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Research Article

COMPARATIVE ASSESSMENT OF AUDITORY AND VESTIBULAR FUNCTIONS IN MULTIPLE SCLEROSIS PATIENTS USING AUDIOLOGICAL DIAGNOSTIC TOOLS

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ABSTRACT

Objective: As a demyelinating disease of the central nervous system, multiple sclerosis (MS) can be marked by tiredness, ataxia, sensory complaints, attention, and motor speech, as well as weakness in the arms and legs. Cortical symptoms, cognitive decline, hearing loss and epileptic seizures are typical symptoms. The aim of this study is to determine the impact of MS on the auditory and vestibular pathways.

Materials and Methods: MS patients mental abilities were assessed in this study, accounting for vestibular and auditory function. Fifteen MS patients and fifteen healthy controls were recruited. The experimental and patient groups underwent vestibular and audiological testing and the results from these two groups were compared. The patients underwent simultaneous impedance audiometry.

Results: The data from our study showed significant results for the right and left ears of MS patients when we used pure tone audiometry. In the Auditory Brainstem Response (ABR) test, unilateral sensorineural hearing loss was observed in seven patients. On the Video Head Impulse Test (VHIT), the vestibulo-ocular reflex (VOR) gains of 9 MS patients were outside normal limits, while the VOR gains of one patient were low in the left lateral canal. On the Vestibular evoked myogenic potentials test, wave latencies were delayed in 12 of the patients and the left P1 and N1 waveforms were not observed in two patients.

Conclusion: Based on the findings of our study, we can say that auditory and vestibular functions are significantly impaired in MS patients. We can recommend that studies with larger patient populations should be developed.

Keywords: ABR, MS, psychosocial problems, vestibular function tests, pure tone audiometry.

INTRODUCTION

Multiple Sclerosis (MS) is a chronic, inflammatory, demyelinating disease that is usually seen in young adults and causes neurological and cognitive function loss (1). It has been shown that gray matter and white matter are affected. Genetic and various environmental factors influence the disease's development (2). Movement issues, migraines, epileptic seizures, hearing loss, cognitive decline, and cortical symptoms are typical symptoms (3). MS symptoms may occur as prodromal or acute episodes. Although the disease's first findings are mostly in remission, remission or partial attacks are seen or not seen in later ataxias (4, 5). Evoked potential (EP) examinations are most frequently applied in the clinic to diseases that cause demyelinating lesions in the central nervous system, especially MS (6). The electrical potentials are recorded by applying sensory stimuli to MS patients through the scalp, and their formation times are evaluated with evoked potentials. Visual Evoked Potentials (VEP) and Somatosensory Evoked Potentials (SEP) applications applied to MS patients are essential for both diagnosis and patient follow-up (7, 8). Demyelinating plaques can also form in the vestibular and central pathways, resulting in hearing and balance disorders. For example, these plaques can also develop in the brainstem, where the auditory and vestibular pathways are located (9). In addition, it has been suggested that the vestibular nuclei and root vestibule of the 8th cranial nerve are one of the most common anatomical sites for inflammation (10). Peripheral nerve connections within the cochlea may be affected by demyelination, resulting in peripheral auditory and vestibular involvement in people with MS (11, 12). This study hypothesizes that MS patients will exhibit significant auditory and vestibular dysfunction compared to healthy controls. While previous studies have explored auditory and vestibular dysfunctions in MS, few have systematically compared these functions using comprehensive diagnostic tests such as ABR, Vestibular evoked myogenic potentials (VEMP), and Video Head Impulse Test (VHIT) in a controlled setting. This study, which compared hearing and balance levels between MS patients and healthy controls, has the potential to significantly enhance our understanding of MS's impact on auditory and vestibular functions. The findings could provide valuable insights into the fields of neurology, audiology, and otolaryngology, sparking further research and discussion in these areas.

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MATERIALS AND METHODS

The methodology of the study was comprehensive. All stages of the study are summarized in Figure 1. A total of 15 MS patients aged between 27 and 55 years, with or without hearing and balance problems, who were diagnosed with definite MS at the Neurology Department from the Adana MS Patients and Relatives Association, and who had not had an attack for at least two months were included in the study. The control group we included in the study consisted of 15 individuals and the age range was between 27 and 55, as in MS patients.

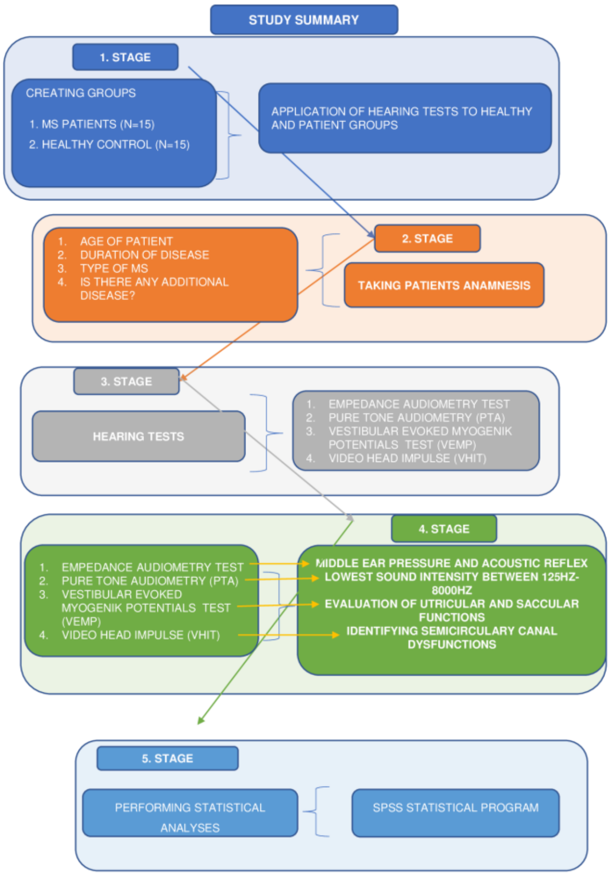

Figure 1. Experimental Design

The number of patients and controls to be used in the study was determined based on the reference article by performing a power analysis. The α value was taken as 0.05 and the beta value as 0.95. As a result of these calculations, the effect size was found to be 1.2456822. As a result, the total number was determined as 30, with 15 people per group (13). The control group consisted of individuals who were examined at the ENT Department and who had no hearing or balance problems. Participants who had previously been diagnosed with hearing loss, had a history of vestibular disorder or had an attack in less than two months, had a lower extremity fracture within two months before inclusion in the study and/or had other medical conditions that would affect the study procedures were not included in the study. The audiologic and vestibular function tests of the study were performed at the Audiology Unit of the ENT Department of the Çukurova University Faculty of Medicine, ensuring the reliability and validity of the results. The first immitansmetric measurements (Interacoustics brand AT-235 model device) were made on the study participants. Thus, it was determined that the patients did not have a middle ear pathology that prevented hearing, and pure tone signals with decreasing intensity were sent to them at random rhythmic intervals via pure tone audiometer (Interacoustics brand AC-40 model). In this way, the right and left hearing thresholds recorded on the pure tone audiometer were marked on the audiogram. Then, speech tests were performed, and the patient's speech discrimination scores (SD = speech discrimination) were determined. Then, brainstem auditory response audiometry (with GSI-Audera model device) was performed on the patients while resting and in their natural sleep using insert headphones (TDH-39 model). Responses obtained from the brainstem were recorded by sending click stimuli via a computer and electrodes. In the recording, an average was made by giving approximately 1500-2000 stimuli. ABR testing included variations in click stimulus frequency to evaluate its effects on auditory brainstem responses in MS patients. Then, a VEMP test was performed on the patients via ABR equipment. In the cVEMP test, the responses recorded from the SCM muscle were obtained via surface electrodes attached to 1/3 or ½ of the patient's SCM muscle, the middle of the forehead and the sternum. signals were sent via insert earphones (TDH 39 model) attached to both ears of the patient, and positive waves (P1) and negative waves (N1) were obtained with the ABR device (GSI-Audera model device) via electrodes placed on the SCM muscle. In response to the high-intensity sound stimulus, the SCM muscle contracted using various methods, and the latencies of the biphasic waves obtained in the electromyographic recording were evaluated. The functions of the saccule, inferior vestibular nerve, and lower brainstem were assessed in the cVEMP test. Measurements were made using 30 msec AC sound stimuli at 100 dB SPL. In the

VHIT test, patients were made to look at a previously determined fixed point; their heads were tilted forward by 30 degrees, and the lateral semicircular canals were made parallel to the ground plane. The patients were turned forward, backwards, right, and left with sudden, small, rapid movements. The movement was sudden (>3000 degrees/s2), unexpected by the patient and at angles less than 20-30 degrees. To obtain high-resolution and fast recordings, VOR gains were calculated numerically with the help of a computer to determine saccades that were not seen and detected with the naked eye. In the VHIT device used in this study, eye movements were recorded with a camera placed on the glasses. Measurements were made with the EyeSeeCam VHIT (Interacoustics, A/S DK-5610) device and evaluated with the OtoAccessTM computer program. Before starting the test, the device was calibrated. Participants were asked to read the informed consent form at the beginning of the study and their approval was obtained. The Çukurova University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee evaluated the study's compliance with ethical principles and obtained ethical approval (31.08.2018/5).

Statistical analysis

Sample T-test was used to compare the left and right high-frequency hearing and balance thresholds of MS and control groups according to age range at a 5% significance level. In examining the factors affecting MS disease, the data were checked for normal distribution, and the patient and healthy groups were compared by applying sample T-test to those with normal distribution. The significance level between the variables was accepted as statistically significant for $p<0.05$. The dependent variables in this study were the balance and hearing thresholds of the right and left ears, and the independent variables were age, gender, marital status, disease duration, etc. The results were analyzed in the IBM SPSS 22.0 statistical program.

RESULTS

The socio-demographic characteristics of the patient and control groups participating in the study are shown in tables as supplement data. The mean age of the healthy control group participating in the study was 39.26±6.75, and the mean age of MS patients was 38.80±9.14.

Results of pure tone hearing thresholds test

Pure tone hearing thresholds of the patient group were found to be statistically significant in the right ear (p=0.001) and left ear (p=0.002) compared to the control group (Table 1). According to these results, hearing thresholds were significantly increased in MS patients compared to healthy controls, indicating hearing loss. In our study, according to the pure tone audiometry results applied to MS patients, a higher degree of hearing loss was observed in the right ear compared to the left ear.

Table 1: Analysis Results of Pure Tone Audiometry Test Applied to Groups

Parameters	Control Group (n=15)	Patient Group (n=15)	F	p
Pure Tone R	6.53 ± 3.29 dB	21.8 ± 14.45 dB	21.84 dB	0.001
Pure Tone L	8.8 ± 3.74 dB	17.4 ± 12.81 dB	11.61 dB	0.002

The data were represented as mean ± standard error of mean. Differences in means were compared by sample t-test. Statistical significance was defined as p-values of 0.05 or less. In the patient group, right (R) (p=0.001) and left (L) (p=0.002) ear hearing thresholds were found to be statistically significant compared to the control group.

Results of ABR test

Hearing thresholds in the ABR test were found to be statistically significant in the right (p=0.001) and left (p=0.002) ears in the patient group compared to the control group (Table 2). According to these results, ABR thresholds were significantly increased in MS patients compared to healthy controls, indicating hearing loss. Looking at the ABR results we applied to MS patients, we obtained higher thresholds in the right ear compared to the left ear, indicating a greater degree of hearing loss in the left ear.

Table 2: Analysis results of ABR test applied to groups

Parameters	Control Group (n=15)	Patient Group (n=15)	F	p
R	20.0 ± 0.001 dB HL	27.14 ± 14.23 dB HL	12.8 dB	0.001
L	20.66 ± 2.58 dB HL	30.0 ± 13.0 dB HL	11.89 dB	0.002

The data were represented as mean ± standard error of mean. Differences in means were compared by sample t-test. Statistical significance was defined as p-values of 0.05 or less. It was observed that the right (R) (p=0.001) and left (L) (p=0.002) ear hearing thresholds in the patient group were statistically significant compared to the control group.

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Results of VEMP test

VEMP score enables better evaluation of brainstem involvement; while also correlating well with disability and disease duration. In the VEMP test records applied to the participants, the latencies of the electrical waves (P1 and N1) obtained from the sternocleidomastoid (SCM muscle) were measured. The SCM muscle is a large muscle pair located in the neck region. The SCM muscle provides neck movements and facilitates head rotation. The right ear P1 (RP1), right ear N1 (RN1), left ear P1 (LP1) and left ear N1 (LN1) latencies of the patient and control groups were measured. It was observed that the right P1 (p=0.05), right N1 (p=0.05) and left P1 (p=0.01), left N1 (p=0.002) wave latencies in the patient group were statistically significant compared to the control group (Table 3). In the VEMP test, it was determined that 40% of the patients (n=12) had delayed latency values of the P1 and N1 waves. The values of the participants in the control group were within normal limits.

Multiple sclerosis (MS) lesions may impair VEMP responses affecting the vestibular fascicles, vestibular nuclei and their efferents, and cerebellum all of which are all involved in relaying and processing of the vestibular signals. These delays in the latency values of the patient waves indicate brainstem involvement, and more delay was observed in the left ear of the patients than in the right ear.

Table 3: Analysis results of left ear vemp test applied to groups

Parameters	Control Group (n=15)	Patient Group (n=12)	F	p
LP1	14.16 ± 1.70 ms	15.86 ± 5.85 ms	6.45 ms	0.01
LN1	22.94 ± 1.39 ms	23.75 ± 4.62 ms	12.16 ms	0.002
RP1	13.66 ± 1.88 ms	16.90 ± 5.56 ms	4.15 ms	0.05
RN1	23.6 ± 1.97 ms	25.60 ± 2.83 ms	3.95 ms	0.05

The data were represented as mean ± standard error of mean. Differences in means were compared by sample t-test. Statistical significance was defined as p-values of 0.05 or less. It was observed that the right P1 (RP1) (p=0.05), right N1 (RN1) (p=0.05) and left P1 (LP1) (p=0.01), left N1 (LN1) (p=0.002) latencies of wave in the patient group were statistically significant compared to the control group.

Results of VHIT test

In VHIT recordings, right anterior semicircular canal (RA), right lateral semicircular canal (RL), right posterior semicircular canal (RP) (p<0,004), left anterior semicircular canal thresholds (LA) (n=15), left lateral canal gains (LL), and left posterior semicircular canal gains (LP) (p<0.01) were measured. According to the

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results of the VHIT test, 27% of the patients (n=8) were seen to have gain values outside the normal range compared to the control group (Table 4). According to VHIT test results, low channel gains in MS patients indicate that the functions in the vestibular channels are impaired.

Table 4: Analysis Results of Right Ear VHIT Test (Anterior, Posterior, Lateral Canals)

Parameters	Control Group (n=15)	Patient Group (n=14)	F	p
RA	0.90 ± 0.17	0.73 ± 0.21	0.74	0.39
RL	0.91 ± 0.19	0.89 ± 0.21	0.55	0.46
RP	1.02 ± 0.23	0.86 ± 0.35	0.10	0.004
LA	0.98 ± 0.14	0.81 ± 0.28	0.67	0.41
LL	0.90 ± 0.14	0.90 ± 0.10	3.92	0.05
LP	1.03 ± 0.10	0.80 ± 0.21	6.24	0.01

The data were represented as mean ± standard error of mean. Differences in means were compared by sample t-test. Statistical significance was defined as p-values of 0.05 or less. In VHIT recordings, the mean Right Anterior (RA) values in the experimental group were 0.73±0.21 (p=0.39), Right Lateral (RL) values were 0.89±0.21 (p=0.46), and Right Posterior (RP) values were 0.86±0.35 (p=0.004); Left Anterior (LA) values were found to be 0.81±0.28 (p=0.41), Left Lateral (LL) values were found to be 0.90±0.10 (p=0.05) and Left Posterior (LP) values were found to be 0.80±0.21 (p=0.01). In our study, in the VHIT test, 27% of the patients (n=8) were found to have gain values outside the normal range.

DISCUSSION

MS is a chronic inflammatory disease affecting the central nervous system, and its etiology is unknown (14). It is essential to equalize the variables in case-control type studies. The variables in this study were age, gender, marital status, disease duration, hearing, and balance thresholds. These variables affect the social lives of the patients (15). Hearing loss due to demyelination in MS patients may be of peripheral or central origin (16). PTA was measured with a dual-channel Interacoustics AC40 Clinical Audiometer calibrated at frequencies of 250, 500, 1000, 2000, 4000 and 6000 Hz according to the modified Hughson-Westlake ascending method (Jerger et al., 1959) in a soundproof booth. Hearing loss was calculated separately for each pure tone frequency stimulus, and the amount of threshold shift above the standard audiometric zero (dB HL) was also calculated. In our study, sensorineural hearing loss was detected in 27% of the patients in the pure tone audiometry test applied to the patients. Bilateral hearing loss was present in 23% (n=7) of 8 patients, while unilateral sensorineural hearing loss was observed in 4%. Middle ear pressures were Type A tympanogram in 100% of patients, and acoustic reflex was obtained in all patients. In a study, according to the results of pure tone audiometry test and acoustic reflex test applied to 30 MS patients and 23 healthy volunteer participants, no significant results were obtained in MS patients compared to healthy volunteers (17). In another study, case history assessment, otoscopic examination, pure tone audiometry, and ABR testing were performed on 45 MS patients, and it was predicted that the results could be a valid and useful measure in the evaluation of brainstem functions and prediction of disability in MS (18). In a prospective study, ABR testing was performed on 40 participants, and a total of 160 BERA recordings obtained from 80 ears of 40 participants were examined. 20 of these were MS patients and 20 were healthy volunteers in the control group. Significant prolongation of wave latencies was observed in the right and left ears of patients in the MS group (19). In our study, when the click stimulus frequency was 20 per second in the ABR applied to 30 participants in all groups, the right and left ear thresholds were observed as 20 dB HL, and in the patient group, the hearing threshold of the right ear was observed as 20 dB HL and the left ear as 30 dB HL. However, when we increased the click stimulus frequency, the wave morphology in the ABR was distorted in all groups and even artifactual waveforms were observed. cVEMP results allow assessment of brainstem involvement. VEMP are feedforward, low-latency electromyographic responses induced by acoustic stimuli. cVEMP test activates an inhibition reflex (the vestibulocollic reflex) that is recorded from the tonically contracted ipsilateral SCM muscle, reflecting vestibulospinal pathway activity. This reflex arc consists of neuroreceptors of the saccular macula, inferior vestibular nerve, lateral vestibular nucleus, medial vestibulospinal tract, and spinal cord motor neurons supplying muscles in the neck. While the VEMP test has used for the assessment of acoustic neuroma and peripheral vestibular disorders such as Meniere disease and vestibular neuritis, it can provide a stream of information about brainstem function as most of the vestibulocollic reflex arc is centered in the brainstem (20).

In 2008, Zeigelboim et al. conducted a study to define vestibular abnormalities in 30 MS patients. The study group included patients without psychological or oculomotor paresis, internuclear ophthalmoplegia or severe visual impairment. The evaluation phase of vestibular function tests consisted of labyrinth function and ocular tests—the results of the electronystagmography test provided information about changes in corneoretinal potentials. Vestibular changes were observed in 86% of the patients evaluated. Bilateral peripheral vestibulopathy was detected in 20% of the patients, and left peripheral vestibulopathy was detected in 17% (21).

In a study conducted with the participation of 35 adult patients, VEMP test was applied to patient and control groups and then the results of the groups were compared. There was no significant difference between the groups in terms of c-VEMP results, there was no significant difference between the o-VEMP results except for N1-P1 amplitudes. When N1-P1 amplitudes were compared with controls, it was observed that they were significantly lower (22).

vHIT can be used as a diagnostic test for brainstem lesions, so any decrease in vHIT results may predict the onset of brainstem involvement in MS patients. Therefore, it seems necessary to include a VOR function test during the clinical practice of MS patients (23). Our study aims to evaluate the vestibular semicircular canal function in MS using vHIT to determine the angular vestibular reflex associated with stimulation of the six semicircular canals. Our findings revealed that there may be VOR dysfunction in MS and that there was a significant correlation between the VOR gains of the vertical canals and balance clinical scales.

The limitations of our study are the small number of patients, being a single-center study, and the inability to make gender-based comparisons due to gender inequality in patient numbers.

CONCLUSION

As a result of the literature review and the data obtained from our study, significant results were obtained for the right and left ears of MS patients to whom we applied the pure tone audiometry test. There was evidence that it impacted these patients' high frequency hearing sensitivity. In the ABR test, unilateral hearing loss was observed in seven patients when the click stimulus frequency was 20 per second. When the click stimulus frequency was 70 per second, no waveform was observed in any patient. In the VHIT test, while the VOR gains of 9 MS patients were outside the normal limits, the VOR gains of one patient in the left lateral canal were low. The gain values obtained in the anterior and lateral canals in the right and left ears were statistically insignificant.

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In contrast, the posterior canal gains in the right and left ears were statistically significant. In the VEMP test, the P1 and N1 wave latencies of 14 patients in the control group were close to normal limits, and the wave latencies of patients were outside the normal limits. The wave latencies of 12 patients in the patient group were delayed, and the two patients' left-side P1 and N1 waveforms were not observed. The VEMP test showed that the left P1 and N1 waves showed statistically significant results, while the right P1 and N1 waves showed statistically insignificant values. While the average EDSS score of the patients in the control group according to the BDI scale was 1.13 points, the average of the patients with MS was 4.23. More patients and more research are needed to obtain reliable results.

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Authorship contributions

S.U.; Design, Data Collection, Analysis and Interpratation, Literature Search, Writing-Original Draft. Ö.S.; Concept, Design. H.D.; Design, Analysis, Writing-Original Draft.

Data availibity statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declaration of competing interest

No conflict of interest was declared by the authors

Ethics

The Çukurova University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee evaluated the study's compliance with ethical principles and obtained ethical approval (31.08.2018/5).

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