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## **Vestibular evoked myogenic potentials and video head impulse test in patients with vertigo, dizziness and imbalance**

### **Abstract**

The aim of this study was to compare vestibular evoked myogenic potentials (VEMP) and video head impulse test (vHIT) results in patients presenting with vertigo and dizziness. We retrospectively analyzed data of all patients with the chief complaint of vertigo, dizziness, or imbalance that underwent VEMP and vHIT from January 2015 to January 2016. A total of 117 patients (73 females, mean age  $53.92 \pm 16.76$ ) fulfilled inclusion criteria: group 1 included patients with the final diagnosis of vestibular neuritis (VN) (N=31 (16 right and 15 left VN)), group 2 included patients with the final diagnosis of vertigo of central origin (N=23) and group 3 included patients with the final diagnosis of unspecified dizziness (N=63). There was significant correlation between oVEMP asymmetry and asymmetry of the lateral canals 60ms gains on vHIT ( $r=0.225$ ,  $p=0.026$ ). Significant correlation between oVEMP and vHIT asymmetry was present in VN patients ( $r=0.749$ ,  $p<0.001$ ), while no correlation was found in the groups 2 and 3. oVEMP and vHIT lateral canals asymmetries were significantly greater in patients with vestibular neuritis. Furthermore, positive correlations of oVEMP amplitudes with 60ms gain of the lateral semicircular canal and slope of the anterior semicircular canal on vHIT, and cVEMP with slope of the posterior semicircular canal on the vHIT were found. These changes were significantly more pronounced in patients with vestibular neuritis. In conclusion, VEMPs and vHIT data should be used complementarily; asymmetry on both tests strongly supports peripheral vestibular system involvement.

**Key words:** vertigo, dizziness, vestibular evoked myogenic potentials, video head impulse test

## **Introduction**

Vestibular evoked myogenic potentials (VEMPs) are becoming widely used for detailed neurophysiological assessment of the vestibular system. Ocular VEMPs (oVEMPs) measure the function of the vestibulo-ocular reflex arc (utricle, superior vestibular nerve, brainstem vestibular nuclei, medial longitudinal fasciculus, inferior oblique muscle) (1). Cervical VEMPs (cVEMPs) measure the integrity of the vestibulo-collic reflex (saccular afferents, inferior vestibular nerve, the brainstem vestibular nuclei, the medial vestibulospinal tract, upper cervical motor neurons and the accessory nerve) (1). VEMPs have mainly been used to assess peripheral neurovestibular disorders; however, recently the focus increased on VEMPs in central neurological disorders as well (2).

The disadvantage of the caloric test, a gold standard in vestibular disorder testing, over VEMPs is that the caloric test measures the function of only the lateral semicircular canals. Furthermore, the disadvantage of VEMPs is that they do not measure dynamic function; and recently, the video head impulse test (vHIT) has been introduced as a clinical test to measure the dynamic function of all three semicircular canals separately (3).

From all of this, it is evident that no one particular test can assess all of the structures of the vestibular system. This is important because appropriate use and interpretation of different tests can lead to accurate diagnosis and treatment of patients presenting with dizziness and vertigo. In line with this, several studies have shown the usefulness of vHIT or VEMPs in differentiating central from peripheral vestibular disorders. For example, it has been shown that vHIT can reliably distinguish vestibular neuritis and stroke, while VEMPs can be successfully used in monitoring the progression of

multiple sclerosis on the central vestibular pathways (4,5). On the other hand, combinations of different methods like VEMPs and vHIT allow for a better differentiation of receptor involvement in peripheral vestibular disorders (6). Therefore, the aim of this study was to compare VEMP and vHIT results in patients presenting with vertigo and dizziness with a hypothesis that compatibility or dissociation of vHIT and VEMP in patients with dizziness can help to differentiate patients with peripheral and central vestibular disorders.

## **Methods**

Study design: We retrospectively analyzed data of all patients with the chief complaint of vertigo, dizziness, or imbalance that underwent VEMP and vHIT testing from January 2015 to January 2016 at the University Hospital Center Zagreb.

Neurologists from the tertiary medical center gave the indication for the combined VEMP and vHIT. All other tests were performed when indicated by the referring neurologist. Only patients with the final diagnosis of vestibular neuritis (group 1), vertigo of central origin (group 2) and patients without known cause of vertigo (group 3) were further analyzed.

Patients with vestibular neuritis were diagnosed on the basis of neurological examination and the caloric test. Central causes of vertigo were defined when neurological examination or neuroimaging (CT and/or MRI) revealed central nervous system involvement. Unspecified dizziness was defined if the patient had normal neurological examination and all other performed test results were normal.

We excluded patients with the final diagnosis of benign paroxysmal positional vertigo, migrenous vertigo and Meniere's disease.

Before the study, indications and procedures were explained and discussed with the patients. All procedures were performed only after informed consent for each test was signed. The ethics committee of the University Hospital Center Zagreb approved the study.

VEMPs: Methods of recording and analysis of obtained data were performed according to previously described details. (7,8) Stimuli used in the experiment were acoustic clicks of 1ms duration and intensity of 130 dB SPL with stimulation frequency of 1 Hz, administered by a pair of headphones. Each ear was stimulated twice in series of 50 stimuli in order to provide reproducibility. Evoked response from the sternocleidomastoid muscle (SCM) was recorded from two electrodes placed on the belly and tendon of the same SCM, ipsilateral to stimulated ear. Response from the ocular muscle (OM) was recorded from two surface electrodes placed two cm below the eye contralateral to stimulated ear. During the experiment participants sat in a chair and were instructed to slightly move their head away from the back of the chair and push it against the elastic band around the forehead in order to activate sternocleidomastoid muscle. The muscle contraction was maintained due to the cooperation of patients in keeping the same position during the test. Participants were also instructed to direct their gaze to the ceiling in order to activate the ocular muscles. Recordings and analysis were performed using a Brain Products Brain Vision Recorder and Brain Products Brain Vision Analyzer (Brain Products GmbH Munich, Germany). Signals were divided in segments of 120 ms duration (20 ms before the stimulus appearance and 100 ms after the stimulus appearance) and

averaged for each set of 50 trials. From the averaged responses of the two sets, the grand average was computed and used for further analysis. The following VEMP parameters were analyzed: peak-to-peak OM amplitude (OL N10-P13, OR N10-P13), normalized SCM amplitude (SCMR CorAmp, SCML CorAmp) and asymmetry ratio for OM and SCM amplitudes. Asymmetry ratio was calculated according to formula:  $AR=(A_{Right}-A_{Left})/(A_{Right}+A_{Left})$  and it was considered pathological if it was  $\geq 33\%$ .

vHIT: vHIT was performed using EyeSeeCam vHIT (Interacoustics, 5500 Middelfart, Denmark) as previously described. (9,10) Before the test it was checked that the patient can perform all neck movements and that they are painless. The patient was seated 1.5 m directly in front of a fixation target at eye level. (11) The target was fixed according to the patient height. Goggles were fitted tightly to the patient's head to reduce slippage. The camera was focused on the eye while the subject fixated on the target. The patient was instructed to keep his/her eyes open widely so as not to obscure the pupil. The system was calibrated for the eye and head movements of each patient before formal testing. The examiner stood behind each patient and rotated the head unpredictably (in direction and time) to the left and right along the longitudinal axis (peak head velocity 150 °/s to 300 °/s). For LARP and RALP positions, the examiner unpredictably moved the head of the patient in the upward and downward direction of the sagittal plane towards right and left side. Each participant underwent a minimum of 5 head impulses in each plane and in each direction.

The following vHIT parameters were analyzed: for the right and left lateral canals (RL and LL, respectively) gain at 60ms, presence of covert and overt saccades and gain asymmetry; for right anterior (RA), left posterior (LP), left anterior (LA) and right posterior (RP) slope and presence of covert and overt saccades. Oto Access



automatically calculated gain, slope and asymmetry. Each test was visually inspected for presence of saccades. LL and RL gains at 60 ms were considered pathological if  $<0.75$ .

Outcomes: The primary outcome was to correlate findings of oVEMP with vHIT of the lateral and anterior semicircular canals, and cVEMP with vHIT of the posterior semicircular canals.

Secondary outcomes were to see whether there is a difference in concordance of the results between the two tests, between three groups, and whether there is a difference in pathological findings of each test between groups.

Statistics: The Kolmogorov-Smirnov test was applied to see whether the data have a normal distribution. Differences in the distribution of qualitative variables were determined with the  $\chi^2$  test and Fisher's Exact test, while the differences in quantitative variables were determined with the use of the ANOVA and Kruskal-Wallis tests. Correlations were tested with Pearson's and Spearman's correlation methods. P values less than 0.05 were considered as significant. Software used for statistical analysis was IBM SPSS, version 20.

## Results

Patients: Out of 144 reviewed patients, a total of 117 patients (73 females, mean age  $53,92 \pm 16,76$ ) fulfilled inclusion criteria: group 1 included patients with the final diagnosis of vestibular neuritis (N=31 (16 right and 15 left VN)), group 2 included patients with the final diagnosis of vertigo of central origin (N=23) and group 3 included patients with the final diagnosis of unspecified dizziness (N=63). There was no difference in age and gender between three groups ( $p>0.05$ ).

Results of VEMP and vHIT parameters and differences between groups are presented in Table 1.

Primary outcomes: For the whole cohort there was significant correlation between oVEMP asymmetry and asymmetry of the lateral canals 60 ms gains on vHIT ( $r=0.225$ ,  $p=0.026$ ). Significant correlation between oVEMP and vHIT asymmetry was present in VN patients ( $r= 0.749$ ,  $p<0.001$ ), while no correlation was found in the groups with central and unspecified dizziness ( $r=-0.312$ ,  $p=0.193$ ; and  $r=-0.205$ ,  $p=0.133$ ; respectively) (Figure 1). Furthermore, both oVEMP and vHIT lateral canal asymmetries were significantly greater in group 1 compared to groups 2 and 3 (Table 2).

For the whole group, OL N10-P13 amp [ $\mu$ V] correlated with the RL gain (60ms) ( $0.298$ ,  $p=0.001$ ). In the VN group, OL N10-P13 amp [ $\mu$ V] correlated with the RL gain (60ms) and RA slope ( $0.489$ ,  $p=0.005$  and  $0.581$ ,  $p=0.001$ , respectively). No correlations were found for groups 2 and 3.

For the whole group, OR N10-P13 amp [ $\mu\text{V}$ ] correlated with the LL gain (60ms) (0.238,  $p=0.010$ ). In the VN group, OR N10-P13 amp [ $\mu\text{V}$ ] correlated with the LL gain (60ms) (0.408,  $p=0.023$ ). No correlations were found for groups 2 and 3.

For the whole group, SCML CorAmp correlated with the LP slope (0.222,  $p=0.022$ ) and SCMR CorAmp correlated with the RP slope (0.293,  $p=0.003$ ). No correlations were found when analyzing each group separately.

Secondary outcomes: In group 1, significant oVEMP asymmetry was present in 7 patients (43.8% of patients with right VN) on the right and 12 (80% of patients with left VN) on the left side. Decreased lateral canal 60 ms gain on vHIT was present in 16 (93.8% patients with right VN) on the right and 13 (86.7% of patients with left VN) on the left side.

In group 2, significant oVEMP asymmetry was present in 7 (30.4%) patients on the right and 4 (17.4%) patients on the left side. Decreased lateral canal 60 ms gain on vHIT was present in 6 (26.1%) patients on the right and 4 (17.4%) on the left side.

In group 3, significant oVEMP asymmetry was present in 13 (20.6%) patients on the right and 15 (23.8%) patients on the left side. Decreased lateral canal 60 ms gain on vHIT was present in 14 (22.2%) patients on the right and 2 (3.2%) on the left side.

When interpreting results as normal or pathological, we found no difference between groups for right and left oVEMP asymmetry ( $p=0.669$  and  $p=0.168$ , respectively). For vHIT results there was a significant difference in pathological results between groups for both left and right response ( $p<0.001$  and  $p=0.014$ , respectively). Concordance between oVEMP and vHIT findings is presented in Table 3.

## Discussion

The main aim of this study was to evaluate the relationship between vHIT, which is able to reveal deficits of the semicircular canals and their ampullary nerves, and VEMPs in a clinical population of patients attending a balance disorder clinic. The vestibular nerve is composed of the superior vestibular nerve, which can further be divided into the utricular nerve, the superior and lateral ampullary nerves, and the inferior nerve, consisting of the saccular nerve and posterior ampullary nerve. Since oVEMPs evaluate the function of utricular nerves, cVEMPs of the saccular nerves, and vHIT of individual ampullary nerves, it is obvious that the combined use of VEMPs and vHIT we can analyze the peripheral vestibular function to far greater detail than by only using the caloric test (12). The results have shown that the oVEMP and cVEMP amplitude changes correspond to the functional impairment of vestibular system indicated by vHIT in patients with vertigo and dizziness. This is evident from positive correlations of oVEMP amplitudes with 60ms gain of the lateral semicircular canal and slope of the anterior semicircular canal on vHIT, and cVEMP with slope of the posterior semicircular canal on the vHIT. Furthermore, it seems that these changes are significantly more pronounced in patients with peripheral vestibular loss (i.e. vestibular neuritis). In our cohort, in which all the patients had their superior vestibular nerve affected, we found excellent correlations between oVEMP asymmetry and lateral semicircular canals asymmetry on vHIT, as well as between oVEMP amplitudes and 60ms gain of the lateral and slope of the anterior semicircular canal on vHIT. However, we found no correlation between cVEMP and the slope of the posterior semicircular canal on the vHIT in the VN group. A similar observation

was found in the previous study, which investigated simultaneous use of VEMPs and vHIT. (13)

The second conclusion of this study is that, for differential diagnosis of patients with vertigo and dizziness, concomitant application of VEMPs and vHIT enables better physiopathological evaluation and helps to differentiate between peripheral and other causes of vertigo and dizziness. VEMPs have initially been used to investigate peripheral vestibular disorders; however, recently there has been a shift in their use in central neurological disorders, with most studies being performed in stroke and multiple sclerosis (2). In brainstem stroke patients, VEMP changes are mostly undistinguishable from those of patients with vestibular neuritis. Most VEMP abnormalities in brainstem stroke consist of absent responses, followed by diminished amplitudes. (14,15) Similar observations are seen in MS patients as well, in which absent responses correlate well with brainstem disease burden (16). Unlike VEMPs, it seems that the vHIT could be used to discriminate central from peripheral causes of acute vestibular syndrome. One study has shown that posterior inferior cerebellar artery (PICA) strokes, presenting with acute vestibular syndrome, have normal lateral semicircular canals vHIT gains. (17) On the other hand, a prior study found that 22% of PICA stroke patients had abnormal caloric responses despite a normal head impulse test. (18). This discrepancy between caloric test and vHIT in PICA stroke can be explained by previous investigations that have shown consistently that even though a caloric asymmetry becomes clinically significant at ~22 to 25%, the asymmetry must equal or exceed ~40 to 60% for the performance characteristics of the vHIT to be sensitive to canal paresis (19,20). Furthermore, it has been suggested that a caloric asymmetry of 39.5% is needed to optimize the discrimination between an abnormal and normal vHIT. (21) Anterior inferior cerebellar artery (AICA) strokes, on the other

hand, are associated with a wide distribution of individual lateral semicircular canals vHIT gains, ranging from asymmetric, bilaterally low to normal gains. (17)

Conversely, significant differences were not observed in the vestibular test battery between the PICA and AICA stroke, where cVEMPs were abnormal in 50% of the PICA stroke patients and 66% of the AICA stroke patients. (22)

The limitations of our study are retrospective data collection, the fact that all patients came from tertiary medical center and the relatively large number of patients with unexplained dizziness.

Nevertheless, our findings suggest that the VEMPs and vHIT data are not redundant but, instead, are complementary; asymmetry on both tests strongly supports peripheral vestibular system involvement.

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## Tables

**Table 1.** Results of VEMP and vHIT parameters and differences between groups.

	Group	Mean	SD	Significance
OL N10-P13 amp [ $\mu$ V]	1	4,74	4,67	0.229
	2	4,23	6,73	
	3	5,06	5,76	
OR N10-P13 amp [ $\mu$ V]	1	3,43	4,88	0.113
	2	4,02	5,21	
	3	4,93	4,95	
SCMR CorAmp	1	0,98	0,79	0.071
	2	0,89	0,82	
	3	1,23	0,59	
SCML CorAmp	1	0,83	0,93	0.098
	2	0,78	0,54	
	3	1,23	1,73	
LL gain (60ms)	1	0,63	0,34	0.000*
	2	0,80	0,29	
	3	0,90	0,17	
RL gain (60ms)	1	0,61	0,30	0.000**
	2	0,71	0,31	
	3	0,83	0,21	
LA slope	1	0,92	0,45	0.003*
	2	1,11	0,50	
	3	1,24	0,30	
RA slope	1	0,70	0,35	0.004*
	2	0,76	0,31	
	3	0,90	0,22	
LP slope	1	0,73	0,24	0.114
	2	0,70	0,37	
	3	0,83	0,23	
RP slope	1	1,05	0,28	0.072
	2	0,97	0,42	
	3	1,15	0,28	

Bonferoni post hoc analysis revealed significant difference between \*groups 1 and 2, 1 and 3; \*\*groups 1 and 3;

OL left ocular, OR right ocular, SCMR right sternocleidomastoid, SCML left sternocleidomastoid, LL left lateral canal, RL right lateral canal, RA right anterior canal, LA left anterior canal, RP right posterior canal, LP left posterior canal.

**Table 2.** Differences in oVEMP and vHIT lateral canals asymmetry between groups.

<b>oVEMP asymmetry</b>				
Group	Mean	Standard deviation	Median	Significance
1	65.95	42.60	90.84	p<0.001*
2	-7.55	69.57	-4.35	
3	4.91	55.86	-0.43	
<b>vHIT lateral canals asymmetry</b>				
Group	Mean	Standard deviation	Median	Significance
1	35.65	21.81	37	p<0.001*
2	9.17	12.76	4	
3	5.44	9.11	3	

\*Kruskal-Wallis test, post hoc analysis revealed significant difference between groups 1 and 2, and groups 1 and 3.

**Table 3.** Concordance between oVEMP and vHIT findings.

<b>Vestibular neuritis</b>				
		R_vHIT		significance
		N	P	
R_AS	N	15	9	0.007
	P	0	7	
		L_vHIT		
		N	P	
L_AS	N	16	3	0.000
	P	2	10	
<b>Vertigo of central origin</b>				
		R_vHIT		significance
		N	P	
R_AS	N	12	4	1.000
	P	5	2	
		L_vHIT		
		N	P	
L_AS	N	16	3	1.000
	P	3	1	
<b>Unspecified dizziness</b>				
		R_vHIT		significance
		N	P	
R_AS	N	39	11	1.000
	P	10	3	
		L_vHIT		
		N	P	
L_AS	N	46	2	1.000
	P	15	0	

AS assymetry, R right, L left.

## Figures

Figure 1. Scatterplot showing individual patient's oVEMP asymmetry and vHIT asymmetry of the lateral canals.

