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ORIGINAL ARTICLE

Video Head Impulse Test and Vestibular-Evoked Myogenic Potentials: Simple Clinical Tools for Assessment of Multiple Sclerosis Patients

Walid Ibraheem[1], Eman Shahba[2*] Nadia Elnabtity[1]

1. Otorhinolaryngology Department, Faculty of Medicine, Zagazig University, Egypt.
2. Otorhinolaryngology Department, Om El Masreyeen General Hospital, Giza, Egypt

***Corresponding author:**
Eman Shahba
ENT Department, Om El Masryeen General Hospital, Giza, Egypt

E-mail:
eman.gamal136@gmail.com

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ABSTRACT

Background: In multiple sclerosis (MS) patients, because there is a weak correlation between radiological extend determined by magnetic resonance imaging (MRI) and its clinical presentation, it is essential to find potential methods for testing brainstem affection in these patients. Consequently, we aimed to investigate the clinical value of the video head impulse test (vHIT) and vestibular evoked myogenic potential (VEMP) tests in the diagnosis of brainstem affection in MS patients, as well as to correlate them with clinical symptoms and MRI findings.

Methods: This study included fifty subjects in 2 groups; the control group included 25 normal subjects, and the study group consisted of 25 MS patients. The study group was divided into 2 subgroups according to MRI findings: MS patients without brainstem lesions (n=14) and MS patients with brainstem lesions (n=11).Basic audiological evaluation, vHIT and VEMPs were conducted to all subjects in the study.

Results: There was a statistically significant difference between control and MS patients with lesions in the brainstem in the vHIT gain of lateral and posterior canals. Both study subgroups had significantly delayed cVEMP and oVEMP latencies in comparison to the control group. Regarding cases with brainstem symptoms, they had significantly lower lateral and posterior canal gains. Moreover, they had significantly delayed cVEMP and oVEMP latencies.

Conclusions: vHIT and VEMPs are valuable tools in evaluating the involvement of the brainstem in patients with MS. Moreover, these tests can be useful in recognizing undetected brainstem lesions and thus have a predictive value for the disease progress.

Keywords: Vestibular evoked myogenic potentials; Video head impulse test, Brainstem lesion, Multiple sclerosis

INTRODUCTION

Multiple sclerosis (MS) is a central nervous system chronic demyelinating neurodegenerative disease that can be triggered by autoimmune, genetic, or environmental causes [1, 2]. MS patients may experience sensory, motor, and/or autonomic dysfunction. Cerebellar symptoms, ocular neuritis, trigeminal neuralgia, dizziness, or vertigo may also develop [3].

Demyelination of the brainstem and cerebellum is common in MS. As a result, it is unsurprising that abnormal vestibular sensations are MS prevalent features. True vertigo occurs in about 20% and can be the presenting complaint in up to 5% of MS patients [4]. Vestibular dysfunction may be clinically undetected but is diagnosed with neuro-otological examination and testing. While magnetic resonance imaging (MRI) is the primary diagnostic test for multiple sclerosis (MS), it may not adequately correlate with clinical signs of brainstem affection [5].

Many tests are thought to be able to detect brainstem involvement in MS. vHIT is a video-

based equipment test that uses sudden head impulse stimulations to measure the gain of the vestibulo-ocular reflex (VOR) and detect refixation saccades (both covert and overt saccades) [6].Some researchers have demonstrated that VOR can be reduced when the vestibular system's central component is injured [7]. Moreover, ocular vestibular evoked myogenic potential (oVEMP) and cervical vestibular evoked myogenic potential (cVEMP) can provide useful information about brainstem functions as their neural pathways pass through the brainstem [8].

The purpose of this study was to assess the clinical utility of vHIT, ocular, and cervical VEMPs in the diagnosis of brainstem affection in MS patients and their relationship with clinical symptoms and MRI findings. The correlation between VEMPs and vHIT findings in MS patients was further investigated.

METHODS

Study design and subjects

The work was done in the unit of Audio-Vestibular medicine, Department of Otorhinolaryngology, Faculty of Medicine and Zagazig University, Egypt

In this case-control study, fifty participants underwent vHIT and VEMPs at Zagazig University Hospitals, Audio-Vestibular Medicine unit from 2019 to 2020. The ages of the participants ranged from 20 to 50 years old, with no sex predilection. They were separated into two groups: 25 healthy control participants and 25 MS patients previously diagnosed with multiple sclerosis (MS) using the revised McDonald criteria. [9].

The study group was divided into two subgroups according to MRI findings: 14 MS patients without brainstem lesions and 11 MS patients with brainstem lesions. All patients had otoscopic and basic audiological evaluation before the study. All participants who had peripheral vestibular disorders, conductive hearing loss, were using medications known to have a vestibular system-altering effect, or who had a cervical lesion limiting their neck range of motion were excluded from the study in both groups.

Clinical and MRI examinations

The clinical involvement of the brainstem in all patients was evaluated using history and clinical examination. Vertigo, facial sensory symptoms, and/or diplopia were among the most prevalent brainstem symptoms [10].

We assessed the brainstem for demyelinating lesions using multi-planar dual fast spin-echo PD and T2-WI MRI sequences using 1.5 T MRI. An experienced neuro-radiologist analysed MRI scans blinded to the goal of the study.

vHIT recording

We used EYESEECAM vHIT from Interacoustics. The patients sat 1meter away from the target mark, wearing tightly fitted lightweight goggles. The goggles had a small video camera, and a half-silvered mirror reflected the patient's right eye image. The patients were instructed to fixate on this target with wide-open eyes and minimal blinking [11].Before testing, the eyes and head movements were calibrated. The goggles' sensor measured head movement while the high-speed camera (250 Hz) captured the eye velocity.

To generate the VOR, the examiner rotated the subject's head in unpredictable directions. The head impulses were administered in three planes: lateral, right anterior-left posterior (RALP), and left anterior-right posterior (LARP) with at least 20 impulses provided in each plane [11, 12].

At the completion of the whole test, stimuli and responses were displayed on the computer screen, along with a graph depicting the calculated VOR gain (ratio of eye velocity to head velocity) for each head rotation. Refixation saccades were sampled and classified as covert if they occurred before the end of the head impulse or as overt afterward[11,12,13].The existence of a lateral canal gain of less than 0.8 or less than 0.75 for the anterior and posterior canals was characterized as abnormal vHIT. Gain asymmetry of ≥8% was considered abnormal .vHIT was considered abnormal when the reduction of canal gain was associated with overt or covert saccade [14].

VEMP recordings

Using *Otometrics"ICSchartr EP 200"* device*;* 500 Hz tone burst stimulus was applied to the tested ear at a rate of 5/s and an intensity of 95dB.Each response was analyzed for 50 ms, with 100 sweeps for each run. Between 30 and 1500 Hz, the response was band-pass filtered.These parameters were used for both c VEMP and o VEMP. However, in O VEMPthe stimulus was delivered to the tested ear which is the contralateral ear to the measured eye. For the cVEMP test, the patients sat with their heads tilted by 45º to the contralateral side and slightly flexed by ~30º. The active electrode was positioned on the middle part of the ipsilateral SCM muscle, whereas the ground electrode was put on the forehead and the reference one over the upper sternum [15].

The active electrode for the oVEMP test was positioned 1 cm below the centre of the contralateral lower eyelid. The reference electrode was 15 mm below it and the ground one over the forehead. During the test, patients were instructed to stare upward to a fixed point 2 meters away and 30–35°above the horizontal line [16].

To evaluate the peak latency and peak to peak amplitude in both ears, the biphasic wave with a positive (P) and negative (N) peak was recorded for both VEMPs. The amplitude asymmetry ratios (AR) were also determined using the formula: AR = (A_{Right} _ A_{Left}) / (A_{Right} + $_{left}$), and it was termed abnormal if it was ≥33% [17].

The Research Ethics Committee at the Faculty of Medicine, Zagazig University Hospitals approved this study with the number 5243-23-2-2019. Written informed consent was obtained from all participants after the test procedures had been explained. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans

STATISTICAL ANALYSIS

IBM SPSS version 20 was used to analyze the data. Quantitative variables were described using their means and standard deviations. Chi-square test ($\chi 2$) compared qualitative variables. The means of two or more groups were compared using independent t-tests and one-way ANOVA respectively. Correlations were assessed using *Pearson's* correlation coefficient. The P-value for significant results (*) was ≤0.05, and for highly significant results (**) was ≤0.01

RESULTS

There were 13 male and 37 female patients in this study, the age and gender distribution were calculated in both control and study groups and revealed no significant difference in age or gender between them. All patients with MS had bilateral normal hearing sensitivity. Dizziness and facial symptoms were the most frequent MS symptoms in the study group, particularly in patients with MRI brainstem lesions. There was a statistically significant difference between MS patients with and without brainstem lesions regarding these symptoms. In one case with diplopia and two cases with dizziness, radiological findings were not correlated **(**no brainstem lesion was present)**(Table 1)**.

Regarding vHIT abnormalities, the canal deficit in the study group was detected in three of 14 MS patients without brainstem lesion (21.4%) and six of 11 MS patients with brainstem lesion (54.5%) **(Fig.1)**.The most affected canals were the lateral, followed by the posterior canal. MS patients with brainstem lesions had significantly reduced lateral and posterior canal gain compared to controls. The control and study groups differed significantly in RALP and LARP asymmetry **(Table 2)**.Compared to control group, overt and covert saccades were more frequent in the study groups. Cases with canal deficit were associated with overt or covert saccade.

As regards cVEMP abnormalities, Three MS patients(21.4%) without brainstem lesion showed delayed latency and seven MS Patients (63.5%) with brainstem lesion showed abnormalities in the form of [six patients (54.5%)with delayed latency of P13, N23 of cVEMP and an absent response in one patient (9%)]**(Fig. 1)**. In comparison to control group, there was a statistically significant delay in P13, N23 latency in the study groups and a difference in P13 N23 latency between MS patients with and without brainstem lesions.The asymmetry ratio and P13, N23 amplitude differences between the control and study groups, were insignificant **(Table 3)**.

oVEMP abnormalities were observed in 4 patients (28.5%) in cases without brainstem lesion in the form of delayed latency. In addition 9 patients (81.6%) with brainstem lesion showed abnormalities in the form of (seven patients with delayed latency (63.6%) and two patients (18%) exhibiting no response) **(Fig. 1).** There was a significantly delayed N10 P15 latency in the study groups **(Table 4)**.

In MS patients with brainstem lesions, the gain of the lateral and posterior canals of vHIT correlated negatively with the latencies of cVEMP and oVEMP**(Table 5)**.In contrast, vHIT and VEMPs did not correlate in MS patients without brainstem lesions. Moreover, cases with brainstem symptoms had significantly lower lateral and posterior canal gains. They also had significantly delayed cVEMP and oVEMP latencies **(Table 6)**.oVEMP has the highest sensitivity in detecting the brainstem lesion (85.4%) followed by cVEMP (82.1%) and vHIT (74%) in MS patients with brainstem lesions.

Table (1): Brainstem symptoms in MS patients with and without brainstem lesion:

		Study group		Total (n= 25)	χ2	P
		MS without BS lesions (n=14)	MS with BS lesions (n=11)			
Dizziness	**N**	2	9	11	11.4	0.001**
	%	14.3%	81.8%	44.0%		
Facial symptoms	**N**	0	9	9	17.89	0.001**
	%	0.0%	81.8%	36.0%		
Diplopia	**N**	1	3	4	1.87	0.17
	%	7.1%	27.3%	16.0%		

χ^2 Chi-square test **MS**= Multiple sclerosis **BS**= Brainstem **p<0.01 is highly significant

Table (2): Comparison of vHIT between control and study groups:

		Control	Study group		F	P	LSD
			MS without BS	MS with BS			
Lateral canal gain	**RT**	0.98±0.11	0.92±0.25	0.74±0.24	3.480	0.015*	P1=0.18 P2=0.001** P3=0.005*
	LT	0.99±0.12	0.92±0.25	0.71±0.21	5.380	0.008*	P1=0.19 P2= 0.001** P3=0.035*
Anterior canal gain	**RT**	0.97±0.21	0.91±0.30	0.89±0.28	0.651	0.526	
	LT	1.07±0.19	0.88±0.26	0.81±0.22	1.540	0.225	
Posterior canal gain	**RT**	0.99±0.22	0.95±0.22	0.76±0.22	4.136	0.001**	P1=0.21 P2=0.001** P3=0.004*
	LT	0.98±0.25	0.91±0.24	0.77±0.25	2.581	0.026*	P1=0.09 P2=0.001** P3=0.012*
Lateral canal Asymmetry		5.72±1.7	8.21±2.78	8.45±2.54	2.569	0.087	
RALP Asymmetry		6.04±2.01	9.88±3.24	11.41±3.78	7.403	0.002*	P1=0.001** P2=0.001** P3=0.055
LARP Asymmetry		5.44±1.77	11.85±3.79	12.23±3.11	11.663	0.001**	P1=0.001** P2=0.001** P3=0.06

RALP= right anterior- left posterior **LARP**= Left Anterior-right posterior
P1 between control & case without BSlesion**P2** between control & case with BS lesion
P3 between case without BS & case with BS lesion

Table (3): Comparison of cVEMP parameters between control and study groups:

		Control	Study group				
			MS without BS	MS with BS	F	P	LSD
P 13 latency	RT	14.25±0.95	15.95±1.52	18.01±2.81	14.31	0.001**	P1=0.04* P2=0.001** P3=0.001**
	LT	14.09±0.89	15.7±1.58	18.13±2.82	16.61	0.001**	P1=0.03* P2=0.001** P3=0.001**
N23 latency	RT	23.07±1.1	25.24±1.98	27.74±2.98	14.57	0.001**	P1=0.045* P2=0.012* P3=0.011*
	LT	22.93±1.2	24.74±1.91	27.66±2.97	15.08	0.001**	P1= 0.038* P2= 0.001** P3=0.021*
P13 N23 Amplitude	RT	25.94±6.51	25.25±4.56	24.65±6.61	0.18	0.831	
P13 N23 Amplitude	LT	25.45±6.21	24.01±7.73	25.26±5.83	0.22	0.801	
Asymmetry Ratio		16.68±3.83	13.35±4.09	13.18±4.21	3.17	0.051	

P1between control & case without BS lesions **P2**between control & case with BS lesions
P3between cases without BS & cases with BS lesions

Table (4): Comparison of oVEMP parameters between control and study groups:

		Control	Study group				
			MS without BS	MS with BS	F	P	LSD
N10 Latency	RT	9.86±1.1	12.11±2.03	15.4±2.99	32.84	0.001**	P1=0.02* P2=0.001** P3=0.001**
	LT	10.03±1.1	12.02±1.96	15.28±2.96	26.81	0.001**	P1=0.04* P2=0.001** P3=0.001**
P15 Latency	RT	14.75±0.92	17.55±1.75	20.72±2.37	34.39	0.001**	P1=0.003* P2=0.001** P3=0.0001**
	LT	14.83±1.1	17.41±1.96	20.59±2.5	29.21	0.001**	P1= 0.03* P2=0.001** P3=0.001**

N10 P15 Amplitude	**RT**	6.51±1.68	6.19±1.66	6.19±1.39	3.01	0.082	
N10 P15 Amplitude	**LT**	6.51±2.01	6.37±1.52	6.62±1.04	2.66	0.089	
Asymmetry ratio		8.68±2.71	7.27±2.51	6.41±2.11	1.38	0.259	

P1between control & case without BS lesion **P2**between control & case with BS lesion
P3between case without BS & case with BS lesion

Table (5): Correlation between vHIT and both VEMPs in MS patients with brainstem lesion:

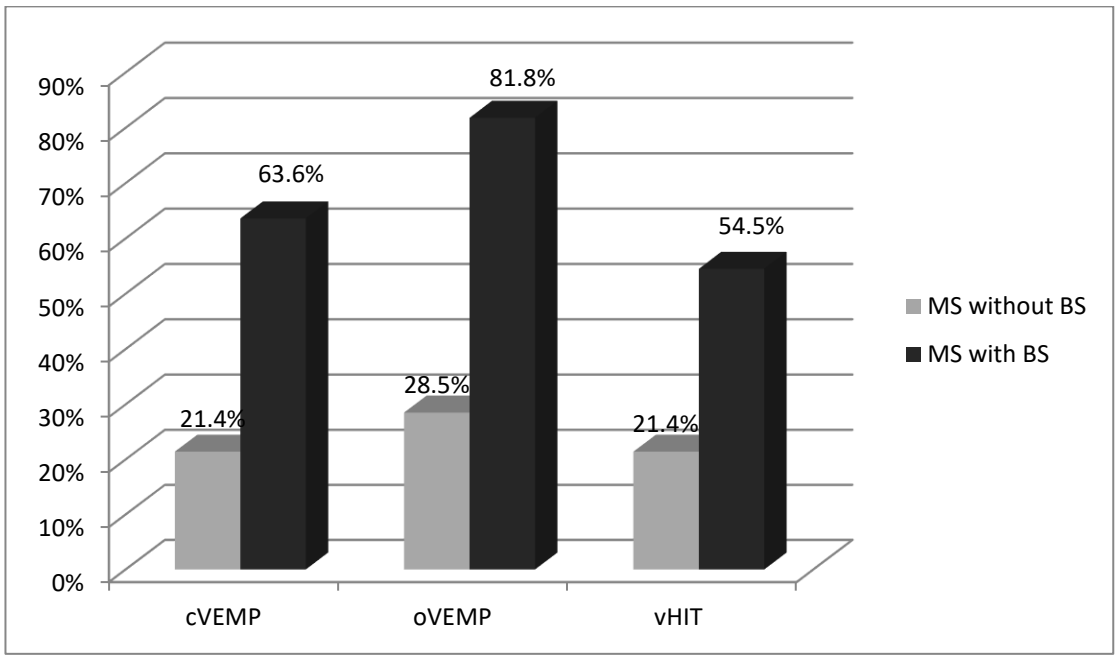
VEMPs		Vhit					
		Lateral RT	**Anterior RT**	**Posterior RT**	**Lateral LT**	**Anterior LT**	**Posterior LT**
cVEMPP 13 RT	**R**	-.518**	.021	-.544**	-.449-**	-.031	-.552**
	P	.0001	.887	.0001	.001	.832	0.002
cVEMPP 13 LT	**R**	-.580**	-.051	-.540**	-.496-**	.053	-.571**
	P	.0001	.727	.0001	.0001	.713	.0001
cVEMPN 23 RT	**R**	-.564**	-.032	-.497**	-.524-**	.018	-.551**
	P	.0001	.824	.002	.0001	.903	.0001
cVEMPN 23 LT	**R**	-.471**	-.025	-.556**	-.437-**	-.002	-.446**
	P	.001	.861	.001	.002	.987	.002
oVEMPN 10 RT	**R**	-.534**	-.098	-.488 **	-.512**	.198	-.544**
	P	.001	.695	.003	.001	.284	.002
oVEMPN 10 LT	**R**	-.431*	-.093	-.586**	-.591**	.098	-.497**
	P	.020	.596	.001	.001	.598	.001
oVEMPP 15 RT	**R**	-.575**	-.198	-.498**	-.597**	.198	-.598**
	P	.001	.398	.001	.009	.169	.000
oVEMPP 15 LT	**R**	-.465**	-.185	-.472**	-.446**	.298	-.486**
	P	.004	.398	.002	.009	.198	.001

Table (6): Comparison of the scores of vHIT, cVEMP and oVEMP in patients with and without brainstem symptoms:

	Symptoms		**t**	**P**
	No	**Yes**		
vHIT lateral RT	1.11±0.21	0.78±0.23	2.356	0.027*
vHIT Anterior RT	1.11±0.31	0.82±0.24	0.076	0.940
vHIT Posterior RT	1.25±0.38	0.86±0.27	2.339	0.010*
vHIT lateral LT	1.15±0.31	0.84±0.41	2.085	0.048*
vHIT Anterior LT	1.31±0.36	0.82±0.24	0.085	0.933
vHIT Posterior LT	1.18±0.14	0.86±0.23	2.846	0.009*
cVEMP P13 RT	13.7±0.27	16.95±2.29	4.669	0.001**
cVEMP P13 LT	13.72±0.32	17.08±2.3	4.777	0.001**
cVEMP N23 RT	23.54±0.38	26.75±2.16	4.818	0.001**
cVEMP N23 LT	23.45±0.34	26.66±2.1	4.972	0.001**
oVEMP N10 RT	10.85±0.98	15.06±2.4	5.421	0.001**
oVEMP N10 LT	10.74±1.13	14.95±2.38	5.348	0.001**
oVEMP P15 RT	15.97±1.1	19.48±1.85	5.625	0.001**
oVEMP P15 LT	15.76±1.02	19.4±1.82	5.878	0.001**

*p<0.05 is statistically significant**p<0.01 is highly significant

Figure (1): **Percentage of patients with VEMPs and vHIT abnormalities in the study group**:



DISCUSSION

Detection of brain stem involvement in MS is one of the major predictors of a clinically relevant disability.Although brain MRI is the 'gold standard' approach for diagnosing MS, it was noted that it was not capable of detecting all lesions in MS patients.MRI abnormalities were observed in less than 60% of patients with brainstem symptoms [17]. In the current study, no radiological evidence of brainstem involvement was seen in two cases of dizziness and one with diplopia (Table 1). This stresses the need for novel, potentially diagnostic brainstem dysfunction testing.

In agreement with *Pavlović* et al. [12] our vHIT results demonstrated a statistically significant reduction in lateral and posterior canal gain in MS patients with brainstem lesions and a statistically significant difference between the control and both study groups regarding RALP and LARP asymmetry (table 2).This effect can be attributed to demyelinating lesions in the vestibular nerve's root exit zone, vestibular nucleus, or deep cerebellar nuclei that modulate the VOR. The high level of affection for lateral and posterior canals could be explained by the increased prevalence of lesions in medial longitudinal fasciculus (MLF) in MS [19].

Consistent with earlier findings [20, 21], we observed statistically significant prolongation of cVEMP and oVEMP latencies in MS patients, significantly greater in individuals brainstem lesion (table 3, 4). Delayed latency in MS patients is due to demyelinating lesion affecting the axons that leads to reduction in the conduction velocity [20].

However, *Kavasoğlu et al*. [22] documented that investigating cVEMPs in MS is not a sensitive technique for determining brainstem involvement, even though delayed latencies, mostly involving p13, were found in 23.3% of MS participants. Additionally, *Eleftheriadou et al*. [23] reported that VEMP latency prolongations are not specific to MS, and it had been reported in other brainstem-related illnesses such as stroke and tumors. These findings do not negate the importance of VEMP testing as a simple and easy-to-use technique to supplement other approaches (particularly clinical and radiological testing) for MS diagnosis and follow-up.

As with previous publications on VEMPs in MS [23, 24], our study's abnormal vHIT, cVEMP, and oVEMP results in MS patients without radiological brainstem lesion (**Fig. 1;** subgroup 1) suggest brainstem lesion despite normal MRI. This may indicate the effectiveness of these tests in detecting silent brainstem lesions. One possibility is that minor demyelinating lesions in the brainstem can result in conduction slowness while remaining undetected by MRI. Despite their silence, these lesions may have a future impact on MS impairment and thus have predictive value for disease progression.

In MS patients with brainstem lesions, the sensitivity of oVEMP is the highest (85.4%), followed by cVEMP (82.1%) and vHIT (74%). The VEMP results agreed with *Rosengren et al.*

[25] who reported that oVEMP more sensitive than cVEMP in MS patients, this was related to the increased prevalence of lesions in MLF. oVEMP and cVEMP were more sensitive than vHIT because they assess both ascending and descending vestibular pathways in the brainstem respectively, resulting in a higher rate of abnormalities.

In MS patients with brainstem lesions, gains in both the lateral and posterior canals of vHIT were negatively correlated with the latencies of both cVEMP and oVEMP (table5). This could be explained by many researches: while Gazioglu and Boz [21] found a statistically significant prolongation in both VEMPs' latencies, Pavlović et al [12] observed a significantly reduced gain on vHIT in MS patients.

In line with previous findings [21, 26], MS patients with clinical symptoms of brainstem involvement had a higher VEMP abnormality (delayed latency) than patients with no symptoms of brainstem involvement. Furthermore, our cases that had brainstem symptoms had significantly lower vHIT lateral and posterior canal gains (table 6). As a result, vHIT and VEMP, particularly the oVEMP test, can be used as valuable tools with predictive value in evaluating brainstem involvement in MS patients.

CONCLUSIONS

The vHIT and VEMP tests are simple and valuable methods for assessing brainstem involvement in MS patients. The most frequently observed abnormalities in MS patients were delayed VEMP latencies and decreased vHIT lateral and posterior canal gain. Additionally, these tests may be beneficial in detecting silent brainstem lesions, providing predictive value for disease diagnosis and progression.

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