Research Article

The Effect of Sensorimotor Synchronization on Gait Spatiotemporal Parameters in Women with Multiple Sclerosis: A Quasi-Experimental Study

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Running Title: Sensorimotor Synchronization in Multiple sclerosis

Abstract

Background: Although gait rehabilitation based on sensorimotor synchronization (auditory and visual) is interesting for other patients with neurological disorders and the elderly, there is little evidence in patients with multiple sclerosis. Therefore, this study investigates the effect of synchronization with rhythmic visual stimulus on gait Spatiotemporal parameters, bilateral symmetry, and locomotor rehabilitation index in women with multiple sclerosis.

Material and Methods: Spatiotemporal parameters, bilateral symmetry, and the locomotor rehabilitation index were obtained before and after six weeks (three times per week, 30 min) of locomotor training, comparing these findings between two groups of 10 patients, each with Expanded disability status scale (EDSS) 3-6 who performed the gait training with vs. without rhythmic visual stimulus.

Results: Time*group interaction effects indicated greater significant improvements in the group with rhythmic visual stimulus in self-selected walking speed (p=0.041), stride frequency (p=0.009), stance time (p=0.021), and locomotor rehabilitation index (p=0.036). stride length, double stance and swing time improved in the group with rhythmic visual stimulus but this change was not significant. Also, bilateral symmetry did not change significantly in the experimental group. Therefore, rhythmic visual stimulation can help improve functional mobility and locomotor rehabilitation index in patients with multiple sclerosis, especially due to the improvements in the temporal parameters of gait.

Conclusions: Therefore, synchronizing gait with a rhythmic visual stimulus can be an effective therapeutic strategy to improve gait and main temporal parameters in patients with multiple sclerosis.

Keywords: Multiple Sclerosis, Sensorimotor, Synchronization, Gait

Introduction

Multiple Sclerosis (MS) is a demyelinating disease of the central nervous system, leading to a wide range of disabilities and disorders in the transmission of neural messages throughout the brain and spinal cord (1, 2). Gait disorder is one of the most common problems reported in these patients (3). Liparoti et al. (2019) reported that patients with MS show longer stance time, double stance, and swing time compared to healthy people (4). Bilateral coordination is also worsened, and reduced gait speed seems to be a decisive factor in this impairment (5). This indicates that gait mechanics is impaired in these patients (5). which is reflected in changes in gait Spatiotemporal parameters (6). Therefore, it is crucial to develop treatment strategies to improve gait biomechanics parameters in these patients.

Sensory disorders play a major role in hampering motor control and coordination in patients with MS (7). Therefore, treatment strategies based on providing additional sensory cueing with the aim of supporting movement performance can be a suitable method to overcome motor control and coordination disorders in patients with MS (8), such as sensorimotor synchronization exercises. Sensorimotor synchronization consists of generating a sequence of motor responses at a frequency similar to a sensory stimulus, i.e., producing a motor response that coincides with a sensory stimulus (9). Motor and cognitive rehabilitation (such as sensorimotor synchronization exercises) can enhance the functional and structural plasticity of the brain in patients with MS (10). In patients with MS, the evidence shows that plasticity limits the clinical effects of injury by creating patterns of brain activity different from healthy volunteers, and improvement in motor function following exercises is accompanied by reorganizing those altered patterns (11). Also, exercising a practical movement under time constraints can be effective for practicing timing and treating patients coordination problems (12). So, it seems exercises based on sensorimotor synchronization can help in improving gait mechanics of these patients.

A limited number of studies have investigated the effect of synchronization with different sensory stimuli in patients with MS (13-15). In most studies, the effect of synchronization with rhythmic auditory stimulus on the gait performance of these patients has been investigated, which indicates the positive effects of this type of stimulus on the improvement of the gait mechanic of patients with MS (13, 14). However, as far as we know, only one study investigated the effect of synchronization with rhythmic visual stimulus on gait performance in patients with MS (15). The findings of this study showed that practicing gait with a rhythmic visual stimulus improved stride length, stride time, double support time, gait cadence, and speed. However, this difference was not statistically significant between the experimental group and the control group (15). Further studies have also reported a positive effect of this type of intervention for people suffering from other neurological diseases, such as Parkinson's disease (16). Research design problems in these studies include: short time of intervention and missed control. Despite these limitations, the improvement of gait Spatiotemporal parameters of these patients shows that gait training with rhythmic sensory stimuli can be a promising rehabilitation strategy in patients with MS. Researchers state that more research and better evidence and more quality are required to ensure the extent and extent of the positive effects of this type of intervention on the gait rehabilitation of patients with MS (13-15).

The present study is the first study that, while controlling the limitations of previous studies, investigates the effect of gait synchronization with the rhythmic visual stimulus on gait spatiotemporal parameters, motor rehabilitation index, and bilateral symmetry in patients with MS.

We hypothesized that gait training synchronized with rhythmic visual stimuli would improve gait spatiotemporal parameters, including self-selected walking speed, stride frequency, stride length, stance time, and swing, double stance and locomotor rehabilitation index to a greater extent compared to gait training alone. Also, we hypothesized that bilateral symmetry would improve significantly by adding the synchronization method to gait training due to the inherent stimulus of controlling the stepping and additional gains in the gait speed already observed in the previous study.

Methods

Twenty women with MS (Relapsing - remitting MS) members of the Zahedan MS Association were selected using available and targeted sampling methods (17). The criteria for participating in the present research included: 1) being 18 years old or more, 2) presenting an extended disability status scale three to six, 3) walking ability of at least 100 feet without physical assistance, 4) lack of treatment and recurrence and exacerbation of the disease in the past 30 days, 5) lack of cardiovascular and rheumatic diseases, 6) lack of severe pain in the lower joints, 7) lack of participation in any regular exercise for the past three months, 8) normal or corrected vision with glasses (15). The degree of disability of the patients was determined by the neurologist with an Expanded disability status scale questionnaire for MS patients. This study was approved by the ethics committee at the University of Mazandaran with the code IR.UMZ.REC.1399.012. All participants completed a written informed consent form to participate in the study. They were divided by the simple random method into an experimental group with 10 participants (gait training with rhythmic visual stimulus) and a control group with 10 participants (simple gait). In order to measure gait biomechanics eight Qualisys motion analysis cameras and the Qualisys Track Manager software were used. In order to measure the parameters of gait stability, right and left leg stance time, and swing time, after extracting the gait cycle and Toe off event, the time interval between Heel contact (HC) to Toe off has been considered as stance time and the time interval between Toe off to HC was considered as swing time (18). After measuring the temporal-spatial parameters of gait, the symmetry index was used to evaluate the bilateral symmetry (5). Also, the locomotor rehabilitation index was determined through the ratio of self-selected walking speed to optimal walking speed (19)

Exercises were performed for six weeks, three sessions per week, and 30 minutes per session. The exercises consisted of gait synchronization with a rhythmic visual stimulus. The stimulus was created with the design of a device including a Musedo (MT-100) metronome, an optical LED connected to the metronome, and a piece of wire 10 cm in front of the right inner edge of a hat. At the beginning of the first session of the experimental group exercise program, the visual stimulus frequency was set 10% higher than each participant's preferred walking cadence (15), determined during a 10-meter walking test. In this test, a 10-meter route was covered at a preferred speed, the number of steps and the time of covering the mentioned distance were recorded, and the number of steps in one minute was calculated as the preferred walking cadence of each participant (20). After setting up the device for each participant, they were asked to cover a distance of six meters after adapting their steps to the desired stimulus frequency, rotate 180 degrees, and return to the beginning of the route (16). In each exercise session, it was possible for the participant to split the 30-minute time into smaller intervals if it were difficult for them to walk for 30 minutes consecutively. At the end of each week, each participant's preferred walking cadence was measured using a 10-meter walking test at the preferred speed (20). Then, based on the preferred walking cadence plus 10%, the visual stimulus frequency was set for the following week's exercises. The exercises were performed individually, and an instructor walked two steps behind the examinees to support and prevent the participants from falling. The participants in the control group performed only simple gait (Figure 1 shows the consort chart of the study). Three participants, including two in the experimental group and one in the control group, were excluded from the initial statistical sample due to receiving corticosteroids and not attending regularly in the exercise sessions. It should be noted that the pre-test and post-test were conducted by people who were blind to the grouping. (Table 1 shows the general characteristics of the groups participants).

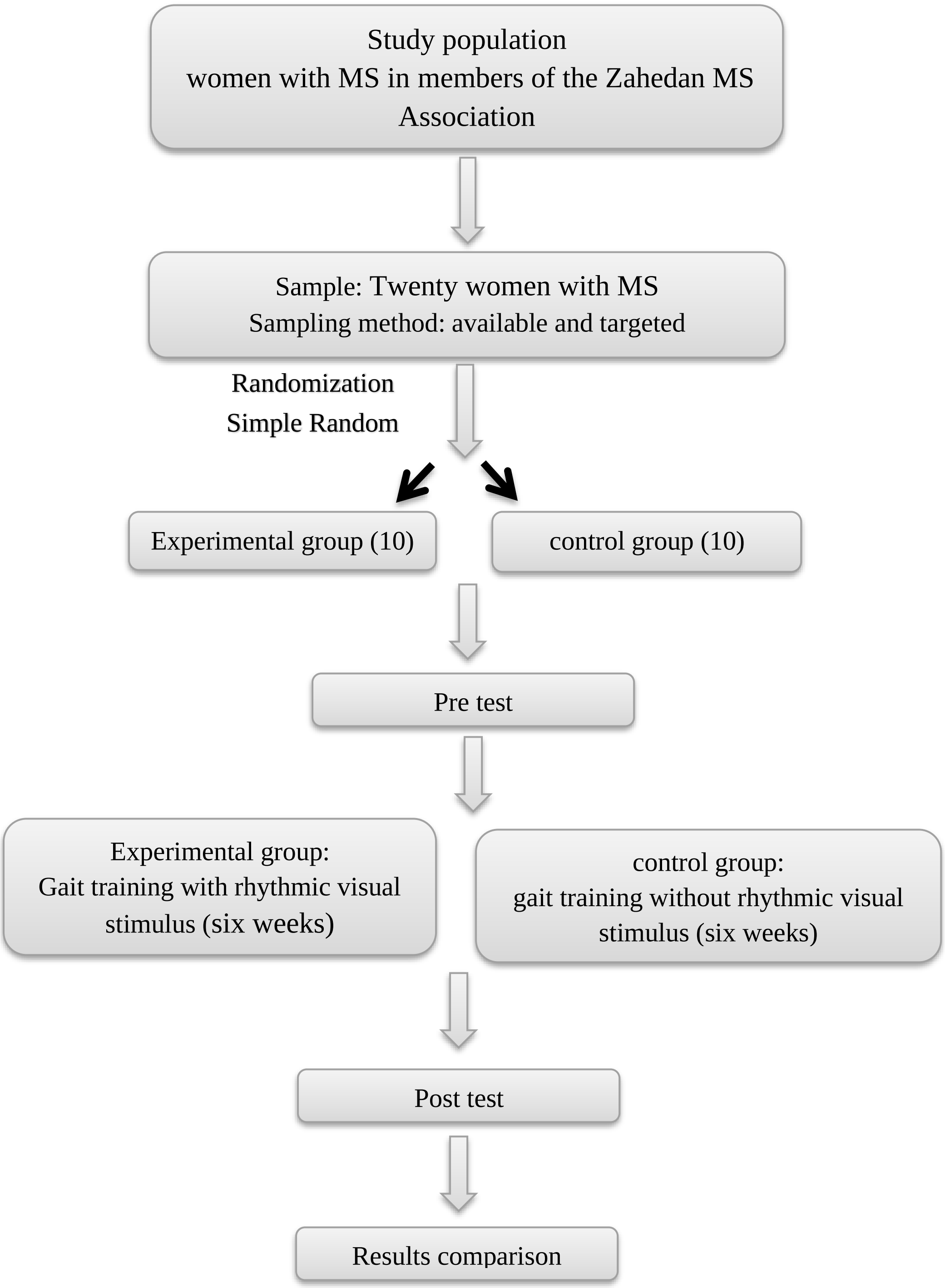

Figure 1. The consort chart of the study:

Table 1. General characteristics of the participants in the groups (n=20)

Variables	**Control group**	**Experimental group**	**p-value**
Participants (male/female)	10 (0/10)	10 (0/10)	-
Age (years)	40.9 ± 9.2	38.1 ± 12.1	0.149
Height (cm)	1.63 ± 0.06	1.60 ± 9.70	0.195
Body mass (kg)	60.9 ± 11.5	66.1 ± 7.2	0.753
BMI (kg*m^{-1})	25.6 ± 3.4	26.5 ± 3.5	0.585
EDSS	4±0.8	4.2±0.9	0.684
Lower Limb Length (m)	0.88 ± 0.03	0.87 ± 0.05	0.368

The results for independent t-test comparing Control and Experimental group. Body mass index (BMI); Values are presented by mean and standard deviation.

Statistical analysis

Firstly, we analyzed the data qualitatively for the normal distribution using the Shapiro-Wilk test and the homogeneity of the variances, which was confirmed by the Levene test. To evaluate the effect of different interventions a mixed model ANOVA was used with interventions (gait with and without rhythmic visual stimulation) and time (pre- and post-training) as fixed factors and subjects as random factors (Jasp). Data were reported as mean and standard deviation, with alpha adopted of p=0.05. Finally, Hedges's *g* and 95% confidence interval (CI) were used to determine the magnitude of the changes, bringing a more practical approach to the obtained results (Nakagawa et al., 2007). The Effect Size (ES) was classified as trivial (<0.19), small (0.20–0.49), medium (0.50–0.79), and large (0.80–1.29) (21).

Results

Time*group interaction effects indicated greater significant improvements in the group with rhythmic visual stimulus in self-selected walking speed (p=0.041), stride frequency (p=0.009), stance time (p=0.021), and locomotor rehabilitation index (p=0.036). stride length, double Stance and swing time improved in the group with rhythmic visual stimulus but this change was not significant. Also, bilateral symmetry did not change significantly in the experimental group (see Table 2).

Table 2. Mixed Model ANOVA test results for gait Spatiotemporal parameters, bilateral symmetry, and locomotor rehabilitation index in groups

Variables	**Control group**		**Experimental group**		**p-value**		
	pre	post	pre	Post	Group	Time	Group* Time
Self-Selected Walk Speed (m/s)	0.55±0.23	0.61 ± 0.29	0.43 ± 0.19	0.75 ± 0.32	0.885	0.006	0.041*
Stride length (m)	0.75 ± 0.26	0.80 ± 0.29	0.71 ± 0.26	0.95 ± 0.30	0.598	0.009	0.074

Stride frequency (Hz)							
	0.77 ± 0.06	0.75 ± 0.13	0.60 ± 0.12	0.77 ±0.14	0.086	0.037	0.009*
Stance time (s)							
	0.99 ± 0.22	0.95 ± 0.20	1.19 ± 0.23	0.86 ± 0.21	0.485	0.004	0.021*
Swing time (s)	0.40 ± 0.05	0.41 ± 0.06 ‡	0.49 ±0.10	0.47 ± 0.23 §	0.137	0.945	0.604
Locomotor rehabilitation index (%)				§			
	51.6 ± 17.4	55.1 ± 20.8	28.3 ± 12.8	50.4 ± 21.9	0.068	0.006	0.036*
Relative stance time (%)							
	70.3 ± 3.6	68.8 ± 3.5	69.3 ± 4.1	64.5 ± 7.0	0.092	0.045	0.292
Double Stance (s)							
	0.30 ± 0.1	0.29 ± 0.13	0.35 ± 0.1	0.23 ± 0.1	0.960	0.028	0.060
SL Symmetry (%)	32.3±17.7	29.8±17.3	4.88±4.27	3.80±2.71	<0.001	0.495	0.780
SF Symmetry	8.75±11.1	8.78±8.02	5.28±6.73	6.45±6.35	0.371	0.758	0.768
ST Symmetry	13.5±12.2	9.6±10.4	7.1±4.13	10.4±11.9	0.490	0.889	0.131
SW Symmetry	14.1±11.4	32.5±46.3	16.1±9.15	12.5±7.35	0.295	0.314	0.138
DC Symmetry	27.1±17.9	29.7±26.9	21.3±16.7	25.7±17.2	0.518	0.491	0.854

Values are presented by means and standard deviation. Superscript symbols indicate statistically significant differences ($p <0.01$ and $p< 0.05$) within-effect (s) in group (†),Control (‡), between-effect (versus control) in conditions (§). SL: Stride length, SF: Stride frequency, ST: Stance, SW: Swing.

Violin plots showing the distribution of the gait spatiotemporal parameters and locomotor rehabilitation index according to the time conditions (pre and post) for the control group (just gait, pink) and the synchronization group (gait synchronization with rhythmic visual stimulus, green). Moreover, the two-sided violin plots indicate the data distribution for each variable (Figure 2).

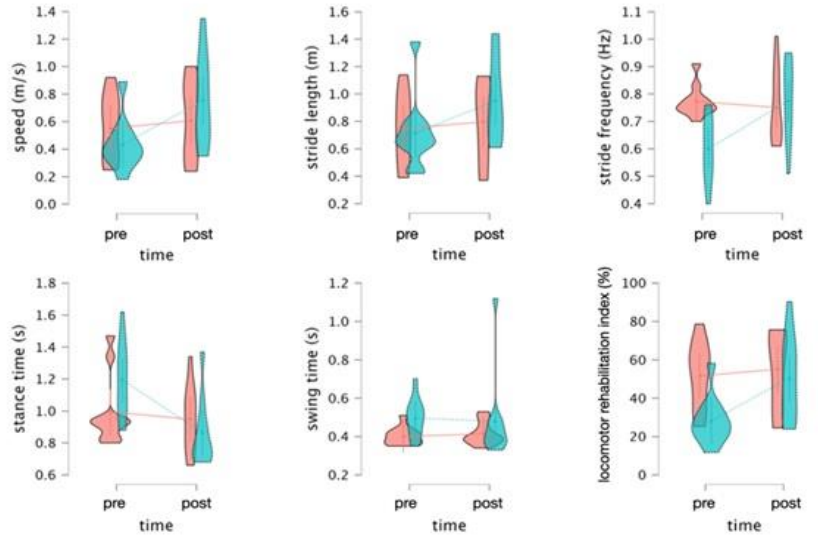

Figure 2. Violin plots: The distribution of the gait spatiotemporal parameters and locomotor rehabilitation index according to the time conditions (pretest and posttest). the control group, pink and the experimental group, green.

The ES was 0.15 with a 95% CI from -0.26 to 0.57 between pre and post conditions. On the other hand, in the rhythmic training with unequalized total training volume (RTUV) condition the ES was 0.51 (i.e., medium) with 95% CI from 0.09 to 0.97. For cross-sectional area (CSA) values, the ES between the different frequencies of the rhythmic training with equalized total training volume (RTEV) condition was -0.02 (i.e., insignificant) with a 95% CI from -0.43 to 0.40, while in the RTUV condition, the ES was 0.63 (i.e., medium) with 95% CI from 0.21 to 1.10 (Fig 2).

Discussion

The present study compared the changes in gait spatiotemporal parameters, Locomotor rehabilitation index and bilateral symmetry after a 6-week between gait training executed with and without synchronization with rhythmic visual stimuli in a group of patients with MS.

Our main findings showed that the self-selected walk speed, stride frequency, stance time, and locomotor rehabilitation index significantly improved after synchronizing gait with the rhythmic visual stimulus. However, despite improvements in stride length, double Stance and swing time, no significant change was observed. These findings confirm our first hypothesis. Also, bilateral symmetry did not show significant improvement, which rejected our second hypothesis.

Our findings confirm the previous results from studies on spatiotemporal parameters of gait with shorter periods of training (15). Shahraki, Sohrabi, et al. (2019) showed in a study that gait training with the rhythmic visual stimulus improves stride length, stride time, double support time, cadence, and speed. However, this difference between the experimental and control groups was not statistically significant (15). The results of the present study with a longer training period than the previous study (15) suggest that the specific improvements due to the inclusion of rhythmic visual stimulus as a mode to synchronize the stepping gait were related to temporal parameters more than spatial parameters. These specific adaptations positively impacted the functional mobility observed here as gait speed. In addition to the observed biomechanical improvements, the bilateral coordination was probably enhanced due to higher self-selected walking speed done by the synchronized group. Previous evidence has demonstrated that the bilateral accuracy (temporal symmetry between right-left stepping) and bilateral consistency (variability of the temporal symmetry) are increased at a faster speed than self-selected in patients with MS (22). Furthermore, the improvements found in the temporal variables of gait are particularly interesting as they impact cardinal points of movement disorders in MS (23). Indeed, impairments in stride frequency and stance time are extremely related to gait speed and even related to disease staging (EDSS). Although reductions in temporal gait parameters due to MS could be part of adopting a more cautious gait strategy, these impairments result in a higher risk of falls (24).

Temporal-specific adaptations in response to an intervention based on temporal gait control raise the question of whether training with visual-spatial stimuli (e.g., visual cues) could bring superior adaptations in spatial variables such as stride length. Future studies could test these possible specific adaptations on mobility gains. This study provides pertinent information for the organization and application of interventions for patients with MS. Individuals with high levels of bilateral asymmetry and low bilateral coordination may likely have important benefits with the use of the rhythmic visual synchronization used in the present study.

Abnormalities in postural control during gait in patients with MS are related to slow movement toward stability limits and delayed responses to perturbations and displacements during gait (25). The improved responses in the present study may be related to the mitigation of this slowness of movement during gait.

The improved locomotor rehabilitation index indicates that subjects, after the intervention, perform their routine gait activities with greater economy and improved pendulum mechanics (19,26). The locomotor rehabilitation index, which expresses the relationship between the

Conceptually, self-selected walking speed (SSWS) is defined as the speed at which people choose to walk in their daily lives because it is the most comfortable speed, and optimal walking speed (OWS) is defined as the speed at which the contribution of mechanical parameters is optimized and the metabolic energy expenditure is minimized, is a complementary analysis of spatiotemporal parameters in gait assessment. According to this index, walking is functional and healthy when the SSWS and OWS are coincident. Therefore, the locomotor rehabilitation index can be considered an important performance marker with clinical relevance (19). This improved metabolic economy may result in an increase in physical activity performed as well as an increase in the quality of movements other than walking (e.g., load lifting, instrument handling) due to the lower degree of fatigue (27). Given that gait is the most commonly reported exercise among adults, walking at faster than usual paces may signalize additional gains in primary health-related outcomes in the follow-up (27).

Patients with MS adopt a conservative strategy to maintain stability by increasing the duration of the walking cycle (4). Besides, gait disorder in patients with MS indicates motor control disorder in these patients, which is inversely related to gait speed (4). Hence, as shown in this study, it seems that improvements in spatiotemporal parameters, especially temporal parameters of gait, following sensory-motor synchronization training with a rhythmic visual stimulus may indicate increased motor control and improve the stability of gait in patients with MS. As previously mentioned, treatment strategies based on providing additional sensory cueing to support movement performance can be a good way to overcome motor control and coordination disorders in patients with MS (8). Sensorimotor synchronization activates several motor areas of the brain, including the prefrontal cortex, supplementary motor area, premotor cortex, right lower parietal lobe, posterior superior temporal gyrus, anterior insula, cerebellum, and putamen (28). Activation of motor areas of the brain improves muscle activation and leads to better motor control (29).

The EDSS was used to homogenize the study groups, allowing them to assess gait disorders in these patients. On the other hand, the walking training route in this study was 6 meters; that is, the participants in the study returned to the beginning of the route after a distance of 6 meters and walked along this route during the entire training period (16). However, it seems that in this protocol, the participants restarted the synchronization process in each turn instead of walking slowly and evenly in a straight line for a long time. Similarly, in daily life, people rarely walk in a straight line and often stop, change direction, and start again, and these protocols are more like people’s normal lives.

It seems that no studies have been performed to evaluate the effect of synchronizing gait with a rhythmic visual stimulus on brain plasticity in patients with MS (30). The effect of synchronization with the rhythmic visual stimulus on the improvement spatiotemporal parameters of gait in these patients may be the result of the effect of this type of rehabilitation intervention on the reorganization or restoration of the altered brain patterns. Also, these changes may be the consequence of activity-dependent myelination. Future studies are suggested for clinicians to investigate this issue. Also, clinicians can recommend the above protocol as an effective, cheap and usable rehabilitation method as a complementary treatment along with drug treatment to patients, medical and rehabilitation centers.

Here, we investigated spatiotemporal parameters, bilateral symmetry, and locomotor rehabilitation index recovery after six weeks of locomotor training, comparing these findings between two groups of 10 patients each performed the gait training with vs. without rhythmic visual stimulus. We demonstrated that rhythmic visual stimulus improved functional mobility and locomotor rehabilitation index in patients with MS. These improvements were possible because of the rhythmic visual stimulus employed in the present study, which constitutes an effective method to qualify gait training methods. In addition, we showed that the ability to walk was additionally improved, specifically due to temporal adjustments of gait provided by the rhythmic visual stimulation. Here, we showed that patients living with multiple sclerosis sparing improved about ≈74% of their initial functional mobility adding rhythmic visual stimulation—a proportion much higher compared to just gait.

Research limitations This study also had limitations, including that there was no control group with no exercise. It was not possible to control the eating patterns, daily activity patterns, and rest of the participants. Also, it was not possible to match the social, economic, cultural, and health status, mental health, and motivation levels of the participants.

Ethical Considerations

All procedures performed in this study were in accordance with ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Compliance with ethical guidelines Institutional

Review Board in Mazandaran (IR.UMZ.REC.1399.012) approved Informed Consent The study. Participants were informed about the purpose and benefits of the research then they signed the written content. In addition, they were allowed to leave the study whenever they wanted, and if desired, the research results would be available to them.

Authors contributions

Data collection and writing the original draft: M M, and M S. Review, editing, and supervision: M M, M S, B M O, L C, L A P T.

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Conflict of Interest

No conflict of interest has been declared.

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