The Journal of International Advanced Otology

J Int Adv Otol 2024; 20(3): 247–254 • DOI: 10.5152/iao.2024.231269

Original Article

Cervical and Ocular Vestibular Evoked Myogenic Potentials in Fibromyalgia Syndrome Patients

Abeir Osman Dabbous[1], Noha Mahmoud Abdel Baki[2], Malak Medhat Hassanein [1], Sarah Mohamed Sheta[1]

[1]Department of Otolaryngology, Audio-Vestibular Unit, Cairo University, Kasr-Al-Ainy Faculty of Medicine, Cairo, Egypt
[2]Department of Rheumatology, Cairo University, Kasr-Al-Ainy Faculty of Medicine, Cairo, Egypt

ORCID iDs of the authors: A.O.D. 0000-0003-0288-077X, N.M.A.B. 0000-0003-1012-259X, M.M.H. 0009-0003-5258-2049, S.M.S. 0000-0001-5623-2722

Cite this article as: Dabbous AO, Abdel Baki NM, Hassanein MM, Sheta SM. Cervical and ocular vestibular evoked myogenic potentials in fibromyalgia syndrome patients. *J Int Adv Otol.* 2024;20(3):247-254.

BACKGROUND: Fibromyalgia syndrome (FMS) is a chronic pain condition that may be associated with dysfunction in the central nervous system.

OBJECTIVE: The aim of this study was to assess the vestibulo-spinal reflex (VSR) and vestibulo-ocular reflex (VOR) in FMS using the cervical vestibular evoked myogenic potential (cVEMP) and ocular vestibular evoked myogenic potential (oVEMP) tests, respectively, and to evaluate their relation to disease severity.

METHODS: This study included 30 female FMS patients and 30 well-matched healthy controls. They underwent full history taking and assessment of the severity of dizziness/vertigo using the Dizziness Handicap Inventory; assessment of the severity of FMS symptoms using the Revised Fibromyalgia Impact Questionnaire; bedside examination of the dizzy patient; videonystagmography, cVEMP, and oVEMP tests; basic audiologic evaluation; and uncomfortable loudness level (UCL) testing.

RESULTS: Dizziness was reported in 46.6% and vertigo in 11.1% of patients. Abnormalities in cVEMP (50%) and oVEMP (63.3%) were mostly unilateral, irrespective of FMS severity. Disease duration affected only the oVEMP amplitude. Fibromyalgia syndrome patients had a statistically significant lower UCL and narrower dynamic range compared to controls.

CONCLUSION: The VSR and VOR are commonly affected in FMS patients, and findings suggest central sensitization involving the brain stem. We recommend routine cVEMP and oVEMP testing to assess brainstem function in FMS patients.

KEYWORDS: cVEMP, dizziness, fibromyalgia syndrome, oVEMP, vestibulo-spinal reflex, vestibulo-ocular reflex

INTRODUCTION

Fibromyalgia syndrome (FMS) is a well-established central sensitivity-related pain syndrome. Fibromyalgia syndrome is characterized by widespread or multisite muscle pain lasting longer than 3 months, frequently accompanied by chronic fatigue, problems in memory, phonophobia, and photophobia as well as sleep and mood disturbances. Dizziness, vertigo, and imbalance are common complaints in FMS.[1,2] But patients show normal findings when clinically examined musculo-skeletally and neurologically.[3] The etiology of FMS is still unknown,[4] although genetic predisposition, prior physical or psychological trauma, or other risk factors. The prevalence of fibromyalgia is 2.1%, with a tendency to occur more in women. Fibromyalgia increased with age: 0.8%, 2.5%, and 3% in those <40, 40-59.9, and >60 years of age, respectively.[3]

A short-latency electromyographic response known as the vestibular evoked myogenic potential (VEMP) is recorded when the vestibular receptors are activated by sound or vibration. Cervical VEMP (cVEMP) is used to evaluate the saculo-colic reflex descending in the brainstem, while ocular VEMP (oVEMP) is used to evaluate the utriculo-ocular reflex ascending in the brainstem. The cVEMP pathway involves neural impulses from the saccular maculae to the inferior vestibular nerve (IVN) reaching the brainstem; the vestibular nucleus then descends through the medial vestibulospinal tract to the spinal accessory nerve to supply the sternocleidomastoid muscle in the neck. The cVEMP pathway involves impulses from the utricular maculae to the superior vestibular nerve

Corresponding author: Abeir Osman Dabbous, e-mail: abeirdabbous@kasralainy.edu.eg

Received: July 1, 2023 • **Revision requested:** August 27, 2023 • **Last revision received:** November 9, 2023 • **Accepted:** November 29, 2023 • **Publication Date:** May 23, 2024

Available online at www.advancedotology.org

and then the brainstem. The vestibular nucleus then ascends in the medial longitudinal fasciculus after crossing in the upper medulla and pons, to the oculomotor nuclei supplying the inferior oblique muscle of the eye.[5]

Although the audiologic findings have been previously studied,[6,7] in fibromyalgia syndrome patients, as far as we know, few studies about vestibular brainstem pathways,[6] in fibromyalgia syndrome patients, namely the saculo-colic and the utriculo-ocular reflexes, have been conducted.

This study aims to assess the vestibulospinal reflex as well as vestibulocular reflex pathways' integrity in the brain stem in patients with FMS through testing the cVEMP and oVEMP tests, respectively, and to evaluate their relation to disease symptom severity.

MATERIAL AND METHODS

Sample size in this cross-sectional study was calculated using Epi-calc 2000, taking into account preceding research evidence and the percentage of negative VEMP response outcomes in FMS. A rate of 80% was taken for power, and significance was set at a level of .05, 12.12% of FMS exposed, to detect odds ratio (OR) = 6 and a ratio of cases to controls = 1. Sample size would be 54 participants equally distributed in the 2 groups (27 each). A rate of 10% was taken for dropouts, so the sample size would finally include 60 participants equally distributed in the 2 groups (30 each). It included 30 FMS patients diagnosed at the Department of Rheumatology and Rehabilitation, aged between 20 and 50 years old, who were compared to 30 healthy volunteers matched to controls regarding age and gender.

Inclusion Criteria

Patients with FMS were diagnosed at the Department of Rheumatology and Rehabilitation according to the following diagnostic criteria: (a) pain on the left and right sides of the body, pain above and below the waistline, and pain in the axial skeleton that has lasted for at least 3 months (cervical column or anterior thoracic column, or thoracic column or lumbar column). Pain on either the shoulder or the buttock is considered pain on both sides. (b) Pain in at least 11 of the 12 palpated "tender points" with a strength of roughly 4 kg. To be considered a positive "tender point," the patient must state that palpation was painful. It was conducted in the period from April 2022 to April 2023, in the Audio-Vestibular Medicine Unit, ENT Department, Faculty of Medicine in the Cairo University, after the approval of the Otolaryngology Department Council and Medical Research Ethical Committee (Approval No: MS-203-2022). Informed consent was obtained from all subjects.

Exclusion Criteria

The following are the exclusion criteria: history of surgery in 1 or both ears, previous head trauma, brain tumor, anatomical abnormalities of the external auditory canals, conductive hearing loss, other peripheral or central vestibular disorder, any other rheumatological co-morbidities, other neurological, psychiatric, or significant medical disorder, oculomotor nerve lesion hindering the testing, anatomical abnormalities in facial muscles hindering the testing, other neck problems hindering the testing, or absence of 1 or both sternocleidomastoid muscles hindering the testing. Participants in this study had undergone: *(*1) comprehensive history taking; (2) evaluation of dizziness/vertigo severity by the Dizziness Handicap Inventory (DHI)[8] in its Arabic-translated form;[9] 3) otoscopy; (4) audiometric testing: air and bone conduction *Pure tone* thresholds at octave intervals, Speech Recognition threshold, and Word Recognition score by Itera II audiometer (Madsen from GN Otometrics, Denmark); (5) tympanometry by the 226Hz middle ear analyzer Zodiac 901 (Madsen from GN Otometrics, Denmark); (6) testing for the pure tones' intensity uncomfortable loudness level by at 0.5, 1, 2, and 4kHz; (7) assessing the severity of fibromyalgia syndrome by the Arabic-translated[10] Revised version of the Fibromyalgia Impact Questionnaire (FIQ-R);[11] (8) bedside examination of dizzy patient; (9) videonystagmography to exclude peripheral vestibular lesion, using Visual Eyes™, Micromedical Technologi es(Micromedical Corporation, USA); and (10) cVEMP and oVEMP: using Neuro-Soft version 1.0.96.0. (Neurosoft Ltd., Russia). It was ensured that the FMS cases were not in a flare-up (attack) during the recording. After exclusion of conductive hearing loss, a 0.5 kHz tone burst, having a rise and fall time of 1 ms and a plateau of 2 ms, was delivered by air conduction at a level of 95 dB nHL through ER-3A insert earphones. The impedance was maintained below 5 kOhms, respectively. Rectification was used to normalize electromyographic activity. In cVEMP, surface electrodes were symmetrically applied on the SCM mid-third (inverting electrodes) and on the upper sternum laterally (non-inverting electrodes). Participants were instructed to elevate their head from supine or to have their neck rotated in an upright position. P13 and N23 latency (in ms) and P13-N23 peak-to-peak amplitude (in μV) and the amplitude asymmetry ratio (interaural amplitude difference (IAD)) were assessed. During the oVEMP test, the noninverting electrode was placed at 1 cm, the inverting electrode was 3 cm below the middle of the opposite lower eyelid, and the ground electrode was applied on the forehead. Subjects were asked to have their gaze elevated from 30˚ to 35˚ when recording. N10 and P15 latencies, and N15-P10 peak-to-peak amplitude and IAD were assessed.

Statistical Analysis

Data were entered in Microsoft Excel 365 and analyzed by the the Statistical Package for Social Science Statistics software version 24.0 (IBM SPSS Corp.; Armonk, NY, USA). Results were statistically described quantitatively by the arithmetic mean and SD and qualitatively by frequency and percent. Correlations were made by Pearson correlation coefficient bivariate relationship quantitatively and chi-square (or Fisher's exact test if needed) qualitatively. Comparisons were made quantitatively by t-independent test (or Mann–Whitney if needed). A *P*-value less than .05 was taken as statistically significant.

MAIN POINTS

- Dizziness is more common than vertigo in Fibromyalgia syndrome.
- cVEMP and oVEMP abnormalities are common in Fibromyalgia syndrome but are not correlated to disease severity.
- Findings suggest central auditory sensitization involving the brainstem in Fibromyalgia syndrome.

RESULTS

The mean age of the study group was 34 ± 8.16 (21-49) years and was 100% female. The mean age of the control group was 31.07 ± 7.83 (21-48) years, with 27 females and 3 males. The mean symptom

Table 1. The mean, SD, and Range of the Revised Fibromyalgia Impact Questionnaire in Fibromyalgia Syndrome patients (n = 30), and the Dizziness Handicap Inventory Scores in Fibromyalgia Patients with Dizziness and/or Vertigo (n = 14)

	Mean	SD	Minimum	Maximum
FIQR				
FIQR function	15.47	3.64	9	25.5
FIQR overall	12.2	2.59	7	16
FIQR symptoms	29.16	5.91	20	42
FIQR total score	56.84	10.42	36	76
DHI				
DHI—functional score	10.71	4.99	2	20
DHI—physical score	10	6.61	2	26
DHI—emotional score	10.86	4.62	2	20
DHI—total score	31.57	10.76	16	52

DHI, Dizziness Handicap Inventory; FIQR, Fibromyalgia Impact Questionnaire.

duration was 5.93 ± 25 (2-11) years. Cases and controls did not differ statistically significantly regarding age or gender distribution. Participants in this study had normal middle ears reflected in the type A tympanograms bilaterally. Fourteen of 30 patients (46.7%) had dizziness, and 3/30 (10%) had vertigo. The FIQ-R and DHI scores in FMS patients are shown in Table 1 (n = 14). Nine patients (64.3%) had a mild degree of dizziness handicap, and 5 (35.7%) had a moderate degree of dizziness handicap. While vertigo was reported in 3 patients in addition to the dizziness, all the cases had normal posture and gait on bedside examination. None had nystagmus, and all had normal oculographic test findings.

The biphasic cVEMP was recorded in all cases in both ears, while the biphasic oVEMP was unilaterally lost in 2 cases only. Table 2 shows a comparison between cases having FMS and controls as regards cVEMP latencies, amplitudes, and Inter-aural amplitude difference (IAAD) and rectified IAAD. Table 3 shows the results of cVEMP in the cases. Table 4 shows a comparison between cases having FMS and controls as regards oVEMP latencies, amplitudes, and IAAD and rectified IAAD. Table 5 shows the results of oVEMP in the cases.

No statistically significant correlation was found between latencies of cVEMP or amplitude of cVEMP in either ear or cVEMP IAAD with the FIQ-R scores or with any of the DHI subscale scores or total scores. The same was true for oVEMP, except for a direct correlation between oVEMP Inter-aural amplitude difference ratio (IAAR) and Fibromyalgia Impact Questionnaire (FIQR) scores, and except for a direct correlation between the functional subscale score of the dizziness handicap inventory (DHI- F score) and both left N10 and P15 latencies (i.e., the worse [greater] the DHI F score, the more delayed were N10 and

Table 2. Cervical Vestibular Evoked Myogenic Potential Latencies and Amplitudes (Right and Left Ears) and IAAD and Rectified IAAD in Cases and Controls

	Group	Cervical Vestibular Evoked Myogenic Potential				*t* Value	*P*
		Mean	SD	Minimum	Maximum		
Right							
Latency P13 (ms)	Cases	14.05	2.11	9.1	18.3	−0.654	.516
	Controls	14.34	1.25	12.4	16.9		
Latency N23 (ms)	Cases	22.06	3.65	16.7	30.8	−0.399	.692
	Controls	22.38	2.28	16.7	27.2		
Amplitude P13-N23 (μv)	Cases	37.37	23.36	0.6	109.9	1.645	.105
	Controls	28.94	15.55	9.7	69.3		
Rectified Amplitude P13-N23 (μv)	Cases	0.72	0.39	0.3	2.1	1.815	.075
	Control	0.55	0.31	0.2	1.4		
Left							
Latency P13 (ms)	Cases	14.98	2.92	10.8	26.3	1.396	.188
	Controls	14.15	1.41	12.5	16.7		
Latency N23 (ms)	Cases	22.45	3.27	17.7	34.3	1.736	.088
	Controls	21.17	2.36	16.8	26.9		
Amplitude P13-N23 (μv)	Cases	40.75	0.51	0.8	108.5	2.287	.026
	Controls	30.01	0.22	12	60		
Rectified Amplitude P13-N23 (μv)	Cases	0.77	33.06	0.2	2.9	1.654	.103
	Control	0.53	13.08	0.2	1		
IAAD	Cases	21.89	19.58	0.43	69.34	2.897	.005
	Controls	10.95	6.68	1.2	25.67		
Rectified IAAD	Cases	17.55	19.47	0	71.43	1.186	.241
	Controls	13.07	7.02	0	25		

IAAD, Inter-aural amplitude difference.
A *P*-value less than 0.05 was taken as statistically significant

Table 3. Results of Cervical Vestibular Evoked Myogenic Potentials in the Right and Left Ears in Cases

		Cases (n = 30)			
		Right Ear		Left Ear	
		n	%	n	%
P13 latency	Delayed	4	13.3	4	13.3
	Normal	26	86.7	26	86.7
N23 latency	Delayed	5	16.7	4	16.7
	Normal	25	83.3	26	83.3
Amplitude P13-N23	Normal	26	86.6	29	96.6
	Decreased amplitude	4	13.3	1	3.3

P15 latencies), and a direct correlation between the total score and left N10 latency (i.e., as the total score was worse [greater], the more delayed was N10 latency).

No statistically significant correlation was found between cases with mild and cases with moderate dizziness handicap as regards the cVEMP or oVEMP latencies or amplitudes.

No statistically significant correlation was found between the duration of FMS symptoms and DHI scores or with cVEMP or oVEMP, except for a direct correlation between the duration of symptoms and oVEMP IAAD scores.

No statistically significant correlation was found between cases with dizziness and those without dizziness as regards cVEMP and oVEMP, except that the right ear N10-P15 amplitude in FMS cases having dizziness was statistically significantly larger compared to FMS cases not complaining of dizziness. oVEMP was abnormal in 78.6% of fibromyalgia patients with dizziness and in 50% of those not complaining of dizziness. And this distribution was statistically significant.

Table 6 shows a comparison between cases and controls as regards the dynamic range. 70% (21/30) of fibromyalgia patients complained of intolerance to loud sounds. But all had within normal dynamic range except for a mildly contracted dynamic range (75 dB) in 2 patients at frequencies 500, 2000, and 4000 kHz and 1 patient at 1000 kHz, in the right ear, and 1 patient at 1000 and 4000 kHz, and 2 patients at 2000 kHz in the left ear. All had excellent speech discrimination scores. No statistically significant correlation was found between cases and their controls regarding Word discrimination score (WDS) in either ear.

DISCUSSION

Dizziness was found in 46.6% of FMS patients in the current study, and vertigo was found in 11.11%. In comparison to our study, Zeigelboim and Moreira[12] found that 84% of 25 female fibromyalgia patients had dizziness. Mohamed et al[13] found that 78% of their FMS patients had imbalance and chronic vertigo (with an average duration of 30 months). They explained the dizziness to be related to

Table 4. Ocular Vestibular Evoked Myogenic Potential Latencies and Amplitudes (Right and Left Ears) and IAAD and Rectified IAAD in Cases and Controls

	Group	Ocular Vestibular Evoked Myogenic Potential				*t* Value	*P*
		Mean	SD	Minimum	Maximum		
Right							
N10 latency (ms)	Cases	11.21	1.29	13.5	17.2	2.639	.011
	Controls	10.46	0.83	12.2	17.2		
P15 latency (ms)	Cases	16.11	1.79	9.2	15.7	4.742	.000
	Controls	14.24	1.19	9.4	12.8		
Amplitude N10-P15 (μv)	Cases	3.36	3.89	0.3	13.6	−0.584	.562
	Controls	3.9	3.22	0.6	17.2		
Rectified amplitude N10-P15 (μv)	Cases	0.43	0.51	0.1	1.9	−0.607	.546
	Controls	0.49	0.22	0.2	1		
Left							
N10 latency (ms)	Cases	11.27	1.59	13.2	19.8	1.387	.171
	Controls	10.81	0.85	11.6	16.3		
P15 latency (ms)	Cases	15.77	1.45	8.8	16.1	2.632	.011
	Controls	14.89	1.11	9.5	12.8		
Amplitude N10-P15 (μv)	Cases	3.39	4.22	0.3	15.2	−0.944	.349
	Controls	4.31	3.22	0.7	17		
Rectified amplitude N10-P15 (μv)	Cases	0.37	0.38	0.1	1.5	0.152	.419
	Controls	0.43	0.19	0.1	0.9		
IAAD (uv)	Cases	29.91	27.16	1.69	100	0.38	0.000
	Controls	10.54	6.46	0.58	47.37		
Rectified IAAD (uv)	Cases	28.19	27.34	0	100	2.313	.024
	Controls	16.06	8.78	0	33.33		

Table 5. Results of Ocular Vestibular Evoked Myogenic Potential in the Right Ear in Cases and Controls

		Cases (n = 30)	
		n	%
Right ear			
N10 latency	Delayed	4	13.3
	Normal	26	86.7
P15 latency	Delayed	5	16.7
	Normal	25	83.3
Wave morphology	Normal	30	100
	Abnormal	0	0
Amplitude N10-P15	Normal	26	86.6
	Decreased amplitude	4	13.3
Left ear			
N10 latency	Delayed	3	10
	Normal	27	90
P15 latency	Delayed	3	10
	Normal	27	90
Wave morphology	Normal	30	100
	Abnormal	0	0
Amplitude N10-P15	Normal	21	70
	Decreased amplitude	9	30

musculoskeletal abnormalities and impaired proprioception, which were significantly more prevalent in FMS.

Koca et al[14] found a higher frequency of vertigo (84%) and imbalance complaints (61.3%) in their 44 FMS patients. They suggested that this may be related to the impact of fibromyalgia on the central nervous system, which can affect various bodily functions, and suggested that the presence of comorbid conditions such as vestibular dysfunction or anxiety may exacerbate these symptoms.

Bellato et al,[15] have reported that FMS can be associated with specific diseases such as rheumatic pathologies, psychiatric or neurological disorders, infections, and diabetes. However, in the present study, FMS patients with previous head trauma, brain tumors, peripheral or central vestibular disorders, any other rheumatological co-morbidities, and other neurological, psychiatric, or significant medical disorders have been excluded. So, any neurological disorder could not have been the reason for the association with a balance disorder in these patients.

Núñez-Fuentes et al[16] showed that FMS patients had worse scores of the vestibular ratio and visual ratio than the healthy controls in the Sensory Organization Test and were dependent on their somatosensation,[16] due to vestibular disorders, which affected their ability to perform daily activities independently.[17]

Mucci et al[18] found that their FMS patients suffered from vertigo and dizziness, characteristics suggestive of migraine-like central vestibular impairment. Peinado-Rubia et al,[2] showed that the FMS severity, according to the overall FIQ score, was correlated with vertigo severity, according to the DHI, which affected the stability of postural. They found that vertigo severity and severity of central sensitization, according to the central sensitization index, accounted for half of the causes behind the quality-of-life affliction in FMS.

In comparison to the cVEMPs and oVEMPs results in the present study, Tuncer et al[6] found that cVEMPs could not be obtained in 15.15% of the right ears and 12.12% of the left ears, and oVEMPs could not be

Table 6. Comparison Between Cases and Controls as Regards Dynamic Range in Right and Left Ears

Frequency			Dynamic Range				*t* value	*P*
			Mean	SD	Minimum	Maximum		
RT ear	500 Hz	Cases	89	6.49	75	95	−2.616	.011
		Controls	92.5	3.41	75	95		
	1000 Hz	Cases	87.5	6.53	75	95	−2.745	.008
		Controls	91.67	5.14	75	95		
	2000 Hz	Cases	88.17	7.01	75	95	−2.775	.007
		Controls	92.33	4.3	75	95		
	4000 Hz	Cases	87.5	7.04	75	95	−3.361	.001
		Controls	92.5	4.1	75	95		
LT ear	500 Hz	Cases	90.17	5.49	75	95	−1.701	.094
		Controls	92.33	4.3	75	95		
	1000 Hz	Cases	88.5	6.97	75	95	−3.063	.003
		Controls	92.83	3.39	75	95		
	2000 Hz	Cases	89.17	7.2	75	95	−1.447	.153
		Controls	91.5	5.11	75	95		
	4000 Hz	Cases	90.33	5.86	75	95	−1.688	.097
		Controls	92.5	3.88	75	95		

obtained in 1.21% of the right ears and 30.30% of the left ears of their 33 patients compared to none of the healthy participants.

In the present study, FMS cases showed a significantly greater mean of left cVEMP P13-N23 amplitude and significantly delayed right ear oVEMP latency than their controls and significantly delayed right ear oVEMP latency compared to controls. Dealing individually with results, cVEMPs were abnormal in 50%, of which (33.3%) had delayed latency (P13 and/or N23) and 16.67% had amplitude asymmetry. Of all FMS with abnormal cVEMPs, 93.3% showed unilateral abnormality.

In the present study, cVEMP and oVEMP mean IAAD were greater in FMS cases than controls, but only the mean rectified inter-aural amplitude difference (rIAAD) of oVEMP was greater in FMS cases than controls. However, 30% and 20% showed IAAD and rIAAD abnormalities in cVEMP, and 33.3% showed IAAD and rIAAD abnormalities in oVEMP. This reflects amplitude asymmetry between ears in fibromyalgia patients.

Bayazit et al[19] found that only the cVEMP n23 latency and the inter-peak latencies were significantly longer in FMS cases than their controls, which suggests that the sacculo-collic reflex arc and likely saccular dysfunction in FMS may have been affected. On the other hand, Zeigelboim and Moreira[12] found that the oVEMP amplitudes, but not latencies, were significantly affected in FMS patients.

It is possible that the pathophysiological mechanisms underlying fibromyalgia, such as central sensitization, may contribute to the vestibular dysfunctions observed in this population.[20] Central nervous system sensitization is a process by which the central nervous system becomes more sensitive to pain and other sensory stimuli over time. This process may affect the vestibular system by altering the way the brain processes vestibular signals, leading to greater asymmetry in vestibular function between the ears.[21]

The current study did not show any correlation between VEMP findings and the severity of FMS, as assessed by the FIQR scores. This reflects that the FMS disease process itself affects the brain stem irrespective of its severity. The current study did not show any correlation between either cVEMP or oVEMP results and duration of fibromyalgia except for a direct correlation with oVEMP IAAD, reflecting that the longer the disease duration, the more the possibility was for ear amplitude asymmetry in oVEMP. There was no correlation between the duration of fibromyalgia symptoms and dizziness severity as assessed by the DHI. Taken together, this reflects that the FMS disease process itself affects the brain stem, which can be detected as VEMP asymmetry irrespective of the dizziness complaint.

Mohamed et al[13] found that their FMS patients who had vertigo had a significantly longer duration of the disease (an average of 4.5 years) compared to patients who did not complain of vertigo (an average of 1.5 years). Hashimoto et al[22] stated that persistent postural-perceptual dizziness may be exaggerated by central nervous system sensitization. Mucci et al[18] found that dizziness and vestibular symptoms in their FMS participants correlated well with all FMS symptoms, especially the psychological depressive symptoms. However, their female participants were all of perimenopausal and menopausal age, so they would have been at risk for symptoms aggravation,[23] while the present study's mean age was 35 years.

The present study showed that most fibromyalgia patients with dizziness showed abnormal oVEMP compared to only 50% of those without dizziness, and this was statistically significant. Also, 42.90% of those with dizziness showed abnormal cVEMP compared to only 56.3% of those without dizziness, and this was not statistically significant. Moreover, the worse [greater] the DHI F score, the more delayed were N10 and P15 latencies, and as the total score was worse (greater), the more delayed was N10 latency, and as the DHI P score was worse (greater), the IAAD and rIAAD were greater.

The DHI showed that about 75% of FMS patients with absent both VEMPs, complained of vertigo.[6]

There may be other symptoms related to central sensitization that affect VEMP findings.[20] Migraine patients exhibit abnormal pain processing and increased pain sensitivity compared to healthy participants, indicating the presence of central nervous system sensitization, which is a common pathogenesis between migraine and other pain conditions like FMS. Central brainstem sensitization changes involve neuronal excitability, neurotransmitter release, and ion channel function that can result in the development of central sensitivity syndromes.[24,25]

The present study showed that although pure-tone audiometry (PTA) thresholds were statistically significantly worse in cases than controls regarding the right ear 500 Hz and average and left ear 8 kHz PTA thresholds, all were within normal hearing threshold levels.

In accordance with our study, Mohamed et al[13] reported that all FMS patients had normal hearing as assessed by PTA. Also, Bayazit et al[26] found that the audiometry results in 95.83% of patients with FMS were normal. Accordingly, they suggested that fibromyalgia does not have a direct effect on the cochlea. Kapusuz Gencer et al[7] found that FMS patients had within the normal hearing threshold at low frequencies (250-2000 Hz), but significant hearing loss at higher frequencies. However, in Kapusuz Gencer et al[7] study, the mean age of the patients was 48.1 $\pm$ 9.4 years (range: 30-65 years). This age was higher than the current study mean (35 years), with a minimum of 27 and a maximum of 57 years, and was higher than the mean age in the Mohamed et al[13] study (36 years), with a minimum of 22 and a maximum of 50 years, suggesting the possibility of the presence of presbycusis as an explanation for high-frequency hearing loss.

In the current study, all FMS cases had within a normal dynamic range except for a mildly contracted dynamic range (75 dB) in 3 FMS patients compared to controls. However, cases had a statistically significant narrower dynamic range compared to their controls at 1,2 & 4kHz in the right ears and at 1kHz in the left ears. In accordance with our study, Staud et al[27] investigated the presence of hyperacusis (sound sensitivity) in patients with FMS by measuring their UCL. They found that FMS cases had significantly decreased UCL than their controls, indicating the presence of hyperacusis in this population, as part of the central auditory nervous system sensitization.[28,29] Hyperacusis may also be due to mandibular joint dysfunction, which is also common in FMS.

Word discrimination score (WDS) in FMS cases in the present study did not significantly differ from the controls. Fibromyalgia syndrome may have a mild effect on speech discrimination ability but is not significant enough to cause clinically relevant hearing difficulties.[13]

The presence of normal PTA in the current study reflected normal peripheral hearing. However, the presence of statistically significantly lower UCL and narrower dynamic range in FMS cases compared to controls, in addition to the presence of sacculocolic and utriculo-ocular reflex dysfunction, are suggestive of brain stem involvement in hyperacusis, i.e., central hyperacusis, which reflects increased central auditory gain, further highlighting the presence of central sensitization in FMS. This is in accordance with the central pain pathogenesis in FMS, the increased central gain in fibromyalgia, and how it may contribute to the widespread pain experienced by patients with this condition. Thus, the oVEMP and cVEMP can objectively reflect brain stem dysfunction in the form of central sensitization occurring in FMS patients irrespective of the disease severity or duration.

Fibromyalgia patients exhibit changes in pain processing in the form of increased excitability and changes in sensory integration within the brain.[29] Fibromyalgia syndrome patients also exhibit increased levels of substance P and other neuropeptides that are involved in central sensitization. Central pain and sensitization are believed to be a result of changes in the processing of pain signals within the central nervous system.[28,30] These changes can be caused by a variety of factors, such as injury, inflammation, or prolonged exposure to nociceptive stimuli.[31] Fibromyalgia syndrome results from dysfunction in the processing of pain centrally rather than peripherally.[20]

Limitations of This Study

Limitations in the current study include the subjects' small number and the fact that most cases showed a mild degree of dizziness handicap, limiting the ability for correlation with the VEMP parameters.

Ocular vestibular evoked myogenic potentials and cVEMP are commonly affected (in 63.7% and 50% of FMS, respectively), reflecting urticulo-ocular and sacculo-colic reflex dysfunction, mostly unilaterally, where latency was more affected than amplitude in cVEMP, while amplitude was more affected than latency in oVEMP. Vestibular-evoked myogenic potential abnormalities were not dependent on disease severity, reflecting that the reflex dysfunction is caused by the occurrence of the disease process itself. Ocular-VEMP amplitude decreases as the FMS duration of symptoms increases, but cVEMP is not affected by the FMS duration. Fibromyalgia syndrome is associated with hyperacusis, which could be of a central etiology due to central sensitization, i.e., increased central auditory gain involving the brain stem.

We recommend routine cVEMP and oVEMP in the assessment of sacculo-colic and urticulo-ocular reflexes in FMS patients as an objective tool to assess the brainstem. As of yet, there are neither objective laboratory nor radiological investigations to diagnose FMS. We recommend assessment of the afferent and efferent brain stem auditory pathways in fibromyalgia syndrome, through testing by the auditory brain stem response and contralateral suppression of otoacoustic emission respectively. We also recommend studying the effectiveness of vestibular rehabilitation therapy in improving dizziness symptoms in patients with FMS. A better understanding of the underlying mechanisms of FMS can help develop effective treatments for this condition.

Ethics Committee Approval: This study was approved by Ethics Committee Approval: This study was approved by Ethics committee of Cairo University (Approval No: MS-203-2022).

Informed Consent: Informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.D.; Design – A.D.; Supervision – A.D., N.A., S.S.; Resources – M.M.; Materials – M.M.; Data Collection and/or Processing – M.M.; Analysis and/or Interpretation – M.M, A.D., N.A., S.S.; Literature Search – M.M.; Writing – A.D., M.M.; Critical Review – A.D., N.A., S.S.

Declaration of Interests: The authors have no conflicts of interest to declare.

Funding: The authors declared that this study had received no financial support.

REFERENCES

1. Clauw DJ. Fibromyalgia: a clinical review. *JAMA*. 2014;311(15):1547-1555. [CrossRef]
2. Peinado-Rubia A, Osuna-Pérez MC, Rodríguez-Almagro D, Zagalaz-Anula N, López-Ruiz MC, Lomas-Vega R. Impaired balance in patients with fibromyalgia syndrome: predictors of the impact of this disorder and balance confidence. *Int J Environ Res Public Health*. 2020;17(9):3160. [CrossRef]
3. Gilliland BC. Fibromyalgia, arthritis associated with systemic disease, and other arthritides. In: Kasper D. L., Harrison T. R., eds. *Harrison's Principles of Internal Medicine*, Vol 2, 16th edn. New York, NY, USA: McGraw-Hill, Medical Publication Division; 2005: 2055-2064.
4. Bohn D, Bernardy K, Wolfe F, Häuser W. The association among childhood maltreatment, somatic symptom intensity, depression, and somatoform dissociative symptoms in patients with fibromyalgia syndrome: a single-center cohort study. *J Trauma Dissociation*. 2013;14(3):342-358. [CrossRef]
5. Rosengren SM, Colebatch JG, Young AS, Govender S, Welgampola MS. Vestibular evoked myogenic potentials in practice: methods, pitfalls and clinical applications. *Clin Neurophysiol Pract*. 2019;4(4):47-68. [CrossRef]
6. Tuncer M, Çoban K, Erbek S, Erbek HS. Audiovestibular dysfunction in patients with fibromyalgia syndrome. *J Int Adv Otol*. 2021;17(4):348-352. [CrossRef]
7. Kapusuz Gencer Z, Balbaloğlu Ö, Özkırış M, Saydam L. Does fibromyalgia have an effect on hearing loss in women? *Turk J Med Sci*. 2017;47(6):1699-1702. [CrossRef]
8. Jacobson GP, Newman CW. The development of the Dizziness Handicap Inventory. *Arch Otolaryngol Head Neck Surg*. 1990;116(4):424-427. [CrossRef]
9. Alsanosi AA. Adaptation of the dizziness handicap inventory for use in the Arab population. *Neurosciences (Riyadh)*. 2012;17(2):139-144.
10. Abu-Dahab S, AbuRuz SM, Mustafa K, Sarhan Y. Validation of the Arabic version of the revised Fibromyalgia Impact Questionnaire (FIQR_A) on Jordanian females with fibromyalgia. *Clin Rheumatol*. 2014;33(3):391-396. [CrossRef]
11. Bennett RM, Friend R, Jones KD, Ward R, Han BK, Ross RL. The revised Fibromyalgia Impact Questionnaire (FIQR): validation and psychometric properties. *Arthritis Res Ther*;11(5):R120. [CrossRef]. Erratum in: *Arthritis Res Ther*. 2009;11(5):415. (https://doi.org/10.1186/ar2830)

12. Zeigelboim BS, Moreira DN. Vestibular findings in fibromyalgia patients. *Int Arch Otorhinolaryngol*. 2011; 15(3):283-289.
13. Mohamed AS, Abousetta AA, Hefny MA, Farid AM. Peripheral vestibular function in patients with fibromyalgia. *EJENTAS*. 2018;19(3):217-221.
14. Koca TT, Tugrul A, Eksioglu M. Evaluation of hearing in patients with fibromyalgia syndrome. *J Craniofac Surg*. 2018;29(5):e463-e466.
15. Bellato E, Marini E, Castoldi F, et al. Fibromyalgia syndrome: etiology, pathogenesis, diagnosis, and treatment. *Pain Res Treat*. 2012;2012:426130. [CrossRef]
16. Núñez-Fuentes D, Obrero-Gaitán E, Zagalaz-Anula N, et al. Alteration of postural balance in patients with fibromyalgia syndrome-A systematic review and meta-analysis. *Diagnostics (Basel)*. 2021;11(1):127. [CrossRef]
17. Pérez-de-Heredia-Torres M, Huertas-Hoyas E, Martínez-Piédrola R, et al. Balance deficiencies in women with fibromyalgia assessed using computerised dynamic posturography: a cross-sectional study in Spain. *BMJ Open*. 2017;7(7): e016239.
18. Mucci V, Demori I, Rapallo F, et al. Vestibular disability/handicap in fibromyalgia: a questionnaire study. *J Clin Med*. 2022;11(14):4017. [CrossRef]
19. Bayazit YA, Celenk F, Gunduz AG, Gunduz B, Ondag N, Meray J. Vestibular evoked myogenic potentials in patients with fibromyalgia syndrome. *J Laryngol Otol*. 2010;124(6):610-615. [CrossRef]
20. Staud R, Smitherman ML. Peripheral and central sensitization in fibromyalgia: pathogenetic role. *Curr Pain Headache Rep*. 2002;6(4):259-266. [CrossRef]
21. Yunus MB. Fibromyalgia and overlapping disorders: the unifying concept of central sensitivity syndromes. *Semin Arthritis Rheum*. 2007;36(6):339-356. [CrossRef]
22. Hashimoto K, Takeuchi T, Ueno T, et al. Effect of central sensitization on dizziness-related symptoms of persistent postural-perceptual dizziness. *Biopsychosoc Med*. 2022;16(1):7. [CrossRef]
23. Martínez-Jauand M, Sitges C, Femenia J, et al. Age-of-onset of menopause is associated with enhanced painful and non-painful sensitivity in fibromyalgia. *Clin Rheumatol*. 2013;32(7):975-981. [CrossRef]
24. Burstein R, Noseda R, Borsook D. Migraine: multiple processes, complex pathophysiology. *J Neurosci*. 2015;35(17):6619-6629. [CrossRef]
25. Dodick DW. A phase-by-phase review of migraine pathophysiology. *Headache*. 2018;58(suppl 1):4-16. [CrossRef]
26. Bayazit YA, Gürsoy S, Ozer E, Karakurum G, Madenci E. Neurotologic manifestations of the fibromyalgia syndrome. *J Neurol Sci*. 2002;196(1-2):77-80. [CrossRef]
27. Staud R, Godfrey MM, Robinson ME. Fibromyalgia patients are not only hypersensitive to painful stimuli but also to acoustic stimuli. *J Pain*. 2021;22(8):914-925. [CrossRef]
28. Latremoliere A, Woolf CJ. Central sensitization: a generator of pain hypersensitivity by central neural plasticity. *J Pain*. 2009;10(9):895-926. [CrossRef]
29. Cagnie B, Coppieters I, Denecker S, Six J, Danneels L, Meeus M. Central sensitization in fibromyalgia? A systematic review on structural and functional brain MRI. *Semin Arthritis Rheum*. 2014;44(1):68-75. [CrossRef]
30. Woolf CJ. Central sensitization: implications for the diagnosis and treatment of pain. *Pain*. 2011;152(3suppl):S2-S15. [CrossRef]
31. Basbaum AI, Bautista DM, Scherrer G, Julius D. Cellular and molecular mechanisms of pain. *Cell*. 2009;139(2):267-284. [CrossRef]