Postural Control in Relapsing-Remitting Multiple Sclerosis

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Abstract

Introduction Postural instability is considered one of the most disabling symptoms of relapsing-remitting multiple sclerosis (RRMS).

Objective To evaluate postural control in patients with RRMS.

Method A total of 79 individuals between 18 and 65 years old, of both genders, were distributed into an experimental group composed of patients with RRMS ($n = 51$) and in a control group composed by healthy individuals ($n = 28$). The evaluation consisted of anamnesis, Dizziness Handicap Inventory (DHI), visual vertigo analog scale (VVAS), and static posturography (Tetrax IBS).

Results Patients with RRMS presented mild degree in the DHI and in the VVAS; in Tetrax IBS, they presented higher or lower values of the indices of general stability, weight distribution, synchronization of postural oscillation, fall risk, and frequency bands of postural oscillation in two, five or all eight sensory conditions, in relation to the control group. Vestibular, visual and/or somatosensory dysfunction of peripheral type (51.0%) prevailed over the central type. The RRMS group, with an expanded scale of disability status > 3 points, presented a higher fall risk than with a score ≤ 3 points ($p = 0.003$). There was a positive correlation of the Fall Risk Index with the total DHI Score ($s = 0.380$; $p = 0.006$) and with the VVAS score ($s = 0.348$; $p = 0.012$).

Conclusion Patients with RRMS may present with inability to maintain postural control due to general instability, desynchronization and increased postural oscillation at frequencies that suggest deficiencies in the vestibular, visual, and somatosensory systems; as well as fall risk related to the state and intensity of functional disability and self-perception of the influence of dizziness on quality of life.

Keywords

- multiple sclerosis
- relapsing-remitting
- postural balance
- dizziness
- quality of life

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Introduction

Multiple sclerosis (MS) is an autoimmune, chronic, and demyelinating disease of the central nervous system (CNS). It is more common in young adults and has unpredictable, complex, and heterogeneous evolution due to the involvement of various pathophysiological processes.[1,2] It is characterized by an inflammatory reaction that damages the myelin sheaths of the axons of the brain and spinal neurons, causing demyelination and the appearance of a vast picture of signs and symptoms.[2]

The diagnosis of MS is established based on clinical history and on physical and complementary examinations; there is no pathognomonic marker for the diagnostic definition of the disease. The diagnostic criteria that highlight the temporal and spatial distribution of the disease[3] should be supplemented with the results of magnetic resonance imaging (MRI) of the brain and the spinal cord, when necessary.[4] The evolution of MS follows certain clinical patterns characterized by relapses and progression, classified as relapsing-remitting, primary progressive, secondary progressive, and progressive-relapsing.[1]

Relapsing-remitting multiple sclerosis (RRMS) is the most common pattern, reaching 85.0% of cases. Symptoms occur in the form of clinically well-defined relapses. Recovery is variable; 40.0% of relapses result in persistent neurological deficiencies and patients may accumulate progressive disability.[5]

Physical disabilities during the evolution of MS over time can be classified using the expanded disability status scale (EDSS) in eight functional systems: pyramidal, cerebellar, brainstem, sensory, vesical and/or intestinal, visual, mental, and other functions.[6] The score ranges from zero to 10; zero corresponds to a normal neurological examination, and ten to death due to MS. Scores > 4.5 are greatly influenced by the ability of the individual to walk, especially the ability to walk certain distances and the need for aids, such as unilateral, bilateral, or wheelchair support.[7]

Due to the variable distribution of demyelination in the CNS, patients with MS may present with disorders of coordination, sensitivity, strength, and body balance.[8] Abnormalities of body balance are described in 78.0% of patients with MS,[9,10] accompanied by a high incidence of falls[8,11–13] over a period of 2 to 6 months in $> 50.0\%$ of cases.[8,14–16] The high prevalence of changes in body balance in patients with MS reinforces the relevance of a comprehensive diagnostic investigation of postural control, since this symptom may have peripheral vestibular origin, regardless of signs of CNS impairment, enabling relevant therapeutic interventions.[17,18]

The present study is justified by the importance of setting up a functional evaluation protocol to show objective signs of impairment of postural control in patients with MS, allowing to customize the appropriate therapeutic conduct according to the findings in each case, when necessary. The hypothesis for the present study is that patients with MS, even without postural instability and who did not meet the clinical criteria for physical disability in the medical evaluation using the EDSS, may present with objective signs of postural control impairment.

The overall objective of the present study is to evaluate postural control in patients with RRMS. The specific objectives are to compare the results of the body balance of patients with RRMS those of a control group and with reference values, checking whether there is an association between the fall risk over time in the disease state, the functional ability, the intensity, and the self-perception of the influence of the dizziness on the quality of life, the postural instability, and the practice of physical activity of the patient.

Method

The present analytical cross-sectional study, conducted in patients with RRMS[4] under regular follow-up in the outpatient clinic of demyelinating diseases of the discipline of Neurology in the outpatient clinic of demyelinating diseases of the Department of Neurology and Neurosurgery, Universidade Federal de São Paulo, was approved by the Research Ethics Committee under number 3114893. The individuals were informed about the procedures performed and signed the Informed Consent Form, enabling their participation, as well as subsequent analysis and dissemination of the results.

The present study was conducted in the discipline of Otology and Otoneurology of the Department of Otorhinolaryngology and Head and Neck Sugery, Universidade Federal de São Paulo.

The experimental group was composed of patients with a diagnosis of RRMS, selected from January 2017 to July 2018 during the weekly follow-up at the outpatient clinic of demyelinating diseases of the discipline of Neurology, outpatient clinic of demyelinating diseases of the Department of Neurology and Neurosurgery, Universidade Federal de São Paulo. The inclusion criteria were neurological medical diagnosis of RRMS,[4] EDSS score ≤ 6 points, and age between 18 and 65 years old.

The control group consisted of healthy individuals from the community, caregivers of patients, and students, and was homogeneous in terms of age, gender, height, and body mass index (BMI) in relation to the experimental group. The inclusion criteria for the control group were absence of a history of vestibular, auditory, body imbalance and/or headache symptoms, and absence of symptoms or of a diagnosis of neurological disease.

Patients in exacerbation (relapse) of demyelination in the previous 8 weeks, presenting with other neurological conditions not associated with MS, and under corticoid pulse therapy in the previous 3 months were excluded from the experimental group. In both groups, individuals who presented with inability to understand and meet simple verbal commands, with inability to remain independently in the orthostatic position, with severe or uncompensated visual impairment with the use of corrective lenses, with orthopedic disorders that result in limitation of movement or require the use of prostheses in the lower limbs, with a history of otological past, who had used medications that affect the vestibular system, and who had performed rehabilitation of body balance in the previous 6 months were excluded.

The evaluation consisted of anamnesis, application of the Dizziness Handicap Inventory (DHI) in the Brazilian

Portuguese version, visual vertigo analog scale (VVAS), and evaluation of postural control through static posturography.

Anamnesis was performed through a detailed interview, with the application of a questionnaire focused on the clinical history of the patients, including information on complaints of dizziness, postural instability, physical activity practice, and medications in use.

The DHI questionnaire on quality of life,[19] in the Brazilian Portuguese version,[20] was applied to assess the self-perception of disability imposed by dizziness. Twenty-five questions evaluated the physical, emotional, and functional aspects. The questionnaire was read by the researcher to all participants, who answered the questions with "yes," "no" or "sometimes." For each "yes" answer, four points were assigned; for "no," zero points; and for "sometimes," two points. The higher the score, the greater the loss in quality of life.[19] Self-perception of dizziness was considered mild between zero and 30 points; moderate between 31 and 60; and severe between 61 and 100 points.[21]

The self-perception of the intensity of dizziness was evaluated by the VVAS, consisting of a graduated line from zero to 10, in which zero corresponded to the absence of dizziness, and 10 to maximum dizziness.[22]

Postural control evaluation was performed with static posturography (Tetrax IBS, Sunlight Medical Ltd, Tel Aviv, Israel), which consists of a computer program, a platform with four integrated but independent plates (A-B-C-D), which capture the variations of weight distribution, handrails, and foam mattresses.

The participants were barefoot, with their toes and heels resting on the indicative design of the platform, fixed their gaze on a target in front of them and kept their posture upright and stable, with their arms extended along the body for 32 seconds, in each of the 8 sensory conditions. The examiner remained close to the participant during the procedure.

The sensory conditions evaluated were: 1) Stable surface, face forward, eyes open (NO); 2) Stable surface, face forward, eyes closed (NC); 3) Unstable surface, face forward, eyes open (PO); 4) Unstable surface, face forward, eyes closed (PC); 5) Stable surface, head with 45° rotation to the right, eyes closed (HR); 6) Stable surface, head with 45° rotation to the left, eyes closed (HL); 7) Stable surface, head tilted 30° back, eyes closed (HB); and, 8) Stable surface, head tilted 30° forward, eyes closed (HF).

The sensory condition in a stable surface, face forward and eyes open, which is in the neutral position, analyzes the visual, somatosensory, and vestibular systems; and the condition on a stable surface, face forward and eyes closed limits vision effect, testing the somatosensory and vestibular systems; and the condition of unstable surface, face forward and eyes open limits the effect of proprioception by stimulating the visual and the vestibular systems; the conditions of stable surface, head rotated 45° to the right or to the left and eyes closed also eliminate the vision and stimulate the vestibular system; and the conditions stable surface, head tilted 30° backward or forward and eyes closed eliminate the vision and stimulate the vestibular and cervical systems.[23]

The posturography measured the variations of the vertical force exerted by the heels and toes, allowing the characterization of the oscillation of the body according to the displacement of the pressure center. Tetrax IBS evaluated the indices of stability, weight distribution, synchronization of right/left postural oscillation and of toes/heels, frequencies F1 to F8, and frequency bands F1, F2–F4, F5–F6, F7–F8 of postural oscillation, in each of the 8 sensory conditions, and the Fall Risk Index.[23,24]

The stability index mathematically indicated the overall stability and the ability to compensate for postural modifications and evaluated the number of oscillations on the four platforms, according to body weight; the higher the score, the greater the instability.[23]

The weight distribution index compares the weight distribution on each of the four plates. The theoretically lowest limit is zero, with 25% of the weight distributed on each plate. In normal individuals, a value between 4 and 6% is expected. The higher the score, the greater the difficulty in maintaining balance. Very low values, close to zero, indicate postural stiffness, which is common in compensation mechanisms.[23]

The right/left and heel/toe synchronization postural oscillation indices measured the coordination between the lower limbs and symmetry in weight distribution. For each condition, six synchronizations were measured: heels and toes of each foot (AB, CD), two heels and toes of both feet (AC, BD), and the two diagonals, between the heel of one foot and the contralateral toes (AD, BC). The synchronization indices AB, CD, AD and CB are negative, and the BD and AC are positive. Values with inverted signals suggest excessive postural oscillation; low values indicate impairment; high values may be due to postural stiffness or to intentional simulation of lateral oscillation.[23]

The frequencies of postural oscillation vary in a spectrum between 0.01 and 3.0 Hz and were measured by Fourier transformation, a mathematical treatment that indicates the intensity of body oscillation at different frequencies.

Tetrax IBS subdivided the spectrum of postural oscillation into 4 frequency bands: low (F1), < 0.1 Hz; low-medium (F2–F4), between 0.1 and 0.5 Hz; medium-high (F5–F6), between 0.5 and 1.0 Hz; and high (F7–F8), > 1.0 Hz.

Each postural oscillation frequency band enhances the use of a certain postural subsystem. Prevalence of postural oscillations in the low frequency band suggests postural control and integrity of the vestibulovisual-otolytic systems; in the low-medium frequency band, it suggests peripheral vestibular dysfunction, physical fatigue or exhaustion, and alcohol intoxication; in the medium-high frequency band, it suggests somatosensory reactions mediated by the motor system of the lower limbs and the spine; and, in the high frequency band, it suggests CNS impairment.[23]

The fall risk index, expressed as a percentage, weighs the results of the Tetrax IBS parameters in the eight sensory conditions. It can vary between zero and 100; a value between zero and 36% is considered as mild risk (marked in green on the Tetrax IBS chart); a value between 37 and 58%, moderate risk (in yellow); and between 59 and 100%, high risk (in red). The higher the score, the higher the fall risk.

The individual performance of the patient in the analysis of all parameters in the eight sensory conditions allowed to identify the altered sensory systems involved in maintaining postural control,[23] according to the following characteristics: a) Substantial difference in weight or desynchronization of one of the feet from the other, consistent in all positions, would indicate deficiency in one of the lower extremities, as a function of an orthopedic problem or neurological dysfunction; b) Low and consistent performance in sensory conditions HR, HL, HF and HB in relation to NO, NC, PO and PC conditions would indicate cervical vestibular disorders; c) Low and consistent performance in the values of the Stability Index and increased postural oscillation in different frequency bands would indicate impairment in the vestibular and somatosensory systems or CNS impairment. Consistently low performance in weight distribution and synchronization indices of postural oscillation points in the direction of orthopedic problems; d) Consistently poor results in all conditions and parameters suggest a generalized lower limb problem or severe CNS disorder; e) Consistently poor performance in all sensory conditions in the values of the Stability Index and increase of postural oscillation in different frequency bands, with normal or close to normal results, in all conditions in the weight distribution and synchronization of postural oscillation indices, often indicates intentional simulation of body oscillation; f) Inconsistent responses in some sensory conditions, with others without change, imply test repetition; g) Low performance in a specific postural oscillation frequency band could be related to one of the following changes: F1) visual dysfunction; F2–4) vestibular dysfunction, mainly peripheral; F5–6) somatosensory dysfunction; and, F7–8) central vestibular dysfunction; h) Changes in all frequency bands would indicate widespread disturbance of the postural system, provided that the weight distribution and synchronization indices of the postural oscillation also show poor results; i) Increased body oscillation in the low-medium frequency band (F2–F4), altered weight distribution to compensate for loss of balance, relatively worse performance in sensory condition PC, discrepancy between performance in sensory conditions HR and HL related to lateralization of vestibular dysfunction, normal synchronization and normal stability, if vestibular dysfunction is well compensated, suggest peripheral vestibular system dysfunction; j) Increased and abnormal body oscillation in the high frequency band (F7–F8), low synchronization in general and, in particular, in the stressful vestibular sensory condition PC and altered performance in general stability and weight distribution suggest central vestibular system dysfunction.

The statistical analysis was initially performed in a descriptive way through the average, median, minimum and maximum values, standard deviation (SD), and absolute and relative frequencies (percentage). The inferential analyses employed to confirm or refute evidence found in the descriptive analysis were:

- Mann-Whitney[25] to compare the characteristics of quantitative nature between groups (experimental and control); and the Fall Risk Index (%), according to time of disease ($\leq$10 years, $>$10 years), EDSS ($\leq$ 3 and $>$3 points), complaint of postural instability, and the practice of physical activity;
- Kruskal-Wallis[25] to compare the fall index, according to the degree of fall risk (mild, moderate, or high); and the Fall Risk Index (%), according to dysfunction in Tetrax IBS (peripheral, central, or absent);
- Pearson chi-squared test, Fisher exact test, or its extension[26] to compare the groups (experimental and control), according to characteristics of a qualitative nature.

In all conclusions of the inferential analyses, the level of Alpha significance equal to 5.0% was used. The data were entered into Microsoft Excel 2010 for Windows (Microsoft Corporation, Redmond, WA, USA) spreadsheets for proper information storage. Statistical analyses were performed with the statistical program R version 3.3.2. (R Foundation, Vienna, Austria).

Results

Of the 352 patients referred to the Outpatient Clinic of Demyelinating Diseases of the Discipline of Neurology, outpatient clinic of demyelinating diseases of the Department of Neurology and Neurosurgery, Universidade Federal de São Paulo, 106 consecutive patients met the inclusion criteria for the experimental group and were asked by telephone contact to perform the procedure; and 55 did not show up on the scheduled day or refused to participate in the trial. The final sample of the experimental group consisted of 51 patients diagnosed with RRMS and 28 healthy individuals from the control group.

►**Table 1** shows the demographic data and clinical characteristics of the two groups.

►**Table 2** shows the results of the DHI and of the VVAS of the experimental group.

►**Table 3** shows the descriptive values and comparative analysis of the weight distribution index and the general stability index of the experimental and control groups in the eight sensory conditions in Tetrax IBS. The weight distribution index was higher in the experimental group under sensory conditions head with rotation of 45° to the right on firm surface (HR) and head tilted 30° back on firm surface (HB), with a statistically significant difference. The experimental group presented a higher overall stability index than the control group in all the conditions evaluated, with a statistically significant difference.

►**Table 4** presents the descriptive values and comparative analysis of the synchronization indices of the experimental and control groups in the eight sensory conditions in Tetrax IBS. There was no statistically significant difference between the groups in the condition of eyes closed on a firm surface (NC), in the synchronization between the toes and the heel of the left foot (AB) and the toes of the right foot and the toes of the left foot (BD); in the conditions with the head rotated 45° to the left on a firm surface (HL), and eyes closed on an unstable surface (PC), the synchronization between the toes

Table 1 Descriptive values and comparative analysis of demographic data and clinical characteristics of experimental and control groups

Demographics and clinical characteristics		RRMS ($n = 51$)		CO ($n = 28$)		*p*-value
Gender	Female	34	66.7%	23	82.1%	0.142 [b]
	Male	17	33.3%	5	17.9%	
Age (years old)	Median	39.0		29.0		0.148 [a]
	Minimum	18.0		18.0		
	Maximum	65.0		58.0		
Weight (kg)	Median	68.6		63.5		0.085 [a]
	Minimum	40.8		41.6		
	Maximum	129.2		101.7		
Height (cm)	Median	167.0		163.5		0.240 [a]
	Minimum	149.0		130.0		
	Maximum	190.0		187.0		
BMI (kg/m2)	Median	24.9		23.5		0.241 [a]
	Minimum	17.2		16.3		
	Maximum	40.8		60.2		
Physical activity	Yes	17	33.3%	14	50.0%	0.147 [a]
	No	34	66.7%	14	50.0%	
Postural instability	Yes	32	62.7%	–	–	
	No	19	37.3%	–	–	
Fall	Yes	18	35.3%			
	No	33	64.7%			
Time of disease (years)	Median	12.0		–		
	Minimum	1.0		–		
	Maximum	20.0		–		
EDSS	Median	2.0		–		
	Minimum	0.0		–		
	Maximum	6.0				

Abbreviations: CO, control; EDSS, Expanded Disability Status Scale; RRMS, relapsing-remitting multiple sclerosis.
[a]Mann-Whitney Test.
[b]Pearson chi-squared test.
*Statistically significant value at the level of 5% ($p < 0.05$).

of the right foot and the toes of the left foot (BD); on the condition with the head tilted 30° backward, firm surface (HB), the synchronization between the toes and the heel of the left foot (AB), or between the toes and the heel of the right foot (CD) and between the toes of the right foot and the toes of the left foot (BD); and the condition with the head tilted 30° forward, firm surface (HF), the synchronization between the toes and the heel of the left foot (AB).

►**Table 5** shows the descriptive values and the comparative analysis of postural oscillation frequency bands (F1, F2–F4, F5–F6, F7–F8) of the experimental and control groups in the 8 sensory conditions in Tetrax IBS. In the conditions of closed eyes on firm surface (NC); head with rotation of 45° to the right on firm surface (HR); head with rotation of 45° to the left on firm surface (HL); head tilted 30° backward on firm surface (HB); head tilted 30° forward on firm surface (HF); and closed eyes on unstable surface (PC), the experimental group presented higher values than those of the control group in all frequency bands, with a statistically significant difference. In the conditions of open eyes on a firm surface (NO), and of open eyes on an unstable surface (PO), the experimental group presented higher values than those of the control group in the frequency bands F2–F4, F5–F6, and F7–F8, with a statistically significant difference.

►**Table 6** presents the descriptive values and the comparative analysis of the fall risk index of the experimental and control groups in Tetrax IBS. The experimental group had a higher Fall Risk Index than the control group, with a statistically significant difference.

In the control group, the 28 (100.0%) individuals had a mild degree fall risk in Tetrax IBS. ►**Table 7** shows the distribution of patients in the experimental group according to the degree of fall risk in Tetrax IBS. The proportion of patients at moderate and high fall risk was significantly

Table 2 Descriptive values of the Dizziness Handicap Inventory and of the visual vertigo analogue scale of the experimental group

Assessments		RRMS (51)	
Physical DHI	Median	6.0	
	Minimum	0.0	
	Maximum	28.0	
Functional DHI	Median	2.0	
	Minimum	0.0	
	Maximum	30.0	
Emotional DHI	Median	0.0	
	Minimum	0.0	
	Maximum	36.0	
Total DHI	Median	10.0	
	Minimum	0.0	
	Maximum	94.0	
DHI degree (*n*, %)	Asymptomatic	20	39.2%
	Light	20	39.2%
	Moderate	08	15.7%
	Severe	03	5.9%
VVAS	Median	3.0	
	Minimum	0.0	
	Maximum	10.0	

Abbreviations: DHI, Dizziness Handicap Inventory; RRMS, relapsing-remitting multiple sclerosis; VVAS, visual vertigo analogue scale.

higher in the experimental group compared with the control group ($p < 0.001$).

The general analysis of postural performance identified, in the experimental group, 26 (51.0%) patients with main pattern of impairment of the vestibular, visual and/or somatosensory systems of peripheral type, namely, 15 (29.5%) cases of the vestibular system, 8 (15.7%) of the vestibular and somatosensory systems, 2 (3.9%) of the vestibular, visual and somatosensory systems, 1 (1.9%) of the vestibular and visual, and 11 (21.6%) with vestibular, visual and/or somatosensory impairment of the central type, with 7 (13.7%) of the vestibular system, 4 (7.8%) of the vestibular system with cervical impairment, and 14 (27.4%) without alterations. In the control group, no change was found in the maintenance of postural control in the 28 (100.0%) individuals evaluated.

►**Table 8** shows the type of dysfunction as peripheral, central or absent in relation to the Fall Risk Index in Tetrax IBS in the experimental group. Patients with peripheral and central dysfunction had a higher fall risk than patients without dysfunction, with a statistically significant difference ($p < 0.001$). There was no statistically significant difference ($p = 0.295$) between patients with peripheral and central dysfunction in relation to the fall risk index.

►**Table 9** shows the distribution of patients according to the time of disease, EDSS score, symptoms of dizziness, postural instability, physical activity practice, DHI and VVAS in relation to the Fall Risk Index of Tetrax IBS in the experimental group. There was no statistically significant difference ($p = 0.932$) between the fall risk index of the experimental group and time of disease $\leq$ 10 years (24 cases [47.1%]) or $>$ 10 years (27 cases [52.9%]). Patients in the experimental group with EDSS $>$ 3 points (14 [27.5%]) had a higher fall risk than those with EDSS $\leq$ 3 points (37 [72.5%]), with a statistically significant difference ($p = 0.003$). There was a positive correlation between the fall risk index and the total DHI score ($s = 0.380$; $p = 0.006$) and the VVAS ($s = 0.348$; $p = 0.012$), when estimating the Spearman correlation coefficient in the experimental group. There was no relationship between the fall risk index and the complaint of dizziness ($p = 0.192$), the complaint of postural instability ($p = 0.148$), and the practice of physical activity ($p = 0.706$).

Discussion

In the present study, the postural control of patients with RRMS was evaluated by static posturography with Tetrax IBS. The group of patients with RRMS had a predominance of women, with a median age of 39.0 years old, which is in line with other authors, who reported a higher occurrence of the condition in women and young adults.[5]

Patients with RRMS presented a mild degree in the total DHI score, identifying a mild impact of dizziness on functional, physical, and emotional well-being.[20,27] The EDSS also demonstrated low functional disability in patients with RRMS.

Postural instability was reported in 62.7% of the cases, and 35.3% of the evaluated patients reported falls. Body balance disorders were described in 78.0% of patients with MS.[9,10]

Table 3 Descriptive values and comparative analysis of the weight distribution index and the general stability index in the eight conditions of the Tetrax Interactive Balance System (Tetrax IBS) of the experimental and control groups

		Weight distribution index			Stability Index		
		RRMS ($n = 51$)	CO ($n = 28$)	*p-value*	RRMS ($n = 51$)	CO ($n = 28$)	*p-value*
NO	Median	4.98	5.00	0.862	15.53	10.99	$< 0.001^*$
	Minimum	1.30	1.69		7.46	5.38	
	Maximum	11.83	11.43		58.36	18.97	
NC	Median	5.04	4.63	0.197	23.86	16.61	$< 0.001^*$
	Minimum	1.35	0.94		8.11	6.66	
	Maximum	13.30	10.82		77.02	24.98	
HR	Median	6.07	4.33	0.048^*	21.26	13.93	$< 0.001^*$
	Minimum	1.76	0.86		9.02	6.25	
	Maximum	13.98	11.60		84.65	24.17	
HL	Median	5.27	4.69	0.219	21.73	14.24	$< 0.001^*$
	Minimum	2.14	1.25		9.24	5.96	
	Maximum	12.84	12.54		76.34	21.39	
HB	Median	5.67	4.06	0.007^*	23.81	15.67	$< 0.001^*$
	Minimum	2.11	1.31		11.21	6.40	
	Maximum	15.86	13.83		91.31	23.28	
HF	Median	5.83	5.37	0.351	21.43	14.60	$< 0.001^*$
	Minimum	1.90	2.27		11.36	6.75	
	Maximum	15.00	14.34		62.54	27.06	
PO	Median	5.37	5.04	0.846	25.38	16.20	$< 0.001^*$
	Minimum	1.57	1.91		12.64	10.34	
	Maximum	14.38	10.88		60.25	29.85	
PC	Median	4.56	4.68	0.846	38.56	21.49	$< 0.001^*$
	Minimum	0.81	1.64		17.19	12.17	
	Maximum	13.26	10.82		87.60	39.36	

Abbreviations: CO, control; HB, eyes closed, head tilted 30° backward, on a firm surface; HF, eyes closed, head tilted 30° forward, firm surface; HL, eyes closed, head rotated 45 ° to the left, and on a firm surface; HR, eyes closed, head rotated 45 ° to the right, on a firm surface; NC, eyes closed, firm surface; NO, eyes open, firm surface; PC, eyes closed on an unstable surface; PO, eyes open on an unstable surface; RRMS, relapsing-remitting multiple sclerosis.
Mann-Whitney test.
*Statistically significant value at the level of 5% ($p < 0.05$).

Postural instability is considered one of the most disabling symptoms of the disease, as it generates negative effects on mobility and independence, leading to injuries, falls, and, consequently, impacting on the quality of life.[28] Postural control, often impaired in MS patients, is a complex skill based on the sensory integration of visual, somatosensory, and vestibular information in the brainstem.[29] Thus, the importance of a diagnostic method that evaluates this information individually becomes evident. Static posturography with Tetrax IBS uses different parameters and procedures from other types of posturographies, which makes it difficult to compare the results quantitatively with those from other devices.

The group of patients with RRMS showed higher values of the weight distribution index in Tetrax IBS only in two sensory conditions on a stable surface with closed eyes: in the head rotation to the right and in the head backward inclination, characterizing irregular weight distribution in the platform plates. Change in weight distribution index, predominantly in closed-eye sensory conditions, was described in 58% of the patients with MS.[30] No studies were found in the literature on posturography weight distribution index in Tetrax IBS in RRMS.

The overall stability index of patients with RRMS in Tetrax IBS showed increased values in relation to controls in all eight sensory conditions, revealing postural control inability. Reduced overall stability was also described in the four evaluated sensory conditions – with open and closed eyes, on a stable surface, and on an unstable surface – in cases of MS, when compared with controls, in Tetrax IBS.

Regarding the control group, the patients with RRMS presented on Tetrax IBS a reduction in the synchronization indices of the postural oscillation: between the right toes and the left toes in four of the eight sensory conditions, and an

Table 4 Descriptive values and comparative analysis of the synchronization indices in the eight conditions of the Tetrax Interactive Balance System (Tetrax IBS) of the experimental and control groups

		AB			CD			AC			BD			AD			BC		
		RRMS	CO	*p*-value	RRMS	CO	*p*-value	RRMS	CO	*p*-value	RRMS	CO	*p*-value	RRMS	CO	*p*-value	RRMS	CO	*p*-value
		(*n* = 51)	(*n* = 28)		(*n* = 51)	(*n* = 28)		(*n* = 51)	(*n* = 28)		(*n* = 51)	(*n* = 28)		(*n* = 51)	(*n* = 28)		(*n* = 51)	(*n* = 28)	
NO	Median	−831.93	−869.70	0.219	−869.03	−889.19	0.461	635.67	706.72	0.967	767.99	836.80	0.137	−851.53	−872.92	0.616	−907.23	−872.21	0.053
	Minimum	−981.16	−985.59		−991.18	−978.90		−155.32	−102.29		−57.16	153.01		−987.84	−967.41		−986.73	−960.79	
	Maximum	−80.67	−205.42		−286.10	−97.60		969.14	868.03		976.72	951.92		−260.84	−402.23		−231.33	−430.22	
NC	Median	−861.06	−920.75	0.031*	−904.04	−909.57	0.207	727.43	734.20	0.539	820.52	881.93	0.028*	−882.64	−903.96	0.566	−914.99	−906.88	0.330
	Minimum	−989.79	−986.57		−989.26	−985.72		−430.96	80.00		19.06	−86.13		−979.75	−976.66		−981.65	−972.19	
	Maximum	677.38	−744.95		423.88	−645.89		941.34	931.69		976.43	980.81		−420.06	−189.09		−596.03	13.92	
HR	Median	−876.54	−908.20	0.062	−894.34	−901.94	0.870	738.60	721.62	0.862	847.50	891.55	0.068	−893.49	−918.07	0.406	−916.89	−900.69	0.601
	Minimum	−980.03	−989.37		−986.67	−988.27		−651.09	77.94		−195.12	631.09		−972.49	−985.92		−982.85	−981.92	
	Maximum	503.68	−592.61		312.76	−385.32		957.94	952.65		964.19	989.21		−180.66	−666.18		−158.16	−444.97	
HL	Median	−841.20	−842.40	0.412	−894.48	−877.52	0.927	543.93	660.27	0.518	797.93	837.88	0.045*	−856.35	−879.37	0.239	−885.47	−886.18	0.902
	Minimum	−977.42	−977.71		−990.63	−977.93		−251.77	−336.19		−177.39	636.60		−976.60	−972.81		−981.66	−975.71	
	Maximum	12.53	−289.86		304.68	74.38		904.66	923.64		965.00	981.06		−16.89	−319.57		−355.88	−277.62	
HB	Median	−865.04	−921.48	0.013*	−876.86	−936.90	0.043*	687.18	761.27	0.190	776.86	883.82	0.021*	−888.12	−899.12	0.190	−914.64	−896.72	0.935
	Minimum	−986.93	−991.37		−989.69	−985.22		−463.45	212.95		−147.46	−7.34		−967.96	−976.39		−985.41	−985.07	
	Maximum	196.12	−236.91		9.39	−336.87		929.99	926.26		983.71	987.48		202.11	−631.60		−250.41	−356.97	
HF	Median	−839.36	−916.92	0.004*	−907.61	−909.67	0.406	634.93	708.75	0.239	819.95	864.23	0.055	−863.04	−876.48	0.727	−910.74	−866.07	0.103
	Minimum	−989.09	−980.24		−991.23	−991.11		−727.61	92.29		−6.13	635.11		−987.67	−956.12		−987.28	−966.70	
	Maximum	287.60	−304.73		789.54	−711.61		968.96	917.98		974.39	973.07		−81.40	−534.96		−304.63	−581.76	
PO	Median	−750.41	−799.16	0.095	−811.91	−824.82	0.854	642.21	806.13	0.081	663.79	757.91	0.320	−911.61	−918.77	0.927	−926.95	−947.02	0.239
	Minimum	−986.52	−963.23		−977.45	−983.70		−332.84	285.97		−748.72	87.70		−982.37	−990.61		−992.12	−992.88	
	Maximum	625.59	−334.90		47.40	−161.11		977.85	959.51		972.45	958.72		−115.90	−484.03		−50.64	−581.46	
PC	Median	−776.46	−836.07	0.054	−852.33	−890.31	0.095	745.61	771.60	0.148	755.21	848.09	0.048*	−935.67	−936.29	0.325	−943.43	−952.41	0.362
	Minimum	−978.68	−984.79		−981.96	−972.60		−164.12	312.42		19.00	339.71		−989.30	−984.93		−989.98	−993.51	
	Maximum	519.49	−565.85		549.51	−373.60		977.82	964.21		967.98	980.78		−633.73	−761.35		−629.05	−815.00	

Abbreviations: AB, index of synchronization between platforms related to toes and the heel of the left foot; AC, index of the synchronization between the right and the left heels; AD, index of synchronization between the left heel and the toes of the right foot; BC, index of synchronization between the toes of the left foot, and the heel of the right foot; BD, index of synchronization between the toes of the right foot and the toes of the left foot; CD, index of synchronization between toes and the heel of the right foot; CO, control; HB, eyes closed, head tilted 30° backward, on a firm surface; HF, eyes closed, head tilted 30° forward, firm surface; HL, eyes closed, head rotated 45° to the left, and on a firm surface; HR, eyes closed, head rotated 45° to the right, on a firm surface; NC, eyes closed on firm surface; NO, eyes open, firm surface; PC, eyes closed on an unstable surface; PO, eyes open on an unstable surface; RRMS, relapsing-remitting multiple sclerosis; Mann-Whitney test.
*Statistically significant at the 5% level ($p < 0.05$).

Table 5 Descriptive values and comparative analysis of postural oscillation frequency bands (F1, F2–F4, F5–F6, F7–F8) in the eight conditions of the Tetrax Interactive Balance System (Tetrax IBS) of the experimental and control groups

		BAND F1			BAND F2-F4			BAND F5-F6			BAND F7-F8		
Condition		RRMS ($n=51$)	CO ($n=28$)	*p*-value	RRMS ($n=51$)	CO ($n=28$)	*p*-value	RRMS ($n=51$)	CO ($n=28$)	*p*-value	RRMS ($n=51$)	CO ($n=28$)	*p*-value
NO	Median	16.02	12.80	0.143	7.54	5.50	< 0.001*	3.22	2.39	0.002*	0.49	0.41	0.030*
	Minimum	6.68	5.71		2.91	2.75		1.12	1.09		0.24	0.18	
	Maximum	49.92	22.59		21.14	8.43		13.12	3.89		1.44	0.69	
NC	Median	14.57	10.01	0.029*	10.46	8.35	0.004*	4.60	3.06	< 0.001*	0.70	0.53	0.018*
	Minimum	4.55	5.07		4.52	4.31		1.57	0.93		0.30	0.17	
	Maximum	45.38	25.08		43.95	12.74		14.16	5.07		3.02	0.95	
HR	Median	15.41	10.99	0.004*	10.31	6.59	< 0.001*	4.07	2.49	< 0.001*	0.72	0.38	< 0.001*
	Minimum	4.49	4.67		4.26	4.56		1.32	0.90		0.28	0.19	
	Maximum	44.90	32.05		49.10	11.12		12.59	3.92		3.23	0.91	
HL	Median	13.28	10.08	0.010*	9.89	6.25	< 0.001*	3.96	2.58	< 0.001*	0.66	0.44	< 0.001*
	Minimum	4.89	5.16		4.30	3.52		1.56	1.17		0.29	0.18	
	Maximum	36.52	29.70		32.81	9.89		11.14	4.31		2.87	0.85	
HB	Median	16.74	10.79	0.009*	11.22	7.45	< 0.001*	4.23	2.72	< 0.001*	0.74	0.47	< 0.001*
	Minimum	5.66	2.44		4.32	4.10		1.63	0.90		0.38	0.19	
	Maximum	42.94	34.44		51.58	11.63		15.21	4.20		2.56	0.86	
HF	Median	15.49	12.83	0.024*	11.16	7.33	< 0.001*	4.22	2.74	< 0.001*	0.71	0.53	0.001*
	Minimum	2.63	3.87		2.62	3.50		2.02	1.27		0.34	0.19	
	Maximum	69.70	25.27		28.06	14.35		11.05	5.14		3.13	1.00	
PO	Median	20.69	21.23	0.559	9.19	6.31	< 0.001*	5.00	3.43	< 0.001*	0.81	0.54	0.001*
	Minimum	7.27	10.83		4.70	4.18		2.36	2.12		0.25	0.35	
	Maximum	64.57	37.22		38.55	8.96		11.97	5.91		1.98	1.01	
PC	Median	27.69	17.24	0.005*	15.18	9.89	< 0.001*	7.27	3.68	< 0.001*	1.30	0.79	< 0.001*
	Minimum	6.41	8.08		6.45	6.87		2.59	1.93		0.54	0.37	
	Maximum	90.91	40.96		38.10	20.18		17.62	6.94		3.98	1.36	

Abbreviations: CO, control; F1, F2-F4, F5-F6, F7-F8, postural oscillation frequency bands; HB, eyes closed, head tilted 30° backward, on firm surface; HF, eyes closed, head tilted 30° forward, on firm surface; HL, eyes closed, head 45° to the left, on firm surface; HR, eyes closed, head 45° to the right, on firm surface; NC, eyes closed, on firm surface; NO, eyes open, on firm surface; PC, eyes closed on an unstable surface; PO, eyes open on an unstable surface; RRMS, relapsing-remitting multiple sclerosis.
Mann-Whitney test.
*Statistically significant value at the level of 5% ($p < 0.05$).

Table 6 Descriptive values and comparative analysis of the Fall Risk Index (%) in the Tetrax Interactive Balance System (Tetrax IBS) of the experimental and control groups

		Fall Risk Index (%)		
	RRMS	CO	Total	*p-value*
n	51	28	79	< 0.001*
Average	52.51	10.86	37.75	
Median	42.00	7.00	26.00	
Minimum	4.00	2.00	2.00	
Maximum	100.00	28.00	100.00	
Standard deviation	33.48	8.19	33.82	

Abbreviations: CO, control; RRMS, relapsing-remitting multiple sclerosis.
Mann-Whitney Test.
*Statistically significant value at the level of 5% ($p < 0.05$).

Table 7 Distribution of patients according to the degree of fall risk in the Tetrax Interactive Balance System (Tetrax IBS) in the experimental group

	Degree of Fall Risk				
	Light	Moderate	HIgh	Total	*p-value*
n	22	8	21	51	< 0.001*
Average	21,0	43.5	89.0	52.5	
Median	16.0	43.0	94.0	42.0	
Minimum	4.0	38.0	64.0	4.0	
Maximum	36.0	52.0	100.0	100.0	
Standard deviation	10.7	4.6	12.5	33.5	

Kruskal-Wallis test.
*Statistically significant value at the level of 5% ($p < 0.05$).

increase in the synchronization index of the postural oscillation between the toes and the right or left heel in three sensory conditions, characterizing incoordination between the lower limbs and asymmetry in weight distribution. No studies were found in the literature that evaluated the postural oscillation synchronization indices in RMSS.

Patients with RRMS showed greater postural oscillation in Tetrax IBS than the control group in six of the eight sensory conditions evaluated in all frequency bands and in two of the sensory conditions in all frequency bands, with the exception of the low-frequency band. Postural performance without alteration is characterized by greater postural oscillation at low frequency (F1), suggesting integrity of the vestibular visual and otolithic systems. Each postural oscillation frequency band enhances the use of a certain functional subsystem. When the low-frequency oscillation does not maintain body balance effectively, the oscillation in the low-medium band (F2–F4) prevails, suggesting peripheral

Table 8 Distribution of patients according to the type of dysfunction: peripheral, central or absent, and Fall Risk Index in the Tetrax Interactive Balance system (Tetrax IBS) in the experimental group

Type of dysfunction in	Fall Risk Index (%)						
Tetrax IBS	*n*	Average	Median	Minimum	Maximum	Standard deviation	*p-value*
Peripheral	26	62.8	58.0	26.0	100.0	26.9	< 0.001*
Central	11	76.9	94.0	34.0	100.0	27.4	
Absent	14	14.1	14.0	4.0	30.0	6.0	
Total	51	52.5	42.0	4.0	100.0	33.5	

Kruskal-Wallis test.
*Statistically significant value at the level of 5% ($p < 0.05$).

Table 9 Distribution of patients according to the time of disease, score on the expanded disability status scale, postural instability, physical activity practice, Dizziness Handicap Inventory, and visual vertigo analogue scale in relation to the Fall Risk Index in the Tetrax Interactive Balance system (Tetrax IBS) in the experimental group

	Fall Risk Index (%)						
	n	Average	Median	Minimum	Maximum	Standard deviation	*p-value*
Time of disease							
≤ 10 years	24	54.3	39.0	4	100.0	33.8	0.932
> 10 years	27	50.9	44.0	6	100.0	33.7	
Total	51	52.5	42.0	4	100.0	33.5	
EDSS							
≤ 3	37	43.7	36.0	4	100.0	30.9	0.003*[a]
> 3	14	75.7	87.0	18	100.0	29.4	
Total	51	52.5	42.0	4	100.0	33.5	
Postural instability							
Yes	32	57.2	45.0	14.0	100.0	31.70	0.148
No	19	44.5	36.0	4.0	100.0	35.71	
Physical activity							
Yes	17	57.8	46.0	14.0	100.0	33.0	0.706
No	34	49.9	39.0	4.0	100.0	33.9	
	Correlation analyses						
	n		*p-value*	r			
DHI	51		0.006*[c]	0.380			
VVAS	51		0.012*[c]	0.348			

Abbreviations: DHI, Dizziness Handicap Inventory; EDSS, Expanded Disability status Scale; VVAS, visual vertigo analog scale.
[a]Mann-Whitney test.
[c]Spearman(s) correlation test.
*statistically significant value at the level of 5% ($p < 0.05$).

vestibular dysfunction; and/or in the middle-high band, suggesting somatosensory reactions; and/or in the high band, indicating CNS impairment.[23] One study identified greater postural oscillation in the frequencies F2, F4, and F5 in patients with MS in Tetrax IBS compared with healthy individuals, and all altered cases presented clinical or imaging signs, indicating brainstem injury.[30]

In Tetrax IBS, the group of patients with RRMS showed higher fall risk values compared with the control group, as well as a higher proportion of patients with moderate and high fall risk. In agreement with this finding, just over a third of the number of RRMS cases reported at least one episode of fall during the course of the disease. Patients with peripheral or central dysfunction in Tetrax IBS had a higher fall risk than patients without abnormalities, while the fall risk was similar in cases with peripheral and central dysfunction.

In patients with MS, the incidence of falls is considered high, and its prevalence can vary from 31.0 to 63.0%,[8,14,16,28,31] often resulting in a decrease in functional capacity due to the fear of new falls, present in ~ 63.5 to 69.0% of patients with MS.[14,28,32] Postural control depends on the integration of visual, somatosensory, vestibular systems and adequate motor responses, which are often impaired in patients with MS, contributing to increase the fall risk.[33]

The analysis of postural performance identified in most patients with RRMS the pattern of peripheral dysfunction, showing changes in the vestibular; vestibular and somatosensory; vestibular, visual and somatosensory; and vestibular and visual systems, in descending order of prevalence, and, with a lower occurrence, the pattern of central dysfunction, indicating changes in the vestibular and/or cervical systems. Studies using different types of posturographies also reported the impairment of different systems involved in maintaining body balance in patients with RRMS.[18,34–38]

Postural instability is greater in more challenging sensory conditions, reducing the support base, suppressing visual or vestibular information and/or altering the proprioceptive system in patients with RRMS.[39,40] Even in the sensory condition of open eyes and stable surface, using all sensory inputs, two thirds of the total number of patients with MS present abnormal postural performance, which can reach 82.0% of cases when there is disturbance of one of the sensory information.[29]

There was a correlation between the fall risk index and the EDSS, of ≤ 3 or > 3 points, in patients with RRMS. The EDSS is used by the neurologist to assess the neurological disability of patients with MS; scores > 4.5 are greatly influenced by the ability to walk; therefore, the higher the EDSS score, the higher the fall risk.[14,41] No studies were found in the literature on the fall risk measured by static posturography and by the EDSS in patients with RRMS. However, there is a positive relationship between static and dynamic posturography parameters and the EDSS.[38,42] Important postural imbalance at dynamic posturography and low functional disability in patients with MS indicate that this examination is a valuable method of disease monitoring.[18]

There was no correlation between the fall risk index and time of disease $\leq$ 10 years or $>$ 10 years in the group with RRMS. Studies evaluating the fall risk index measured by a posturography and the time of disease were not found in the literature. Some authors have described a positive correlation between the time of disease and the overall body performance score by means of dynamic posturography in patients with MS.[43]

In patients with RRMS, there was a positive correlation between the Fall Risk Index and the score of the DHI and VVAS quality of life questionnaires, demonstrating the relevance of the DHI and the VVAS in the assessment of the fall risk in patients with RRMS and justifying its use in evaluation protocols. The reliability and validity of the DHI in patients with MS have been demonstrated in previous studies.[29,44] The DHI was considered a good predictor of fall in cases of MS with and without falls, and the questionnaire score was 31.0% higher in the group with reported falls, with the physical and functional aspects being the most impaired.[29] The impact of dizziness and/or imbalance on the functional, physical, and emotional well-being of patients with MS was demonstrated with the DHI score when compared with healthy individuals.[45] No research was found in the literature that evaluated the Fall Risk Index and the VVAS.

There was no relationship between the Fall Risk Index, the complaint of postural instability, and the practice of physical activity in the group with RRMS, and more than one-third of the sample practiced physical activity with nonspecific exercises. The practice of physical activity in patients with MS should be performed after assessment and individual counseling, considering the severity of the disease, the type of MS, age, the degree of disability and of functional disability.[46,47]

Similar to the findings regarding RRMS in Tetrax IBS posturography, other posturographic evaluations were also able to identify changes in body balance, even in RRMS without complaint of postural instability and with a low degree of functional disability in the EDSS, in the clinical evaluation.[37,39,40]

Conclusion

Patients with RRMS may present inability to maintain postural control due to general instability, desynchronization and increased postural oscillation at frequencies that suggest deficiencies in the vestibular, visual, and somatosensory systems; fall risk was related to the state of functional disability and to the intensity and self-perception of the influence of dizziness on the quality of life of the patient.

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