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ORIGINAL ARTICLE

Integrated Cognitive Training and Vestibular Rehabilitation Therapy in Management of Imbalance in Patients with Remitting Relapsing Multiple Sclerosis

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ABSTRACT

BACKGROUND Remitting Relapsing MS (RRMS) is the most prevalent type of MS. During the course of their illness, patients reported symptoms related to vestibular, visual, and somatosensory problems. The main objective of the study was to assess the effect of customized VRT versus integrated cognitive training and customized VRT on balance problems in RRMS patients. **METHODS** This interventional prospective cohort study was conducted from January 2021 to March 2022 at the Audio-Vestibular Medicine Unit, ENT Department, Faculty of Medicine, Zagazig University. A comprehensive sample included 48 participants with RRMS; were randomized into three groups (n=16 each), who attended the Outpatient Clinic of the Neurology Department of Zagazig University Hospitals for 12 months (nearly 4 cases per month). The period of intervention lasted for a total of six weeks for each participant who were subjected to Full history taking, neurological evaluation, Magnetic resonance imaging , Otological examination, Basic audiological assessment, Vestibular evaluation, Cognitive assessment. **RESULTS** The three study groups were comparable in age, sex, clinical history related to RRMS, dizziness history, and associated symptoms. the cognitive evaluation revealed average scores that reflect moderate impairment across participants. Importantly, there were no statistically significant differences in vestibular and cognitive deficits among the three groups ($p \geq 0.05$). **CONCLUSIONS** Abnormalities indicating central vestibular pathology are significant findings in patients with RRMS as well as a moderate cognitive impairment linked to white and grey matter abnormalities. Integrating cognitive training with VRT has been shown to be more effective in improving stability than using customized VRT alone

KEYWORDS Multiple sclerosis; Vestibular rehabilitation therapy; cognitive impairment

INTRODUCTION

Multiple sclerosis (MS) is the most prevalent chronic autoimmune disease of the central nervous system (CNS), in which inflammation, demyelination, and axonal loss occur even in the early stages of the disease. MS is mainly diagnosed during adulthood, typically between 20 and 40 years of age with women affected three times as frequently as men [1]. Remitting Relapsing MS (RRMS) is the most prevalent type of MS, impacting roughly 85% of MS patients. It is characterized by exacerbations of symptoms followed by periods of remission during which the symptoms diminish or subside. The pathogenesis of this disorder involves the destruction of the myelin sheath, thereby disturbing the communication to and from the brain. Therefore, MS is associated with manifestations such as cognitive impairment, loss of coordination, and imbalance[2].

During the course of their illness, patients with RRMS reported symptoms that are related to vestibular, visual, and somatosensory problems. Vestibular symptoms, such as vertigo, imbalance, unsteadiness, and nausea frequently appear during the onset of the disease. The type and severity of vestibular symptoms differ from one patient to another. Visual manifestations such as diplopia, nystagmus, abnormal saccades, and optic neuritis are also common in MS .Moreover, patients could require great assistance in their daily living activities [3].

Progressive cognitive impairment is considered the most debilitating symptom of MS as it leads to significant social and economic problems. Information processing speed, complex attention, episodic memory, executive functioning, navigation, and visuospatial abilities are typically the most commonly affected abilities [4].

There is a physiological connection between cognitive function and postural control, which are respectively controlled by specific cortical areas and the cerebellum with a series of interconnecting neural networks. Cognitive domains are necessary for postural control. Therefore, a combined investigation of the higher cognitive function and balance control provides insight into real-life affectations in MS patients who experience cognitive and balance disorders [2].

Vestibular rehabilitation therapy (VRT) is an exercise-based strategy that enhances gaze and postural stability through a customized exercise program. It is believed that standard neuro-rehabilitation training in RRMS patients should include VRT strategies [5]. Moreover, cognitive training therapy was found to improve cognitive function in RRMS patients with subsequent improvement of balance and postural control [6]. Computer-based cognitive training (CCT) is one specific type of cognitive intervention. It usually consists of computer exercises that resemble games, are customizable to each person's performance, and can target several cognitive domains [7].Little is known about the impact of integrated cognitive training and customized VRT on life quality in subjects with RRMS. Therefore, the current study was conducted on patients with RRMS who had dizziness or a sense of imbalance. The objectives of the study were to (1) assess both vestibular and cognitive functions and (2) evaluate the effectiveness of customized VRT against the integrated cognitive training and VRT in enhancing stability and life quality in these patients.

METHODS

Participants

A comprehensive sample included all patients with RRMS, complaining of dizziness or imbalance who attended the Outpatient Clinic of the Neurology Department of Zagazig University Hospitals for 12 months (nearly 4 cases per month). Therefore, the sample size was calculated to be 48 cases. To be involved in the study, participants were over 18 years old and of both genders, diagnosed with RRMS by an expert neurologist based on the “Revised McDonald’s criteria” [8], had a complaint of dizziness or imbalance, and exhibited an “Expanded Disability Status Scale”(EDSS)score of ≤ 6/10[9].They had no previous experience inVRT or cognitive training therapy and were able to walk ten meter sat least without aid, enabling them to perform the dynamic gait index (DGI).

Patients were excluded from the study if they had a history of ear infections or conductive hearing loss that could hinder the Vestibular-Evoked Myogenic Potentials (VEMP) testing, blindness, significant visual impairment, or cervical lesions limiting neck range of motion to be able to perform the vedio nystagmography (VNG), conditions increasing fall risk (e.g. arthritis and foot, visual, or cardiovascular issues), and/or other comorbidities that limit exercise participation. Additionally, patients with neurological problems other than MS, those with depression as identified by “Beck’s Depression Inventory” (BDI) [10], and patients taking antidepressant drugs were not involved.

Procedure

This interventional prospective cohort study was conducted from January 2021 to March 2022 at the Audio-Vestibular Medicine Unit, ENT Department, Faculty of Medicine, Zagazig University. Participants in the study were tested pre-and post-intervention. The period of intervention lasted for a total of six weeks for each participant.

Ethical considerations A written consent was given by each participant to take part in the research. The International Review Board of the Faculty of Medicine, Zagazig University has approved this study with ID: ZU-IRB #6700/26-1-2021.

Examinations

Participants underwent a thorough assessment involving:

1- Full history taking:

This covered personal, otological, vestibular, neurological, and general medical history.

2- Neurological evaluation:

Diagnosis of RRMS was established using the Revised McDonald's criteria [8] at the Neurology Department. Disability severity was assessed with the EDSS [9], while the BDI screened for depression. A general neurological evaluation was also conducted to exclude other neurological conditions.

3- Magnetic resonance imaging (MRI):

It was used to classify brain lesions in MS as infratentorial (affecting the brainstem and cerebellum) or supratentorial (not affecting these areas).

4- Otological examination:

It was carried out to exclude ear infections.

5- Basic audiological assessment:

It involved pure-tone audiometry, speech audiometry, and immittancemetry to exclude conductive hearing loss and ensure normal middle ear function.

6- Vestibular evaluation

Comprehensive vestibular evaluation was performed to examine peripheral and central vestibular functions. This included office tests such as ocular-motor, vestibulo-ocular reflex (VOR), posture, and gait measures; the oculomotor test battery of VNG (including saccadic, smooth pursuit, optokinetic, and gaze tests and searching for spontaneous nystagmus), positional, and positioning (Dix-Hallpike and roll maneuvers)tests; and the VEMP both cervical and ocular.

7- Cognitive assessment

Cognitive assessment was performed to evaluate the presence and severity of cognitive impairment, as well as the primarily affected domains, using the Arabic versions of the Montreal Cognitive Assessment (MoCA) [11] and the Mini-Mental State Examination (MMSE) [12].

Based on the pattern of previous responses, the participants were classified as having: a) No vestibular pathology and they were not included in the study, b) Central vestibular impairment (45 cases) and they were included in the study, and c) Combined central and peripheral vestibular impairment (three cases diagnosed with BPPV in addition to central vestibular pathology) and they were also included in the study.

Outcome measures

Both subjective (Arabic version of Dizziness Handicap Inventory [DHI])[13]and objective (DGI) [14]measures were applied before and after rehabilitation to evaluate the programs. The DHI is a 25-item questionnaire assessing the self-perceived level of handicap due to dizziness, divided into emotional (nine items), functional (nine items), and physical (seven items) subscales[13].The DGI evaluates dynamic postural stability in fall-risk patients through eight walking tasks, with scores based on gait deviation or imbalance[14].

Intervention

In this study, 48 participants were randomized into three groups(n=16 each): Group I (GI) received disease-modifying therapy (DMT), which is used as routine management for RRMS[15] with a placebo (tonics or vitamins); Group II (GII) received customized VRT in addition to the DMT; and Group III (GIII) received integrated CCT and customized VRT along with DMT.

1- Disease-modifying therapy (DMT):

Ten therapies approved for MS include four forms of interferon beta (from four different companies), glatiramer acetate, natalizumab, fingolimod, alemtuzumab, teriflunomide, and dimethyl fumarate [15].

2- Customized VRT:

This program involved home-based exercises for gaze stability that the patient performed four to five times daily for a total of 20-40 minutes/day, plus 20 minutes/day for postural stability exercises for six weeks. Patients diagnosed with left posterior BPPV first underwent an Epley canal repositioning maneuver[16]before VRT.

3- Computer-based cognitive training (CCT):

A six-week home-based CCT using the RehaCom program was implemented to assess focus, attention, memory, and perception. It included 45-minute sessions three times a week[17].The patients were telephoned every week during the entire study period to encourage their adherence/compliance and to provide solutions to any possible difficulties. All therapeutic session data and scores obtained were recorded and stored by the RehaCom software

Statistical analysis

Data were coded, entered, and analyzed using Microsoft Excel and SPSS version 20.0. Chi-square test (X^2), one-way ANOVA test (F),least significant difference test (LSD), paired sample t-test (t), Kruskal-Wallis test(H), Wilcoxon Signed-Rank (W), and Pearson's correlation coefficient (r)were utilized. The significance was set at p-value < 0.05.

RESULTS

The three study groups were comparable in age, sex, clinical history related to RRMS, dizziness history, and associated symptoms (Table 1). MRI demonstrated a uniform distribution of brainstem and cerebellar lesions (Table 2). All participants exhibited normal middle ear function (bilateral type A tympanogram with preserved acoustic reflex) and average hearing sensitivity of 25 dB HL or less across 0.25 to 8 kHz, with consistent word recognition scores within the groups.

The vestibular evaluation included office tests, VNG test battery (oculomotor, positional, and positioning tests), and VEMPs. Concerning office tests, abnormal findings were noted in 43% of ocular-motor examinations, 80% in tandem gait and tandem Romberg tests, 55% swaying in condition 3 of the Modified Clinical Test for Sensory Interaction on Balance (mCTSIB),and 100% in condition 4. The parameters of the saccadic, smooth pursuit, and optokinetic nystagmus tests revealed abnormalities when compared to the normal cutoff values established by Abuzagaya et al.[18].However, all patients showed no spontaneous or gaze-evoked nystagmus. Positional nystagmus occurred in 4 patients in GI (25%), 6 in GII (37.5%), and 7 in GIII (43.8%), with nystagmus either horizontal or vertical, not latent, and not fatigable, consistent with the criteria of central nystagmus. Moreover, both cVEMP and oVEMP tests showed prolonged latency measures with intact amplitude and asymmetry ratio measures when compared to the cutoff values reported by Elsayed et al.[19]. On the other hand, the cognitive evaluation revealed average scores that reflect moderate impairment across participants. Importantly, there were no statistically significant differences in vestibular and cognitive deficits among the three groups ($p \geq 0.05$).

The main objective of the study was to assess the effect of customized VRT versus integrated cognitive training and customized VRT on balance problems in RRMS patients. Both subjective (DHI) and objective (DGI) measures were used. The pre-intervention DHI subscales and total scores were statistically non-significantly different among the three groups (Supplementary Table 1).However, the difference became statistically significant post-intervention for the functional subscale and total scores(Supplementary Table 2).Comparison of pre-versus post-therapy outcomes revealed non-significant differences for GI and significant differences (improvement) for GII and III(Figure 1). Furthermore, the pre-intervention DHI degrees of severity exhibited a consistent distribution across the three study groups. The most common degree of severity was moderate, detected in 58.3% of participants, followed by severe at 35.4%, and mild at 6.3% (Supplementary Table 1). After the intervention, the distribution of DHI severity levels remained consistent, though some changes were observed: the moderate category increased to 66.7%, the mild category rose to 18.7%, and the severe category decreased to 14.6%(Supplementary Table 2). Specifically, post-intervention, GI demonstrated no changes in the frequency of DHI degrees of severity, while GII and III showed improvements. Notably, GIII achieved the best results (Figure 2).

An objective evaluation of the three study groups revealed no statistically significant differences in the pre-intervention DGI total scores (Supplementary Table 1). However, post-intervention, the differences in the DGI total score became significant. The LSD test indicated that GIII had a significantly higher score than the other two groups(Supplementary Table 2). When comparing pre-versus post-intervention scores, GII and III demonstrated significant improvements in their DGI total scores, while GI showed no change (Figure 3).

Moreover, the outcomes of the RehaCom training were evaluated in GIII. Statistically significant differences were found between the starting and end-level scores of the attention, memory, and executive function components of the RehaCom training. indicating post-intervention improvement in cognitive function (Table 3).

The study also examined how various factors influenced the post-intervention DHI and DGI outcome measures .Most variables showed weak correlations. However, there was a moderate positive correlation between the duration of dizziness and the pure tone average (PTA) with the total DHI scores in GII and III. In contrast, there was a moderate negative correlation of both dizziness duration and PTA with the total DGI scores in GII and III (Table 4).

Table (1): Personal and history-related criteria of the three study groups.

Personal data	Group 1 (N=16)		Group 2 (N=16)		Group 3 (N=16)		Test value	p
Age (years):								
• Mean ± SD	31.7 ± 4.9		32.4 ±6.9		31.4 ± 6.2		0.01*	0.99
• Range	24-39		20-42		22-43			
Sex (N,%):								
• Male	6	37.5	7	43.8	9	56.3	1.2ˣ	0.56
• Female	10	62.5	9	56.3	7	43.8		
RRMS history-related data								
-Age of onset of RRMS(years)								
• Mean ± SD	28.3 ± 3.8		27.6 ± 5.3		27.5± 5.6		0.18*	0.84
• Range	22-35		19-36		19-36			
Absolute duration of RRMS (years):								
• Mean ± SD	4.1 ± 3.1		3.9 ± 2.8		4.1± 1.9		0.04#	0.96
• Median	3		3.5		4			
• Range	1-12		0.67-9		0.75-8			
- Relative duration of RRMS‡(%)	12.9		12		13		0.06*	1
- Annual relapse rate⁂	0.66		0.57		0.5		10.2#	0.99
Dizziness-related history								
-Dizziness duration (months)								
• Mean ± SD	12.3 ± 9.7		10.5 ± 9.7		10.4± 7.5			
• Median	10		7.5		8		0.22#	0.80
• Range	3-36		1-36		2-24			
-Dizziness / RRMS duration (months)								
• Mean ± SD	4 ± 3.1		2.7 ± 3.5		2.5± 3.9		0.86#	0.43
• Median	3.3		2.1		2			
-Dizziness description (N,%)								
• Imbalance	10 (62.5)		11 (68.8)		13 (81.3)			
• Rotation	0 (0)		1 (6.3)		2 (12.5)		5.8ˣ	0.21
• Light-headedness	6 (37.5)		4 (25)		1 (6.3)			
Associated symptoms (N,%)								
• Hearing loss	2	12.5	7	43.8	4	24	4ˣ	0.13
• Tinnitus	2	12.5	5	31.3	3	18.8	1.8ˣ	0.41
• Headache	10	62.5	9	56.3	13	81.3	2.4ˣ	0.30

* F-value of One-way ANOVA test; # Kruskal-Wallis H test;ˣChi-square test (X^2).‡Relative duration = (RRMS absolute duration ×100) / age; ⁂ annual relapse rate = total number of relapses / the total number of patient-years (duration of MS).

Table (2): MRI findings among the three studied groups.

MRI findings	Group I(N=16)		Group II (N=16)		Group III (N=16)		X^2	p
	N	%	N	%	N	%		
• ***No brainstem or cerebellar lesions***	11	68.8	13	81.3	8	50	3.6	0.17
• ***Brainstem and cerebellar lesions***	5	33.3	3	18.8	8	50		

Table (3): RehaCom training score among Group III.

REHACOM training module	Starting level	End level	W	*p*
Attention				
• ***Selective attention***				
Mean	4.6 ±1.7	14.8±4.5		
Median	4.5	15.5	8.7	**<0.001***
Range	2-8	5-22		
• ***Divided attention***				
Mean	4 ± 1.4	13.9±3.6		
Median	4	15	10.3	**<0.001***
Range	2-8	6-9		
Memory				
• ***Topological***				
Mean	4.1 ± 1.5	11.6±2.4		
Median	4	13	10.6	**0.001***
Range	2-7	8-16		
• ***Verbal***				
Mean	1.3 ± 0.95	6.9±1.4		
Median	2	7	10.9	**0.001***
Range	1-5	5-10		
Executive functions				
• ***Logical reasoning***				
Mean	5.2 ± 2.2	15.1±3.2		
Median	5	15.5	10.2	**<0.001***
Range	1-10	9-20		
• ***Shopping***				
Mean	2.6 ± 1.9	11.5±2.7		
Median	3.5	11.5	9.6	**<0.001***
Range	1-7	6-16		

Table (4): Effect of different variables (personal, RRMS criteria, dizziness criteria, neurological and audiological findings) on post-intervention DHI and DGI total scores in the three study groups.

Variables	Post-intervention DHI total score			Post-intervention DGI total score		
	Group I	Group II	Group III	Group I	Group II	Group III
Age [r(*p*)]*	-0.064 (0.51)	-0.088 (0.75)	-0.212 (0.43)	0.343 (0.13)	-0.312 (0.24)	0.273 (0.31)
Sex [*H*(*p*)]#	0.84 (0.15)	0.77 (0.46)	-1.3 (0.22)	0.64 (0.24)	0.63 (0.54)	1.2 (0.26)
Age of onset of RRMS [r(*p*)]*	-0.057 (0.19)	0.017 (0.95)	-0.189 (0.48)	-0.233 (0.98)	-0.321 (0.18)	0.260 (0.33)
Absolute duration [r(*p*)]*	0.136 (0.46)	-0.238 (0.38)	0.321 (0.17)	0.151 (0.74)	-0.065 (0.81)	0.132 (0.63)
Relative duration [r(*p*)]*	-0.344 (0.42)	-0.282 (0.29)	0.037 (0.89)	0.024 (0.61)	0.030 (0.91)	0.052 (0.85)
Duration of dizziness[r(*p*)]*	0.0193 (0.59)	**0.372 (0.03)**	**0.561 (<0.001)**	-0.054 (0.50)	**-0.41 (0.01)**	**-0.60 (0.002)**
Dizziness/ RRMS duration [r(*p*)]*	-0.301 (0.19)	-0.213 (0.43)	-0.342 (0.20)	0.139 (0.27)	0.085 (0.76)	0.035 (0.90)
Dizziness description [F(*p*)]∴	0.62 (0.74)	0.83 (0.38)	0.09 (0.76)	0.46 (0.38)	0.96 (0.41)	0.68 (0.42)

Variables	Post-intervention DHI total score			Post-intervention DGI total score		
	Group I	Group II	Group III	Group I	Group II	Group III
MRI findings [*H*(*p*)]#	0.55 (0.467)	0.91 (0.379)	0.31 (0.764)	-0.76 (0.26)	-0.97 (0.35)	-0.78 (0.45)
PTA [r(*p*)]*	0.026 (0.43)	**0.39 (0.01)**	**0.52 (0.003)**	-0.234 (0.20)	**-0.642 (0.007)**	**-0.590 (<0.001)**
Annual relapse rate [r(*p*)]*	0.126 (0.46)	-0.256 (0.35)	0.256 (0.52)	0.073 (0.74)	-0.063 (0.81)	0.034 (0.90)

PTA= Pure tone average.*Pearson's correlation; # Kruskal-Wallis H test; ∴ One-way ANOVA test.

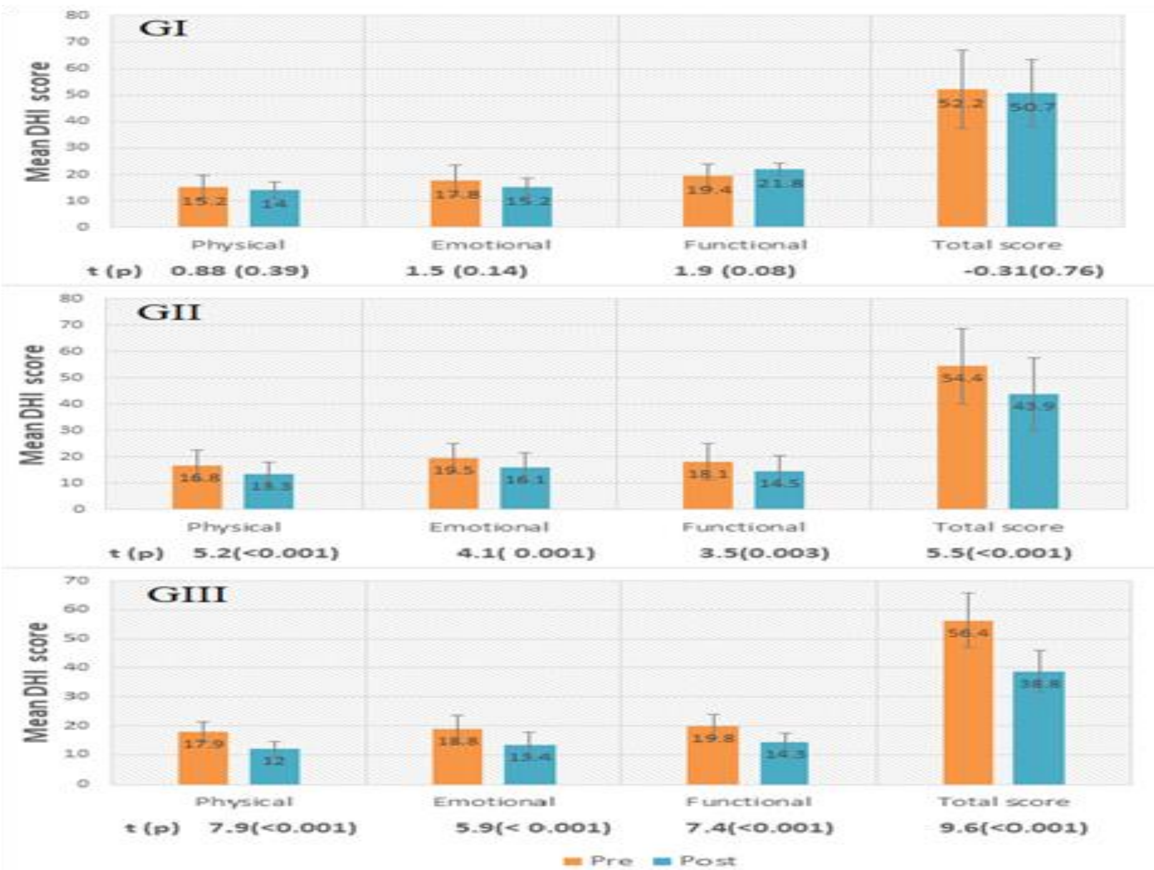

Figure (1): Comparison between pre-and post-intervention DHI subscales and total scores in each of the three study groups.

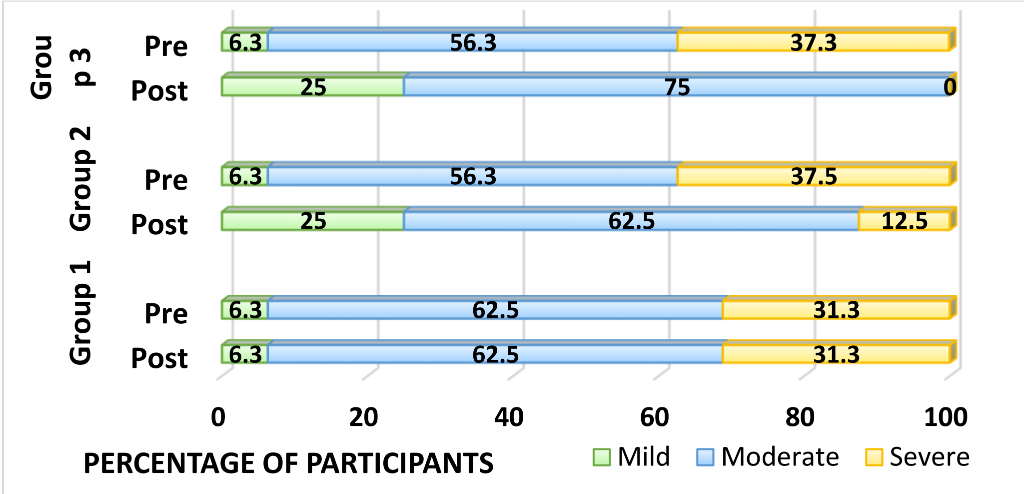

Figure (2): Comparison of pre-and post-intervention DHI degree of severity in each of the three study groups.

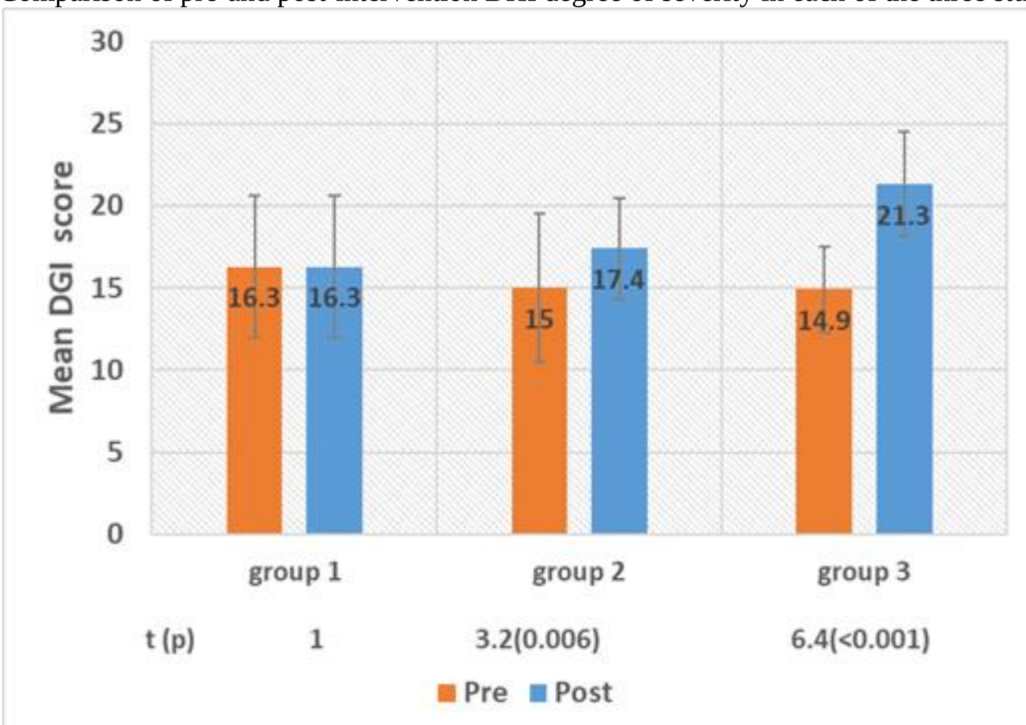

Figure (3): Comparison between pre-and post-intervention DGI total scores in each of the three study groups.

DISCUSSION

The RRMS is the most common MS phenotype. It is characterized by alternating periods of relapses and remissions. An identified sign of the disease is plaques in the brain or spinal cord, detectable via MRI [1]. In this study, MRI findings were classified as infratentorial (with brainstem and cerebellar affection) or supratentorial (without such affection). Among RRMS participants, 67% had supratentorial lesions, while 33% had infratentorial lesions. Similarly, Degirmenci et al. [20] evaluated 30 adult MS patients and found that 30% had infratentorial lesions as detected with MRI.

The current study aimed to evaluate vestibular and cognitive functions in RRMS patients with balance issues. Vestibular assessments showed abnormalities in ocular-motor tests (43%), tandem gait, and tandem Romberg tests (80%), as well asmCTSIB results (55% in condition 3, 100% in condition 4).Saccade, smooth pursuit, and optokinetic nystagmus abnormalities were noted that agreed with the research results reported by

Degirmenci et al. [20]and Zeigelboimet al. [21].Overall, these results suggest central vestibular involvement, commonly seen in MS. Remarkably, spontaneous and gaze-evoked nystagmus were absent in all patients as was reported in adult RRMS patients [22] supporting the findings that these are more prevalent in progressive MS forms, not the RRMS [23]. Additionally, prolonged latencies were observed in both cVEMP and oVEMP, matching research findings of adult MS patients [24, 25]. This is caused by demyelination reducing conduction speed due to conduction block or desynchronized conduction [26].

Cognitive evaluation using the Arabic version of the MMSE and MoCA revealed equivalently impaired cognitive function across the studied groups, consistent with previous research on adults with RRMS [27].Cognitive impairment in MS may stem from brain disconnection due to white matter tract abnormalities and functional disconnection in grey matter structures [28].Importantly, vestibular and cognitive evaluations revealed no significant differences among our three RRMS groups, indicating they were relatively homogeneous at the start of the different interventions that we carried out.

The main objective of this study was to assess the effect of customized VRT versus integrated cognitive training and customized VRT on balance problems in RRMS patients, using subjective (DHI-Arabic version) and objective (DGI) tests. Pre-intervention DHI subscales and total scores were nearly similar among the three groups (Supplementary Table 1), but this equivalency was lost post-intervention (Supplementary Table 2), likely due to varying improvements in balance function and quality of life using different therapies across the groups. GI showed minimal improvement, GII had better outcomes with customized VRT, and GIII achieved the best results overall with integrated cognitive training and customized VRT (Figure 1). This underscores the effectiveness of non-pharmacological approaches for balance dysfunction in MS patients [29].

Moreover, there was a homogenous distribution of DHI degrees of severity among the three study groups before therapy, with moderate being the most common, followed by severe and mild (Supplementary Table 1). However, this distribution persisted post-therapy with some changes (Supplementary Table 2). Post-intervention, GI showed no changes in DHI severity, while GII and GIII demonstrated improvements, particularly GIII, which had the best results (Figure 2).

An objective evaluation of the three study groups showed similar pre-intervention DGI total scores (Supplementary Table 1). Post-therapy, the analogy of DGI total score was lost with GII and III showing better results (Supplementary Table 2). On comparison between pre-versus post-intervention scores, GII and GIII demonstrated significant improvements in DGI total scores, unlike GI, which showed no change (Figure 3).

RehaCom training aimed at enhancing cognitive functions (attention, memory, and executive functions) in GIII resulted in notable improvements, as indicated by higher-end levels of training scores (Table 3). This aligns with Naeeni Davarani et al.[30]who found that RehaCom software enhances cognitive performance in MS patients.

Based on the aforementioned results, it can be concluded that pharmacologic therapies are ineffective in managing balance dysfunction in MS patients[29].For GI, a placebo using vitamins and tonics did not produce significant changes. Conversely, customized VRT proved effective in improving dizziness, shown by significant changes in the DHI and DGI compared to standard treatments [31]. This improvement is linked to VRT exercises that enhance the physiological process of compensation through habituation, substitution, and adaptation, maintaining cerebral cortex activation at a homeostatic level by a process similar to conditioning [32]. Hence, frequent exercise repetition is essential for better results.

The effect of integrated cognitive training and customized VRT in MS patients aligns with findings by Veldkamp et al.[33]on the benefits of dual-task training for dizziness and postural stability. Patients exhibited improved mobility measures, including the Timed-Up-And-Go test and DGI, post-intervention. Jonsdottir et al. [34] also reported higher DGI scores following integrated rehabilitation, while Monjezi et al. [35]noted enhancements in gait and balance. These improvements may stem from the strong correlations between central vestibular integration and cognitive functions in MS, highlighting the physiological relationship between cognition and balance[36]. Since both functions rely on interconnected brain circuits, interventions targeting these pathways can potentially enhance both balance and cognitive function. Additionally, postural control and cognition share limited resources, suggesting that integrated training may better activate motor performance, ultimately reducing treatment time and costs[6]. Consequently, integrated approaches may be the most beneficial option for managing imbalance in MS patients, offering better outcomes and efficiency.

The current study examined the effect of various variables on the post-intervention DHI and DGI outcomes (Table 4). Most variables showed no significant impact, but a positive, moderate correlation was found between dizziness duration and PTA with post-intervention DHI scores, while a negative, moderate correlation was noted with post-intervention DGI scores. These findings agree with previous research indicating that longer dizziness duration before rehabilitation correlates with poorer balance outcomes at discharge [37,38]. Consequently, an earlier referral for rehabilitation therapy would be beneficial. Additionally, PTA affected both DHI and DGI scores, supporting literature that MS patients with hearing loss face greater challenges in regaining balance and have a higher fall risk [39]. This can be attributed to the close anatomical relationship between the cochlea and vestibular system and the cognitive load on patients with hearing loss [40].

Limitations of the current study involved a small sample size that prevented comparison between patients with and without brainstem and cerebellar lesions. Additionally, participants were restricted to an EDSS of 6/10 or less to ensure they could safely complete gait and balance measures. Our findings may be slightly biased, as we did not control for socioeconomic status, which can affect cognitive performance. We also limited patients' ages to a maximum of 45 years to reduce the impact of aging on balance. Finally, incorporating specific measures of balance, such as dynamic posturography, would help investigate other mechanisms affecting balance and clarify intervention outcomes in RRMS patients

CONCLUSIONS

Abnormalities indicating central vestibular pathology are significant findings in patients with RRMS as well as a moderate cognitive impairment linked to white and grey matter abnormalities .A tailored six-week VRT significantly improved balance and reduced dizziness-related disability in these patients. Furthermore, CCT using RehaCom software effectively enhances cognitive function for individuals with RRMS. Integrating cognitive training with VRT has been shown to be more effective in improving stability than using customized VRT alone. This suggests a physiological connection between cognitive function and balance, emphasizing the crucial role that cognitive abilities play in maintaining balance.

Disclosure of potential conflicts of interest:

The authors report no conflicts of interest.

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Supplementary Table (1): Comparison of the pre-intervention outcome measures' scores between the three study groups.

Subjective and objective outcome measures	***Pre-intervention outcomes***							
DHI subscales and total scores	**Group 1** (N=16)		**Group 2** (N=16)		**Group 3** (N=16)		**F**	***p***
Physical: • ***Mean ± SD*** • ***Range***	15.2 ± 4.5 6-22		16.8 ±5.6 8-28		17.9 ± 3.3 1-4		4.5	0.53
Emotional: • ***Mean ± SD*** • ***Range***	17.8 ± 5.9 8-26		19.5 ± 5.6 10-28		18.8± 4.9 8-28		0.41	0.66
Functional: • ***Mean ± SD*** • ***Range***	19.4 ± 4.6 10-30		18.1 ±6.9 10-30		19.8 ± 4.1 8-24		0.33	0.72
Total score: • ***Mean ± SD*** • ***Range***	52.2 ± 14.8 23-76		54.4 ±14.2 30- 78		56.4 ± 9.4 30-68		0.98	0.38
DHI degree of severity	**N**	**%**	**N**	**%**	**N**	**%**	**χ 2**	***p***
• *Mild* • *Moderate* • *Severe*	1 10 5	6.3 62.5 31.3	1 9 6	6.3 56.3 37.5	1 9 6	6.3 56.3 37.5	0.20	0.99
DGI total score	**Group 1** (N=16)		**Group 2** (N=16)		**Group 3** (N=16)		**F**	***p***
• ***Mean ± SD*** • ***Range***	16.3 ± 4.3 10-24		15 ± 4.5 9-23		14.9 ± 2.6 9-17		2.9	0.29

Supplementary Table (2): Comparison of the post-intervention outcome measures' scores between the three study groups.

Subjective and objective outcome measures	*Post-intervention outcomes*								
DHI subscales and total scores	**Group 1** (N=16)		**Group 2** (N=16)		**Group 3** (N=16)		**F**	***p***	**LSD**
Physical: • ***Mean ± SD*** • ***Range***	14± 3.1 10-18		13.3 ±4.6 8-20		12 ± 2.6 8-16		1.3	0.29	------
Emotional: • ***Mean ± SD*** • ***Range***	15.2±3.4 8-18		16.1 ± 5.4 8-28		13.4 ±4.2 8-24		1.6	0.22	-------
Functional: • ***Mean ± SD*** • ***Range***	21.8±2.3 8-22		14.5 ±5.9 8-28		14.3 ±3.2 8-20		17.4	**<0.001**	**P1=0.001** **P2=0.001** P3= 0.99
Total score: • ***Mean ± SD*** • ***Range***	50.7±12.7 30-72		43.9±13.7 24- 70		38.8 ±7.1 28-50		4.3	**0.02**	**P1= 0.02** **P2<0.001** **P3= 0.04**
DHI degree of severity	**N**	**%**	**N**	**%**	**N**	**%**	X^2	***p***	
• *Mild* • *Moderate* • *Severe*	1 10 5	6.3 62.5 31.3	4 10 2	25 62.5 12.5	4 12 0	25 75 0	2.2	0.34	
DGI total score	**Group 1** (N=16)		**Group 2** (N=16)		**Group 3** (N=16)		**F**	***p***	**LSD**
• ***Mean ± SD*** • ***Range***	16.3 ± 4.3 10-24		17.4± 3.1 12-23		21.3± 3.2 10-22		2.7	**0.02**	P1= 0.72 **P2<0.001** **P3= 0.02**

Citation

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