

Vestibular-evoked myogenic potential: an easy neurophysiological tool for evaluating brain stem involvement in multiple sclerosis

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Background

Vestibular-evoked myogenic potentials (VEMPs) are an applicable neurophysiological technique that can be used for diagnosis of brain stem involvement in patients with multiple sclerosis (MS).

Aim

The aim was to evaluate the relationship between VEMP parameters, clinical characteristics, and brain stem lesions in patients with MS.

Patients and methods

The study was a case–control study done on 20 patients with MS and 10 normal controls. The disability level of the patients was assessed by the expanded disability status scale and brain stem functional system score (FSS). Location of demyelinating lesions was determined from brain and spinal cord MRI scans. VEMP was done for all patients and controls.

Results

Overall, 60% ($n=12$) of patients with MS were found to have absent VEMP latency (P13–N23) in both right and left side. Patients with preserved VEMP latency were found to have significantly delayed latency (P13–N23) in both right and left sides than controls. Comparison between patients with delayed VEMP latency and those with absent VEMP latency in disease characteristics revealed that there was a statistically significant difference between them in disease duration ($P=0.001$), expanded disability status scale score ($P=0.01$), and functional system score ($P=0.04$). The group of patients with vestibular symptoms or brain stem lesions was found to have significantly more absent VEMP latency than those without.

Conclusion

Patients with MS may have abnormal VEMP, especially those with long disease duration, vestibular symptoms, greater disability, and brain stem lesions.

Keywords:

expanded disability status scale, functional system score, multiple sclerosis, vestibular, vestibular-evoked myogenic potentials

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Introduction

Multiple sclerosis (MS) is a chronic neurodegenerative demyelinating disorder of the central nervous system. Till now, the definite causes that can provoke it are unknown, although various autoimmune mechanisms are known to be involved. The hypothesis has been proposed that MS can be produced by multiple genetic and environmental factors; these may include some viral infections or other factors in childhood or during pregnancy that may cause abnormal reaction of the immune system [1,2].

Diagnosing MS is a complex task. In fact, reliable diagnosis of MS is through postmortem autopsy or biopsy, although it can be clinically diagnosed through the presence of disseminated neurological deficits in both time and space [3].

During the course of MS, ~65% of patients may develop one or more clinical symptoms or signs of brain stem affection. The importance of brain stem involvement in MS has been investigated in several studies revealing good prediction of future disability [4]. Anatomical localization of brain stem lesions on the MRI does not show adequate correlation with clinical signs of brain stem affection; ~60% of patients with brain stem signs have corresponding MRI lesions [5]. Patients with MS frequently report vestibular symptoms like vertigo and dizziness, in the course of their illness [6].

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The vestibular-evoked myogenic potentials (VEMPs) are considered a good neurophysiological tool that can be used in the diagnosis of brain stem involvement and demonstrating the presence of demyelinating lesions in the vestibulospinal tract in patients with MS [7,8].

VEMP is a myogenic potential generated by a sound stimulus that allows noninvasive exploration of the vestibular sense organ (sacculae and inferior vestibular nerve). VEMP acoustic stimulus can be evoked by presenting clicks through headsets. The macula is activated by sound stimulus, generating an electrical potential which goes through the pathway of the inferior vestibular nerve, lateral vestibular nerve, vestibulospinal tract, and finally, ipsilateral motor neuron of neck muscle [9].

In the cervical VEMP test, an inhibitor reflex (the vestibulocollic reflex) is activated, and recording is performed from the tonically contracted ipsilateral sternocleidomastoid muscle to provide information about the vestibulospinal pathway. This reflex arc includes neuroreceptors of the saccular macula, inferior vestibular nerve, lateral vestibular nucleus, medial vestibulospinal tract, and spinal cord motor neurons that supply the neck muscles [10].

Aim of work

The aim of this study was to evaluate the relationship between VEMP parameters, clinical characteristics, and brain stem lesions in patients with MS.

Patients and methods

Study design and population

This is a case–control study carried out on 20 patients with MS and 10 normal controls. They were recruited from the Neurology Outpatient Clinics of Bani-Suef University Hospital.

Inclusion criteria

A total of 20 patients fulfilled the McDonald diagnostic criteria for MS, 2010. Controls were recruited from medical personnel and healthy volunteer relatives of patients. All individuals participated willingly in the study.

Exclusion criteria

Both patients with MS and control groups who had conductive or sensorineural hearing loss, peripheral vestibular disease, or sternocleidomastoid muscle pathology (traumatic injury or weakness) were excluded from the study. Moreover, in both MS and

control groups, hearing thresholds were less than or equal to 25 dB hearing level at 250, 500, 1000, 2000, 4000, and 8000 Hz.

Methods

Demographic characteristics of the patients, disease duration, presence of an MS attack within the previous year, and neurologic assessment were recorded. Vestibular symptoms like dizziness and vertigo which occurred within 3 months before the VEMP testing and were still present were recorded. The disability of the patients was assessed by the expanded disability status scale (EDSS) and brain stem functional system score (FSS). Location of demyelinating lesions in the brain and spinal cord was determined from MRI scans. All patients and controls had otoscopic examination, pure tone audiometry, tympanometry, and stapedial reflex tests.

Vestibular-evoked myogenic potentials

VEMP was performed using Interacoustic Eclipse 'EP15' (Interacoustics, Denmark). The surface electrodes were placed as follows: the active (positive) electrode placed on both right and then left sided of the upper two-thirds of the sternocleidomastoid muscles, the inverting (negative) electrode placed on the upper sternum (suprasternal notch), and the ground electrode placed on the forehead. Two repeatable recordings were obtained for each condition. Participants were given 30–60 s to relax between each recording to avoid fatigue. During recording, the participant is instructed to raise his head and tilt it away from the stimulated side throughout the test to ensure good muscle tone. The VEMP responses were obtained by binaural acoustic stimulation and recorded from bilateral sternocleidomastoid muscles. Short tone burst was initiated at frequency of 500 Hz of a rarefaction polarity, with 4 ms rise/fall time and 2 ms plateau. Blackman ramp was used for stimulation. Intensity used is 95 dBHL presented through TDH39 headphones. Stimulus repetition rate is 5.1. The accepted number of response was 200. VEMP response was judged as either present or absent according to the presense or absence of P13–N23 biphasic response.

Statistical methods

The data were coded and entered using the statistical package for the social sciences version 15 (SPSS v 15; SPSS Inc., Chicago, Illinois, USA). Descriptive statistics were reported as mean±SD for continuous variables and number (%) for categorical variables. Student's *t*-test was used for comparison between means of two groups of quantitative variables. χ^2 -Test was used for comparison between two

groups of categorical data or frequency of events. The Pearson correlation coefficient (r) was used to describe the degree of relationship between two variables. The sign of correlation coefficient (+, -) defines the direction of the relationship, either positive or negative. The probability/significance value of greater than or equal to 0.05 is not statistically significant and less than 0.05 is statistically significant.

Results

The mean age of patients with MS was 36.80 ± 4.514 years, whereas the mean age of controls was 34.40 ± 6.43 years. Overall, 65% ($n=13$) of the included patients with MS were females and 35% ($n=7$) were males. Regarding controls, 60% ($n=6$) of the included participants were females and 40% ($n=4$) were males (Table 1).

Regarding disease characteristics in the included patients with MS, the mean value for disease duration was 4.4 ± 1.81 , the mean value for EDSS score was 4.68 ± 1.2 , and the mean value for FSS score was 1.6 ± 1.2 . Overall, 40% ($n=8$) of the patients has vestibular symptoms, 75% have at least an MS attack within the current year, and 45% had brain stem lesions (Table 2).

VEMP was done for all patients with MS and controls included in this study. Overall, 60% ($n=12$) of patients with MS were found to have absent VEMP latency (P13–N23) in both right and left sides and 40% ($n=8$) were found to have preserved latency (Table 3). Patients with preserved VEMP latency were found to have significantly more prolonged latency (P13–N23) in both right and left sides than controls (Table 4). There were no statistically significant differences between patients with preserved VEMP and controls in the mean value of VEMP amplitude or interaural amplitude ratio in right or left side (Table 4).

Comparison between patients with delayed VEMP latency and those with absent VEMP latency in disease characteristics revealed that there was a statistically significant difference between them in

Table 1 Demographics of patients with multiple sclerosis and controls

	Patients ($n=20$)	Controls ($n=10$)	<i>P</i> value
Age [mean (SD)]	36.80 (4.514)	34.40 (6.43)	0.244
Sex [n (%)]			
Male	7 (35)	4 (40)	0.789
Female	13 (65)	6 (60)	

$P \geq 0.05$, nonsignificant. * $P < 0.05$, significant.

disease duration ($P=0.001$), EDSS score ($P=0.01$), and FSS ($P=0.04$). The group of patients with vestibular symptoms or brain stem lesions was found to have significantly higher number of patients with absent VEMP latency than those without (Table 5).

On correlating VEMP latency with clinical characteristics of patients with MS, there was a statistically significant correlation between right N23 latency and EDSS ($P=0.023$), but there was no statistically significant correlation between VEMP latency and disease duration or FSS on right side or between VEMP latency and disease duration, EDSS, or FSS on left side (Table 6).

Discussion

VEMP recording is considered a simple technique to investigate the integrity of the vestibulospinal pathways. It provides rapid and accurate information about vestibular and vestibulospinal reflex function. Such test is very important in patients with MS, because they frequently experience vestibular symptoms related to vestibulospinal system involvement [8]. Previous studies revealed that the diagnostic sensitivity of VEMP testing in patients with MS may vary between 31 and 70% [11,12]. The present results differed from the findings obtained by several previous studies, which revealed that prolonged p1 latency may be the most common finding in patients with MS [7,9,13,14]. However, the present results are consistent with a

Table 2 Disease characteristics in patients with multiple sclerosis

	MS patients ($n=20$)
Disease duration [mean (SD)]	4.4 (1.81)
EDSS [mean (SD)]	4.68 (1.2)
FSS [mean (SD)]	1.6 (1.2)
Vestibular symptoms [n (%)]	
With	8 (40)
Without	12 (60)
MS attack [n (%)]	
With	15 (75)
Without	5 (25)
Brain stem lesion	
With	9 (45)
Without	11 (55)

EDSS, expanded disability status scale; FSS, functional system score; MS, multiple sclerosis.

Table 3 Distribution of vestibular-evoked myogenic potential response in patients with multiple sclerosis

VEMP response	Number of patients (%)
Present	8 (40)
Absent	12 (60)

VEMP, vestibular-evoked myogenic potential.

Table 4 Comparison between patients with present vestibular-evoked myogenic potential and controls in mean value of vestibular-evoked myogenic potential parameters

	Controls (n=10) [mean (SD)]	Patients with present VEMP (n=8) [mean (SD)]	P value
Right VEMP			
P13 latency	13.83 (1.145)	17.14 (0.71)	>0.001*
N23 latency	20.76 (3.43)	26.82 (0.84)	>0.001*
Left VEMP			
P13 latency	14.43 (0.702)	17.2 (0.56)	<0.001*
N23 latency	22.30 (1.725)	27.17 (0.75)	<0.001*
Right Amplitude P13–N23	61.18 (34.64)	41.88 (19.71)	0.181
Left Amplitude P13–N23	65.74 (18.51)	54.95 (28.27)	0.371
Interaural amplitude ratio (IAAD)	16.0875 (8.96)	23.3700 (10.05)	0.125

IAAD, interaural amplitude difference; VEMP, vestibular-evoked myogenic potential. $P \geq 0.05$, nonsignificant. * $P < 0.05$, significant.

Table 5 Comparison between patients with delayed vestibular-evoked myogenic potential latency and those with absent vestibular-evoked myogenic potential wave in disease characteristics

	Patients with delayed VEMP (n=8)	Patients with absent VEMP (n=12)	P value
Disease duration [mean (SD)]	2.88 (0.3)	5.42 (1.56)	0.001*
EDSS [mean (SD)]	3.88 (0.99)	5.21 (1.03)	0.01*
FSS [mean (SD)]	0.88 (0.84)	2.08 (1.38)	0.04*
Vestibular symptoms [n (%)]			
With	1 (12.5)	7 (58.3)	0.04*
Without	7 (87.5)	5 (41.6)	
MS attack [n (%)]			
With	5 (62.5)	10 (83.3)	0.29
Without	3 (37.5)	2 (16.7)	
Brain stem lesions [n (%)]			
With	0 (0)	9 (75)	0.001*
Without	8 (100)	3 (25)	

EDSS, expanded disability status scale; FSS, functional system score; MS, multiple sclerosis; VEMP, vestibular-evoked myogenic potential. $P \geq 0.05$, nonsignificant. * $P < 0.05$, significant.

Table 6 Correlation between vestibular-evoked myogenic potential latency and clinical characteristics of patients with multiple sclerosis

	Right P13 latency		Right N23 latency		Left P13 latency		Left N23 latency	
	(r) coefficient	P value	(r) coefficient	P value	(r) coefficient	P value	(r) coefficient	P value
Disease duration	-0.063	0.882	0.475	0.234	-0.182	0.666	0.239	0.569
EDSS	0.514	0.192	0.778	0.023*	0.538	0.169	0.683	0.062
FSS	-0.063	0.882	-0.056	0.895	-0.213	0.613	0.125	0.769

EDSS, expanded disability status scale; FSS, functional system score; r, Pearson's coefficient. $P \geq 0.05$, nonsignificant. * $P < 0.05$, significant.

previous study that reported absent response as the most common abnormality [11].

Prolonged latency in patients with MS has been attributed to reduced conduction velocity because of demyelination of vestibulospinal tract axons or primary afferent axons in the nerve root entry zone [6,15]. In the present study, absence of VEMP waves in 60% of patients with MS may be attributed to advanced damage to the myelin sheath or axonal degeneration because none of the patients had conductive hearing loss or history/current symptoms/signs of peripheral vestibular disease that may influence VEMP results. Although demyelinating lesions typically cause reduced conduction, severe demyelination

may cause conduction block and desynchronized conduction and phase loss, which may result in decreased amplitude or loss of response [8,11].

In the present study, patients with absent VEMP wave were found to have significantly higher disease duration than those with preserved VEMP wave, and this was consistent with a previous study that showed a statistically significant positive correlation between P13–N23 latencies and disease duration [15], and in another study 75% patients with VEMP abnormalities were found to have disease duration longer than 10 years [11]. However, another study revealed that VEMP abnormalities were not correlated with disease duration [13].

In the present study, the absence of P13–N23 waves was more frequent in patients with greater than those with lesser EDSS score, and this was consistent with the findings obtained from multiple previous studies that investigated the relationship between EDSS scores and VEMP abnormalities [13,15]. Our results also demonstrated that VEMP abnormalities were more common in patients with elevated brain stem FSS. This may be explained by the association between brain stem dysfunction and severe disability.

In the present study, absence of P13–N23 waves was more frequent in patients with MS with vestibular symptoms, greater disability, and brain stem lesions. Multiple studies had investigated the relationship between VEMP abnormalities, clinical signs, and presence of brain stem lesions. In a previous study, VEMP abnormality was consistent with clinical vestibular symptoms in 55% patients and brain stem lesions in 65% of patients [6]. Another study revealed abnormal VEMP only in the MS group that had clinical signs of brain stem involvement and found a relation between VEMP abnormalities and brain stem lesions in 36% of patients [15]. However, another study showed no relation between VEMP abnormalities and clinical vestibular signs, but there were VEMP abnormalities in 60% patients who had brain stem lesions [11]. Other studies did not show a correlation between VEMP abnormalities and clinical signs of brain stem involvement [8,13] or brain stem lesions on MRI [12,13].

Conclusion

The present study revealed that VEMP latency may be abnormal in patients with MS, especially in patients with vestibular symptoms, greater disability, and long disease duration. Furthermore, absence of VEMP waves in patients with MS may suggest involvement of the brain stem.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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