Contents lists available at Islamic World Science Citation Center (ISC)

International Journal of Motor Control and Learning (IJMCL)

Journal Home page: http://www.ijmcl .com

Training with Non-dominant Limb: A Helpful Strategy for Motor Function and Dual-task Cost in Multiple Sclerosis Patients

Shahzad Tahmasebi Boroujeni [a*], Arash Abbasnia [b], Masoumeh Doosti [c]

[a] Associate Professor, Department of Behavioral and Cognitive Sports Sciences, Faculty of Sport Sciences and Health, University of Tehran, Tehran, Iran. Email: Shahzadtahmaseb@ut.ac.ir

[b] MS. Department of Behavioral and Cognitive Sports Sciences, Faculty of Sport Sciences and Health, University of Tehran, Tehran, Iran. Email: arash.abasnia@ut.ac.ir

[c] PhD Candidate in Motor Learning, Department of Behavioral and Cognitive Sports Sciences, Faculty of Sport Sciences and Health, University of Tehran, Tehran, Iran. Email: m.doosti@ut.ac.ir

ARTICLE INFO

Article history:

Received: 2023/04/24

Accepted: 2023/07/29

Available online: 2023/08/03

Keywords:

Functional mobility

Manual dexterity

Upper extremity

Motor control

ABSTRACT

Background: The use of the inter-limb transfer mechanism in the rehabilitation of Multiple sclerosis (MS) patients is unclear. This study aimed to investigate the effect of non-dominant hand training on motor function and dual-task cost in MS patients. **Methods:** 22 women with a mean age of 44.09 ± 7.26 years and the Expanded Disability Status Scale (EDSS) 3.83 ± 0.76 were randomly divided into control (n=11) and experimental (n=11) groups. Nine Hole Peg Test (NHPT), Box and Block Test (BBT), and Dual-Task Cost test (DTC) took as pre-tests from the participants. Post-test was taken 24 hours after the last intervention session and the retention test one week later. **Results:** The results showed that the motor function (NHPT and BBT) of the experimental group improved in both dominant and non-dominant hands ($P \leq 0.05$). However, a significant decrease was observed in both dominant and non-dominant hands in the control group for NHPT and BBT ($P \leq 0.05$). Also, the experimental group had a lower Dual-Task Cost than the control ($P < 0.001$) in the post-test. **Conclusion:** According to the results, inter-limb transfer mechanisms can be used in the rehabilitation of MS patients in both motor and cognitive dimensions.

1. Introduction

Multiple sclerosis (MS) is a chronic inflammatory and neurodegenerative immune-mediated disease of the central nervous system (CNS) that affects most middle-aged men and women in the busiest years of their lives and career advancement. As the disease progresses, physical and mental disorders cause problems such as fatigue, weakness of the limbs, altered motor coordination of the upper limbs, and fine movements (Lamers et al., 2016). Upper extremity dysfunction may be present in 80% of people with MS (Kraft et al., 2014). A review of the findings shows that different upper limb rehabilitation strategies all improve, but research should move towards comparing them and choosing the most appropriate method (Lamers et al., 2016). Two general issues can be seen in previous studies for upper limb rehabilitation; First, the nature of the training is considered to be increasing, which has recently been enhanced by robots and virtual reality and computer training, which have generally seen improvements (Bonanno et al., 2019; Cuesta-Gómez et al., 2020; Jonsdottir et al., 2019). However, for MS patients, the availability of these exercises and the possibility of performing them easily is an issue that can be problematic for MS patients. The second is related to the intervention results; most studies have reported performance improvements only in the trained hand; while, most Activities of daily life (ADL) are done in two hands (Yang et al., 2021). This issue is crucial due to the Hemispheric Asymmetry Reduction in Older Adults (HAROLD) (Cabeza et al., 2002). Neuroscientists use the term HAROLD for this phenomenon, and reduce the difference between dominant and non-dominant hands in terms of power, accessibility, targeting, and accuracy (Cabeza et al., 2002), increasing age in these patients, becomes especially important. According to the neurogenic view (Hill et al., 2020), it seems that effective rehabilitation methods should seek to increase upper limb function in both hands.

One of the mechanisms that lead to improved function in both the limbs is inter-limb transfer mechanisms (de Oliveira et al., 2013). In the arguments of inter-limb transfer, the results of recent findings showed that task training with the non-dominant hand (N-DH) is well transferred to the dominant hand (DH) and the direction of transfer from the N-DH to DH is greater than the DH to the N-DH (De Almeida Batista et al., 2017; Tilsley et al.,2021; Xiao et al., 2020). In general, DH change creates plasticity mechanisms that lead to the reorganization of specific brain areas (Nicholls et al., 2010).

Generally, when performing multiple tasks, there is ample evidence that individuals with cognitive-motor interference (CMI) develop (Shumway-Cook & Woollacott, 2001). In particular, CMI refers to cognitive, motor function defects or both when performed concurrently compared to when performed in isolation. These changes are quantified by the difference in performance between dual-task and single-task conditions, known as dual-task cost (DTC)

Corresponding author: Shahzad Tahmasebi Boroujeni, Associate Professor, Department of Behavioral and Cognitive Sports Sciences, Faculty of Sport Sciences and Health, University of Tehran, Tehran, Iran. E-mail addresses: Shahzadtahmaseb@ut.ac.ir

[DOI: 10.61186/ijmcl.5.3.24]

(Wajda et al., 2016). MS patients have been hypothesized to have higher DTC (Lemmens et al., 2018). Research has shown that these changes are related to the degree of disability (Sosnoff et al., 2011), gait, and cognitive function in MS patients (Motl et al., 2014). The results of studies show that gait performance in MS patients is significantly reduced in the presence of dual-task (Motl et al., 2014; Raats et al., 2019). Also, some gait studies have analyzed the movements, patterns, and functions of the upper extremity segments in normal gait (Carmo et al., 2012) and showed upper limb movements help maintain balance (Kavanagh et al., 2004) in normal gait. Studies showed that children with diplegic and hemiplegic cerebral palsy adopt specific arm postures related to their gait instability (Meyns et al., 2012). In hemiplegic CP, the unaffected arm seemed to contribute more to COM deceleration during (pre) swing, while the affected side contributed to COM acceleration (Meyns et al., 2017). Improved upper extremity function may positively change the phasing relationship between the arms and legs in gait (Jongen et al., 2012). It has been suggested that cognitive-behavioral therapy programs, exercise, and education can be used in this direction (Jongen et al., 2012).

Given the above, the authors of this study seek to answer two questions 1) Does non-dominant hand training improve motor functions in the DH in MS patients? In this study, considering the importance of improving function in both upper limbs for functional independence and ADL in MS patients, it is expected that N-DH training will lead to DH transfer according to the predictions of inter-limb transfer. 2) Does non-dominant hand training reduce CMI in these patients? Given the simultaneously cognitive and motor needs of most ADLs and because practice interventions with levels of task difficulty lead to task-related adaptations (Zimmer, Javelle, & Lampit, 2021), we are expected that challenges reduce the CMI, which the DTC will measure, by practicing the non-dominant hand and the resulting increased attention needs. The authors also answer this question based on the results that confirm the effect of upper limb function on gait, hypothesizing that improved upper limb function can lead to improved gait function and ultimately lower DTC during gait.

2. Materials and Methods

2.1. Participants

Participant flow through the study is presented in Fig. 1. Participants were female MS patients of Fars's Association with a mean age (44.09 ± 7.26) years and Expanded Disability Status Scale (EDSS) EDSS (3.83 ± 0.76) and disease duration (10.93 ± 2.02) who were voluntary and after completing the informed consent form. The number of samples was determined 22 subjects using G-Power software for Mixed Analysis of Variance with a test power of 0.85, an effect size of 0.3, and an alpha level of 0.05. Finally, 22 participants were selected by simple random sampling, and divided into two control (n= 11) and experimental (n= 11) groups. At the entrance stage of the study, all participants received the Mini Mental State Exam (MMSE) dementia test, upper limb physical examination, active and inactive range of motion test, and Annett's handedness questionnaire.

2.2. Task and apparatuses

2.2.1. Nine Hole Peg Test (NHPT)

The test consists of a plastic console with pegs on one side and holes for each peg. From the time the participant touches the first peg to the time the last peg is inserted into the hole, time is calculated. Participants made a practice trial before performing the test, and in the main test conditions, two trials were made for each DH and N-DH, and the average of these two trials was used in the analysis (Grice et al., 2003). This test has validity and reliability for people with MS (Johansson et al., 2012; Jonsdottir et al., 2019).

2.2.2. Box and Block Test (BBT)

The test is performed so that the participant sits facing a rectangular box that is divided into two square compartments of equal size using a wall. One hundred and fifty 2.5 cm wooden blocks are placed in one of the compartments. The person is obliged to move the blocks one by one to the other side within 1 minute. To score each block, the patient's hand must cross the wall. Better performance is shown by moving more blocks. The validity and reliability of BBT are excellent for MS patients (Desrosiers et al., 1994).

2.2.3. Dual-Task Cost (DTC)

The DTC calculated as the difference between the scores of dual and single-task conditions. To measure the DTC, we use the Timed Up and Go test (TUG) in two conditions: walking without a secondary task (ST) and walking with a secondary cognitive task (DT) (which in this study, the subjects counted three digits back from the number 100) were used. The DTC was calculated using the following formula (Brustio et al., 2018):

Formula 1. (Single-task performance − dual-task performance)/ (single-task performance) × 100

2.2.4. Jebsen Hand Function Test (JHFT)

This test evaluates the function of the upper extremities and assesses fine and gross motor skills, weighted and non-weighted hand function activities during the performance of activities of daily living in neurological patients. The JHFT consists of 7 items that measure: (a) fine motor skills, (b) weighted functional tasks, and (c) non-weighted functional tasks. These items include: writing a short sentence (24 letters, 3rd-grade reading difficulty), turning over a 3×5 inch card, picking up small everyday objects, simulated feeding, stacking checkers, picking up large light cans, and picking up large, heavy cans (Schaefer et al., 2018).

[DOI: 10.61186/ijmcl.5.3.24]

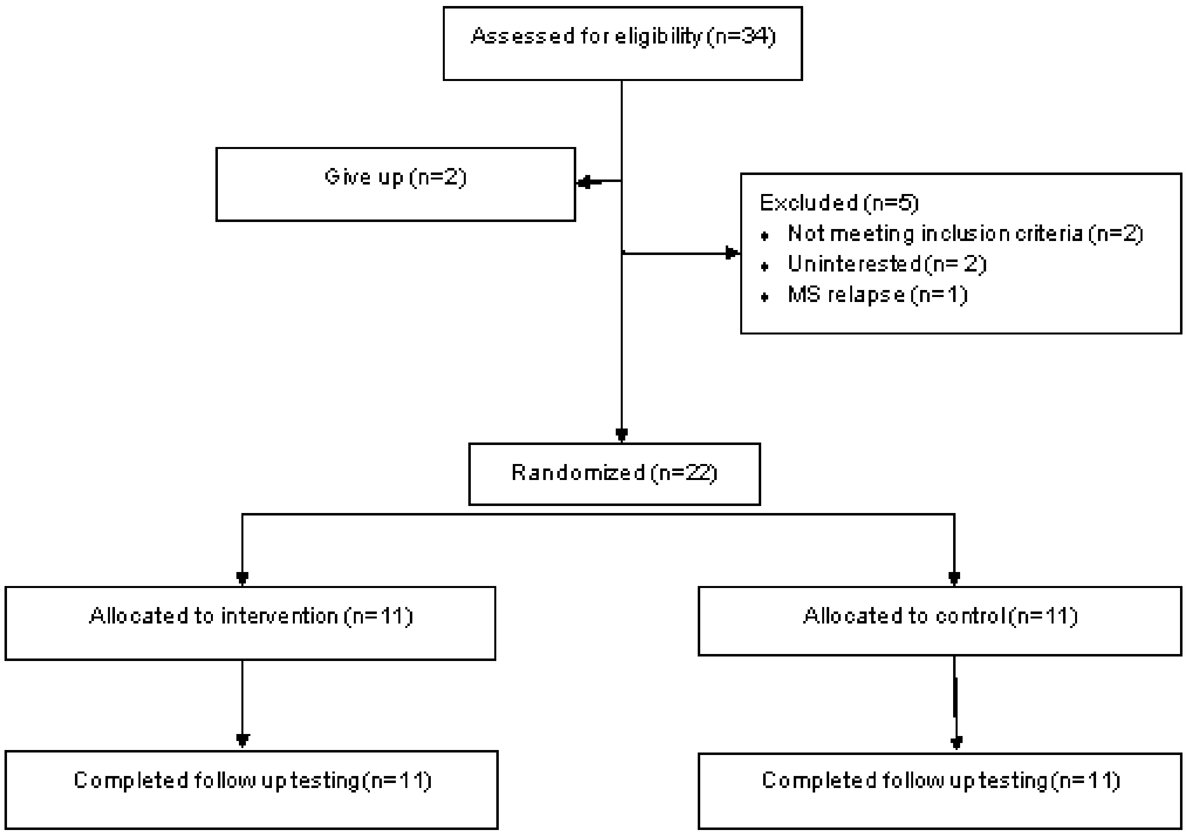

Figure. 1. CONSORT diagram

2.6. Procedure

The study received an ethics code number IR.SSRC.REC.1400.028 from the Research Ethics Committees of Sport Sciences Research Institute (SSRI). Participants completed and signed an informed consent form to participate in the study. Then, participants were randomly divided into experimental and control groups. The participants took NHPT, BBT, and DTC tests in the pre-test. In the intervention phase, the experimental group performed 16 supervised sessions (4 times a week) of rehabilitation training taken from the JHFT with the N-DH. Each session consisted of 3 practice sets. In each set, each training was performed for 45 seconds. There were 30 seconds between each workout and 5 minutes between each set. We changed the volume and intensity of the exercise by asking patients and reporting their condition. Therefore, the duration of each training session was between 30 and 60 minutes. It changed progressively from the beginning to the end of the training period. The control group did not undergo any intervention during the intervention and went about their daily lives. In the post-test phase, which was 24 hours after the last training session, the tests were taken similar to the pre-test phase, and the delayed retention test was taken from the participants a week later. All tests were performed by an examiner unaware of the purpose of the study before and after 16 training sessions.

2.7. Data Analysis

First, we used the Shapiro-Wilk test to check the normality of data distribution and the Leven test to check the homogeneity of variances. In each of the functional variable's HPT, BBT, and DTC, 2 (group) in 3 (test) mixed ANOVA were used. Pairwise comparisons were performed with Bonferroni modification using syntax at the significance level of $P \leq .05$. Data analysis was performed by SPSS25 software, and Excel16 software was used to draw the graphs.

3. Results

The descriptive information for the research variables in different stages (pre-test, post-test, and retention) is shown in **Table 1**.

[DOI: 10.61186/ijmcl.5.3.24]

International Journal of Motor Control and Learning 2023; 5 (3) 24-29

Table 1.

Mean ± SD of variables

Variable	Group	n	Hand Performance	M ± SD		
				Pre test	Post test	Retention
NHPT (s)	Experimental	11	DH	25.72 ± 1.50	22.97 ± 1.57	22.89 ± 2.72
			N-DH	30.10 ± 5.72	27.66 ± 4.98	26.47 ± 4.97
	Control	11	DH	27.22 ± 4.75	29.26 ± 1.35	27.53 ± 5.42
			N-DH	31.46 ± 6.07	35.28 ± 1.39	35.48 ± 5.63
BBT (n)	Experimental	11	DH	59.9 ± 3.64	66.18 ± 11.02	67.00 ± 8.08
			N-DH	52.27 ± 8.54	61.27 ± 2.40	56.45 ± 6.39
	Control	11	DH	60.72 ± 8.55	58.27 ± 6.85	59.18 ± 8.31
			N-DH	50.72 ± 6.78	45.90 ± 9.1	47.09 ± 8.89
DTC (%)	Experimental	11	-	-26.41 ± 11.27	-23.99 ± 14.17	-25.47 ± 10.96
	Control	11	-	-32.9 ± 9.24	-45.07 ± 14.36	-49.27 ± 19.09

Note: DH= dominant hand; N-DH= non- dominant hand.

3.1. NHPT

There was no significant difference between groups in NHPT pretest none of the DH ($F_{(1, 20)} = 0.99$, $P = 0.31$) and N-DH ($F_{(1, 20)} = 0.29$, $P = 0.593$). The results of Mixed ANOVA in NHPT showed that in the DH, the main effect of the test ($F_{(2,40)}= 4.16$, $P = 0.023$, $\eta2P = 0.172$), group ($F_{(1,20)} = 7.51$, $P = 0.013$, $\eta2P = 0.273$) and interaction test * group ($F_{(2,40)}= 14.58$, $P < 0.001$, $\eta2P = 0.422$), and in the N-DH, the main effect of the group ($F_{(1,20)}= 7.52$, $P = 0.013$, $\eta2P = 0.273$) and interaction test*group ($F_{(2,40)}= 25.19$, $P <0.001$, $\eta2P = 0.558$) was significant, but the main effect of test was no significant ($F_{(2,40)}= 0.76$, $P = 0.473$, $\eta2P = 0.037$).

Within group comparison, the experimental group in the DH showed the NHPT time significantly reduced from pre-test (25.72 ± 1.50) to post-test (22.97 ± 1.57; P <0.001), and retention (22.89 ± 2.72; P =0.002). Also significant improvement in NHPT time in N-DH from pre-test (30.10 ± 5.72) to post-test (27.66 ± 4.98) and retention (26.47 ± 4.97; P = 0.003) was observed in experimental group. However, in the control group, the NHPT time in the DH had a significant increase from pre-test (27.22 ± 4.75) to post-test (29.26 ± 1.35; P = 0.002).

In between-group comparisons (Figure 2), the experimental group in the post-test of the DH (P <0.001) and N-DH (P = 0.001) and in retention of DH (P = 0.02) and N-DH (P =0.001) performed significantly better than the control group **(Figure 2).**

3.2. BBT

In the BBT, the results of the mixed ANOVA showed that in the DH, the effect of the interaction test * group (F)2,40(= 7.73, P =0.001, η2P = 0.27) and in the N-DH, the main effect of the group (F)1, 20(= 8.182, P = 0.01, η2P = 0.29) and interaction test * group (F)2,40(= 13.75, P <0.001, η2P = 0.409) were significant; the other main effect didn't significant.

In within-group comparisons, in the DH of the experimental group, significant performance improvement from pre-test (59.9 ± 3.64) to post-test (66.18 ± 11.02; P =0.015) and retention (67.00 ± 8.08; P <0.001) was observed. Also, in N-DH, performance from pre-test (52.27 ± 8.54) to post-test (61.27 ± 2.40; P <0.001) had a significant improvement in experimental group. In contrast, in the control group, the hand function of N-DH from pre-test (50.72 ± 6.78) to post-test (45.90 ± 9.1; P = 0.038) had a significant decrease. The other comparisons did not significant.

In between-group comparisons (Figure 3), the experimental group in the post-test of N-DH (P < 0.001) and retention of DH (P = 0.037) and N-DH (P = 0.01) performed significantly better than the control group **(Figure 3).**

3.3. DTC

In the DTC variable, the results of mixed ANOVA showed that only the main effect of the group was significant (F)1,20(= 29.47, P <0.001, η2P = 0.596) and the experimental group (-25.29%) showed lower DTC from the control group (-42.42%) **(Figure 4).**

[DOI: 10.61186/ijmcl.5.3.24]

International Journal of Motor Control and Learning 2023; 5 (3) 24-29

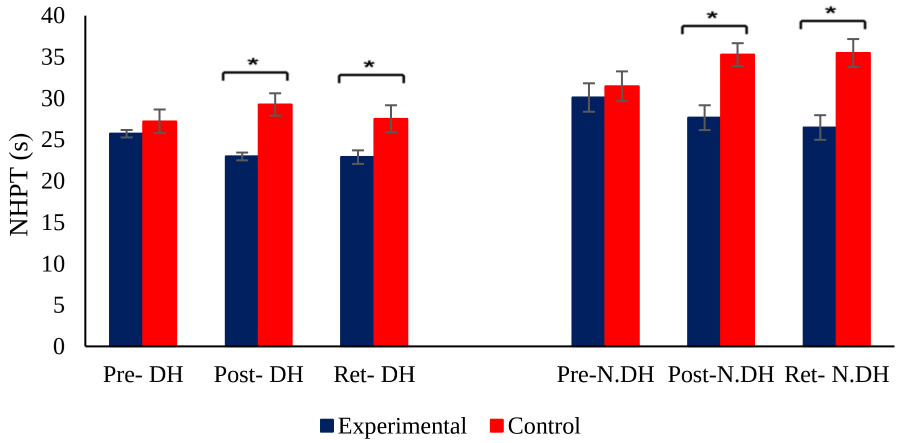

Figure. 2. Between-group differences in NHPT. Note: the value represents mean with standard error bars; * P≤0.05.
***Note**: DH= dominant hand; N-DH= non- dominant hand.*

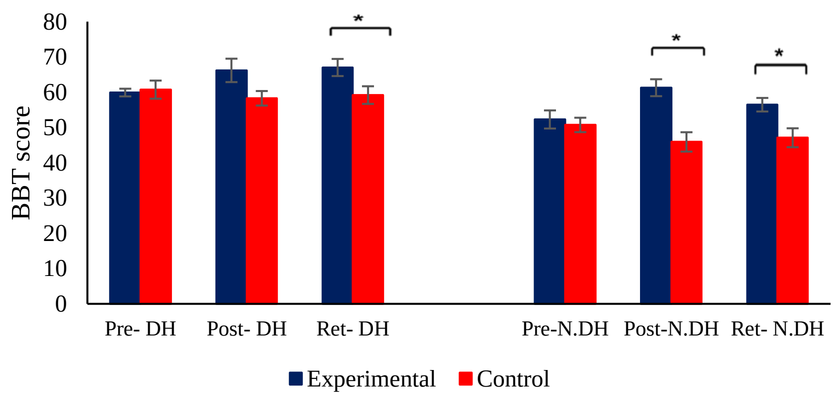

Figure. 3. *Between-group differences in BBT. Note: the value represents mean with standard error bars; * P≤0.05*
***Note**: DH= dominant hand; N-DH= non- dominant hand.*

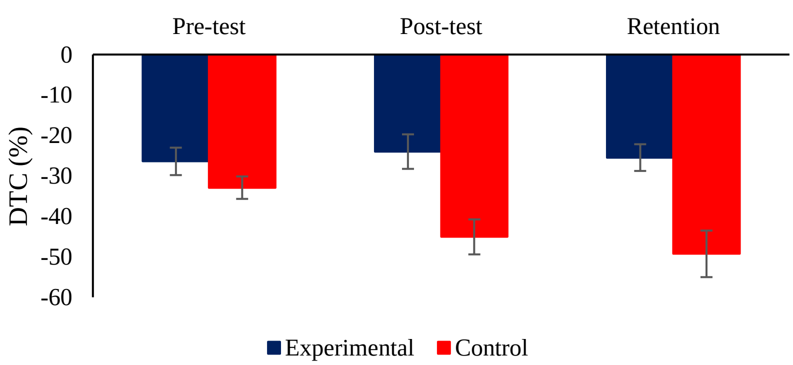

Figure. 4. *Between-group differences in DTC. Note: the value represents mean with standard error bars; * P≤0.05*
Note: *DH= dominant hand; N-DH= non- dominant hand.*

.

[DOI: 10.61186/ijmcl.5.3.24]

International Journal of Motor Control and Learning 2023; 5 (3) 1-12

4. Discussion and conclusion

MS is an inflammatory disease that destroys the central nervous system and is associated with an impaired motor function (Bonanno et al., 2019). This study aimed to evaluate the effect of non-dominant hand training on motor and cognitive function of MS patients. The findings of this study showed that training with a non-dominant can lead to improved motor function in the dominant hand. The results contradicted the findings inserted in the intervention of virtual reality games and reported that significant performance improvement was only on the affected side (Carpinella et al., 2012; Cuesta-Gómez et al., 2020; Jonsdottir et al., 2019). In the study of Cuesta-Gómez et al. (2020), participants underwent 20 sessions of 15 minutes of virtual reality games (in addition to their usual rehabilitation protocols), and observed effects only on the affected side. The games considered in that research included playing the piano, reaching, grasping, prehension, and positioning the page with both hands (Cuesta-Gómez et al., 2020). One of the limitations of that research is that the considered training is not easily accessible to patients, which poses many challenges for people with the disease. In this regard, the results showed that a 16-session upper limb training session at home improves the motor function of the trained hand (Ortiz-Rubio et al., 2016).

The present study results showed that inter-limb transfer from N-DH to DH occurs in MS patients, and the function of untrained hand movement improves under the influence of trained hands. The present study's findings are consistent with studies showing that transfer from the healthy hand to paretic hand occurs during an NHPT training period in patients with stroke (C. D. Ausenda & Carnovali, 2011; Iosa et al., 2013; Xiao et al., 2020). The present study results also agree with the findings that showed the transfer from N-DH to DH (De Almeida Batista et al., 2017; Tilsley et al., 2021). It has been suggested that cognitive involvement (concentration, attention, and perception) is greater during N-DH training. When in the transfer situation, the person performs the task with her DH; due to more cognitive involvement in the training phase, more transfer to the DH occurs. Complex tasks are also associated with the activity of the dorsal premotor, motor supplementary, cerebellum areas as well as the primary motor cortex; on the other hand, more transfer to the opposite limb with more activity in similar neural structures (such as the cerebellum and motor supplementary region) is associated with complex tasks (Nasios et al., 2020). Thus, despite this overlap in inactive brain regions, challenging and complex tasks also increase transfer. Because the progression of MS-related disability can be adjusted by neuroplasticity, complicated training can be used to delay disease progression; this causes the brain to reorganize, mainly at the synaptic level (Nasios et al., 2020). Complex tasks lead to more cognitive or motor effort and increase neuroplasticity changes through the cognitive-motor neural network necessary for learning and transmission (Lefebvre et al., 2015). So, increasing brain neuroplasticity is the primary goal of all MS disease control methods that can change the duration of the disease (Nasios et al., 2020). Therefore, since N-DH training is considered a more complex level of training than DH training, it is likely to cause more transfer.

At the DTC, the results showed that the experimental group had a lower DTC than the control group. This finding is consistent with the results of studies showing that DTC can be improved by training (Sosnoff et al., 2011). In a way, the DTC improvement may have occurred due to improved gait performance; because the integration of the frontal areas related to executive function is necessary for gait and balance and involves the coordination of different areas in the hemisphere. The responsibility for this integration lies with the corpus callosum, which connects the frontal and anterior frontal cortices in the first place. Therefore, it seems that corpus callosum function in the neural mechanism of bilateral transfer and more activity in areas related to complex training and overlapping of those areas with areas involved in the bilateral transfer, can lead to an integration of different brain regions and improve gait performance and reduce DTC. In confirmation of improved gait performance, the results show that gait performance is correlated with DTC negatively (Raats et al., 2019). Therefore, lower DTC in the experimental group can be associated with better gait performance.

On the other hand, the inferior frontal gyrus (IFG) is one of the main areas of activity of mirror neurons (MN). Since the training considered in the present study was performed in groups and created conditions for observational learning and interpersonal interaction, it may have increased the activity of MN in this area. Activation of this region in the non-dominant hemisphere recovers words from long-term memory in patients with brain lesions and even with language learning disabilities without brain damage (de Oliveira et al., 2013). Previous findings revealed that hand motor function is associated with linguistic (Meister et al., 2006) and cognitive (Carotenuto et al., 2019) abilities. Therefore, the decrease in DTC may be due to the activity of the IFG area and activation of MN and occurred as a result of improved hand motor function. Also, in line with studies that show improved upper limb motor function is related to gait performance (Kavanagh et al., 2004; Meyns et al., 2017), the lower DTC of an experimental group than the control group in gait may be justified by the mediating role of improving upper limb function.

On the other hand, white and gray cortical lesions in MS patients have been introduced as one of the pathological causes of cognitive disorders in MS patients (Nasios et al., 2020) and the results of studies show that, in general, gait function decreases with atrophy of white and gray cortex (Wennberg et al., 2017). As a result, the DTC changes may generally be due to the gray and white cortex changes.

Finally, it can be briefly stated that according to the results of the present study, non-dominant hand training resulted in transfer between the limbs to the dominant hand, as well as improved upper limb motor function and reduced DTC in MS patients. In addition, decreased motor function and increased DTC in the control group indicate that MS, as a progressive disease, requires continuous rehabilitation programs to control the disease process. Because disability control is essential in people with MS due to its relationship with cognitive and motor symptoms, their cognitive and motor abilities should be considered in rehabilitation programs. However, the investigation of parameters and gait patterns, such as step speed and step length that are affected by the secondary task, has not been considered and is one of the limitations of the present study. In addition, however, one of the limitations of the present study is the lack of investigation of structural changes and activity of different brain parts, which we suggested to researcher study in future research.

Authors' contributions

Conception and design of the study: SH.T.B, A.A; Data collection: A.A; Data analysis and/or interpretation: M.D;A.A Drafting of manuscript and/or critical revision: M.D, A.A; Approval of final version of manuscript: SH.T.B, M.D.

Conflict of interests

The Authors declare that there is no conflict of interest.

Funding

This work was supported by university of Tehran [grant Numbers 28202/1/7].

Acknowledgements

The research team of this article is grateful to the MS patients of Eqlid city who patiently accompanied us until the end of the project.

[DOI: 10.61186/ijmcl.5.3.24]

References

Ausenda, C. D., & Carnovali, M. (2011). Transfer of motor skill learning from the healthy hand to the paretic hand in stroke patients: A randomized controlled trial. *European Journal of Physical and Rehabilitation Medicine*, 47(3), 417-425. [PMID]

Bonanno, L., Russo, M., Bramanti, A., Calabrò, R. S., & Marino, S. (2019). Functional connectivity in multiple sclerosis after robotic rehabilitative treatment: A case report. Medicine, 98(17), e15047. [DOI:10.1097/MD.0000000000015047] [PMID] [PMCID]

Brustio, P. R., Rabaglietti, E., Formica, S., & Liubicich, M. E. (2018). Dual-task training in older adults: The effect of additional motor tasks on mobility performance. Archives of Gerontology and Geriatrics, 75(December 2017), 119-124. [DOI:10.1016/j.archger.2017.12.003] [PMID]

Cabeza, R., Anderson, N. D., Locantore, J. K., & McIntosh, A. R. (2002). Aging gracefully: compensatory brain activity in high-performing older adults. NeuroImage, 17(3), 1394-1402. [DOI:10.1006/nimg.2002.1280] [PMID]

Carmo, A. A., Kleiner, A. F. R., Lobo da Costa, P. H., & Barros, R. M. L. (2012). Three-dimensional kinematic analysis of upper and lower limb motion during gait of post-stroke patients. *Brazilian Journal of Medical and Biological Research*, 45(6), 537-545. [DOI:10.1590/S0100-879X2012007500051] [PMID] [PMCID]

Carotenuto, A., Moccia, M., Costabile, T., Signoriello, E., Paolicelli, D., Simone, M., … Lauro, F. (2019). Associations between cognitive impairment at onset and disability accrual in young people with multiple sclerosis. *Scientific Reports*, 9(1), 1-8. [DOI:10.1038/s41598-019-54153-7] [PMID] [PMCID]

Carpinella, I., Cattaneo, D., Bertoni, R., & Ferrarin, M. (2012). Robot training of upper limb in multiple sclerosis: comparing protocols with or withoutmanipulative task components. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, 20(3), 351-360. [DOI:10.1109/TNSRE.2012.2187462] [PMID]

Cuesta-Gómez, A., Sánchez-Herrera-Baeza, P., Oña-Simbaña, E. D., Martínez-Medina, A., Ortiz-Comino, C., Balaguer-Bernaldo-De-Quirós, C., … Cano-De-La-Cuerda, R. (2020). Effects of virtual reality associated with serious games for upper limb rehabilitation inpatients with multiple sclerosis: Randomized controlled trial. *Journal of NeuroEngineering and Rehabilitation*, 17(1), 1-10. [DOI:10.1186/s12984-020-00718-x] [PMID] [PMCID]

De Almeida Batista, S. R., Rodrigues, P., & Vasconcelos, O. (2017). Intermanual Transfer of Learning in a Fine Manual Skill Task. *Motriz. Revista de Educacao Fisica*, 23(1), 7-13. [DOI:10.1590/s1980-6574201700010002]

de Oliveira, F. F., Correia Marin, S. de M., & Ferreira Bertolucci, P. H. (2013). Communicating with the non-dominant hemisphere: Implications for neurological rehabilitation. *Neural Regeneration Research*, 8(13), 1236-1246. [DOI:10.4103/1673-5374.112860] [PMID] [PMCID]

Desrosiers, J., Bravo, G., Hébert, R., Dutil, E., & Mercier, L. (1994). Validation of the Box and Block Test as a measure of dexterity of elderly people: reliability, validity, and norms studies. *Archives of Physical Medicine and Rehabilitation*, 75(7), 751-755. [DOI:10.1016/0003-9993(94)90130-9] [PMID]

Grice, K. O., Vogel, K. A., Le, V., Mitchell, A., Muniz, S., & Vollmer, M. A. (2003). Adult norms for a commercially available Nine Hole Peg Test for finger dexterity. *American Journal of Occupational Therapy*, 57(5), 570-573. [DOI:10.5014/ajot.57.5.570] [PMID]

Hill, C., Van Gemmert, A. W. A., Fang, Q., Hou, L., Wang, J., & Pan, Z. (2020). Asymmetry in the aging brain: A narrative review of cortical activation patterns and implications for motor function. *Laterality*, 25(4), 413-429. [DOI:10.1080/1357650X.2019.1707219] [PMID]

Iosa, M., Morone, G., Ragaglini, M. R., Fusco, A., & Paolucci, S. (2013). Motor strategies and bilateral transfer in sensorimotor learning of patients with subacute stroke and healthy subjects. A randomized controlled trial. *European Journal of Physical and Rehabilitation Medicine*, 49(3), 291-299. []

Johansson, S., Ytterberg, C., Claesson, I. M., Lindberg, J., Hillert, J., Andersson, M., … Idiman, E. (2012). The relationship between walking, manual dexterity, cognition and activity/participation in persons with multiple sclerosis. *Multiple Sclerosis Journal*, 17(1), 733-746. [DOI:10.1016/j.jns.2006.02.018] [PMID]

Jongen, P. J., Ter Horst, A. T., & Brands, A. M. (2012). Cognitive impairment in multiple sclerosis. *Minerva Medica*, 103(2), 73-96. [PMID]

Jonsdottir, J., Perini, G., Ascolese, A., Bowman, T., Montesano, A., Lawo, M., & Bertoni, R. (2019). Unilateral arm rehabilitation for persons with multiple sclerosis using serious games in a virtual reality approach: Bilateral treatment effect? *Multiple Sclerosis and Related Disorders*, 35, 76-82. [DOI:10.1016/j.msard.2019.07.010] [PMID]

Kavanagh, J. J., Barrett, R. S., & Morrison, S. (2004). Upper body accelerations during walking in healthy young and elderly men. *Gait & Posture*, 20(3), 291-298. [DOI:10.1016/j.gaitpost.2003.10.004] [PMID]

Kraft, G. H., Amtmann, D., Bennett, S. E., Finlayson, M., Sutliff, M. H., Tullman, M., … Rabinowicz, A. L. (2014). Assessment of upper extremity function in multiple sclerosis: Review and opinion. *Postgraduate Medicine*, 126(5), 102-108. [DOI:10.3810/pgm.2014.09.2803] [PMID]

Lamers, I., Maris, A., Severijns, D., Dielkens, W., Geurts, S., Van Wijmeersch, B., & Feys, P. (2016). Upper limb rehabilitation in people with multiple sclerosis: A systematic review. *Neurorehabilitation and Neural Repair*, 30(8), 773-793. [DOI:10.1177/1545968315624785] [PMID]

Lefebvre, S., Dricot, L., Laloux, P., Gradkowski, W., Desfontaines, P., Evrard, F., … Vandermeeren, Y. (2015). Neural substrates underlying motor skill learning in chronic hemiparetic stroke patients. *Frontiers in Human Neuroscience*, 9(JUNE). [DOI:10.3389/fnhum.2015.00320] [PMID] [PMCID]

Lemmens, J., Ferdinand, S., Vandenbroucke, A., Ilsbroukx, S., & Kos, D. (2018). Dual-task cost in people with multiple sclerosis: A case-control study. *British Journal of Occupational Therapy*, 81(7), 384-392. [DOI:10.1177/0308022618757936]

Meister, I. G., Sparing, R., Foltys, H., Gebert, D., Huber, W., Töpper, R., & Boroojerdi, B. (2006). Functional connectivity between cortical hand motor and language areas during recovery from aphasia. *Journal of the Neurological Sciences*, 247(2), 165-168. [DOI:10.1016/j.jns.2006.04.003] [PMID]

Meyns, P., Desloovere, K., Van Gestel, L., Massaad, F., Smits-Engelsman, B., & Duysens, J. (2012). Altered arm posture in children with cerebral palsy is related to instability during walking. European Journal of Paediatric Neurology : EJPN : *Official Journal of the European Paediatric Neurology Society*, 16(5), 528-535. [DOI:10.1016/j.ejpn.2012.01.011] [PMID]

Meyns, P., Molenaers, G., Duysens, J., & Jonkers, I. (2017). The differential effect of arm movements during gait on the forward acceleration of the centre of mass in children with cerebral palsy and typically developing children. *Frontiers in Human Neuroscience*, 11(March), 1-6. [DOI:10.3389/fnhum.2017.00096] [PMID] [PMCID]

Motl, R. W., Sosnoff, J. J., Dlugonski, D., Pilutti, L. A., Klaren, R., & Sandroff, B. M. (2014). Walking and cognition, but not symptoms, correlate with dual task cost of walking in multiple sclerosis. *Gait and Posture*, 39(3), 870-874. [DOI:10.1016/j.gaitpost.2013.11.023] [PMID]

[DOI: 10.61186/ijmcl.5.3.24]

Nasios, G., Bakirtzis, C., & Messinis, L. (2020). Cognitive Impairment and Brain Reorganization in MS: Underlying Mechanisms and the Role of Neurorehabilitation. *Frontiers in Neurology*, 11(March), 1-8. [DOI:10.3389/fneur.2020.00147] [PMID] [PMCID]

Nicholls, M. E. R., Chapman, H. L., Loetscher, T., & Grimshaw, G. M. (2010). The relationship between hand preference, hand performance, and general cognitive ability. *Journal of the International Neuropsychological Society*, 16(4), 585-592. [DOI:10.1017/S1355617710000184] [PMID]

Ortiz-Rubio, A., Cabrera-Martos, I., Rodríguez-Torres, J., Fajardo-Contreras, W., Díaz-Pelegrina, A., & Valenza, M. C. (2016). Effects of a Home-Based Upper Limb Training Program in Patients With Multiple Sclerosis: A Randomized Controlled Trial. *Archives of Physical Medicine and Rehabilitation*, 97(12), 2027-2033. [DOI:10.1016/j.apmr.2016.05.018] [PMID]

Raats, J., Lamers, I., Baert, I., Willekens, B., Veldkamp, R., & Feys, P. (2019). Cognitive-motor interference in persons with multiple sclerosis during five upper limb motor tasks with different complexity. *Multiple Sclerosis Journal*, 25(13), 1736-1745. [DOI:10.1177/1352458518808194] [PMID]

Schaefer, S. Y., Saba, A., Baird, J. F., Kolar, M. B., Duff, K., & Stewart, J. C. (2018). Within-session practice effects in the jebsen hand function test (JHFT). *American Journal of Occupational Therapy*, 72(6), 7206345010p1-7206345010p5. [DOI:10.5014/ajot.2018.024745] [PMID] [PMCID]

Shumway-Cook, A., & Woollacott, M. H. (2001). Motor control : theory and practical applications /.

Sosnoff, J. J., Boes, M. K., Sandroff, B. M., Socie, M. J., Pula, J. H., & Motl, R. W. (2011). Walking and thinking in persons with multiple sclerosis who vary in disability. *Archives of Physical Medicine and Rehabilitation*, 92(12), 2028-2033. [DOI:10.1016/j.apmr.2011.07.004] [PMID]

Tilsley, P. A., Romaiguère, P., Tramoni, E., Felician, O., & Sarlegna, F. R. (2021). Interlimb transfer of reach adaptation does not require an intact corpus callosum:Evidence from patients with callosal lesions and agenesis. *Eneuro*, ENEURO.0190-20.2021. [DOI:10.1523/ENEURO.0190-20.2021] [PMID] [PMCID]

Wajda, D. A., Roeing, K. L., Mcauley, E., Motl, R. W., & Sosnoff, J. J. (2016). The relationship between balance confidence and cognitive motor interference in individuals with multiple sclerosis. *Journal of Motor Behavior*, 48(1), 66-71. [DOI:10.1080/00222895.2015.1040110] [PMID]

Wennberg, A. M. V., Savica, R., & Mielke, M. M. (2017). Association between Various Brain Pathologies and Gait Disturbance. *Dementia and Geriatric Cognitive Disorders*, 43(3-4), 128-143. [DOI:10.1159/000456541] [PMID] [PMCID]

Xiao, S., Ye, X., Guo, Y., Gao, B., & Long, J. (2020). Transfer of Coordination Skill to the Unpracticed Hand in Immersive Environments. In 2020 IEEE Conference on Virtual Reality and 3D User Interfaces (VR) (pp. 258-265). [DOI:10.1109/VR46266.2020.00045]

Byung-Il Yang, So-Young Han, Jung-Woo Jeong, Sung-Ryong Ma, Ha-Na Kim, Bo-Kyoung Song. (2021). The Effect of Bilateral Asymmetrical Motion Induction Task Training on Hand Activity in Chronic Hemiplegic Patients -According to the Presence or Absence of Predominant Damage-. *Annals of the Romanian Society for Cell Biology*, 1099–1104.

Zimmer, P., Javelle, F., & Lampit, A. (2021). Comment on: "Effects of Exercise Training Interventions on Executive Function in Older Adults: A Systematic Review and Meta-analysis." *Sports Medicine*, 51(3), 593-595. [DOI:10.1007/s40279-020-01369-7] [PMID] [PMCID]

[DOI: 10.61186/ijmcl.5.3.24]