Routine Vestibular Tests May Point Out Vestibular Subtype of Seasickness Only

Bulent Satar; F. Ceyda Akin Ocal; Ceren Karacayli; Volkan Kenan Coban

BACKGROUND: The vestibular system is important in the pathogenesis of seasickness. Our objective is to investigate whether routine vestibular tests detect seasickness.

METHODS: Included were 17 professional naval personnel (mean age of 29.76 $\pm$ 4.73 yr) diagnosed as having seasickness and 29 healthy age- and gender-matched controls. Cervical (c) vestibular evoked myogenic potentials (VEMP) and ocular (o) VEMP and bithermal caloric tests were performed after ear, nose, and throat examination, pure tone audiometry, and magnetic resonance imaging. Severity of seasickness was evaluated based on the Graybiel scale. P1 latency, N1 latency, P1N1 amplitude, and interaural asymmetry ratios (IAR) of cVEMP and oVEMP were compared between the patients and control groups. Abnormal findings in the caloric test were noted. Presence of an abnormality in any of the three vestibular tests (cVEMP, oVEMP, or caloric test) was accepted as a positive vestibular finding.

RESULTS: According to the Graybiel Scale, severe malaise and frank sickness were observed in 3 patients (18.7%) and 13 patients (81.3%), respectively. Graybiel scoring could not be performed in one patient due to general discomfort and bad general condition. In the caloric test, each of three patients (17.65%) showed canal paresis, an incomplete test because of severe nausea, and vomiting and hyperactive response. There were no significant differences in P1 latency, N1 latency, P1N1 amplitude, or IAR of cVEMP and oVEMP ($P > 0.05$). There were three patients (17.65%) and two patients (11.76%) who had abnormal IAR for cVEMP and oVEMP, respectively.

CONCLUSION: Routine vestibular tests may detect some findings in only a minority of patients with seasickness.

KEYWORDS: Seasickness, motion sickness, cervical vestibular evoked myogenic potentials, ocular vestibular evoked myogenic potentials, bithermal caloric test.

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Motion sickness is a range of autonomic symptoms caused by inappropriate sensory effects when experiencing unfamiliar movement patterns. In other words, it is a state of discomfort that includes different symptoms arising from movement.[26] Cardinal symptoms include nausea and vomiting, pallor, cold sweating, increased salivation, drowsiness, headache, and dizziness. Other common findings are apathy, depression, and decreased cognitive functions.[7,11,22] Motion sickness typically occurs during atypical motion patterns that create mismatches in the sensory motor signals, so that perception of the movement or information about the motion does not match the actual physical reality. Sometimes, the usual movement patterns experienced by individuals may result in motion sickness. Many psychosocial and environmental risk factors may contribute to an individual's sensitivity to motion sickness. These factors may vary from person to person.

Sensory conflicts are the most recent pathophysiological explanation of motion sickness.[1,9,17] Vestibular, visual, and proprioceptive afferents provide complementary information about the movement and position of the body in space. Normally, these three sensor structures work in concordance with each other. In Type A conflict, visual and vestibular afferents are contradictory.

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In Type B conflict, signals from the semicircular canals and otolithic organs in the vestibular apparatus are incompatible.[7,9]

As long as inputs from more than one sensory organ cannot be integrated, the information they provide remains incomplete. Semicircular canals sense the angular acceleration of the head, while otoliths sense the size and direction of linear acceleration. Since the same acceleration direction can be caused by the inclination of the head or a combination of horizontal and vertical acceleration, signals from otolithic organs need to be supported by other afferents. The sensory conflict theory may not easily explain motion sickness in every case (e.g., passive low-frequency vertical acceleration). Some of the studies explain motion sickness with subjective vertical conflict theory based on conflict between personal spatial vertical perception (i.e., subjective perception of verticality based on a person's past experience) and current spatial data that is important for providing postural stability. According to the subjective vertical conflict theory, conditions that provoke motion sickness characteristically include a situation in which the perceived vertical movement does not match what has been learnt from previous similar experience.[22] To support this theory, squirrel monkeys underwent bilateral utriculo-sacculectomy and it was observed that they were subsequently resistant to movement-dependent vomiting.[2] It has also been shown that people with nonfunctional vestibular systems are resistant to motion sickness. However, this may not be true in all circumstances. Some groups of vestibular patients have elevated or decreased motion sickness susceptibility, and in most cases these would be picked up by vestibular testing. Motion sickness sensitivity has been demonstrated in various vestibular diseases and migraines.[3]

Various markers have been proposed to determine the susceptibility of individuals to motion sickness. These are otolith asymmetry between the right and left labyrinth, basal autonomic changes, postural stability, or perceptual style.[7] Some researchers have proposed that longer time constants for vestibular velocity storage predict greater motion sickness susceptibility. These parameters entail using a rotation chair.[10] However, none of these have been proven to be useful predictors for susceptibility to motion sickness.

Vertical movement is perceived by the otolithic organs, which are mainly responsible for maintaining balance during vertical and horizontal linear movements. In addition, if the movement includes angular acceleration, the semicircular canals are also activated. According to this theory, motion sickness and space sickness were assumed to be due to otolithic asymmetry caused by channel-otolithic mismatch or differences of autoconial masses between the two labyrinths. The proposed central role of the subjective vertical is supported by studies showing that the vertical linear acceleration component of ship movement is the most provocative stimulant of motion sickness.[16,24]

Otolithic organs are important for maintaining balance during linear acceleration. It is possible to evaluate otolithic organs with cervical vestibular evoked myogenic potentials (cVEMP) and ocular vestibular evoked myogenic potentials (oVEMP).[5,18] cVEMP evaluates saccular function and the sacculocolic reflex pathway, and oVEMP evaluates the utricle. It appears that cVEMP and oVEMP data in motion sickness is very scarce. Tal et al. reported significantly smaller amplitudes and higher cVEMP thresholds in subjects with seasickness compared to healthy controls.[23] Another study by Tal et al.[22] did not reveal a significant difference in latency and amplitude of cVEMP between subjects with seasickness and healthy controls. In the same study, the number of subjects with an asymmetry rate exceeding 35% was higher in susceptible individuals than in the control group, but no statistically significant difference was found between the two groups.[22] Buyuklu et al. also found no significant difference in latency, amplitude, interpeak latency, or interpeak amplitude of cVEMP between motion sickness susceptible and nonsusceptible groups.[4] It can be argued that there are conflicting cVEMP findings in patients with motion sickness. There is only one study on oVEMP in which no statistically significant difference in any oVEMP parameter was observed between susceptible and nonsusceptible subjects. They observed a trend toward higher asymmetry ratio in the motion sickness-sensitive group, but it was not statistically significant.[26]

Considering the paucity of vestibular data in motion sickness, this study aimed to investigate routine vestibular tests in professional naval personnel who were admitted for seasickness and to determine whether there is a difference between them and healthy individuals. In this study, utricle, saccule, superior and inferior vestibular nerves, and related pathways were evaluated using all three tests together (cVEMP, oVEMP, and the caloric test). We hypothesized that there were significant differences in routine vestibular tests in the seasickness group compared to healthy controls.

METHODS

Subjects

The study was approved by the Ethical Committee (19/351). This retrospective study included 17 (mean age 29.76 $\pm$ 4.73 yr) male patients who were professional naval personnel diagnosed as having seasickness. Diagnosis of seasickness was based on observations (Graybiel scale) of health personnel on several occasions during cruises and on official reports. These personnel had to be permanently disqualified from ship duty since they were unable to fulfill their duties because of various combinations of nausea, vomiting, pallor, cold sweating, increased salivation, drowsiness, headache, and dizziness. Included as controls were 29 healthy male participants (mean age 27.79 $\pm$ 8.01 yr). Control subjects had no symptoms of motion sickness. There was no significant difference in age between the two groups ($P = 0.197$).

Materials

Otoscopic examination, pure tone audiometry, speech tests, cVEMPs and oVEMPs, caloric tests, MRI, and the Graybiel scale, which was used to determine the severity of seasickness, were evaluated.

Procedure

The Graybiel scale includes information about nausea, skin color, cold sweating, increased salivation, drowsiness, headache, and dizziness symptoms and had already been filled out by the health employee on board. The Graybiel scales were filled out during three separate cruises. The data used in this study is the average of the three scales. According to this evaluation: 1–2 scores are "slight malaise"; 3–7 scores are "moderate malaise"; 8–15 scores are "severe malaise"; and scores of 16 or above are "frank sickness"[8,11] (**Fig. 1**). Age- and gender-matched controls were pooled from the database of healthy volunteers in our clinic in order to determine normative values of cVEMP and oVEMP.

cVEMP and oVEMP tests were performed while the patient was in a sitting position in a quiet room. Interacoustic Eclips EP 15 (Interacoustics Eclipse EP15; Assens, Denmark) and insert earphones (E-A-RTone 3A ABR, 3M, St. Paul, MN, USA) were used for the tests. The device was calibrated by licensed technical personnel according to the ISO 389-6 standards. For cVEMP recording, an active electrode was placed over the upper third of the sternocleidomastoid (SCM) muscle, a nonactive electrode over the sternal head of the SCM muscle, and the ground electrode on the center of the forehead. Effective contraction of the SCM muscle was obtained by turning the head to the opposite side of the ear being tested. For oVEMP testing the negative electrode was placed 1 cm below the lower eyelid (on the inferior oblique muscle) of each eye, the positive electrode was placed on the chin, and the ground electrode was placed on the forehead (Ambu®Neuroline™ 720; Ambu, Denmark). Subjects were asked to look at a fixation point approximately 60 cm from the eyes and had an upward gaze of approximately 30°. In both tests, the impedances of the surface electrodes were adjusted to be less than 5 kΩ. Via the insert headphones, 500-Hz tone burst stimulus (rise-plateau-fall time 2-2-2 ms) was given. oVEMPs and cVEMPs were recorded in response to 100 dB nHL. The cVEMP wave was defined as a biphasic P13-N23 wave as a positive polarity (P13) approximately 13 ms after stimulus onset, followed by negative polarity (N23) starting at 23 ms. The oVEMP wave was defined as a biphasic P16-N10 wave as a negative polarity (N10) approximately 10 ms after stimulus onset, followed by positive polarity (P16) starting at 16 ms. EMG was band-pass filtered between 10–1200 Hz and amplified (×10.000). Stimulus rate was set to 5.1/s, analysis time to 55 ms and polarity rarefaction. Total of 250 stimuli were averaged. P1 latency, N1 latency, and P1N1 amplitude were recorded for each ear. Interaural asymmetry ratio was also calculated (IAR: left ear P1N1 amp − right ear P1N1 amp/left ear P1N1 amp + right ear P1N1 amp). Based on our normative data, those IAR of patients with seasickness exceeding mean + 2 standard deviations of IAR of the control group were accepted as abnormal IAR for cVEMP and oVEMP. P1 latency, N1 latency, P1N1 amplitude, and IAR ratios of cVEMP and oVEMP were compared between the patient and control groups.

The bithermal caloric test was performed with ICS Chartr 200 (GN Otometrics A/S, Taastrup, Denmark). The test was done with anteflexion of the patient's head about 30°. A total of 200 ml tap water was given to the outer ear canal for 30 s and videonystagmography recordings were obtained. Water temperature was set to warm (44°C) or cold (30°C). Each caloric stimuli was given with an interval of no less than 5 min to

Category	Pathognomonic 16 points	Major 8 points	Minor 4 points	Minimal 2 points	AQS* 1 point
Nausea syndrome	Vomiting or retching	Nausea II, III	Nausea I	Epigastric discomfort	Epigastric awareness
Skin color		Pallor III	Pallor II	Pallor I	Flushing
Cold sweating		III	II	I	
Increased salivation		III	II	I	
Drowsiness		III	II	I	
Pain					Headache
Central Nervous system					Dizziness Eyes closed>=II Eyes open III

*AQS= Additional qualifying symptoms III=severe or marked, II=moderate, I=slight

Frank sickness	Severe Malaise	Moderate Malaise A	Moderate Malaise B	Slight malaise
(S)	(M III)	(M IIA)	(M IIB)	(M I)
>=16 points	8-15 points	5-7 points	3-4 points	1-2 points

Fig. 1. Motion sickness signs and symptoms and Graybiel scoring system. *AQS = additional qualifying symptoms: III = severe or marked, II = moderate, I = slight.

prevent superimposition or conflicting responses. First warm and then cold stimuli were given. Canal paresis was calculated with Jongkee's formula. In addition, vestibular hyperactive response specific to motion sickness except for cerebellar lesions was sought. The slow phase velocity (V_{max}) of nystagmus of 50°/s and above for cold stimulus or of 80°/s and above for warm stimulus were considered hyperactive responses. Presence of an abnormality in any of the three vestibular tests (cVEMP, oVEMP, or caloric test) was accepted as a positive vestibular finding.

Statistical Analysis

Data were analyzed with SPSS 22 software (SPSS Inc., Chicago, IL, USA). Mean, SD, median, and minimum-maximum values were given for descriptive statistics. Conformity of the data to normal distribution was assessed with the Shapiro-Wilk test, which included P1 latency, N1 latency, P1N1 amplitude, and IAR of cVEMP and oVEMP. When normal distribution was observed, the groups were compared with the Student *t*-test and if normal distribution was not observed, both groups were compared with the Mann-Whitney *U*-test. $P < 0.05$ was considered statistically significant.

RESULTS

The patient group included 17 male patients (mean age 29.76 ± 4.73, 25 to 39 yr), and the control group included 29 male subjects (mean age 27.79 ± 8.01, 18 to 48 yr). There was no significant difference in age between study and control groups ($P = 0.197$). Otoscopic examinations, pure tone audiometries, speech tests, and MRI results were normal in the patient group. The mean Graybiel score for the patient group was 27.37 ± 12.10. When the patient group was evaluated according to the Graybiel Scale, severe malaise and frank sickness were observed in 3 patients (18.7%) and 13 patients (81.3%), respectively.

Graybiel scoring could not be performed in one patient due to general discomfort and bad general condition. In 14 patients (82.35%), bithermal caloric testing was normal. There were some abnormalities in three patients (17.65%). In one (5.9%) of them, canal paresis (25%) was noted. His Graybiel score was 41 (categorized as frank sickness). Another patient (5.9%) could not complete the caloric test because of severe nausea and vomiting. His Graybiel score was 24 (categorized as frank sickness). In the other, responses to warm irrigation showed vestibular hyperactivity in both right and left ears. His Graybiel score was 13 (categorized as severe malaise). **Table I** denotes IAR% for cVEMP and oVEMP, Graybiel scores, and caloric test results for each patient with seasickness.

When oVEMP and cVEMP results were analyzed, no significant difference was observed between the right and left ears in terms of P1 latency, N1 latency, or P1N1 amplitude in both the patient and control groups. In the patient group, *P*-values were found to be 0.263, 0.913, and 0.132, respectively, in terms of P1 latency, N1 latency, and P1N1 amplitude for cVEMP. For oVEMP, *P*-values were found to be 0.198, 0.425, and 0.294, respectively. In the control group, *P*-values were found to be 0.922, 0.709, and 0.116 in terms of P1 latency, N1 latency, and P1N1 amplitude for cVEMP. For oVEMP, *P*-values were found to be 0.661, 0.778, and 0.247, respectively.

In a patient with hyperactive caloric response, cVEMP and oVEMP responses could not be obtained from the right ear (**Fig. 2A and B**). Therefore, cVEMP and oVEMP values of the right ear of this patient were excluded from the calculations only. Also, there was no significant difference between the patient and control groups in terms of P1 latency, N1 latency, or P1N1 amplitude in both cVEMP and oVEMP tests. Even though mean IAR was higher in the study group than the control group for both cVEMP and oVEMP tests, the difference was not significant (**Table II** and **Table III**). **Fig. 3A and B** includes cVEMP and oVEMP images of a patient in the control group.

The upper limit of IAR for cVEMP was 24.86%, whereas it was 34.47% for oVEMP. According to these limits, there were three patients (17.65% including a patient with absent cVEMP) with abnormal IAR for cVEMP and two patients (11.76% including a patient with absent oVEMP) with abnormal IAR for oVEMP. Graybiel scoring of the patient without cVEMP and oVEMP responses could not be made due to general discomfort and bad general condition. The other Graybiel scores of those with cVEMP IAR abnormalities are 13 and 21, respectively, and the Graybiel score of the patient with oVEMP IAR abnormality is 13.

DISCUSSION

Motion sickness is diagnosed based on symptoms provoked by motor vehicle motion, or sea or space travel after exclusion of all other diseases. Today, there are many questionnaires designed to estimate and evaluate motion sickness.[6,8,25,28] In our clinic, we routinely use the Graybiel scoring system for motion sickness. It well reflects severity of the disease. In this study, when our patient group was evaluated according to the Graybiel scale, most of them were classified into frank sickness (81.3%). Therefore, most of our patients have suffered from severe symptoms of seasickness.

In general, studies on motion sickness have emphasized the key role of the vestibular system in the etiology of motion sickness. Conflicts among the peripheral vestibular structures that perceive movement have been brought forward in the pathophysiology of motion sickness.[15] Considering the hypothesis proposing that the vestibular system is an integral part of motion sickness, recent studies on vestibular tests in patients with motion sickness are noteworthy despite their contradictory results. Destruction of vestibular nerves or receptors provides immunity to motion sickness, which supports the proposed idea.[27]

Studies in the literature have tested a portion of the vestibular system only by means of a limited test battery (either cVEMP or oVEMP or caloric test) in patients with motion sickness, thus making it impossible to evaluate all vestibular pathways

Table I. Findings in the Vestibular Tests and Graybiel Scores.

PATIENT NUMBER	IAR % FOR cVEMP	IAR % FOR oVEMP	GRAYBIEL SCORE	CALORIC RESPONSE
1	3.3	13.0	24	Not completed because of severe nausea and vomiting*
2	13.8	5.0	47	Normal
3	12.3	32.6	41	Normal
4	16.1	15.5	41	Left canal paresis (25%)*
5	1.8	24.2	25	Normal
6	30.5*	58.2*	--*	Normal
7	11.1	1.6	38	Normal
8	9.7	20.3	25	Normal
9	No response in right ear*	No response in right ear*	13	Hyperactive caloric response: 94°/s for right ear warm irrigation; 88°/s for left ear warm irrigation*
10	14.2	8.0	17	Normal
11	17.3	6.0	37	Normal
12	19.8	2.2	20	Normal
13	2.6	8.7	14	Normal
14	47.6*	3.7	21	Normal
15	21	14	17	Normal
16	20.6	14.9	13	Normal
17	2	10	45	Normal

* Denotes an abnormal finding. In the sixth patient, Graybiel scoring could not be done because of the patient's general discomfort and bad general condition.

together. In this study, the utricle, saccule, superior and inferior vestibular nerves, and related pathways were evaluated using all three tests together.

There have been ongoing debates on pathophysiological bases and mechanisms triggered by the disease. The most commonly accepted theories are sensory conflict theory, subjective vertical mismatch, and otolithic asymmetry.[17] We thought that otolithic asymmetry would be elicited easily by VEMP testing. Otolithic asymmetry could be in the saccule or utricle or both. This asymmetry, if any, would cause right and left differences in electrical discharge from vestibular cells, which would be expected to be detected by VEMP testing. Therefore, our study protocol included both cVEMP and oVEMP tests. Bearing these in mind, cVEMP and oVEMP of the patients with seasickness were compared with age-and gender-matched healthy controls, and no significant difference was observed in P1 latency, N1 latency, or P1N1 amplitude between the study and control groups in both tests. This finding led us to think that symptoms of seasickness occur during the triggering journey, whereas VEMP testing is performed during resting except for a tightened sternocleidomastoid muscle. So, VEMP might not entirely reflect what is going on inside the labyrinth under the motion sickness conditions. Hypothetically, one may state that VEMP results could have been different if it were performed under motion sickness conditions.

As for IAR, comparison of IARs for cVEMP and oVEMP did not result in significant difference between patients with seasickness and controls. In fact, it was noteworthy to calculate higher mean IAR in patients with seasickness than in the controls for cVEMP, but the difference did not reach significance. It seems likely that the small sample size was an underlying reason as to why the difference was not significant. On the other hand, cVEMP caught three patients and oVEMP two patients with abnormally higher IAR or absent potentials. Interestingly enough, there was no cVEMP or oVEMP in the right ear of a patient with a hyperactive caloric response, which would cause huge asymmetry in the otolithic response.

In the literature, Buyuklu et al. reported that there was no correlation between cVEMP and caloric test results, and these tests were not affected by motion sickness.[4] In a study conducted by Tal et al., the motion sickness group had significantly higher VEMP thresholds and significantly lower P13-N23 amplitudes.[23] However, in another study conducted in 2007, they compared 10 seasickness-susceptible and 14 nonsusceptible marines and they could elicit VEMP responses in 50% of the nonsusceptible group and in 10% of the susceptible group. They found no significant differences in terms of P13, N23 latencies, and P13-N23 amplitudes, interpeak latencies, and IAR between the two groups. They attributed these findings to reduced saccular response due to adaptation to sea conditions.[22] Based on our reinterpretation of their findings, we propose that absence of VEMP may be one component or subtype of seasickness. As for our case with the hyperactive caloric response, he had no cVEMP and oVEMP. His Graybiel score was 13, which corresponds to severe malaise. In the study conducted in 2014, 30 patients with motion sickness, 30 professional drivers, and 30 healthy individuals were compared, and no significant difference was observed among the 3 groups in terms of cVEMP and oVEMP latencies and amplitudes.[21] In another study, no significant relationship was found between oVEMP responses and motion sickness sensitivity.[26] In their study on astronauts, Nooij et al. reported that motion sickness-sensitive individuals showed a higher utricular asymmetry, utricular sensitivity, and semicircular canal sensitivity than the nonsensitive group.[16] As can be seen, quite diverse results have emerged from the studies. Shahal et al. evaluated posturography results in subjects sensitive to motion sickness and indicated that vestibular inputs should be less trusted for postural stability.[19] Similarly, Nachum et al. reported that the visual and vestibular inputs should be less trusted and the somatosensory inputs were the most reliable to maintain balance in patients with Mal de debarquement

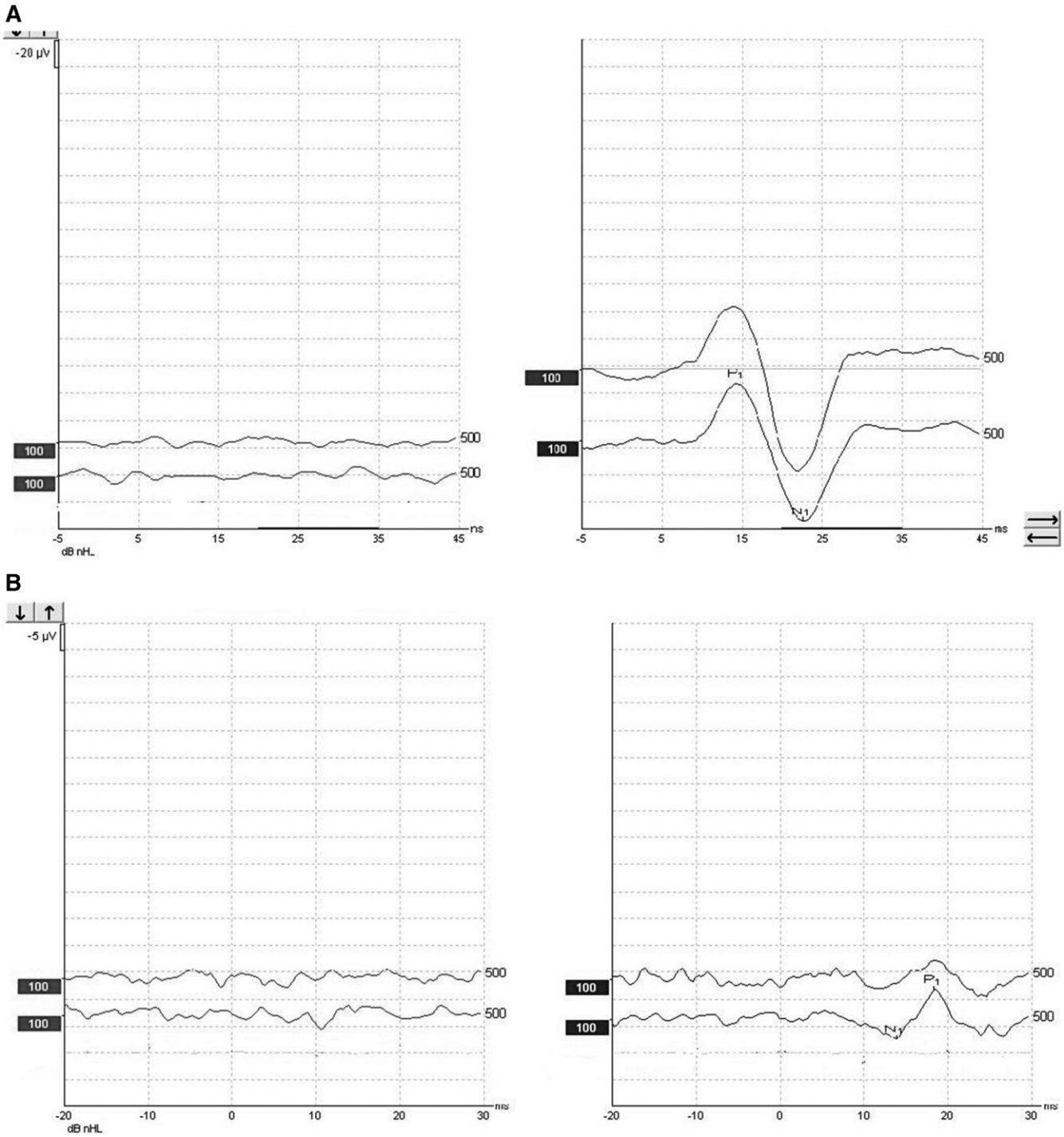

Fig. 2. A.) Images of the patient without cVEMP response in the right ear. B.) Images of the patient without oVEMP response in the right ear.

syndrome.[14] Based on the findings obtained from this study and contradictory findings in the literature, it was concluded that the absence of significant vestibular findings in patients with motion sickness necessitates greater reliance on somatosensory inputs during linear or angular acceleration.

It has been shown in the literature that there may be a hyperactive caloric response in patients with motion sickness.[12,20] However, no significant relationship was found between caloric test and motion sickness in studies.[4,13] In this study, hyperactive caloric response was noted in 1 out of 17 patients. Interestingly enough, there was no cVEMP and oVEMP in the right ear of this patient. Absence of cVEMP or oVEMP in one ear would cause asymmetry in otolithic response to linear stimulus. Another patient could not complete the test since he suffered from severe vomiting. Their Graybiel scores correspond to severe malaise and frank sickness. Since there were only three patients with an abnormal finding in the caloric test, no significant association could be

Table II. Comparison of cVEMP and oVEMP Results of Patient and Control Groups [Mean ± SD, Median, Minimum-Maximum Values, Interquartile Range (IQR)].

	PATIENT GROUP (RIGHT EAR; *N* = 16)	CONTROL GROUP (RIGHT EAR; *N* = 29)	*P*-VALUE	PATIENT GROUP (LEFT EAR; *N* = 17)	CONTROL GROUP (LEFT EAR; *N* = 29)	*P*-VALUE
cVEMP P1 latency (ms)						
Mean ± SD	15.16 ± 2.12	15.52 ± 1.30		15.91 ± 2.48	15.55 ± 1.82	
Median	14.83	15.33	0.229	15.33	15.00	0.544
Min-max	12.25-21.67	13.67-18.33		13.33-24.33	13.33-19.67	
IQR	2.25	1.66		1.25	2.50	
cVEMP N1 latency (ms)						
Mean ± SD	23.49 ± 3.77	24.18 ± 2.33		23.72 ± 3.18	24.06 ± 2.06	
Median	24.00	23.33	0.924	24.00	23.67	0.822
Min-max	13.00-27.33	20.67-28.67		14.00-28.33	20.00-28.33	
IQR	4.26	4.00		3.00	3.00	
cVEMP P1N1amplitude (μV)						
Mean ± SD	91.22 ± 50.77	80.35 ± 83.85		82.32 ± 49.01	74.37 ± 72.96	
Median	80.49	59.30	0.155	70.28	63.68	0.297
Min-max	31.81-200.3	24.62-479.90		27.36-220.10	14.97-420.0	
IQR	80.26	50.30		52.96	48.49	
oVEMP P1 latency (ms)						
Mean ± SD	15.16 ± 0.90	15.73 ± 1.02		15.51 ± 1.12	15.80 ± 0.87	
Median	15.00	15.67	0.071	15.50	15.67	0.337
Min-max	13.67-17.00	13.00-17.67		13.33-17.33	13.33-17.67	
IQR	1.00	1.50		1.58	1.00	
oVEMP N1 latency (ms)				10.59 ± 0.86	10.62 ± 0.85	
Mean ± SD	10.44 ± 1.06	10.63 ± 0.79		10.33	10.33	
Median	10.15	10.33	0.083	9.67-13.25	9.67-12.67	0.809
Min-max	9.33–13.08	9.67–12.67		0.84	1.33	
IQR	0.33	1.16				
oVEMP P1N1 amplitude (μV)						
Mean ± SD	10.39 ± 6.43	9.44 ± 7.72		11.94 ± 8.99	10.11 ± 7.44	
Median	8.98	6.29	0.162	8.30	7.69	0.477
Min-max	1.91-27.03	2.37-34.02		1.69-34.96	1.60-37.55	
IQR	3.15	7.77		10.56	7.57	

$P < 0.05$ was considered statistically significant.

proposed between motion sickness and hyperactive caloric response, which is in accordance with the literature.

Overall, one patient had an abnormality in three tests and another patient had an abnormally higher IAR in both cVEMP and oVEMP. One patient showed abnormal IAR for cVEMP only. Two separate patients showed either canal paresis or an incomplete caloric test because of severe nausea and vomiting. These findings show that routine vestibular tests may miss some of the patients with seasickness. Hyperactive response or an incomplete caloric test due to nausea and vomiting, absence of VEMP, or high asymmetry in right and left amplitudes can be observed in a minority of the patients. Each of these findings may point out a separate subtype of seasickness or overall vestibular or labyrinthine subtype of seasickness since there is an abnormal finding in at least one of the vestibular tests. The patients missed or who were undiagnosed by the mentioned tests are likely to have one of the other subtypes of seasickness that may be detected by further tests.

Table III. Comparison of cVEMP and oVEMP Interaural Asymmetry Ratio (IAR) of Patient and Control Groups (Mean ± SD, Median, Minimum-Maximum Values, Interquartile Range).

	PATIENT GROUP	CONTROL GROUP	*P*
IAR % for cVEMP			
Mean ± SD	15.24 ± 11.78	10.10 ± 7.38	0.172
Median	14.04	10.00	
Min-max	1.82–47.60	0–25.00	
IQR	15.49	13.00	
IAR % for oVEMP			
Mean ± SD	14.89 ± 14.26	14.75 ± 9.86	0.602
Median	11.50	15.00	
Min-max	1.68–58.20	0–36.00	
IQR	13.78	14.50	

$P < 0.05$ was considered statistically significant.

The main limitation of the study was the relatively small sample size in the patient group. However, the patient group was homogeneous in terms of gender, age, and severity of the disease.

In conclusion, the literature on vestibular tests used for evaluation of patients with motion sickness is debatable. Our results showed that routine vestibular tests might detect some findings in only a minority of patients with seasickness. One of the findings was canal paresis, which was deemed not specific to seasickness. However, a hyperactive caloric response, an incomplete test because of severe nausea and vomiting, abnormal IAR, and absent VEMP were considered specific to seasickness. Each of these findings may indicate the presence of a separate subtype of seasickness or an overall vestibular or labyrinthine subtype of seasickness since there is an abnormal finding in at least one of the vestibular tests. The patients missed or who were undiagnosed by the mentioned tests are

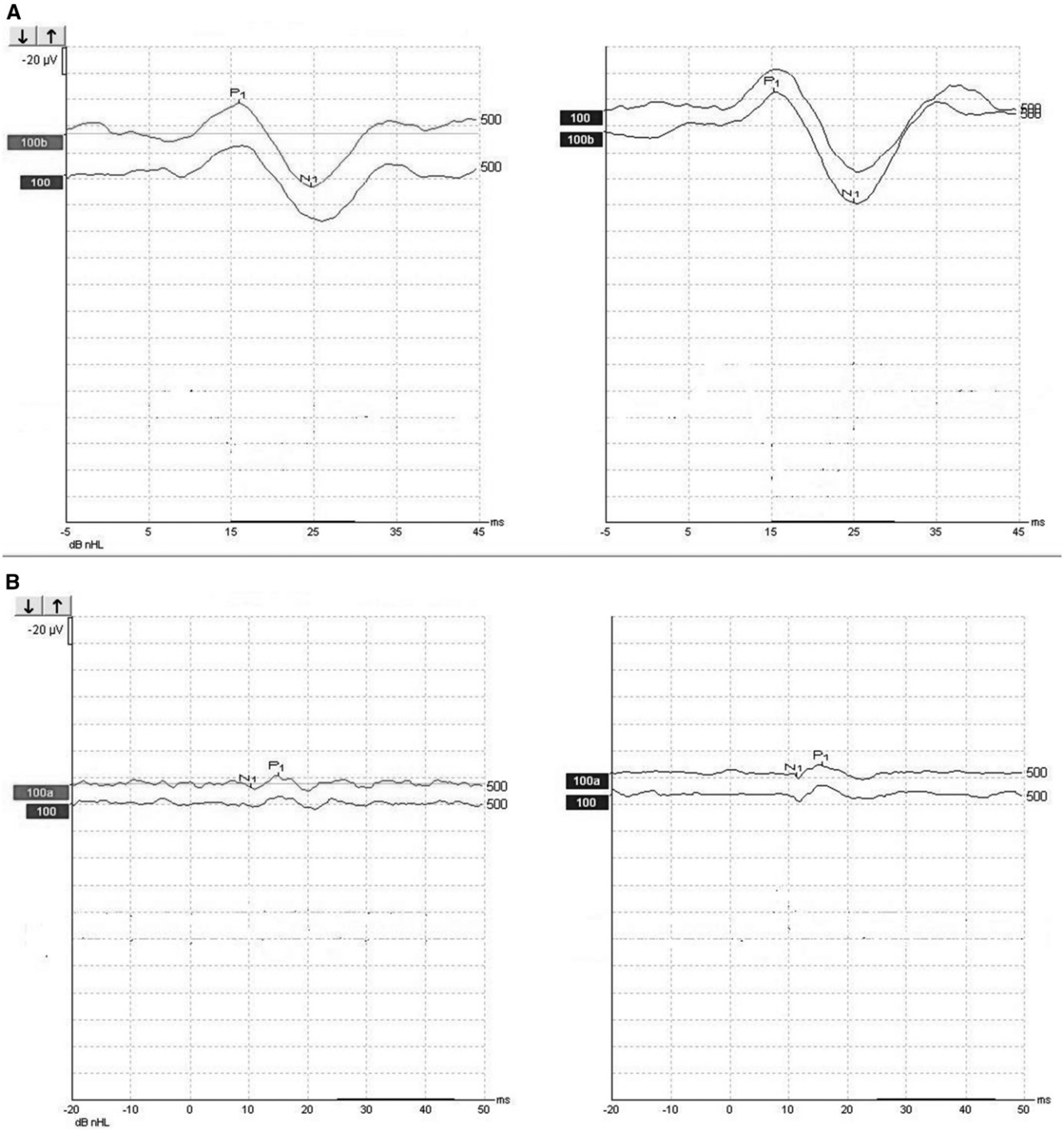

Fig. 3. A.) cVEMP images of a patient in the control group. B.) oVEMP images of a patient in the control group.

likely to have one of the other subtypes of seasickness that may be detected by further tests.

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