed by the participant, keeping his or her head still and viewing a laser light alternately on each side of a target placed 1 m ahead. This was followed by a simple slow head sinusoid with the participant watching the target, thereby allowing a calibration check by ensuring that head and eye velocities were overlaid. Once calibrated, participants were instructed to fix their gaze at a target point, which was kept according to the height of the participant, even when head thrust was given. The head thrust of 40 times was given by the examiner for each of the planes (pitch, roll, and yaw planes) at an angle of 10–20° in randomized order. For LARP and RALP positions, that is, during the vertical canal testing, the head was rotated 30° toward the right or

Table 1. Mean and SD of P1 and N1 Peak Latencies for Both Groups Bilaterally

Group	Right Ear				Left Ear			
	P1		N1		P1		N1	
	Mean (msec)	SD	Mean (msec)	SD	Mean (msec)	SD	Mean (msec)	SD
Individuals with motion sickness	13.59	1.22	20.55	1.79	13.78	1.32	20.97	1.53
Individuals without motion sickness	13.25	0.96	20.77	1.39	13.06	1.02	20.79	1.34

left, whereas gaze was directed and the head impulse was applied in the plane of canals. The VOR gain for all six semicircular canals was measured with the help of a high-speed digital infrared camera attached to the instrument.

Data Analysis

For cVEMP, the absolute latencies, peak to peak amplitude ratio, and asymmetry ratio were measured for both groups. Interaural asymmetry ratio was measured with the formula $-\{[(AI - AS)/(AI + AS)] \times 100\}$, where higher amplitude is AI and lower amplitude is AS between two ears of an individual (Li et al, 1999).

Furthermore, based on the Hex plot, the vHIT response was analyzed, where the VOR gain of all the six semicircular canals were calculated. The refixation saccades (if any) at the time of head thrust (i.e., covert saccade) and after the head thrust (i.e., overt saccade) were also measured. In the present study, we have measured VOR gain, VOR gain asymmetry value, and measurement of refixation saccades in individuals with and without motion sickness. To the best of our knowledge, this is the first study that has analyzed the VOR gain asymmetry values in vHIT.

RESULTS

The latency and amplitude of cVEMP and VOR gain, VOR gain asymmetry, and refixation saccades were calculated for all the participants in both groups.

Cervical Vestibular Myogenic Potentials

cVEMP responses were present for all the participants in both groups. The cVEMP grand averaged waveform of both groups is shown in Figure 1.

SPSS version 23 (IBM Corporation, New York, NY) was used to analyze the data. Descriptive statistics was done to calculate the mean and standard deviation (SD) for latency of P1 and N1 peak and amplitude of P1N1 complex for right and left ears separately in both groups. The mean and SDs for the latency, amplitude, and asymmetry ratio of cVEMP for both groups are given in Table 1, Table 2, and Table 3, respectively.

Table 2. Mean and SD of P1N1 Amplitude for Both Groups Bilaterally

Group	P1N1 Amplitude			
	Right Ear		Left Ear	
	Mean (μ V)	SD	Mean (μ V)	SD
Individuals with motion sickness	70.33	39.22	62.83	30.98
Individuals without motion sickness	80.17	27.88	76.95	29.42

Table 3. Mean and SD of Asymmetry Ratio for Both Groups

Group	Asymmetry Ratio	
	Mean	SD
Individuals with motion sickness	34.56	11.91
Individuals without motion sickness	17.60	13.21

From Table 1, it is evident that there is prolonged mean P1 and N1 latencies for both ears in individuals with motion sickness, except for N1 latency in right ear. The same can be seen in Figure 2.

It can be observed from Table 2 that the mean amplitude of P1N1 complex for both ears is higher in individuals without motion sickness than in the individuals with motion sickness. Similarly, in Figure 3, a bar graph shows the amplitude values of cVEMP for both groups.

It can be observed from Table 3 that the mean asymmetry ratio is higher in individuals with motion sickness than in individuals without motion sickness. The bar graph showing the amplitude asymmetry ratio values of cVEMP for both groups is shown in Figure 4.

The Shapiro–Wilk test was done to check the normality of the data, and it revealed a normal distribution of the data ($p > 0.05$), and hence a parametric independent samples t test was done to check the significant difference in mean latency, amplitude, and asymmetry ratio of cVEMP between the two groups. An independent sample t test between the two groups showed no significant difference for the P1 latency [$t_{(58)} = 1.21$, $p = 0.23$], N1 latency [$t_{(58)} = 0.54$, $p = 0.59$], and P1N1 amplitude complex [$t_{(58)} = 1.120$, $p = 0.27$] for the right ear. Also for the left ear, no significant difference for P1 latency [$t_{(58)} = 2.96$, $p = 0.22$], N1 latency [$t_{(58)} = 0.47$, $p = 0.64$], and P1N1 amplitude complex [$t_{(58)} = 1.81$, $p = 0.75$] was observed. However, the t test revealed significant higher asymmetry ratio in individuals with motion sickness as compared to individuals without motion sickness [$t_{(58)} = 5.22$, $p = 0.00$].

Analysis of VOR Gain Function

Descriptive statistics was used to calculate the mean and SD of VOR gain values, and asymmetry was calculated for all three planes of all six semicircular canals in both groups. The vHIT responses recorded from one of the participants from each group are given in Figures 5 and 6.

Mean and SDs of VOR gain in all three planes in both directions are given in Table 4 and Table 5, respectively. Likewise, the refixation saccades in individuals with motion sickness are represented in Table 6.

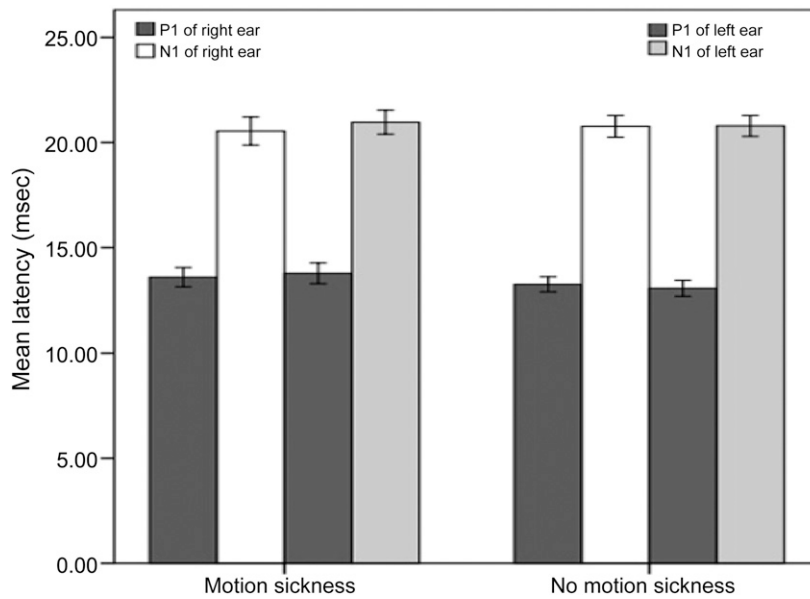


Figure 2. Bar graph represents mean and SD of latency of cVEMP for both groups.

From Table 4, it is evident that there is lower VOR gain in individuals with motion sickness in all six semicircular canals in comparison to normal individuals, except in the left lateral (LL). The mean and SDs of VOR gain values are also represented in Figure 7.

Table 5 reveals higher asymmetry value for all three planes of semicircular canals in individuals with motion sickness than in individuals without motion sickness. The bar graphs showing mean as well as SD for asymmetry of three planes of semicircular canals are given in Figure 8.

A Shapiro–Wilk test revealed normal distribution ($p > 0.05$) of the VOR gain data. Therefore, a parametric independent sample t test performed between two groups for both ears revealed no significant difference

in right lateral (RL) [$t_{(58)} = 2.38, p = 0.02$], LL [$t_{(58)} = 2.38, p = 0.02$], right posterior (RP) [$t_{(58)} = 2.38, p = 0.02$], and left anterior (LA) [$t_{(58)} = 2.38, p = 0.02$], except in the right anterior (RA) and left posterior (LP), with significant difference of [$t_{(58)} = 2.38, p = 0.02$] and [$t_{(58)} = 2.02, p = 0.05$], respectively. Also, the significant difference in asymmetry of lateral [$t_{(58)} = 2.01, p = 0.05$], LARP [$t_{(58)} = 3.77, p = 0.00$], and RALP [$t_{(58)} = 4.06, p = 0.00$] planes were observed, where there were significantly higher asymmetry values in

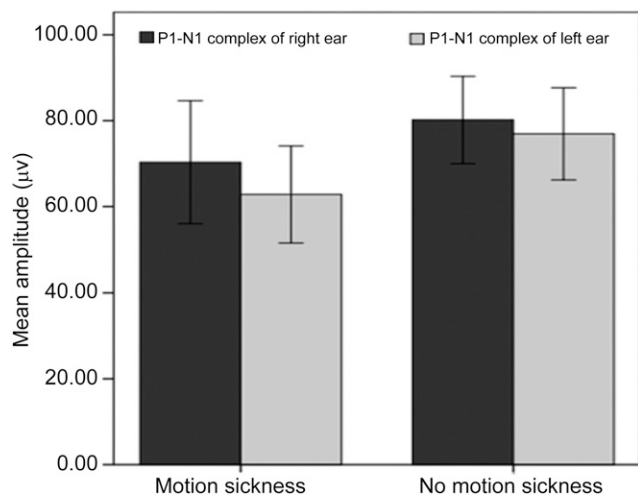


Figure 3. The graph represents mean and SD of amplitude of P1N1 complex of cVEMP for both groups.

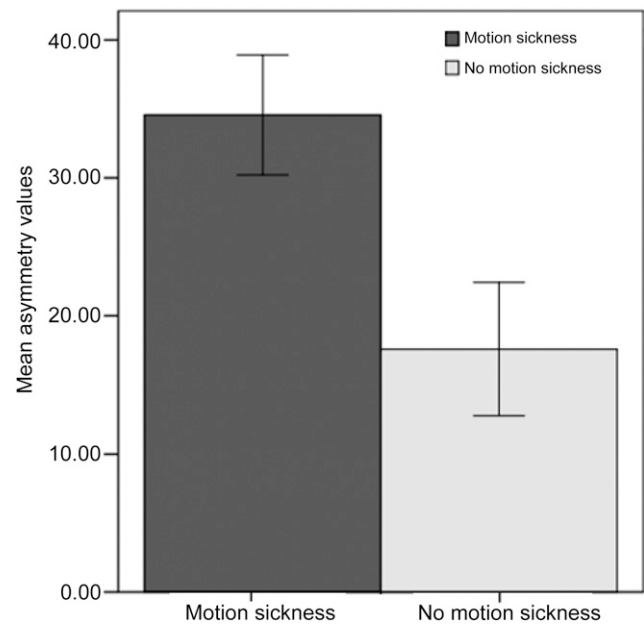


Figure 4. The graph represents mean and SD of asymmetry ratio of cVEMP for both groups.

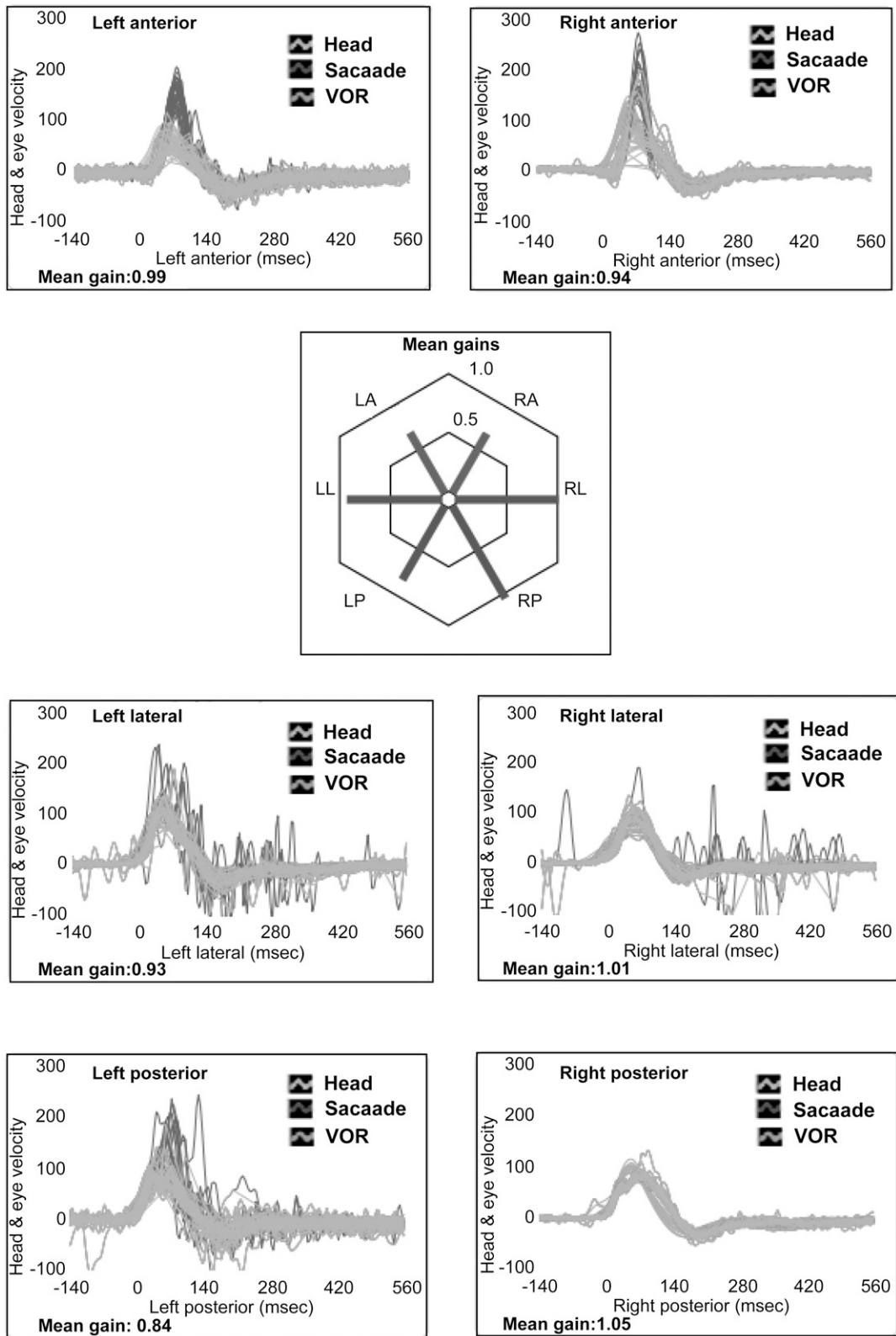


Figure 5. vHIT results in three different planes of an individual with motion sickness. The head and eye velocities throughout different head impulses to the right or left side are shown. The gain values and refixation saccades are also shown.

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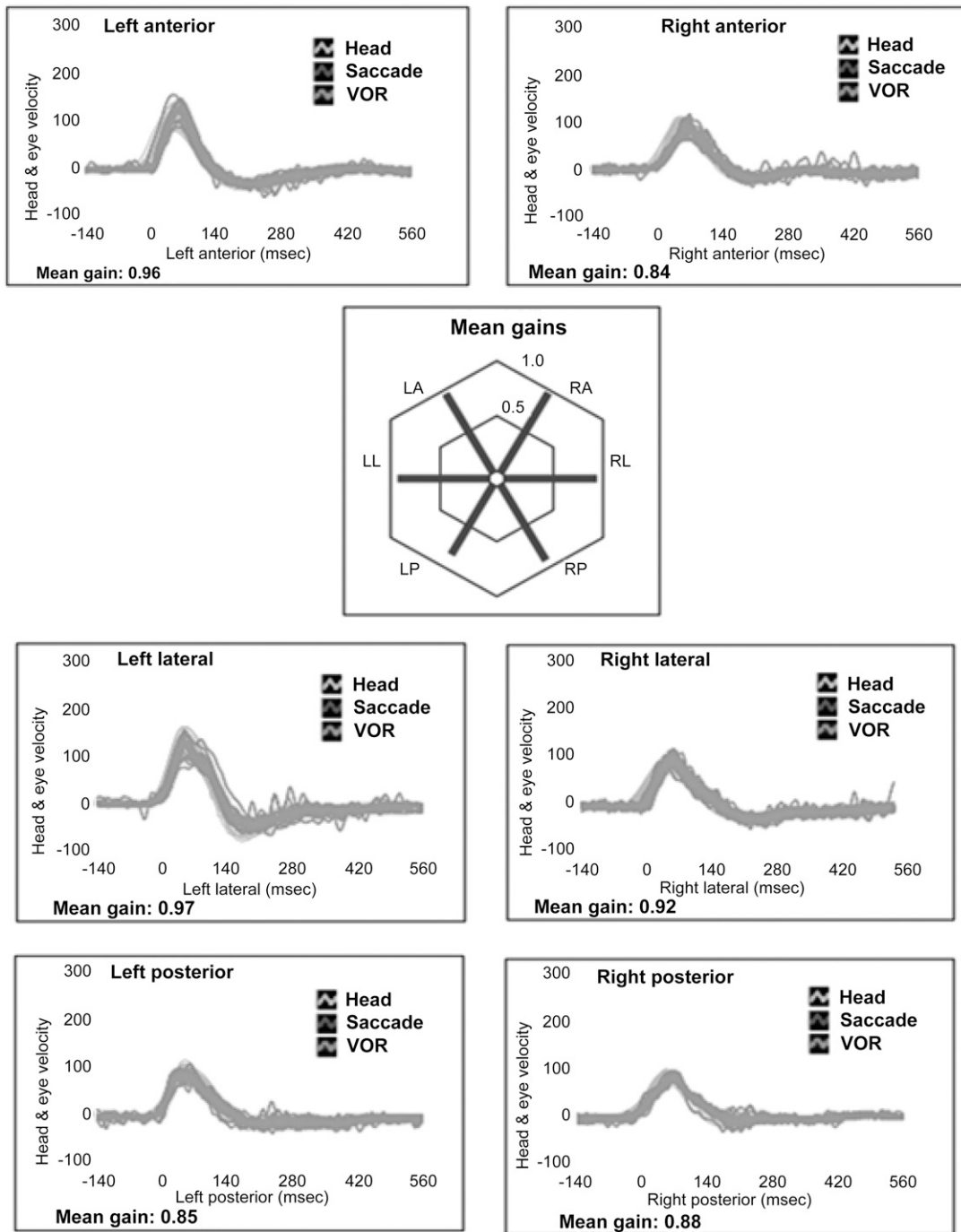


Figure 6. vHIT results in three different planes of an individual without motion sickness. The head and eye velocities throughout different head impulses to the right or left side are shown. Gain values are also shown.

individuals with motion sickness than in individuals without motion sickness.

Also, the refixation saccades were measured in both groups. Refixation saccades were present in individuals with motion sickness and were absent in individuals without motion sickness. Table 6 represents the presence of refixation saccades in different planes in individuals with motion sickness.

DISCUSSION

The present study revealed no significant difference for cVEMP latencies (P1 and N1) in individuals with motion sickness from that of individuals without motion sickness. The results of the present study are in coherence with earlier studies (Tal et al, 2006; Fowler et al, 2014; Singh et al, 2014). The results suggest that

Table 4. Mean and SD of VOR Gain Values for Both Groups

Planes	Individuals with Motion Sickness		Individuals without Motion Sickness	
	Mean	SD	Mean	SD
LL	0.98	0.15	0.97	0.11
RL	1.02	0.17	1.02	0.12
LA	0.84	0.29	0.91	0.17
RP	0.84	0.29	0.91	0.14
LP	0.79	0.19	0.87	0.10
RA	0.83	0.22	0.96	0.17

the neural portion of the sacculocollic pathway is not affected in individuals with motion sickness. It has been reported that affected latencies of cVEMP peaks are the key signs of neural pathologies rather than the labyrinthine pathology (Ochi and Ohashi, 2003; Lee et al, 2008). Therefore, the latency parameter is not a sensitive tool in detecting sacculocollic pathway pathology in individuals with motion sickness.

Similarly, the present study also revealed no significant difference in P1N1 complex amplitudes between the two groups. These findings are consistent with earlier studies (Tal et al, 2007; Buyuklu et al, 2009; Singh et al, 2014). However, a few of the earlier studies (Tal et al, 2006; Fowler et al, 2014) are in incongruity with these findings, where it was reported to have affected amplitude in individuals with motion sickness more than that of individuals without motion sickness. This could be due to the smaller sample size taken in the previous studies. However, the present study includes a comparatively larger sample ($N = 30$). Although the mean amplitude value was smaller in individuals with motion sickness in the present study, a significant difference was not observed between the two groups. This could be because of a larger SD obtained for the amplitude parameters.

However, significantly higher cVEMP asymmetry ratio was observed in individuals with motion sickness than in those without motion sickness. Higher asymmetry ratio of cVEMP amplitude is an indication of pathology in sacculocollic pathway in various vestibular pathologies (Baier et al, 2009; Taylor et al, 2011; Taylor et al, 2012). Thus, it can be interpreted that individuals

Table 5. Mean and SD of Asymmetry of Three Planes of VOR for Both Groups

Planes	Individuals with Motion Sickness		Individuals without Motion Sickness	
	Mean	SD	Mean	SD
Lateral	10.73	8.75	7.00	5.15
LARP	15.30	9.31	7.80	5.68
RALP	21.20	13.36	10.73	4.52

with motion sickness may have pathology of the sacculocollic pathway. This finding is in coherence with the studies reported previously (Helling et al, 2003; Singh et al, 2014). However, a few studies (Tal et al, 2007; Buyuklu et al, 2009; Fowler et al, 2014) show inconsistency with it.

According to Bles (1998), the condition of motion sickness occurred due to the vertical acceleration information achieved, which is in variance with the previous subjective experience of vertical orientation. This incongruence in postural vertical orientation could be due to the difference in otoconial masses of two saccules, thus giving rise to asymmetry. Dysrhythmic discharge due to asymmetry would be balanced and normalized by central compensatory mechanism under normal terrestrial situation in almost all individuals, as it's not large enough to generate an incongruent signal to the cortical areas. However, under the influence of unusual motion patterns, it generates larger asymmetric differences between the otoliths with rarer central compensatory mechanism in individuals with motion sickness. This leads two otoliths to supply an unequal amount of neural impulses to cortical balance areas, therefore generating confusion even when whole body is undergoing the same acceleration (von Baumgarten et al, 1977).

Hence, this phenomenon may end up with symptoms such as dizziness, headache, cold sweats, nausea, and ultimately vomiting as the CNS assumes the occurrence of discordance due to intoxication (Treisman, 1977). A similar result was observed in an animal study where fish with difference in otoconial mass between two labyrinths showed uncoordinated swimming behavior compared to fish with active compensatory mechanism under the Coriolis force environment (Helling et al, 2003). Hence the asymmetry ratio can be taken as one of the parameters of cVEMP in detecting the motion-sickness population in the vestibular test battery.

In the present study, the recent advanced noninvasive instrument, vHIT, was used for the first time in analyzing the functioning of semicircular canals of the individuals with motion sickness. VOR gain analysis of three planes of semicircular canals revealed significant difference, with lower VOR values in RA and LP semicircular canals. Similar results of reduced VOR gain were explained earlier in various peripheral vestibular disorders (Weber et al, 2008; Macdougall et al, 2013; MacDougall et al, 2016). Most of these studies that have reported reduced gain in vestibular pathologies have explained the VOR gain values only in the lateral planes and not in the RALP and LARP planes. In the present study, the significant difference in VOR gain values could be observed only in the RALP plane between the two groups. The VOR gain values have been reported to be less reliable compared to the presence of saccades (Korsager et al, 2016). Thus, Korsager et al (2016) have reported that for diagnosis

Table 6. Refixation Saccades at All Six Semicircular Canals Present in Individuals with Motion Sickness

Semicircular Canals	Covert Saccade	Overt Saccade	Covert + Overt	None
LL	8	4	10	7
RL	4	5	16	3
LA	11	1	8	9
RA	12	1	5	11
LP	6	2	8	12
RP	4	4	8	15

of vestibular pathologies, clinicians shall depend on the presence of saccades followed by the VOR gain values in vHIT recording.

The study revealed significantly higher asymmetry of VOR gain values in three orthogonal planes, that is, RALP, LARLP, and lateral, for individuals with motion sickness than for those without. This explains the intrasensory conflict of semicircular canals (Yates and Miller, 1998; Dai et al, 2007) in individuals with motion sickness. This conflict gives rise to the variance in neural input from different planes to the cortical balance areas, where a dilemmatic situation is generated in understanding the precise postural orientation of the body even when whole body is getting the same acceleration (von Baumgarten et al, 1977). Hence, the CNS intake this discordance as intoxication, resulting in vomiting to flush out the toxins (Treisman, 1977). Although the VOR gain values did not show any significant difference between two groups except for the RALP plane, the asymmetry in VOR gain values did show significant difference between the two groups, suggesting asymmetry values could be a better parameter than the absolute VOR gain values. None of the published studies have reported the asymmetry ratio of VOR gain values in any of the vestibular pathologies.

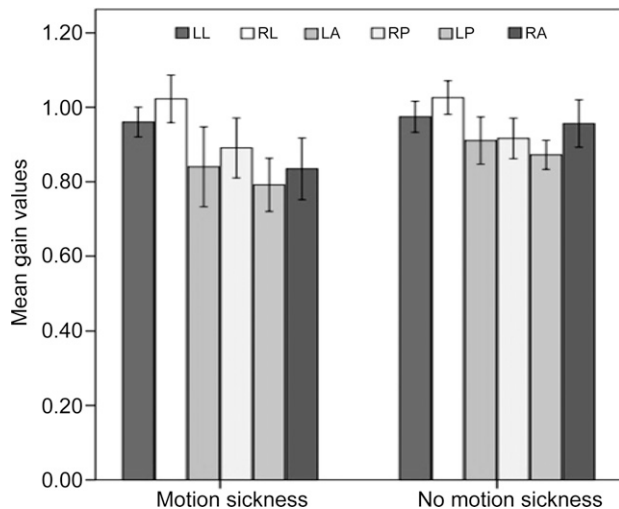


Figure 7. The graph represents mean and SD of VOR gain values for all six semicircular canals in both groups.

This is the first study in which the significant difference in VOR gain values of vHIT in individuals with motion sickness has been reported. However, before VOR gain asymmetry values could be taken as important parameters to detect the semicircular canal pathology, the sensitivity of VOR gain asymmetry values needed to be verified with various other vestibular disorders.

The present study also explains the existence of refixation saccades in 100% of the individuals with motion sickness compared to that of their counterparts. The presence of refixation saccades is in agreement with various studies reported earlier with vestibular-related pathologies (MacDougall et al, 2009; Macdougall et al, 2013; Jiménez and Fernández, 2016; Redondo-Martínez et al, 2016). Refixation saccades occur when the variation is present between the stimulated sides of the coplanar canals and that of the nonstimulated side, therefore making the VOR generate compensatory eye movement to maintain gaze stability even during head rotation (Bronstein and Gresty, 1991). These corrective saccades are suggestive of impaired semicircular canals, such that the gaze stability with movement of the eye in equal velocity and opposite direction to that of the head rotation is unable to be retained (Weber et al, 2008). Therefore, the presence of refixation saccade can be a good indicator in assessing individuals with motion sickness.

CONCLUSIONS

The present study focused on understanding the physiology of saccule and semicircular canals via cVEMP and vHIT, respectively, in a group of individuals with motion sickness. Among the several parameters of cVEMP evaluated, only asymmetry ratio could distinguish the individuals with motion sickness from

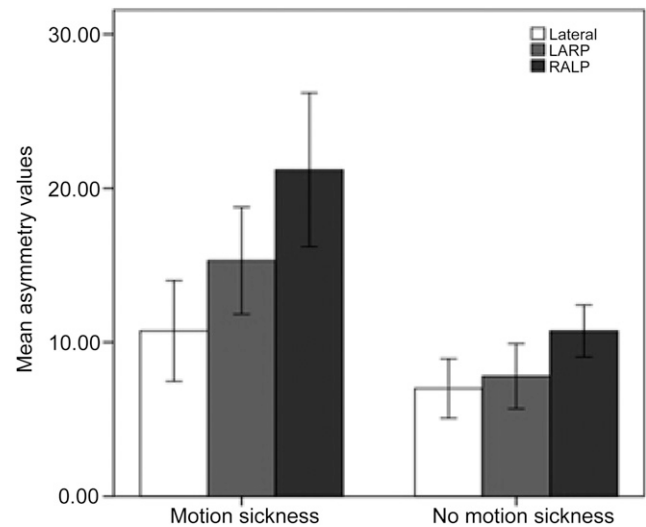


Figure 8. The graph represents mean and SD of asymmetry for all three planes of semicircular canals for both groups.

those without motion sickness. The individuals with motion sickness had higher asymmetry ratio than those without motion sickness; however, no variations were present in latency and peak-to-peak amplitude of cVEMP in between the groups. Also the VOR gain measured in all six semicircular canals revealed the presence of significantly lower gain values in RA and LP semicircular canals in individuals with motion sickness. Furthermore, the present study revealed significantly higher asymmetry differences in three orthogonal planes of semicircular canals across the two groups. Thus, higher asymmetry ratio in cVEMP and vHIT and also refixation saccades can suggest some degree of vestibular anomalies in individuals with motion sickness.

REFERENCES

- Bacal K, Billica R, Bishop S. (2003) Neurovestibular symptoms following space flight. *J Ves Res* 13(2,3):93–102.
- Baier B, Stieber N, Dieterich M. (2009) Vestibular-evoked myogenic potentials in vestibular migraine. *J Neurol* 256(9):1447–1454.
- Baloh RW, Honrubia V, Sills A. (1977) Eye-tracking and optokinetic nystagmus. Results of quantitative testing in patients with well-defined nervous system lesions. *Ann Otol Rhinol Laryngol* 86(1 Pt 1):108–114.
- 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. *Eur Arch Otorhinolaryngol* 271(4):681–688.
- Bles W. (1998) Coriolis effects and motion sickness modelling. *Brain Res Bull* 47(5):543–549.
- Blödow A, Heinze M, Bloching MB, von Brevern M, Radtke A, Lempert T. (2014) Caloric stimulation and video-head impulse testing in Ménière's disease and vestibular migraine. *Acta Otolaryngol* 134(12):1239–1244.
- Böhmer A, Henn V, Suzuki J. (1985) Vestibulo-ocular reflexes after selective plugging of the semicircular canals in the monkey: response plane determinations. *Brain Res* 326(2):291–298.
- Bos JE, Bles W. (1998) Modelling motion sickness and subjective vertical mismatch detailed for vertical motions. *Brain Res Bull* 47(5):537–542.
- Bromberger L. (1996) Pourquoi vous avez mal au coeur. *La Vie du Rail* 2556.
- Bronstein AM, Gresty MA. (1991) Compensatory eye movements in the presence of conflicting canal and otolith signals. *Exp Brain Res* 85(3):697–700.
- Buyuklu F, Tarhan E, Ozluoglu L. (2009) Vestibular functions in motion sickness susceptible individuals. *Eur Arch Otorhinolaryngol* 266(9):1365–1371.
- Carhart R, Jerger J. (1959) Preferred method for clinical determination of pure-tone thresholds. *J Sp Hear Dis* 24:333–345.
- Dai M, Raphan T, Cohen B. (2007) Labyrinthine lesions and motion sickness susceptibility. *Exp Brain Res* 178(4):477–487.
- Fowler CG, Sweet A, Steffel E. (2014) Effects of motion sickness severity on the vestibular-evoked myogenic potentials. *J Am Acad Audiol* 25(9):814–822.
- Golding JF, Gresty MA. (2015) Pathophysiology and treatment of motion sickness. *Curr Opin Neurol* 28(1):83–88.
- Guedry FE Jr, Benson AJ. (1978) Coriolis cross-coupling effects: disorienting and nauseogenic or not? *Aviat Space Environ Med* 49(1 Pt 1):29–35.
- Guerra Jiménez G, Pérez Fernández N. (2016) Reduction in posterior semicircular canal gain by age in video head impulse testing. Observational study. *Acta Otorrinolaringol Esp* 67(1):15–22.
- Halmagyi GM, Curthoys IS. (1988) A clinical sign of canal paresis. *Arch Neurol* 45(7):737–739.
- Heer M, Paloski WH. (2006) Space motion sickness: incidence, etiology, and countermeasures. *Auton Neurosci* 129(1–2):77–79.
- Helling K, Hausmann S, Clarke A, Scherer H. (2003) Experimentally induced motion sickness in fish: possible role of the otolith organs. *Acta Otolaryngol* 123(4):488–492.
- Korsager LH, Wanscher JH, Schmidt JH, Faber C. (2016) Reliability and comparison of gain values with occurrence of saccades in the video head impulse test (vHIT). *Eur Arch Otorhinolaryngol* 273(12):4273–4279.
- Lee SK, Cha CI, Jung TS, Park DC, Yeo SG. (2008) Age-related differences in parameters of vestibular evoked myogenic potentials. *Acta Otolaryngol* 128(1):66–72.
- Li MW, Houlden D, Tomlinson RD. (1999) Click evoked EMG responses in sternocleidomastoid muscles: characteristics in normal subjects. *J Vestib Res* 9(5):327–334.
- Lidvall HF. (1962) Mechanisms of motion sickness as reflected in the vertigo and nystagmus responses to repeated caloric stimuli. *Acta Otolaryngol* 55:527–536.
- MacDougall HG, McGarvie LA, Halmagyi GM, Curthoys IS, Weber KP. (2013) The video head impulse test (vHIT) detects vertical semicircular canal dysfunction. *PLoS One* 8(4):e61488.
- MacDougall HG, McGarvie LA, Halmagyi GM, Rogers SJ, Manzari L, Burgess AM, Weber KP. (2016) A new saccadic indicator of peripheral vestibular function based on the video head impulse test. *Neurology* 26:87(4):410–418.
- MacDougall HG, Weber KP, McGarvie LA, Halmagyi GM, Curthoys IS. (2009) The video head impulse test: diagnostic accuracy in peripheral vestibulopathy. *Neurology* 73(14):1134–1141.
- Mallinson AI, Longridge NS. (2002) Motion sickness and vestibular hypersensitivity. *J Otolaryngol* 31(6):381–385.
- McCaslin DL, Jacobson GP, Bennett ML, Gruenwald JM, Green AP. (2014) Predictive properties of the video head impulse test: measures of caloric symmetry and self-report dizziness handicap. *Ear Hear* 35(5):e185–e191.
- McGarvie LA, MacDougall HG, Halmagyi GM, Burgess AM, Weber KP, Curthoys IS. (2015) The video head impulse test (vHIT) of semicircular canal function: age-dependent normative values of VOR gain in healthy subjects. *Front Neurol* 6:154.
- Ochi K, Ohashi T. (2003) Age-related changes in the vestibular-evoked myogenic potentials. *Otolaryngol Head Neck Surg* 129(6):655–659.

- Owen N, Leadbetter AG, Yardley L. (1998) Relationship between postural control and motion sickness in healthy subjects. *Brain Res Bull* 47(5):471–474.
- Paule MG, Chelonis JJ, Blake DJ, Dornhoffer JL. (2004) Effects of drug countermeasures for space motion sickness on working memory in humans. *Neurotoxicol Teratol* 26(6): 825–837.
- Perez N, Rama-Lopez J. (2003) Head-impulse and caloric tests in patients with dizziness. *Otol Neurotol* 24(6):913–917.
- Persson R. (2008) Motion sickness in tilting trains: description and analysis of present knowledge. VTI Report 614A. Linköping, Sweden: VTI.
- Reason JT. (1978) Motion sickness adaptation: a neural mismatch model. *J R Soc Med* 71(11):819–829.
- Redondo-Martínez J, Bécares-Martínez C, Orts-Alborch M, García-Callejo FJ, Pérez-Carbonell T, Marco-Algarra J. (2016) Relationship between video head impulse test (vHIT) and caloric test in patients with vestibular neuritis. *Acta Otorrinolaringol Esp* 67(3):156–161.
- Scherer H, Helling K, Clarke AH, Hausmann S. (2001) Motion sickness and otolith asymmetry. *Biol Sci Space* 15(4):401–404.
- Simmons RG, Phillips JB, Lojewski RA, Wang Z, Boyd JL, Putcha L. (2010) The efficacy of low-dose intranasal scopolamine for motion sickness. *Aviat Space Environ Med* 81(4): 405–412.
- Singh NK, Pandey P, Mahesh S. (2014) Assessment of otolith function using cervical and ocular vestibular evoked myogenic potentials in individuals with motion sickness. *Ergonomics* 57(12): 1907–1918.
- Tal D, Gilbey P, Bar R, Shupak A. (2007) Seasickness pathogenesis and the otolithic organs: vestibular evoked myogenic potentials study: preliminary results. *Isr Med Assoc J* 9(9): 641–644.
- Tal D, HersHKovitz D, Kaminski G, Bar R. (2006) Vestibular evoked myogenic potential threshold and seasickness susceptibility. *J Vestib Res* 16(6):273–278.
- Taylor RL, Wijewardene AA, Gibson WP, Black DA, Halmagyi GM, Welgampola MS. (2011) The vestibular evoked-potential profile of Ménière's disease. *Clin Neurophysiol* 122(6):1256–1263.
- Taylor RL, Zagami AS, Gibson WP, Black DA, Watson SR, Halmagyi MG, Welgampola MS. (2012) Vestibular evoked myogenic potentials to sound and vibration: characteristics in vestibular migraine that enable separation from Meniere's disease. *Cephalalgia* 32(3):213–225.
- Treisman M. (1977) Motion sickness: an evolutionary hypothesis. *Science* 197(4302):493–495.
- Turner M, Griffin MJ. (1999) Motion sickness in public road transport: the effect of driver, route and vehicle. *Ergonomics* 42(12):1646–1664.
- Turner M, Griffin MJ, Holland I. (2000) Airsickness and aircraft motion during short-haul flights. *Aviat Space Environ Med* 71(12): 1181–1189.
- von Baumgarten RJ, Thümler R, Vogel H. (1977) Motion sickness caused by 'rollercoaster flight'. *S Afr Med J* 52(4):157.
- Weber KP, Aw ST, Todd MJ, McGarvie LA, Curthoys IS, Halmagyi GM. (2008) Head impulse test in unilateral vestibular loss: vestibulo-ocular reflex and catch-up saccades. *Neurology* 70(6):454–463.
- Xie SJ, Chen W, Jia HB, Wang ZJ, Yao Q, Jiang YY. (2012) Ocular vestibular evoked myogenic potentials and motion sickness susceptibility. *Aviat Space Environ Med* 83(1):14–18.
- Yates BJ, Miller AD. (1998) Physiological evidence that the vestibular system participates in autonomic and respiratory control. *J Vestib Res* 8(1):17–25.
- Yates BJ, Miller AD, Lucot JB. (1998) Physiological basis and pharmacology of motion sickness: an update. *Brain Res Bull* 47(5):395–406.