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ORIGINAL ARTICLE

Motor and cognitive effects of video game training in people with multiple sclerosis: a randomized controlled trial

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ABSTRACT

BACKGROUND: Dual-task activities are frequently impaired in people with MS (PwMS), with a high impact on daily life activities. Exergaming may represent a valuable treatment for dual-task abilities as it involves motor and cognitive task.
AIM: To evaluate whether a video game training (VGT) improves mobility, balance, cognitive functions, and dual tasking more than a standardized balance platform training (BPT).
DESIGN: Single-blinded, randomized control trial.
SETTING: Outpatient.
POPULATION: People with multiple sclerosis (PwMS).
METHODS: Forty-eight PwMS were allocated to either VGT or BPT group. VGT was delivered using a commercially available video game console, BPT using a rehabilitative balance platform. Both groups received twelve 1-hour sessions over four weeks. All subjects were evaluated before (T0), after treatment (T1) and at the three-month follow-up (T2). The primary outcome was functional mobility assessed with the Timed Up and Go test. Secondary outcomes included balance, patient-reported measures, cognitive functions, and posturographic assessment in single and dual-task condition.
RESULTS: Mobility significantly improved after treatment in the BPT group. Fatigue and perceived walking ability improved after treatment only in the VGT group. Both treatments significantly improved static and dynamic balance (after treatment and at the three-month follow-up) and quality of life (after treatment). Between-group analysis revealed a significant improvement in reaction time only in people who received VGT.
CONCLUSIONS: Both VGT and BPT were effective in improving balance and quality of life in PwMS. Although no changes in dual-task performance were observed, VGT led to specific improvements in attentional performance.
CLINICAL REHABILITATION IMPACT: Video game rehabilitation may offer a useful and engaging option for improving balance, quality of life, and attention in PwMS. As no improvements were found in dual-task performance, longer-term studies are needed before conclusions can be drawn about its broader rehabilitative impact.

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KEY WORDS: Multiple sclerosis; Exergaming; Balance; Cognitive function; Rehabilitation.

Introduction

Multiple sclerosis (MS) is a chronic inflammatory and neurodegenerative disease of the central nervous system characterized by demyelination and axonal loss. These pathological processes lead to a wide range of neurological signs and symptoms, including motor weakness, balance disturbances, spasticity, sensory deficits, fatigue,

and cognitive impairments.[1] Among the most common disorders are balance and mobility impairments, which are frequently associated with an increased risk of falling and reduced quality of life (QoL).[2] These limitations become more evident during cognitively demanding situations, a phenomenon known as cognitive-motor interference (CMI), whereby performing a cognitive task adversely affects motor performance.[3-5] Although dual-task difficulties are well documented in people with MS (PwMS) and reflect everyday challenges such as walking while talking or performing household tasks, the effectiveness of interventions specifically targeting CMI remains variable.[6] From an anatomical perspective, demyelinating lesions and neurodegeneration affecting brain regions involved in motor learning and dual-task coordination appear to play a central role in CMI.[7] The cerebellum, in particular, is involved not only in postural control and gait adaptation but also in higher-order cognitive processes such as attention and executive functioning. Given its integrative role in motor-cognitive coordination, cerebellar damage may represent a key neural substrate contributing to both motor and non-motor symptoms in PwMS.[8, 9] Dual-task training (DTT) may be an effective intervention for improving motor function during cognitively demanding tasks.[7] However, recent systematic reviews have reported improvements in balance and mobility following DTT, but have found limited and inconsistent effects on cognitive outcomes.[10, 11]

Recently, technological approaches like active video games or exergames have emerged as promising tools in neurological populations rehabilitation.[12] Active video games represent an interactive technology category that combines digital entertainment with physical activity, requiring body movements to control gameplay.[13] Their potential in rehabilitation is due to the possibility to combine physical movement in a virtual environment, offering repetitive, engaging, task-oriented activities that may promote use dependent plasticity in sensorimotor areas.[12, 14] In PwMS, these technological approaches have shown good results on motor aspects, including balance and gait, representing an alternative to conventional rehabilitative approaches.[12, 15] Commercial video game platforms are frequently used in the rehabilitation setting because of their usability at a reasonable cost,[14, 16] despite the limited possibility of personalization of patients' characteristics. In addition, the possibility of exercising in a home-based setting may increase the intensity and frequency of training,[17] promoting neuroplasticity mechanisms.[18]

Beyond motor effects, video game rehabilitation seems to be effective also on cognitive outcomes.[14, 19] Indeed, gameplay commonly requires sustained attention, rapid stimulus processing, response inhibition, error monitoring, and flexible decision-making, aspects frequently impaired in PwMS with negative effects on daily functions. The integration of different types of stimuli in a virtual environment may be relevant for both motor and cognitive functions, but also for understanding CMI. Considering the positive effects of exergaming on motor outcomes and the potential cognitive engagement offered by multisensory tasks, this study aims to compare the efficacy of a commercially available video game therapy and conventional balance platform training (BPT) on mobility, balance, and cognitive function in PwMS, with a specific focus on dual-task ability as a measure of CMI.

Materials and methods

Study design and setting

This parallel-assignment, single-blinded, randomized control trial compares the efficacy of a commercial video game therapy (VGT) to a standardized BPT on mobility, balance, and cognitive outcomes in PwMS. The trial was designed and reported according to the CONSORT 2025 guidelines for randomized controlled trials and the TIDieR checklist for intervention reporting.[20, 21] This study was approved by the Ethics Committee of Ferrara (approval number 170691), and all procedures were conducted according to the ethical standards of the Declaration of Helsinki. The trial protocol has been registered on ClinicalTrials.gov (NCT03353974) and published.[22] Subjects were recruited from patients referred to the Outpatient Rehabilitation Clinic at the University Hospital of Ferrara from December 2017 to October 2022. Written informed consent was obtained before all procedures.

Participants

We included all PwMS who met the following inclusion criteria: men and women aged 18-60 years with a diagnosis of MS (primary or secondary progressive, relapsing-remitting) without relapses in the preceding 3 months, a time window used to determine clinical stability. Disability was defined by an Expanded Disability Status Scale (EDSS) score from 4 to 5.5. Participants were required to have balance impairment associated with an increased risk of falls, defined as a Timed Up and Go (TUG) >8.4s.[23] PwMS were excluded if they presented any additional neurological condition known to affect motor function, musculoskeletal disorders that could impair safe standing, walking, or par-

ticipation in balance exercises, visual impairments (colour blindness or visual acuity deficit) that could interfere with game interaction, medical conditions interfering with the safe completion of the study, or impaired cognitive functioning screened using the Mini-Mental State Examination (MMSE). Because the MMSE has limited sensitivity in MS, we used a cut-off of MMSE<24/30 solely to exclude major global cognitive impairment.[24, 25]

Randomization and blinding

All subjects meeting the inclusion criteria were assigned to one of the two treatment groups through a block randomization approach. Randomization was performed using a computer-generated sequence produced with the randomization.com allocation list generator (tool no longer available online). The randomization list was managed by an external administrator to the research group to prevent selection bias. The outcome assessor and the data analyst were blinded to the subject's allocation group.

Interventions

Subjects allocated to the experimental group received VGT; subjects allocated to the control group received BPT. Both groups received twelve 1-hour therapy sessions over four weeks (three sessions a week). Every session consists of approximately 50 minutes of training and approximately 10 minutes of mobility and flexibility activities performed at the end of the training session. All the activities were delivered in a rehabilitative gym equipped with the instruments needed to administer the treatment and carefully supervised by a physiotherapist with at least 10 years of expertise in MS rehabilitation who monitored subject safety. A log of the sessions was kept daily by the physiotherapist to monitor the progress of the session, the subject's level of improvement, any deviations from the planned treatment, and any adverse event occurring during the treatment. If the subject missed a session, it was rescheduled for the following day. If the subject missed two or more consecutive sessions, it was excluded from the study. All the subjects included in the study were asked to avoid other simultaneous physiotherapy treatments for the duration of the study until follow-up.

VGT

VGT was delivered using a commercially available video game console (Kinect for Xbox 360; Microsoft Corporation, Redmond, Washington, USA), which enables full-body, motion capture-based interaction without the use of handheld controllers. Training activities were selected from the "Kinect Adventures!" and "Kinect Sports" (Microsoft Game Studios) packages and were specifically chosen to promote gross motor function, balance control, and spatial-temporal coordination. The games required participants to perform multidirectional stepping, lateral and anteroposterior weight shifting, walking in all directions within the available space, jumping, and goal-directed upper limb reaching, thereby targeting dynamic balance, postural control, and whole-body coordination. Task difficulty and activity level were individualized by a physiotherapist according to each participant's functional abilities and clinical presentation, with progression based on therapist observation and the intrinsic game difficulty levels. Each session consisted of repeated task blocks lasting 2-5 minutes, followed by a rest periods as needed to manage fatigue.

BPT

BPT was delivered using a balance platform (Biodex Medical Systems, Shirley, New York, USA). The platform trained balance and postural stability through weight-shifting exercises with and without visual feedback. The subject was able to observe their progress toward the target using a monitor positioned in front of it. The level of difficulty was set by a physiotherapist according to the subject's ability and progressively increased based on physiotherapist's judgement.

Outcome measures

All subjects were evaluated before (T0), after treatment (T1) and at the three-month follow-up (T2). Functional assessment was performed by a physiotherapist blinded to the treatment group. The primary outcome was functional mobility, which was assessed using the TUG, a valid and reliable performance-based measure.[23] The secondary outcomes included physical function, patient-reported measures, cognitive and psychological function, and posturographic assessment. Physical function evaluations included the Berg Balance Scale (BBS) for static and functional balance;[26] the Dynamic Gait Index (DGI) for gait, balance and fall risk assessment;[27] the Four Square Step Test (FSST) for balance assessment during rapid changes in direction;[28] the Functional Reach Test (FRT) for stability assessment in the standing position.[29] Patient-reported outcome measures (PROMs) included the following: the Multiple Sclerosis Impact Scale-29 (MSIS-29) for health-related QoL;[30] the Multiple Sclerosis Walking Scale-12

(MSWS-12) for the impact of MS on walking function;[31] and the Modified Fatigue Impact Scale (MFIS) for the perceived impact of fatigue in daily activities.[32] The cognitive and psychological assessments was performed by a blinded neuropsychologist and included the Beck Depression Inventory-Second Edition (BDI-II) for severity of depression;[33] the State Trait Anxiety Inventory (STAI-Y) for the presence and severity of anxiety;[34] the Go/Nogo test to evaluate subject selective visual attention;[35] the Stroop Color-Word Test (SCWT), a neuropsychological task in which individuals name the ink color of incongruent color words, to assess the ability to inhibit cognitive interference;[36] and the Symbol Digit Modalities Test (SDMT) for cognitive processing speed.[37] The posturographic evaluation was performed using force platform (BERTEC Model 4080-10, Bertec, Columbus, OH, USA). During the test, the subjects were asked to stand on the force plate for five 60-second tasks with their eyes open and then with their eyes closed. The force platform recorded the movement of the center of pressure (CoP) of the subjects, and the displacement from the starting position was analysed.[38] A combination of posturographic and neuropsychological test was used to evaluate dual-task ability. The subjects were asked to complete the SCWT while standing on the force platform, and single and dual performances were compared. The magnitude of CMI was estimated as the dual-task cost (DTC), which was calculated as follows: (postural sway [dual-task]postural sway [single-task])/ postural sway [single-task]100.[39]

Statistical analysis

The sample size calculation was based on preliminary pilot observations in PwMS with EDSS score below 6 receiving video game rehabilitation. Assuming a standardized effect size of 0.93, equal allocation between the VGT and BPT groups, and a two-sided significance level of 5%, and 80% statistical power, 40 participants were required. To account for an expected dropout rate of 20%, the final sample size was increased to 48 participants, with 24 subjects per group.[22] The data distributions were assessed with the Shapiro-Francia test. Baseline characteristics are reported as medians and interquartile ranges or frequencies and percentages according to variable type. Baseline characteristics were compared to test the quality of randomization using the Kruskal-Wallis test for continuous variables and the Chi-square Test for discrete variables. Group analysis was performed using the Friedman test for repeated measures; pairwise comparisons were performed using Conover post hoc analysis with Bonferroni correction (adjusting for multiple time-point comparisons within each outcome). Between-group analysis for all outcome measures was performed using the Kruskal-Wallis test. Aligned rank transformation (ART) analysis of variance (ANOVA) was performed to analyse time-treatment interactions. The primary outcome was evaluated at a two-sided significance level of 0.05 without further multiplicity correction. Secondary outcomes were considered exploratory; therefore, no additional correction across different secondary endpoints was applied. Effect sizes and 95% confidence intervals are reported to support interpretation. An intention-to-treat analysis was carried out on all the outcome measures. Missing data were treated using the last observation carried forward approach.

Statistical analysis was performed using Stata Statistical Software (Release V.13., StataCorp) and R Software (Release V.4.5.0, R Foundation for Statistical Computing, Vienna, Austria).

Data availability

The data associated with the paper are not publicly available but are available from the corresponding author on reasonable request.

Results

Fifty-two PwMS were screened for eligibility; four did not meet the inclusion criteria and were excluded. The remaining 48 PwMS were enrolled (median age 55 (47-58), 25% male, 9 (4-16) median years from MS diagnosis). Twenty-four subjects were allocated to the VGT group, and 24 were allocated to the BPT group; all of them received the assigned treatment and completed the rehabilitation protocol without adverse events. A total of 10.4% (four in the VGT group and one in the BPT group) did not return to the hospital during the three-month follow-up (three for personal issues unrelated to the treatment, one due to MS relapse, and one deceased). All 48 randomized PwMS were included in the analyses in accordance with the intention-to-treat approach, using last observation carried forward to handle missing data. The study flow diagram is shown in Figure 1. The two groups were similar in demographic and clinical characteristics (Table I), except for depressive and anxiety symptoms, open eyes posturographic evaluation, and mediolateral DTC.

Primary outcome: Timed Up and Go test

Within-group analysis revealed a significant effect on the TUG score in the BPT group, and post hoc analysis re-

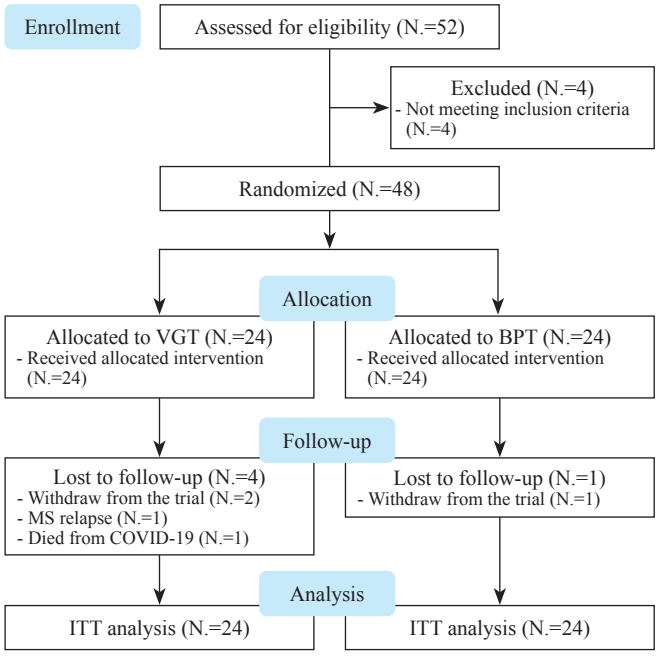


Figure 1.—CONSORT Flow diagram of the study.
BPT: balance platform training; ITT: intention-to-treat; MS: multiple sclerosis; VGT: video game therapy.

vealed an improvement in the post treatment assessment (see Figure 2 and supplementary material). No differences were recorded between the two groups, and no significant time-treatment interaction was detected (Table II).

Secondary outcomes

Within-group analysis revealed that both treatments significantly improved several static and dynamic balance measures at post treatment and follow-up assessments. In terms of PROMs, both treatments significantly improved the impact of MS on QoL (MSIS-29) at the post treatment evaluation. Only the VGT group reported positive effects for perceived walking ability (MSWS-12) and fatigue (MFIS), with post hoc significance at T1 and T2 for the MSWS-12 and at T1 for the MFIS. Within-group analysis revealed that only VGT significantly improved reaction time in the Go/Nogo test, with post hoc significance at the post treatment evaluation (Figure 2). No significant within-group changes were recorded for postural sway during posturographic assessment in either the single- or dual-task modality or the DTC. Detailed results of within-group analysis are available as supplementary material. Between-group analysis revealed no differences for any secondary outcome except for the Go/Nogo reaction time, which improved only in people who received VGT. No significant time-treatment interaction was observed for any secondary outcome measure (Table II).

Discussion

PwMS often experience motor and cognitive impairments, particularly when these tasks are performed simultaneously. This randomized controlled trial aimed to determine whether VGT could improve mobility, balance and cognitive performance, with a specific focus on attentional functions and dual tasking, more than standardized BPT. Considering the primary outcome of our trial, we failed to demonstrate that VGT increases mobility more than a conventional BPT. One of the first aspect to considered is probably that our study is underpowered due to a sample size calculation based on a previous pilot study with a large effect size. Even though the planned sample was consistent with previous randomized controlled trials investigating video game-based balance interventions in PwMS,[40, 41] a larger sample would allow us to observe changes in TUG following treatment. Another aspects to consider is certainly the dose of exercise used in our trial. We can assume that the amount of exercise in both groups is insufficient to generate clinically significant changes

TABLE I.—*Characteristics of the included subjects.*

Characteristics	VGT (N.=24)	BPT (N.=24)	Total (N.=48)	P
Age, median [IQR] (y)	55 [46;58]	55.5 [47.8;59]	55 [46.8;58]	0.54
Sex, N. male (%)	6 (25)	6 (25)	12 (25)	1.00
MS diagnosis, median [IQR] (y)	10 [6;18.2]	8 [3;12.5]	9 [4;15.8]	0.42
MS subtype, N. (%)				0.91
RR	14 (58.3)	13 (54.2)	27 (56.3)	
PP	8 (33.3)	8 (33.3)	16 (33.3)	
SP	3 (12.5)	2 (8.3)	5 (10.4)	
EDSS, median [IQR]	4.5 [4;5.5]	4.5 [4;5]	4.5 [4;5.25]	0.77

BPT: balance platform training; EDSS: Expanded Disability Status Scale; IQR: interquartile range; MS: multiple sclerosis; PP: primary progressive; RR: relapsing-remitting; SP: secondary progressive; VGT: video game therapy; y: years.

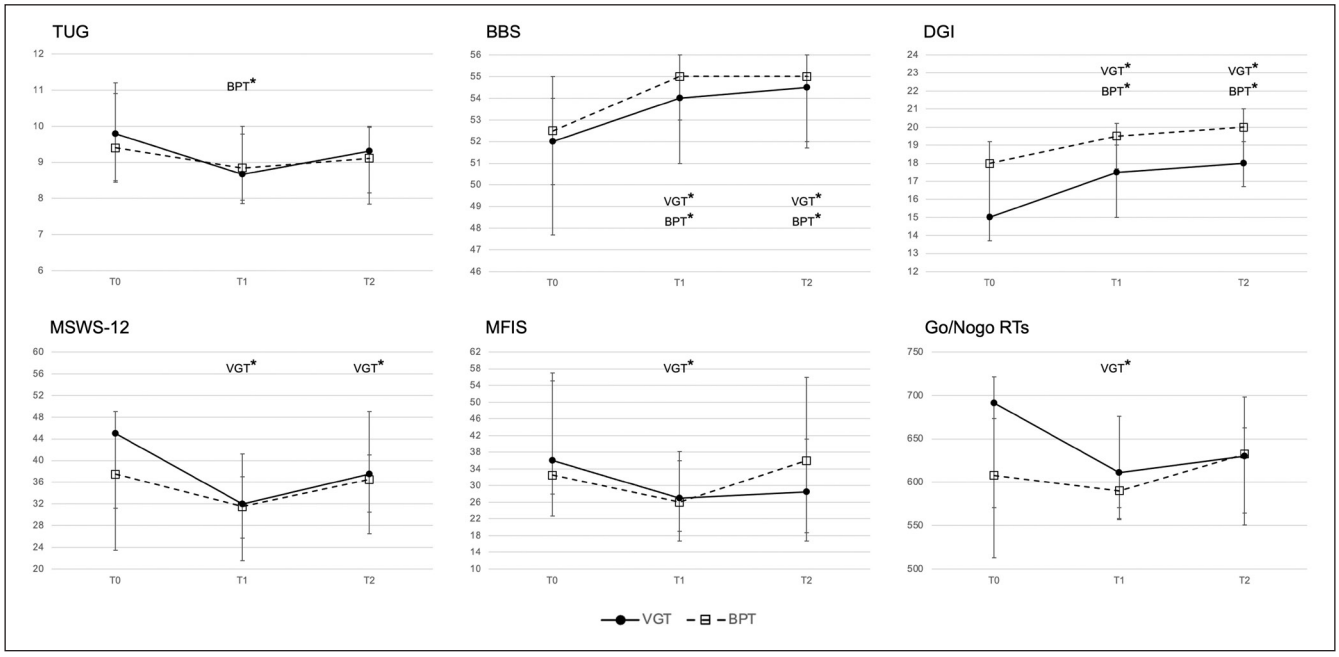


Figure 2.—Within-group changes for the primary and key secondary outcomes.
BBS: Berg Balance Scale; BPT: balance platform training (continuous line); DGI: Dynamic Gait Index; MFIS: Modified Fatigue Impact Scale; MSWS-12: Multiple Sclerosis Walking Scale – 12; RTs: reaction times; TUG: Timed Up and Go test; VGT: video game therapy (dot line).
*P<0.05.

in this functional domain. A previous systematic review has reported larger effects of exergaming on balance in PwMS.[15] However, many of the studies showing superior outcomes used substantially higher training doses than those applied in the present trial. Particularly, studies employing the same gaming system often delivered a greater number of sessions or higher weekly frequency.[42-44] Gutierez *et al.* performed forty sessions in four weeks,[42] and Tollar *et al.* performed twenty-five sessions in five weeks.[44] The importance of a high dose of rehabilitation is also highlighted by Cortes-Perez *et al.* who suggested a minimum effective dose for MS balance rehabilitation of 40 or more virtual reality sessions (five sessions/week).[45] Despite the importance of rehabilitation intensity and duration on neuroplasticity in PwMS,[46, 47] these have not been systematically explored in exergaming trials.[48] It is therefore possible that the treatment dosage used here was insufficient to detect between-group differences. The choice of a 12-session protocol reflected a standard outpatient rehabilitation schedule in a rehabilitation center and aimed to ensure feasibility and patient adherence. When the study was designed, available evidence showed considerable variability in treatment dose, and several trials had reported meaningful improvements with 8-12 sessions. Nonetheless, our findings, together with more recent literature, suggest that a higher number of sessions may be required to maximize the effects of exergaming. In addition to dosage, the baseline motor function of the included subjects must be considered. Participants in our sample exhibited relatively mild mobility and balance impairment compared with other populations studied,[42-44] which may have limited the potential to observe larger changes with both interventions. In a previous study by our group on people with traumatic brain injury, subjects who benefited from VGT had more impaired mobility compared to the subjects in our sample.[38] Taken together, these considerations indicate that VGT at this specific intensity and duration may be more suitable for individuals with greater baseline motor deficits, who may show a larger capacity for improvement. Regarding the other secondary outcomes, both groups showed significant improvements in QoL after treatment. Nevertheless, only the VGT group achieved clinical improvement in both physical and psychological aspects. Previous work in chronic conditions has reported variable effects of exergaming on QoL.[49] We can assume that factors such as motivation or engagement of video game rehabilitation may have contributed to the results observed in our sample,[48] a strong motivational drive to

TABLE II.—*Between-group analysis*

Outcome, median [IQR]	Δ T0-T1			Δ T0-T2		
	VGT	BPT	P	VGT	BPT	P
Motor function						
TUG	-0.96 [-1.59;-0.19]	-0.96 [-1.67;0.15]	0.98	-0.35 [-1.58;0.23]	-0.26 [-1.34;0.21]	1.00
BBS	1 [0;3]	1 [0;3.25]	0.98	1 [0.75;2.25]	1 [0;2.25]	0.59
DGI	2 [0;3]	2 [0;4.25]	0.66	2 [0.75;4]	2 [0.75;3.25]	0.83
FSST	-0.95 [-2.35;-0.14]	-0.82 [-3.46;1.08]	0.89	-0.84 [-1.78;-0.01]	-1.33 [-3.86;0.59]	0.82
FRT	2 [-1.12;4.5]	0.25 [-3.25;4.62]	0.25	2 [-1.12;5.62]	1.75 [-1.5;3.62]	0.56
PROMs						
MSIS-29-PHYS	-6 [-14.75;-1.75]	-8 [-12.5;0.5]	0.70	-1 [-8;4]	-3 [-8.5;0.25]	0.45
MSIS-29-PSY	-2 [-6;0]	-3.5 [-5;0]	0.97	-2 [-4.5;4]	-1 [-3.25;1.25]	0.90
MSWS-12	-8 [-12.25;-2]	-4 [-10.25;1.5]	0.08	-4.5 [-8;0]	-1 [-7;7.5]	0.18
MFIS	-9 [-19;-2]	-6 [-14.25;1]	0.38	-1.5 [-14.;1]	-3 [-9.5;7]	0.83
Psychological function						
BDI-II	-0.50 [-3;0]	0 [-4;0]	0.58	0 [-2.25;0.25]	0 [-0.25;0]	0.96
STAI-Y1	-4 [-8.25;0.25]	-4 [-9;0.75]	0.86	-2.5 [-12.25;1.25]	-1.5 [-6.5;3.5]	0.27
STAI-Y2	-3.5 [-8;0.25]	-2.5 [-7.25;0.25]	0.62	-4.5 [-7.5;2.75]	-0.5 [-8.25;1]	0.64
Cognitive function						
SDMT	0.5 [-5.5;3]	2 [-0.75;6]	0.15	-1 [-19.75;4.5]	-1.5 [-6;4.8]	0.71
Go/Nogo errors	0 [0;1.75]	0 [-2;2]	0.32	0 [0;1]	0 [-1;3]	0.62
Go/Nogo RTs (msec)	-63 [-101.75;9.75]	-8 [-49;50]	0.04	-76 [-475.25;-2]	15 [-39;46]	0.01
SCWT errors	0 [0;1]	0 [0;0]	0.20	0 [0;1]	0 [0;0]	0.13
SCWT time (sec)	3.29 [0.11;7.64]	4.45 [1.61;9.45]	0.42	7.19 [0.36;17.56]	6.18 [2.08;12.03]	0.94
FP total path length						
Open eyes	-2.70 [-73.36;42.19]	-6.31 [-18.24;36.67]	0.73	8.42 [-34.82;65.88]	-4.78 [-35.85;31.4]	0.71
Closed eyes	-18.02 [-110.76;23.36]	6.95 [-29.74;59.21]	0.12	-24.38 [-59.18;9.89]	3.77 [-22.75;36.59]	0.08
Dual task condition	-14.33 [-69.20;79.99]	-14.75 [-98.83;116.95]	0.88	-25.39 [-60.32;92.23]	-28.33 [-141.80;57.77]	0.60
DTC (%)	5.5 [-21.7;44.5]	-13.6 [-49.2;13]	0.31	13.3 [-42.7;40.6]	-14.8 [-29.4;12.9]	0.50

BBS: Berg Balance Scale; BDI-II: Beck Depression Inventory – Second Edition; BPT: balance platform training; DGI: Dynamic Gait Index; DTC: dual-task cost; FP: force platform; FRT: Functional Reach Test; FSST: Four Square Step Test (FSST); MFIS: Modified Fatigue Impact Scale; MSIS-29-PHYS: Multiple Sclerosis Impact Scale – 29 – Physical domain; MSIS-29-PSY: Multiple Sclerosis Impact Scale – 29 – Psychological domain; MSWS-12: Multiple Sclerosis Walking Scale – 12; PROMs: Patient Reported Outcome Measures; RTs: reaction times; SCWT: Stroop Color-Word Test; SDMT: Symbol Digit Modalities Test; STAI-Y-1: State Trait Anxiety Inventory – State anxiety; STAI-Y-2: State Trait Anxiety Inventory – Trait anxiety; T0: before treatment; T1: after treatment; T2: three-month follow-up; TUG: Timed Up and Go test; VGT: video game therapy.

exercise, particularly in PwMS.[14] For such characteristics, video games could be used to increase adherence to home exercise programs, not as an alternative to supervised rehabilitation but as an adjuvant to support long-term symptom management. Although the interventions in this trial were delivered in a supervised, standardized outpatient setting, VGT has the potential to be implemented in home-based or hybrid models (in-hospital familiarization followed by home-based training). Home delivery may improve accessibility and continuity of care, particularly for PwMS facing transportation barriers.[50] Effectiveness in real-world settings may differ due to variability in adherence, home environment constraints (space, distractions), and technology-related factors (equipment availability, usability, technical support) and applicability need therefore to be investigated.

Interestingly, only the VGT group showed a significant effect on perceived walking ability and fatigue. These results might be due to the different characteristics of the two interventions. Indeed, subjects who received VGT had to move into the range of the camera to perform all the activities proposed by the video game platform and were forced to experience more degrees of freedom than subjects who were trained on the balance platform. The possibility for subjects to become involved in more challenging activities during rehabilitation allows them to understand the effective abilities they can spend in daily life. Our results on the effectiveness of VGT for fatigue are consistent with those of previous studies.[51, 52] The greater physical demand of VGT than of BPT might induce muscular and cardiovascular adaptations that can reduce perceived fatigue.

The only secondary outcome significantly different between the two treatment groups was reaction time in the Go/Nogo task. Compared with those in the BPT group, PwMS who received VGT had shorter reaction times at the post treatment assessment. The greater degree of cognitive engagement required by the virtual environment plays a crucial role in cognitive functions needed to respond to a changing scenario. Increased global cognitive function following VR-based rehabilitation may increase cognitive

processing speed, which is useful for suppressing undesired responses.[53] Similar results have been described in older adults with mild cognitive impairment or chronic traumatic brain injury.[38, 54] The possibility of improving reaction time through a video game console opens the door to several rehabilitation options for people with impaired cognitive function in a home setting, increasing adherence and treatment time. However, this attentional improvement did not translate into superior motor performance, possibly due to task specificity and limited transfer of attentional gains to motor skills.

The sway area described by the CoP on the force platform was used to objectively describe changes in the subject's stability in a standing position, with and without cognitive interference. Despite our hypothesis and the rationale based on cognitive-motor interference, neither of the two groups showed significant changes in single- and dual-task postural performance following rehabilitation, and no effect on dual-task cost was observed. This null finding should be emphasized because it contrasts with the expectation that a cognitively engaging training modality could improve motor-cognitive coupling under dual-task conditions. Several studies have investigated the role of CMI in PwMS with different results.[55] The lack of a single interpretation of CMI may lie in the different paradigms used for its evaluation, especially when the effects of different difficulty levels of motor and cognitive tasks on the DTC are unknown.[55] In our case, the absence of change in dual-task cost may reflect a combination of factors, including the relatively short training dose, the characteristics and difficulty of the cognitive task used during posturography and its potential mismatch with the cognitive demands trained during gameplay, and inter-individual variability related to MS severity and symptom burden that may have increased response variability. A different interpretation was proposed by Castelli *et al.*, who assumed that PwMS and low to moderate disability levels during a dual-task activity spend their postural reserve in favor of concurrent cognitive performance.[39] Although comparing cognitive and motor DTCs is beyond the scope of this study, even in our case, it seems that motor rather than cognitive performance is affected by the CMI. Considering these findings, we can suppose that a more difficult motor task would have been more affected by the interference offered by the SCWT.

Limitations of the study

This study has several limitations. First, baseline differences in terms of psychological aspects may have influenced the results of our trial introducing potential uncontrolled variable. Depressive and anxiety symptoms may have affected cognitively demanding assessments and dual-task imbalanced condition may impact postural control. Second, the study was powered on the primary outcome (TUG) and therefore may have been underpowered to detect smaller but clinically relevant differences in dual-task performance or cognitive outcomes. Moreover, the dual-task assessment used in this trial was likely not sufficiently sensitive to discriminate CMI in our sample, employing a more complex motor task might have improved the ability to detect changes following rehabilitation. Third, the three-month follow-up period provides limited insight into the long-term retention of intervention effects. The improvement in reaction time observed immediately after VGT was not maintained at follow-up, suggesting that the cognitive benefits may be short-lasting without sustained or repeated training. Finally, in our trial, video game rehabilitation was administered using a commercially available platform; although testing its effectiveness was one of the study's goals, the use of exergaming devices developed for rehabilitative purposes might be more effective in PwMS.[56]

Conclusions

This randomized control trial evaluated the effect of exergaming as a rehabilitative alternative for PwMS. Our main findings revealed that a rehabilitative program administered using a commercially available video game console is as effective as a conventional BPT in improving static and dynamic balance in PwMS. Using exergaming as a rehabilitation tool particularly improves attention more than conventional treatment does, and its use may be suggested when motor and cognitive functions are both impaired. No differences following treatment were identified in terms of dual-tasking ability.

Considering our results, video game rehabilitation in PwMS may represent a therapeutic option to overcome the long-term disabling effects of neurodegenerative conditions, even in a home context. Despite encouraging results, further studies are needed to confirm our findings.

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Conflicts of interest
The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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Data availability
The data associated with the paper are available from the corresponding author upon reasonable request.

Randomized controlled trials
The trial protocol has been registered on ClinicalTrials.gov (NCT03353974)

Ethical approval
All procedures performed in this study involving human participants received ethical approval from the competent authorities, as described in the appropriate section of the manuscript, and have been conducted in accordance with the 1964 Helsinki Declaration and its later amendments. The authors confirm that this article does not report any studies involving embryos, gametes and human embryonic stem cells conducted by the authors. The authors confirm that this article does not report any studies involving animals conducted by the authors.

Informed consent
Written informed consent was obtained from all participants prior to inclusion in the study and for publication of their data, as described in the appropriate section of the manuscript

Authors' contributions
Andrea Baroni: conceptualization, methodology, data curation, writing - original draft preparation; Giulia Fregna: investigation; Danila Azzolina: data curation; Giacomo Severini: conceptualization, methodology, data curation, writing - review & editing; SS: conceptualization, methodology, writing - review & editing, supervision, funding acquisition. All authors read and approved the final version of the manuscript.

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