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ORIGINAL ARTICLE

Cognitive-motor dual-task training improves dynamic stability during straight and curved gait in patients with multiple sclerosis: a randomized controlled trial

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ABSTRACT

BACKGROUND: Multiple Sclerosis (MS) is a chronic inflammatory, demyelinating, degenerative disease of the central nervous system and the second most frequent cause of permanent disability in young adults. One of the most common issues concerns the ability to perform postural and gait tasks while simultaneously completing a cognitive task (namely, dual-task DT).

AIM: Assessing cognitive-motor dual-task training effectiveness in patients with Multiple Sclerosis (PwMS) for dynamic gait quality when walking on straight, curved, and blindfolded paths.

DESIGN: Two-arm single-blind randomized controlled trial. Follow-up at 8 weeks.

SETTING: Neurorehabilitation Hospital.

POPULATION: A sample of 42 PwMS aged 28-71, with a score of 4.00±1.52 on the Expanded Disability Status Scale were recruited.

METHODS: Participants were randomized in conventional (CTg) neurorehabilitation and dual-task training (DTg) groups and received 12 sessions, 3 days/week/4 weeks. They were assessed at baseline (T0), after the treatment (T1), and 8 weeks after the end of the treatment (T2) through Mini-BESTest, Tinetti Performance Oriented Mobility Assessment, Modified Barthel Index, and a set of spatiotemporal parameters and gait quality indices related to stability, symmetry, and smoothness of gait extracted from initial measurement units (IMUs) data during the execution of the 10-meter Walk Test (10mWT), the Figure-of-8 Walk Test (Fo8WT) and the Fukuda Stepping Test (FST).

RESULTS: Thirty-one PwMS completed the trial at T2. Significant improvement within subjects was found in Mini-BESTest scores for DTg from T0 to T1. The IMU-based assessment indicated significant differences in stability ($P<0.01$) and smoothness ($P<0.05$) measures between CTg and DTg during 10mWT and Fo8WT. Substantial improvements ($P<0.017$) were also found in the inter-session comparison, primarily for DTg, particularly for stability, symmetry, and smoothness measures.

CONCLUSIONS: This study supports the effectiveness of DT in promoting dynamic motor abilities in PwMS.

CLINICAL REHABILITATION IMPACT: Cognitive-motor DT implemented into the neurorehabilitation conventional program could be a useful strategy for gait and balance rehabilitation.

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KEY WORDS: Neurorehabilitation; Postural balance; Multiple sclerosis.

Multiple Sclerosis (MS) is a chronic inflammatory, demyelinating, degenerative disease of the central nervous system and the second most frequent cause of permanent disability in young adults.[1] The clinical features of MS vary widely from one patient to another but 60% of cases manifest both walking and balance difficulties and cognitive deficits.[2, 3] One of the most common issues concerns the ability to perform postural and gait tasks while simultaneously completing a cognitive task (namely, dual-task DT).[4] Indeed, in daily life activities it is frequent that, while walking, it is needed to pay attention to environmental/external stimuli, such as talking on the mobile phone. Considering that attention is a function with limited capacity, dividing it between two simultaneous tasks (motor and cognitive) generates motor-cognitive interference with motor performance remaining stable while cognitive performance deteriorates, or the opposite.[5] This deterioration in terms of cognitive/motor performance could result, consequently, in frequent falls,[6] home and work accidents,[7, 8] driving accidents,[9] and many other adverse events that can even frequently occur in people with MS (PwMS).[10] Balance and gait training programs, historically focused on deficiencies related to compromised visual, somatosensory, or vestibular sensory systems,[11, 12] as well as muscle weakness and spasticity,[13] are known to produce significant beneficial effects in PwMS in terms of cognitive and motor performances. Indeed, conventional rehabilitation programs still suggest separate treatments of motor and cognitive deficits,[13] although task-oriented training focused on the DT paradigm demonstrated superior benefit to single-task interventions in different neurological disorders in improving dynamic motor abilities.[14, 15] A recent systematic review reported that just a few studies investigated the effects of DT training in PwMS with inconsistent evidence in improving balance and gait.[16] In fact, despite several encouraging findings, DT treatments seem to have little effect on clinical balance and gait measurements in PwMS. Clinical measures of balance and gait, as they do not measure dual-task components, may lack the sensitivity to identify dual-task performance improvements. Indeed, Morelli and colleagues[16] suggested that future research using objective measures of postural sway, during static and dynamic balance tasks for single and dual tasks, may show important variations that are not detected by conventional clinical scales. Furthermore, an increasing number of researchers propose to introduce more objective measures of motor performance during dynamic tasks.[17-19] In fact, while motor ability assessment is typically performed using clinical scales, promising results were obtained using instrumental assessments, giving a more accurate and detailed evaluation of gait alterations.[20] Nowadays, many technologies have been used to quantify human motion,[21] but an increasing interest has been directed toward inertial measurement units (IMUs).[22, 23] IMU-based evaluation permits the quantitative estimation of spatiotemporal and gait quality parameters, the latter providing information such as dynamic postural stability and gait smoothness.[24, 25] Indeed, straight walking tests, like the 10-meter Walk Test (10mWT), are frequently used to assess gait impairments,[26] however, these tests are sometimes not sensitive enough to detect motor ability disorders in the activities of daily living.[27] Recently, further dynamic motor tasks have been developed for patients with neurological disorders to test biomechanical characteristics related to gait stability, symmetry, and smoothness while walking following curvilinear paths or stepping while blindfolded.[22, 28, 29] In the literature, an integrated clinical and instrumented-based assessment has been proven to provide quantitative and objective differentiation of various walking levels as well as the correlation between the clinical scale scores and gait stability indices in different neurological populations. This integrated approach has also already been used to assess motor changes following dynamic rehabilitation training in different neurological disorders[30] and could be more sensitive in detecting changes in gait stability with respect to more traditional clinical evaluation. We hypothesize that DT-based training could be useful in improving dynamic stability during dynamic tasks assessed through a combined clinical and instrumental evaluation. Therefore, the aim of this study is to evaluate the effectiveness of cognitive-motor DT training in PwMS on dynamic gait stability during straight, curved, and blindfolded paths.

Materials and methods

Study design

This study was a two-arm single-blind randomized controlled trial. All procedures contributing to this work comply with the ethical standards of the relevant national and institutional guidelines on human experimentation and with the World Medical Association Declaration of Helsinki.[31] This trial was approved by the Local Ethic Committee of “Santa Lucia” Foundation (FSL) Institute for Research and Health Care (IRCCS) (Protocol number CE/PROG.812) and carried out at the FSL IRCCS (Rome, Italy); all participants were included in the study after providing their informed consent. The trial was registered before enrollment on ClinicalTrials.gov with the ID number NCT04619953.

Based on the inclusion and exclusion criteria, a researcher who was not participating in the intervention sessions determined the patients' eligibility to participate. Participants were randomized into one of two groups: a conventional therapy group (CTg) and a dual-task training group (DTg).

Participants

Participants with a diagnosis of MS according to the McDonald Criteria[32, 33] were recruited and enrolled on the basis of consecutive sampling at the FSL between November 2020 and October 2022.

This sample size met the minimum requirements set by an a priori power analysis for nonparametric between-group comparisons conducted on preliminary data ($\alpha=0.05$; $\beta=0.8$; ES=0.6).[34] According to this sample size estimation procedure, each group should have had at least 15 patients.

The following inclusion criteria were applied: 1) diagnosis of relapsing–remitting (RRMS) or secondary-progressive (SPMS) MS diagnosed by a certified neurologist; 2) to be native Italian speakers; 3) aged between 28 and 71 years, 4) Expanded Disability Status Scale (EDSS) score[35] between 0 and 6.5; 5) the ability to walk independently for at least 50 meters. Exclusion criteria consisted of: 1) the presence of psychiatric and neurological disorders (other than MS) and other pathological conditions and/or clinical disorders severe enough to interfere with cognitive functioning and/or the performance of motor or cognitive tasks; 2) the occurrence of a clinical relapse in the three months prior to enrollment; 3) steroid therapies in the 30 days prior to enrolment; 4) the occurrence of a lower extremity fracture within three months prior to enrolment.

Interventions

The enrolled patients underwent 12 individual sessions of conventional or DT intervention, 3 days per week/4 week. Each session lasted 50 min.

All the interventions were performed at the neurorehabilitation gym of the FSL, by physiotherapists with at least 5 years of experience in neurorehabilitation. A Schematic representation of the experimental design is reported in Figure 1.

Conventional therapy

Conventional neuromotor rehabilitation consisted of 30 minutes of muscle stretching, active-assisted mobilizations, neuromuscular facilitation, gait training, and balance exercises using swinging platforms,[11] plus 20 minutes of dynamic postural stability consisted of marching on unstable surfaces and walking on the treadmill both with open and closed eyes.

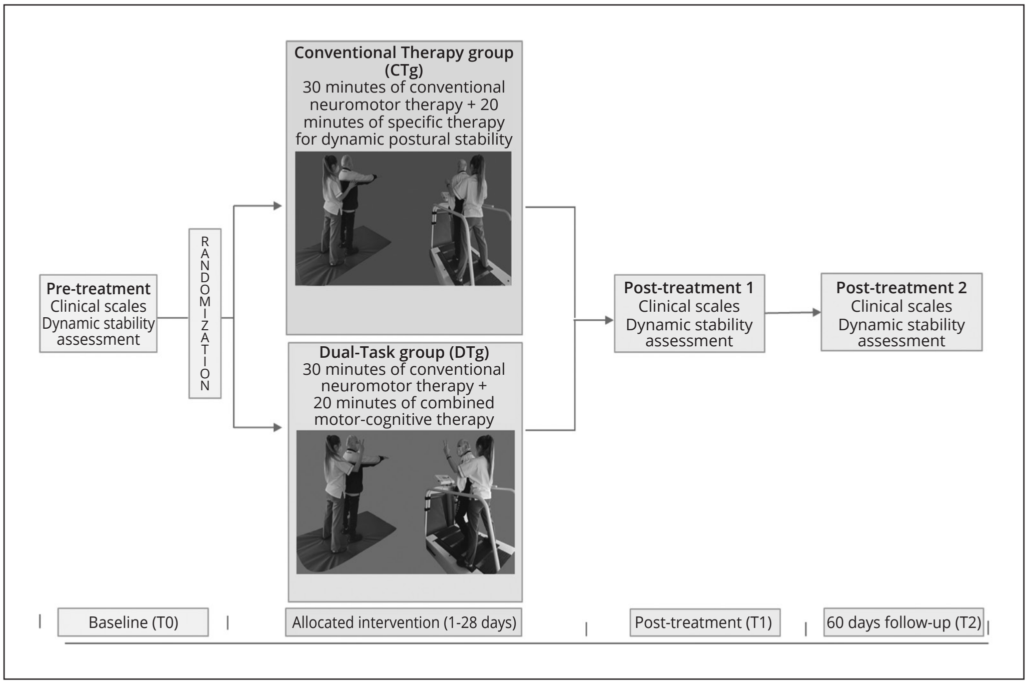

Figure 1.—Schematic representation of the experimental design.

Dual-task training

Twenty minutes of cognitive-motor training was added to conventional therapy and consisted of a dual-task paradigm in which each patient was asked to walk without stopping and was explained that, during the task, they might hear a sound, and in that case, they should have turned their head towards the stimulus' side and recognized a visual target.[36] This dual task was performed both by marching on an unstable surface and walking on the treadmill at different velocities.

Blinding randomization

The randomization was performed by an independent researcher not involved in the decision of the patient's eligibility nor in the intervention sessions. A computer-generated randomization list was used to produce block randomization using a block size. The researcher in charge of randomization stored the list in secure web-based storage. Allocation concealment was ensured by using an automatic random number generator.

Clinical outcome measures

At enrollment, clinical and demographic data were collected. A researcher not involved in the interventions, blinded to allocation, assessed primary and secondary outcomes at baseline (T0), after 4 weeks of training (T1), and 8 weeks after the end of the training (T2).

The primary outcome measure was the Mini-BESTest[37] to assess dynamic balance, postural responses, anticipatory postural adjustments, sensory orientation as well as the ability to modify the gait in response to changing task demands. Secondary outcome measures were the Tinetti Performance Oriented Mobility Assessment (POMA)[38] to evaluate static balance and gait, the Modified Barthel Index (MBI) to evaluate the performance during the activities of daily living (ADL),[39] and an instrumental sensor-based assessment during dynamic motor tasks.

Instrumental assessment

All participants were asked to perform three different motor tasks in a randomized order: the 10-meter Walk Test (10mWT) (Figure 2A), the Figure-of-8 Walk Test (Fo8WT) (Figure 2B)[22] performed both in clockwise and counterclockwise directions, and the Fukuda Stepping Test (FST) (Figure 2C).[40] Each task was performed three times, of which the mean value between trials was subsequently calculated and used for the statistical analysis.

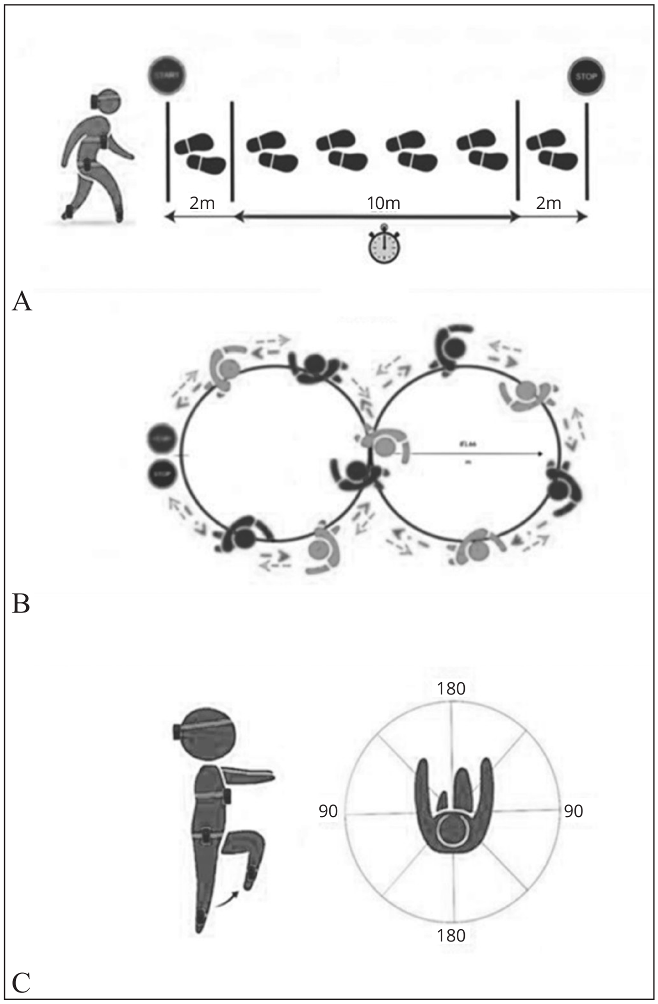

Figure 2.—Schematic representation of the three motor tasks performed: A) 10mWT, patients were asked to walk at their preferred speed on a 14 m trail; B) Fo8WT, clockwise and counterclockwise directions are indicated with blue and green arrows, respectively; C) FST, patients were asked to walk on the spot with eyes closed and arms in front of them.

The instrumental assessments were performed by two physiotherapists specifically trained in gait analysis with inertial sensors.

During the performance of each task (10mWT, Fo8WT, and FST), participants were equipped with five synchronized IMUs (128 Hz, Opal, APDM, Portland, OR, USA), measuring three-dimensional linear accelerations and angular velocities. IMUs were located on the occipital cranium bone, near the lambdoid suture of the head (H), at the center of the sternum (S), and at the L4/L5 level, just above the pelvis (P). For step and stride segmentation, one IMU was placed on each shank, just above the lateral malleoli. All IMUs were attached to the participant's body with Velcro straps. The data were processed in the Matlab® environment (MATLAB R2022b, MathWorks) for the extraction of spatiotemporal and gait quality parameters. The following spatiotemporal parameters and gait quality indices were obtained for the three tasks:

- spatiotemporal:
  - for the gait tasks: 1) average walking speed (WS) as the ratio between total distance and time to complete the test; 2) average stride duration (AD_{stride}) as the ratio between time to complete the test and the number of strides; 3) average stride frequency ($Freq_{stride}$) as the total number of strides divided by the time needed to complete the test. The number of strides was automatically obtained through a peak detection algorithm on the ML angular velocity signals measured by the two IMUs on the shanks;[41, 42]
  - for the FST, the number of steps (Nr_{step}), step frequency ($Freq_{step}$), and step duration (AD_{step}) were taken into consideration;
- stability:
  - normalized root mean square (RMS) of the acceleration measured at the pelvis, trunk, and head levels. The RMS values of each stride acceleration were obtained for the AP, ML, and CC components. To take the influence of the walking speed into account, the AP and ML components were then divided by the CC component, as suggested by.[43] High nRMS values have been associated with higher levels of acceleration, and hence, decreased stability:[18]

$$RMS_j K = \frac{1}{N}\sqrt{\sum\nolimits_{i=1}^{N} a_i^2} \;;$$

$$nRMS_j K = \frac{RMS_j K}{RMS_{CC} K}$$

where *j* represents the component (AP and ML), *K* represents the upper body level (Pelvis, Sternum, Head), *N* is the number of data sample and *a* is the acceleration signal.

  - attenuation coefficients (AC)[42] between each level pair of the upper body (pelvis-sternum, pelvis-head, sternum-head), for each acceleration component (AP, ML, and CC) defined as:

$$ACPS_j = \left(1 - \frac{RMS_{Sj}}{RMS_{Pj}}\right)\cdot 100 \;;$$

$$ACPH_j = \left(1 - \frac{RMS_{Hj}}{RMS_{Pj}}\right)\cdot 100 \;;$$

$$ACSH_j = \left(1 - \frac{RMS_{Hj}}{RMS_{Sj}}\right)\cdot 100$$

where *j* represents the direction AP, ML and CC. Each coefficient represents the variation of the acceleration from lower to upper-body levels. A positive coefficient indicates an attenuation of the accelerations, while a negative coefficient indicates an amplification of the accelerations from the lower to the upper body level. It has been demonstrated that, in typical walking, accelerations are attenuated from the pelvis to the head to stabilize the optic flow and increase the head stability;[44]

- symmetry: improved harmonic ratio (iHR)[45] measured at the level of the pelvis, for each acceleration component (AP, ML and CC). This parameter ranges from 0% (total asymmetry) to 100% (total symmetry). It is calculated as:

$$iHR_j = \frac{\Sigma\text{ power of intrinsic harmonics}}{\Sigma\text{ power of intrinsic harmonics} + \Sigma\text{ power of extrinsic harmonics}}\cdot 100$$

where *j* represents the direction AP, ML and CC.

- smoothness: log dimensionless jerk (LDLJ) measured at the pelvis level, calculated from the linear acceleration and angular velocity signals, LDLJ(a) and LDLJ(v), respectively. With reference to LDLJ(v), it is defined as:[46]

$$LDLJ(v) \triangleq -\ln\left(\frac{(t_2 - t_1)^3}{v_{peak}^2}\int_{t_1}^{t_2}\left\|\frac{d^2}{dt^2}v(t)\right\|_2^2 dt\right) \;;$$

$$v_{peak} \triangleq \max_{t\in[t_1,t_2]}\left\|v(t)\right\|_2$$

where $v(t)$ represents the angular velocity of the movement in the time domain; t_1 and t_2 represent the beginning and end of the movement, respectively. Lower LDLJ values have been associated with a higher level of smoothness of a translational/rotational movement.

Statistical analysis

Statistical analysis was performed using the IBM SPSS Statistics software (v23, IBM Corp., Armonk, NY, USA). Statistical level of significance was set at alpha = 0.05. The normal distribution of each parameter and each clinical scale was verified using the Shapiro-Wilk test. Non-parametric tests were performed for both within and between groups, after the distribution analysis. To evaluate significant differences between the two groups, the Mann-Whitney U-test was used on all estimated parameters. For the within-group analysis, a Friedman test was performed, to investigate if there were significant differences for each group across the three temporal evaluations (T0-T2). When a significant effect was found, a *post-hoc* test with the Wilcoxon rank-sign test with Holm-Bonferroni correction was performed.

Data availability

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

Results

Thirty-nine patients (CTg: 51.60±9.4 years, DTg: 50.40±10.27 years) were enrolled and allocated to the CTg and DTg. The two groups were homogeneous with respect to demographic and anthropometric characteristics, and clinical status as reported in Table I.

Sixteen CTg and twenty DTg patients completed the evaluation at T1 (after the end of the training) and fourteen CTg and seventeen DTg completed the evaluation at T2 (60 days after the evaluation at T1) as reported in Figure 3. The within-subjects comparison over time, showed a significant improvement in Mini-

TABLE I.—*Demographic and clinical characteristics at the baseline.*

Characteristics	CTg (N.=18)	DTg (N.=21)	P value
Age (years)	51.60±9.42	50.40±10.27	0.298
Gender, female	8	14	
Time since MS diagnosis, years	11±10	14±9.55	0.530
EDSS	4.00±1.51	4.00±1.53	0.837
Mini-BESTest	18.15±6.51	18.49±6.59	0.443
POMA	22.61±6.19	22.67±6.29	0.410
MBI	96.92±4.49	96.86±4.52	0.530

Data presented as mean±SD.
CTg: conventional therapy group; DTg: dual-task training group; MS: multiple Sclerosis; EDSS: Expanded Disability Status Scale; POMA: Tinetti Performance Oriented Mobility Assessment; MBI: Modified Barthel Index.

TABLE II.—*Clinical scales scores at time T0, T1 and T2.*

Clinical scales	Group	T0	T1	T2
Mini-BESTest	CTg	18.15±6.51	19.18±7.28	17.71±8.10
	DTg	18.49±6.59	21.75±5.80*	19.05±8.89
POMA	CTg	22.61±6.19	21.81±7.42	21.35±6.10
	DTg	22.67±6.29	25.75±5.80	24.05±5.55
MBI	CTg	96.92±4.49	96.12±5.45	95.35±5.67
	DTg	96.86±4.52	97.6±5.24	96.23±7.25

Data presented as mean±SD.
CTg: conventional therapy group; DTg: dual-task training group; POMA: Tinetti Performance Oriented Mobility Assessment; MBI: Modified Barthel Index; T0: baseline; T1: end of the training; T2: 60 days after the end of the training.
*Statistically significant differences with respect to T0 (P<0.017).

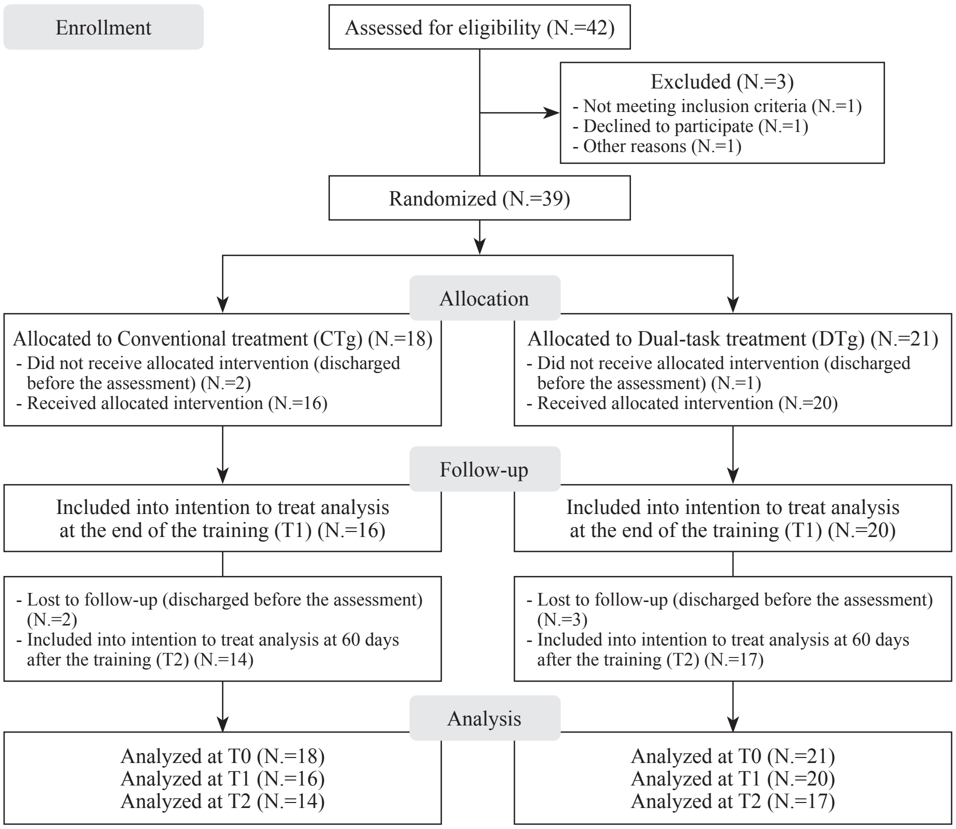

Figure 3.—CONSORT flow diagram of patient enrollment, randomization, and procedures.

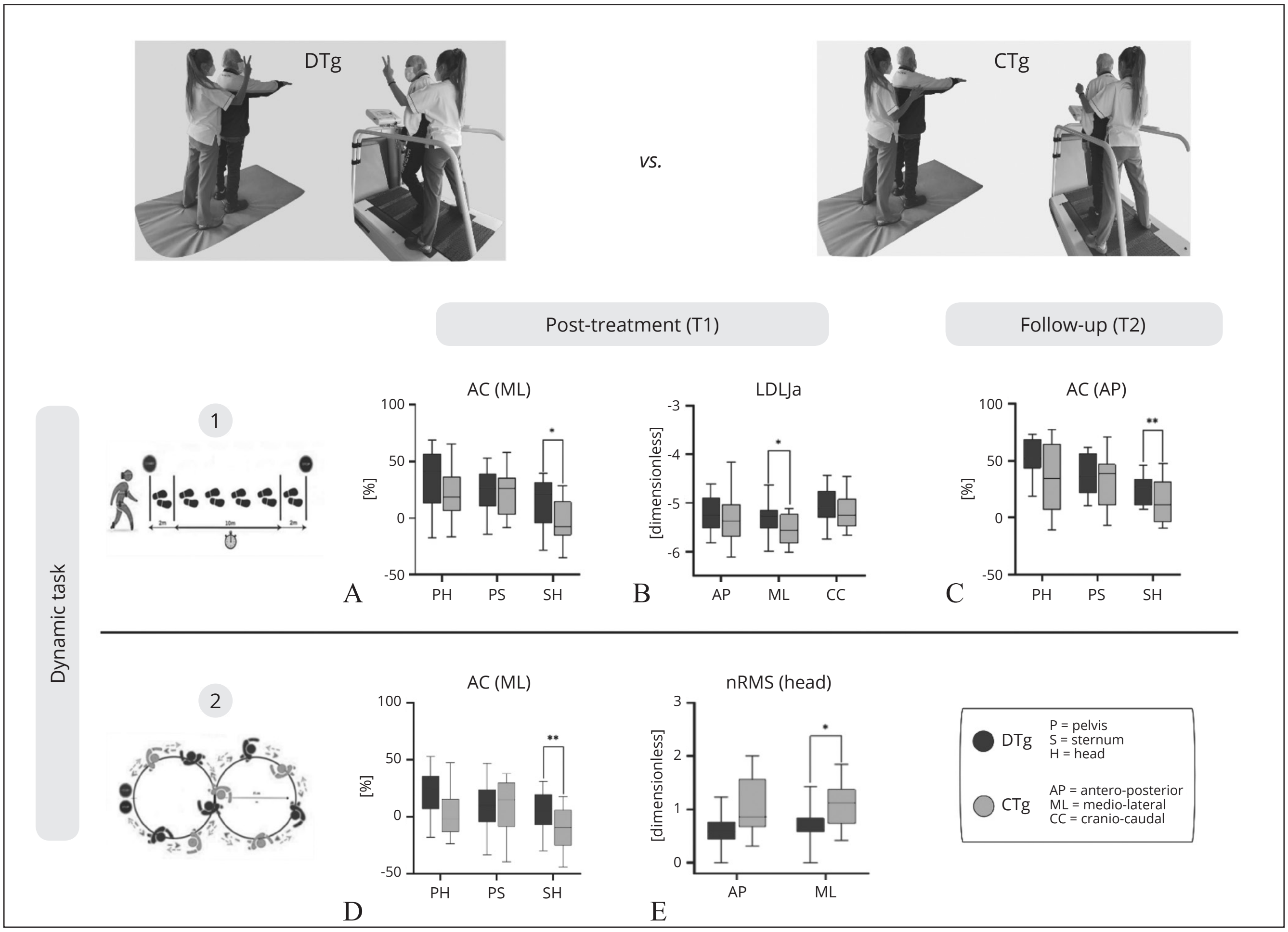

Figure 4.—IMU-based assessment of 10mWT and Fo8WT, between groups analysis at T1 and T2. Normalized root mean square (nRMS), attenuation coefficients (AC) and Log Dimensionless Jerk on acceleration (LDLJa) values for DTg and CTg. Medians and interquartile ranges are reported. AP: antero-posterior; ML: medio-lateral; CC: cranio-caudal; P: pelvis; S: sternum; H: head.
The asterisks indicate statistically significant between-group differences (* P<0.05; **P<0.01).

BESTest scores only for the DTg at T1 with respect to T0 (P=0.013) (Table II).

The IMU-based assessment of linear walking during the 10mWT revealed significant differences between the CTg and DTg in the ML axis for both AC from sternum to head level (U=88.00, *z*=-2.29, P=0.021) and LDLJa from pelvis (U=98.00, *z*=-1.97, P=0.049) at T1 (Figure 4A, B). Also, at time T2, the AC from sternum to head in the AP (U=22.00, *z*=-2.53, P=0.01) and CC axis (U=60.00, z=-2.54, P=0.01) was found significantly different between the groups (Figure 4C). A main effect of the session was highlighted for the iHR parameter in the AP and CC components for CTg, showing a difference in gait symmetry from T1 to T2 (P<0.017).

Significant differences between the CTg and DTg emerged during the curvilinear walking (Fo8WT) at time T1 (Figure 4D, E) in the ML axis for both the nRMS at head level (U=89.00, *z*=-2.26, *P*=0.023) and for the AC from sternum to head level (U=62.00, *z*=-3.11, P=0.001). Furthermore, significant differences (P<0.017) in the within-analysis were found for DTg from T0 to T1 ($Freq_{stride}$, AD_{stride}, WS, nRMS_H_ML) and from T1 to T2 (WS, LDLJv_AP). Whereas for the CTg, for the same task, significant results emerged from T0 to T1 and from T0 to T2 for iHR_CC.

During the FST, in the within-analysis, significant differences (P<0.017) for the DTg were identified from T0 to T2 for $Freq_{step}$. While for the CTg, significant results emerged for Nr_{step}, $Freq_{step}$, AD_{step} from T0 to T1, and from T0 to T2 for Nr_{step}, $Freq_{step}$, AD_{step}, LDLJa_AP, LDLJa_ML, LDLJa_CC parameters. No side effects were reported from all the included participants who completed the study.

Discussion

The aim of this study was to explore the effectiveness of combined motor and cognitive therapy through a dual-task paradigm in PwMS when compared to dynamic postural stability rehabilitation, and to assess the maintenance of possible improvements with an 8- week follow-up. DT, when integrated into a neurorehabilitation program, significantly improved ($P<0.017$) dynamic balance, postural responses, and adjustments assessed by the Mini-BESTest after the end of the training. Although significant improvements were observed only for the Mini-BESTest score from T0 to T1; an increase in clinical scale scores was found also from T0 to T2 in the Mini-BESTest, and from T0 to T1 in the POMA for the DTg with respect to the CTg. A wearable sensor-based protocol was adopted to evaluate gait stability, symmetry, and smoothness of gait during linear (10mWT), curved (Fo8WT), and blindfolded paths (FST). The sensor-based assessment during the dynamic tasks, showed significant improvements in both groups CTg and DTg at T1 during the 10mWT for the AC from sternum to head in AP and ML component (Figure 4, A, C) and for the LDLJa in ML component (Figure 4B), implying greater stability and smoothness during straight walking after the rehabilitation program. Significant differences between groups were found in the ML axis for both AC from sternum to head level ($P=0.021$) and LDLJa ($P=0.049$) at T1, and for the AC from sternum to head in the AP ($P=0.010$) and CC axis ($P=0.01$) at T2. These results suggest that patients who performed the DT training showed more pronounced improvements in the stability and smoothness indices during the linear path when compared to CTg 60 days after the end of the program (T2). Interestingly, significant differences between groups emerged during the curvilinear walking (Fo8WT) at T1 in the ML axis for both the nRMS at head level ($P=0.023$) and for the AC from sternum to head level ($P=0.001$). These findings suggest that undergoing a more dynamic and challenging 4-week program focused on cognitive-motor training allowed PwMS to perform more stable curved paths with respect to a conventional postural stability training (Figure 4E, D). Furthermore, significant improvements were found during the Fo8WT at the end of the training in spatiotemporal ($Freq_{stride}$, AD_{stride}, WS), smoothness (LDLJv in AP direction), and stability (nRMS, head level in the ML component) parameters. Conversely for the CTg, significant results emerged only for symmetry in CC direction. The LDLJv is a significant supplementary metric to measure the effectiveness of rotational movement, showing postural reactions as a result of specific rehabilitation treatment. Because it can quantify motor recovery[47, 48] and forecast the degree of motor independence,[49, 50] the evaluation of smoothness is a helpful index in neurorehabilitation. The increase in LDLJv values during the curvilinear walking test indicates that a combined cognitive-motor training could provide an effective complementary strategy for enhancing dynamic motor abilities when walking along a curved path, especially for a disease that is inherently progressive. Furthermore, during the FST significant differences were found for both DTg and CTg in the spatiotemporal parameters, although LDLJa in all three directions was significant only for the CTg. Indeed, both trainings improved motor abilities during visual deprivation conditions. These results are interesting because only the CTg performed a specific training blindfolded but also the patients who performed a cognitive-motor training reported positive results during this task, suggesting that DT therapy could reduce the visual dependence in PwMS.[49] To the best of our knowledge, this is the first study carried out on PwMS to evaluate the effects of a specific DT training using five synchronized IMUs to measure stability, symmetry, and smoothness of gait with a 2-month follow-up. Similar to previous studies,[51-53] our results support the benefits of complementary integrated cognitive-motor training in PwMS in gait and balance recovery.

Limitations of the study

We acknowledge some limitations in the interpretation of the results. Indeed, this clinical trial was carried out during the COVID-19 pandemic, and this affected the final sample size. Furthermore, we did not report the fatigue and psychological assessment after the training to evaluate the possible effects also on neuropsychological disorders. In fact, as the DT training involves the enhancement of both motor and cognitive functions together, we may expect an improvement in some aspects related to attention and cognition in general. Future research will overcome this limitation.

Conclusions

A combined cognitive-motor DT training integrated into the neurorehabilitation conventional program could enhance the smoothness of gait during the 10mWT and dynamic postural stability during linear and curved paths when compared to conventional postural stability training.

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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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