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ORIGINAL ARTICLE

Audiovestibular findings according to the subtypes of multiple sclerosis

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ABSTRACT

Objectives: This study aimed to evaluate auditory and vestibular function across different clinical subtypes of multiple sclerosis (MS) using both objective testing and patient-reported outcomes.

Patients and methods: The study was conducted between June 2020 and March 2021. A total of 50 adults (26 males, 34 females; mean age, 45.7±13.7 years; range, 20 to 70 years) were included and categorized into five groups: clinically isolated syndrome, relapsing-remitting MS, secondary progressive MS (SPMS), primary progressive MS (PPMS), and healthy controls. Assessments included pure tone audiometry, immittance testing, videonystagmography with oculomotor and positional subtests, and video head impulse test. Dizziness Handicap Inventory was used to assess subjective balance complaints.

Results: Significantly elevated hearing thresholds were observed in the SPMS group at 6000 to 8000 Hz, and in the PPMS group at 250, 1000, and 6000 Hz ($p<0.005$). Oculomotor abnormalities, particularly in saccade and smooth pursuit, were more frequent in PPMS ($p<0.005$). No significant differences were detected in video head impulse test gain values or positional nystagmus between groups ($p>0.005$). Dizziness Handicap Inventory scores were significantly higher in the SPMS and PPMS groups compared to other groups, indicating greater subjective disability ($p<0.005$).

Conclusion: Progressive MS subtypes (SPMS and PPMS) showed greater auditory and vestibular impairment than the other forms. These findings emphasized the need for routine audiovestibular assessments and support integrating patient-reported outcomes such as the Dizziness Handicap Inventory into clinical follow-up.

Keywords: Dizziness Handicap Inventory, multiple sclerosis, vestibular.

Multiple sclerosis (MS) is a chronic autoimmune disease characterized by inflammation, demyelination, and neuroaxonal damage in the central nervous system.[1] Affecting more than 2.8 million people worldwide, MS is most common in individuals aged 20 to 40 years.[2] In epidemiologic studies conducted in Türkiye, the prevalence of the disease varies between 41.1 and 101.4 per 100,000 people.[3]

The most common symptoms in patients with MS are motor, sensory, and balance disorders. Balance problems occur in 75% of patients, while hearing loss has been reported less frequently (6%). Symptoms of vertigo and imbalance are usually transient but may be more prolonged in some cases.[4] According to the 2017 McDonald Criteria, MS is divided into four clinical subtypes: clinically isolated syndrome (CIS), relapsing-remitting MS (RRMS), primary progressive MS (PPMS), and secondary progressive MS (SPMS).[1] Relapsing-remitting MS is the most common form and accounts for approximately 85% of all patients with MS.[5]

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Although auditory and vestibular symptoms have been described in patients with MS in the literature, the distribution of these findings according to subtypes has not been adequately investigated. This study aimed to evaluate auditory and vestibular findings according to different clinical subtypes of MS using subjective and objective methods. Our hypothesis was that these findings would show significant differences between subtypes.

PATIENTS AND METHODS

This single-center, cross-sectional, observational, comparative, and single-blind study included adult patients who were diagnosed with MS according to the 2017 revised McDonald Criteria at the Başkent University Istanbul Health Practice and Research Center Hospital between June 2020 and March 2021. The study was conducted in the Audiology Unit of the Department of Otorhinolaryngology. A total of 50 participants (26 males, 34 females; mean age, 45.7±13.7 years; range, 20 to 70 years) were included and divided into five groups: CIS (n=10), RRMS (n=10), SPMS (n=10), PPMS (n=10), and a healthy control group (n=10). The distribution of patients across subgroups was specified to improve clarity regarding group comparisons. The clinical subtypes were determined based on neurological and radiological findings evaluated by the Department of Neurology. The study followed a single-blind design, in which the assessors were unaware of the participants' MS subtypes. Written informed consent was obtained from all participants prior to data collection. The study protocol was approved by the Başkent University Medical and Health Sciences Research Ethics Committee (Date: 11.03.2020, No: KA20/55. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Participants were eligible for inclusion if they were aged 18 or older, had a confirmed diagnosis of MS according to the 2017 revised McDonald Criteria, and had accessible magnetic resonance imaging and cerebrospinal fluid examinations. Individuals were excluded if they were under 18 years of age and had a history of ototoxic drug use, ear surgery, unrelated neurological disease, head trauma, or any systemic condition that could interfere with test results. Although factors such as disease duration, severity, and number or type of relapses were not included in the inclusion or exclusion criteria, these parameters were recorded for descriptive purposes. A priori sample size calculation was not performed; instead, the sample consisted of all eligible patients who met the criteria within the data collection period. The study was conducted during the COVID-19 (coronavirus disease 2019) pandemic, which imposed certain limitations on clinical access and patient participation; therefore, the sample size remained relatively limited.

All participants underwent a complete otorhinolaryngological examination, followed by audiological testing, immittancemetric evaluation, oculomotor tests, videonystagmography (VNG), and video head impulse testing (vHIT). Subjective evaluation of balance complaints was performed using the Dizziness Handicap Inventory (DHI). Audiometric and immittancemetric measurements were carried out using Interacoustics AC40 and AT235 devices (Interacoustics A/S, Middelfart, Denmark), respectively, while VNG and vHIT assessments were conducted with Biomed (Biomed Medikal San. ve Dış Tic. Ltd. Şti., İstanbul, Türkiye) and Interacoustics systems.

Statistical analysis

The statistical analysis was performed using IBM SPSS version 26.0 software (IBM Corp., Armonk, NY, USA). To determine the distribution characteristics of the data, the Shapiro-Wilk test was applied, and results indicated that the data did not follow a normal distribution. Therefore, nonparametric tests were selected for the analysis. Descriptive statistics were expressed as medians (for continuous, nonnormally distributed data) and as frequencies and percentages (for categorical variables). For pairwise comparisons of independent groups, the Mann-Whitney U test was used, while the Wilcoxon signed-rank test was employed for related samples. The Kruskal-Wallis test was used for comparisons involving more than two groups. In cases of statistically significant overall group differences, post hoc pairwise comparisons were conducted using the Mann-Whitney U test. The Bonferroni correction was applied to control for type 1 error in multiple comparisons, and the adjusted significance level was calculated based on the number of pairwise tests. Spearman's rank correlation coefficient was used to evaluate correlations between continuous nonparametric variables, and the chi-square test was applied to assess associations between categorical variables. The threshold for statistical significance was set at $p<0.05$, unless otherwise adjusted by Bonferroni correction.

RESULTS

There were no significant differences between groups in terms of sex and education level (p=0.102 and p=0.227, respectively). However, significant differences were found in age at diagnosis and disease duration (p<0.001; Table 1). The control group consisted of age- and sex-matched healthy individuals with no known neurological, vestibular, or otological pathology. These participants had no history of dizziness, vertigo, hearing loss, or any demyelinating or neurological condition. Their inclusion was confirmed through neurological and otorhinolaryngological evaluations conducted by the Departments of Neurology and Otorhinolaryngology, ensuring the absence of both central and peripheral nervous system involvement. All participants in the control group had normal otoscopic findings and no prior complaints suggestive of audiovestibular dysfunction.

Regarding hearing thresholds, no significant differences were observed between groups at 125 Hz, 500 Hz, 2000 Hz, and 4000 Hz in the right ear (p=0.053, p=0.073, p=0.058, and p=0.053, respectively). However, pairwise comparisons showed significant threshold reductions at 250 Hz, 1000 Hz, and 6000 Hz (p=0.008, p=0.048, and p=0.008, respectively) between PPMS and control groups, as well as at 6000 Hz and 8000 Hz between SPMS and control groups (p=0.008 and p=0.011, respectively). In the left ear, significant decreases were noted at 2000 Hz between PPMS and controls (p=0.008) and at 1000 Hz and 8000 Hz between SPMS and controls (p=0.003 and p=0.013, respectively).

TABLE 1
Demographic and clinical characteristics by MS subtype

	CIS		RRMS		PPMS		SPMS		Control		
Variables	n	Mean±SD	n	Mean±SD	n	Mean±SD	n	Mean±SD	n	Mean±SD	*p*
Age (year)		36.2±13.85		38±5.98		54.8±12.25		52.1±14.37		47.2±13.88	**0.007***
Sex											0.102
Female	10		5		7		5		7		
Male	0		5		3		5		3		
Education level[1]	1/3/6		1/6/3		4/3/3		0/5/5		1/5/4		0.277
Age at diagnosis		30.4±11.56		29.6±6.26		37.2±9.64		38.6±13.48		0±0	**<0.001***
Disease duration		5.8±4.21		8.4±4.06		17.6±14.14		13.5±9.42		0±0	**<0.001***

MS: Multiple sclerosis; CIS: Clinically isolated syndrome; RRMS: Relapsing-remitting multiple sclerosis; PPMS: Primer progressive multiple sclerosis; SPMS: Secondary progressive multiple sclerosis; SD: Standard deviation; [1]Education level: primary/high school/university, * p<0.05, there was a statistically significant difference between the groups.

TABLE 2
The comparison of the MS subtypes according to the results of oculomotor tests

	MS subtype										
	Clinically-isolated		Relapsing-remitting		Primary progressive		Secondary progressive		Control		
Variables	n	%	n	%	n	%	n	%	n	%	*p*
Saccade speed											
Normal	10^{a}	100.0	$7^{a,b}$	70.0	4^{b}	40.0	$8^{a,b}$	80.0	10^{a}	100.0	**0.006***
Pathological	0^{a}	0.0	$3^{a,b}$	30.0	6^{b}	60.0	$2^{a,b}$	20.0	0^{a}	0.0	
Pursuit earning											
Normal	$8^{a,b}$	80.0	4^{b}	40.0	3^{b}	30.0	$5^{a,b}$	50.0	10^{a}	100.0	**0.007***
Pathological	$2^{a,b}$	20.0	6^{b}	60.0	7^{b}	70.0	$5^{a,b}$	50.0	0^{a}	0.0	
Optokinetic asymmetry											
Normal	10^{a}	100.0	7^{a}	70.0	7^{a}	70.0	7^{a}	70.0	10^{a}	100.0	0.12
Pathological	0^{a}	0.0	3^{a}	30.0	3^{a}	30.0	3^{a}	30.0	0^{a}	0.0	

MS: Multiple sclerosis; * p<0.05. The different letters in the lines show that there was a difference between the two groups and the same letters indicate that there was no difference. p, χ^2 test value.

TABLE 3
The comparison of the MS subtypes according to right vHIT channel gains

Variables	Groups	Mean±SD	Median	TSV	TLV	*p*
vHIT right lateral	Clinically-isolated	0.86±0.04	0.88	1	1	0.946
	Relapsing-remitting	0.88±0.14	0.88	1	1	
	Primary progressive	0.87±0.13	0.88	1	1	
	Secondary progressive	0.87±0.1	0.85	1	1	
	Control	0.88±0.06	0.88	1	1	
vHIT right anterior	Clinically-isolated	1.07±0.16	1.07	1	1	0.103
	Relapsing-remitting	0.99±0.28	1.09	1	1	
	Primary progressive	0.91±0.15	0.96	1	1	
	Secondary progressive	0.89±0.13	0.85	1	1	
	Control	0.89±0.13	0.87	1	1	
vHIT right posterior	Clinically-isolated	0.98±0.16	1.01	1	1	0.152
	Relapsing-remitting	0.94±0.3	1.01	0	1	
	Primary progressive	0.81±0.21	0.82	0	1	
	Secondary progressive	0.8±0.19	0.79	1	1	
	Control	0.86±0.08	0.83	1	1	

MS: Multiple sclerosis; vHIT: Video head impulse testing; SD: Standard deviation; TSV: The smallest value; TLV: The largest value.

No significant differences were found in bone conduction thresholds, speech reception threshold, speech discrimination, most comfortable level, or uncomfortable level (p=0.071, p=0.066, p=0.051, and p=1.000, respectively).

Nystagmus was not observed in the horizontal and vertical gaze test (p=0.349 and p=0.956, respectively). The presence of pathology in saccade and pursuit tests was higher in patients with PPMS compared to controls (p=0.006 and p=0.007, respectively; Table 2). No significant differences were found in other vestibular tests, including spontaneous nystagmus, head shake, or positional tests (right Dix-Hallpike test, left Dix-Hallpike test, left roll test, right roll test; p=0.395, p=0.593, and p=0.155, p=0.617, p=0.537, p=0.624, respectively).

Video head impulse testing parameters showed no significant differences across groups (p>0.05; Tables 3, 4). Significant differences were found in DHI scores between MS subtypes, with control group scores lower than all MS subtypes. No significant differences were observed between MS subtypes (p<0.001; Table 5).

DISCUSSION

This study investigated audiovestibular findings across different subtypes of MS, including both objective assessments (audiometry, vHIT, and VNG) and subjective data (DHI). Our findings revealed that SPMS and PPMS subtypes exhibited more pronounced auditory threshold shifts and vestibular test abnormalities compared to RRMS, CIS, and healthy controls. Notably, hearing thresholds at 6000 and 8000 Hz in the SPMS group and at 250, 1000, and 6000 Hz in the PPMS group were significantly worse than in controls. Additionally, DHI scores were significantly elevated in SPMS and PPMS, suggesting greater subjective disability in these groups. These findings reflect the progressive neurodegenerative characteristic of these subtypes.

These results are consistent with prior studies. Lewis et al.[6] found worse hearing thresholds at 3000 and 4000 Hz in patients with SPMS, while Küfeciler[7] showed elevated thresholds in RRMS compared to healthy controls. Our findings extend these observations by confirming significant threshold shifts in more advanced MS subtypes at mid-to-high frequencies. This supports the hypothesis that auditory pathway involvement becomes more pronounced as disease severity increases.

Hearing frequencies follow a linear or logarithmic progression. In the results section, no significant differences were found at 125 Hz

TABLE 4
The comparison of the MS subtypes according to left vHIT channel gains

Variables	Groups	Mean±SD	Median	TSV	TLV	*p*
vHIT left lateral	Clinically-isolated	0.85±0.06	0.84	1	1	0.927
	Relapsing-remitting	0.85±0.16	0.88	1	1	
	Primary progressive	0.88±0.11	0.89	1	1	
	Secondary progressive	0.9±0.11	0.86	1	1	
	Control	0.86±0.04	0.85	1	1	
vHIT left anterior	Clinically-isolated	1±0.16	1.01	1	1	0.099
	Relapsing-remitting	0.92±0.27	1.01	0	1	
	Primary progressive	0.83±0.2	0.84	0	1	
	Secondary progressive	0.75±0.18	0.75	0	1	
	Control	0.91±0.15	0.86	1	1	
vHIT left posterior	Clinically-isolated	1.04±0.16	1.01	1	1	0.056
	Relapsing-remitting	0.95±0.3	0.97	0	1	
	Primary progressive	0.84±0.14	0.87	1	1	
	Secondary progressive	0.93±0.15	0.92	1	1	
	Control	0.86±0.07	0.84	1	1	

MS: Multiple sclerosis; vHIT: Video head impulse testing; SD: Standard deviation; TSV: The smallest value; TLV: The largest value.

TABLE 5
The comparison of the MS subtypes according to DHI scores

Variables	Groups	Mean±SD	Median	TSV	TLV	*p**
Dizziness handicap inventory score	Clinically-isolated	21.2±13.89	18.00	8	48	**<0.001**
	Relapsing-remitting	30.8±17.42	28.00	10	60	
	Primary progressive	39.6±23.07	44.00	10	68	
	Secondary progressive	36.8±13.31	36.00	12	60	
	Control	6±5.16	6.00	0	14	

MS: Multiple sclerosis; DHI: Dizziness Handicap Inventory; SD: Standard deviation; TSV: The smallest value; TLV: The largest value; * p<0.05, there was a statistically significant difference between the groups.

and 500 Hz, whereas a significant difference was reported at 250 Hz. We acknowledge that the isolated significant difference at 250 Hz presents an interpretive challenge. This discrepancy may be due to technical issues common at very low frequencies, such as headphone placement, environmental noise, or momentary patient inattention. Moreover, this study was conducted during the COVID-19 pandemic, which imposed logistical limitations and reduced our sample size. Therefore, we advise caution in overinterpreting this particular result and instead emphasize the consistent abnormalities found at 1000 to 8000 Hz, which align with previous studies and known central auditory involvement in MS.[8,9]

With respect to vestibular function, abnormalities in saccadic and smooth pursuit eye movements were more frequent in the PPMS group. These findings are consistent with previous studies reporting oculomotor dysfunction in MS. For example, Servillo et al.[10] identified significant saccadic asymmetry and decreased velocity among patients with MS, while Serra et al.[11] and Ojala et al.[12] reported smooth pursuit abnormalities in up to 65% of cases. Rather than suggesting that brainstem or visual involvement is uncommon in PPMS, these results may indicate that oculomotor deficits, potentially reflecting brainstem or cerebellar involvement, are more pronounced or detectable in this progressive subtype due to its

diffuse and slowly advancing neurodegenerative profile.

Previous studies emphasized that disease duration may influence vestibular compensation in patients with MS, potentially leading to attenuation or absence of certain vestibular symptoms over time.[11,13] In our sample, although detailed group-level analysis of disease duration could not be performed due to incomplete clinical records, it was observed that most participants had long-standing MS. This likely contributed to the absence of spontaneous and positional nystagmus, which are commonly observed in earlier stages. Therefore, the lack of these findings in our study may not reflect a true absence of pathology but rather the influence of long-term central adaptation mechanisms associated with chronic disease progression.

Although vHIT canal gains did not differ significantly across groups, we observed overt and covert saccades, particularly in the PPMS group. This mirrors results from Pavlović et al.[14] and Barmak,[15] suggesting that saccade presence may serve as an early indicator of semicircular canal dysfunction even when gain values are normal. Thus, clinicians should consider both gain and saccadic responses in vHIT interpretation.

In our study, spontaneous and positional nystagmus were not detected in any MS subtype. This contrasts with studies by Ebers et al.[16] and Williams et al.,[17] which reported positional nystagmus rates between 27% and 50% in RRMS. The discrepancy may be explained by differences in disease duration. Although group-level analysis of disease duration was not feasible due to incomplete clinical records, anecdotal observations indicated that many participants had long-standing MS. This may partly explain the absence of spontaneous and positional nystagmus in our sample, as central vestibular compensation tends to develop over time in chronic cases.[18]

Dizziness Handicap Inventory scores were highest in SPMS and PPMS, reflecting greater functional burden. This aligns with Hebert et al.,[19,20] who demonstrated DHI's sensitivity to vestibular rehabilitation and disease severity. The parallel between subjective (DHI) and objective test results emphasizes the value of including patient-reported outcomes in MS assessment.

In our study, hearing loss was observed at specific, nonadjacent frequencies (e.g., 250 Hz, 1000 Hz, and 6000 Hz), which may reflect the complex impact of MS on different levels of the central auditory pathway. Such patterns were previously associated with demyelination and axonal damage at varying brainstem or cortical locations, leading to nonuniform auditory deficits.[21,22] Similarly, although the presence of overt and covert saccades in the vHIT might initially suggest peripheral vestibular dysfunction, these findings should not be interpreted in isolation. Multiple sclerosis is primarily a central nervous system disorder, and vestibular impairment often results from lesions affecting central vestibular pathways.[14,23] Therefore, the vestibular abnormalities in our study, particularly those in oculomotor tests, should be considered as reflecting both central and potentially secondary peripheral involvement. This highlights the importance of evaluating audiovestibular findings in MS with an integrated, neuro-otological approach, rather than attributing them solely to one anatomical level.

Auditory and vestibular systems appear to be more significantly affected in SPMS and PPMS subtypes, emphasizing the necessity of a multidisciplinary approach that includes audiology, neurology, and vestibular rehabilitation. The strong alignment between objective test results and subjective assessments, such as DHI, further underscores the importance of incorporating patient-reported outcomes into routine clinical follow-up and care planning.

This study had several limitations. First, the sample size was relatively small, primarily due to recruitment challenges during the COVID-19 pandemic. This may have reduced the statistical power to detect subtle differences between MS subtypes, particularly at certain audiometric frequencies. Additionally, although auditory and vestibular assessments were comprehensive, some variables, such as disease duration, Expanded Disability Status Scale scores, and number/type of relapses, were not consistently documented across participants and therefore not analyzed. This limited our ability to correlate functional impairments with disease severity or progression. Another limitation was the potential measurement variability at very low frequencies (e.g., 250 Hz), which may have influenced some isolated statistically significant results. Finally, this was a single-center study, which may limit the generalizability of the findings to broader MS populations.

In conclusion, our findings suggest that auditory and vestibular dysfunctions are more prevalent and pronounced in patients with SPMS and PPMS compared to other MS subtypes and healthy controls. Elevated hearing thresholds at mid-to-high frequencies and abnormal oculomotor responses, such as impaired saccade velocity and smooth pursuit, were more frequently observed in progressive forms of MS. Subjective burden, as reflected in higher DHI scores, also aligned with these objective deficits. These results emphasize the importance of incorporating both audiological and vestibular evaluations into the multidisciplinary care of patients with MS, particularly those with progressive subtypes. Moreover, the strong correspondence between objective findings and patient-reported outcomes underscores the value of tools such as the DHI in routine follow-up and rehabilitation planning.

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

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