

Effects of Vibration Training on Cognition and Quality of Life in Individuals With Multiple Sclerosis

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ABSTRACT

BACKGROUND: Multiple sclerosis (MS) detrimentally affects cognition and quality of life (QOL). Interventions that can improve cognitive deficit and QOL in individuals with MS are desired. This pilot study investigated the possible effects of vibration training on improving cognition and QOL in individuals with MS.

METHODS: Eighteen adults with MS were randomized into 2 groups: training and control. The training group underwent 6 weeks of vibration training, and the control group maintained their normal lifestyle throughout the study. In both groups, before and after the training course, the disability status was evaluated by the Patient Determined Disease Steps scale and the Multiple Sclerosis Functional Composite (MSFC), cognitive function was assessed by the Behavior Rating Inventory of Executive Function-Adults (BRIEF-A) and the Buschke Selective Reminding Test (SRT), and QOL was gauged by the 36-item Short Form Health Survey (SF-36).

RESULTS: The training was well accepted by the participants, and no major adverse event was reported. All participants finished the entire protocol. Compared with the control group, the training group showed greater improvements in MSFC score, Metacognition Index score of the BRIEF, SRT score, and physical domain score of the SF-36.

CONCLUSIONS: These results suggest that vibration training could be an effective alternative training paradigm to enhance cognition and QOL in individuals with MS, and they provide an encouraging base to conduct a large-scale clinical trial.

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Multiple sclerosis (MS) is one of the leading causes of neurologic disability among young adults in the Western world. It imposes serious adverse effects on individuals, such as limited mobility, impaired physical and cognitive functions, increased risk of falls, and reduced quality of life (QOL).¹ Cognitive impairments are a major challenge in individuals with MS.² Based on 33 studies, a recent meta-analysis concluded that few effective interventions are available to restore or preserve cognitive function for individuals with MS.³ Thus, it is imperative to develop interventions for addressing the impaired physical and cognitive functions of individuals with MS.

Whole-body vibration training, or vibration training, has been increasingly used as a novel clinical prevention and rehabilitation tool in individuals with movement disorders.⁴ During vibration training, trainees stand or sit on a platform vibrating at specific frequencies and amplitudes. The intense mechanical oscillation from the platform stimulates various sensorimotor units of the human body and leads to improvements in sensorimotor functions.^{5,6} Mounting evidence supports that a short-term (6- to 10-week) vibration training course improves physical functions, such as balance, mobility, strength, and power, in older adults.^{7,8} Previous studies also reported positive effects of vibration training on cognitive functions in healthy populations, such as adults⁹ and children,¹⁰ and in individuals with pathologic conditions, such as attention-deficit/hyperactivity disorder⁹ and dementia.¹¹ Vibration training is likely an alternative approach to improving physical and cognitive functions and QOL in individuals with MS.

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Although previous studies have reported vibration-induced physical function improvements in individuals with MS,¹² no study has examined the possible effects of vibration training on changing cognition and QOL in individuals with MS. It remains unknown whether vibration training can improve cognitive functions and QOL in this population. Such a lack of understanding could be an obstacle for the deployment of vibration training to individuals with MS. Therefore, it is of interest to explore the potential impact of vibration training on cognitive function and QOL in individuals with MS.

This study's overall objective was to examine the effect of a 6-week progressive vibration training course on cognition and QOL in individuals with MS, based on a randomized controlled design. Previous studies that adopted an 8-week training program reported health benefits in individuals with MS.^{13,14} The vibration amplitude and bout duration were fixed at 2 mm and 1 minute, respectively, in previous studies. In the present study, the vibration amplitude and bout duration gradually increased from 2 mm and 1 minute, respectively. Given that the training dosage is closely associated with the amplitude and the bout duration, and that the training dosage is strongly related to the training effect,¹⁵ we hypothesized that the 6-week vibration training would improve cognition and QOL in individuals with MS. The findings from this study could furnish preliminary data to design large-scale studies to further test the effectiveness of vibration training in altering cognition and QOL in individuals with MS.

METHODS

Design Overview

This study used a 2-arm randomized controlled design (FIGURE S1, which is published in the online version of this article at ijmsc.org). The training group underwent a 6-week vibration training. The control group did not receive training but maintained their regular lifestyle throughout the study. Before and after the training course, both groups were evaluated for their disability status, cognitive function, QOL, and physical activity level.

Participants

Thirty adults (18 years or older) were screened for participation in this study (Figure S1). Enrollment into the study required a neurologist-confirmed diagnosis of MS, a score of 6 or less on the Patient Determined Disease Steps (PDDS) scale, the ability to stand and walk independently with or without an assistive device, and no clinically significant relapse in the past 8 weeks. Participants had to be free of other major general medical disorders, recent surgery, or pregnancy. Those who had any previous experience with vibration training or had participated in whole-body exercise, balance training, or resistance exercise in the past 6 months

were excluded. All participants gave written informed consent approved by the institutional review board of Georgia State University. The qualified participants were evenly randomized into 2 groups: training and control.

Evaluation of Outcome Measures

The following 3 categories of outcome measurements and the physical activity level were assessed in a research laboratory by the same investigators (F.Y. and P.-S.W.), who were blinded to each participant's group assignment.

Disability Status

Disability level was assessed subjectively using the PDDS scale score and objectively using the Multiple Sclerosis Functional Composite (MSFC) score and fast gait speed. For PDDS scale assessment, participants read the definitions and rated their perceived disability status from 0 (normal) to 8 (bedridden).¹⁶ A lower PDDS scale score indicates less disability.

The MSFC assessment consists of 3 components: lower extremity motor function, evaluated by the Timed-25-Foot Walk test (T25FW); upper extremity motor function, assessed by the 9-Hole Peg Test; and processing speed, working memory, and calculation ability, measured by the Paced Auditory Serial Addition Test-3" (PASAT-3"). The scores from these 3 assessments were combined to form a composite MSFC score.¹⁷ The higher the MSFC score, the lower the disability level.

Based on participant performance during the T25FW, fast gait speed was calculated. Specifically, gait speed was calculated by dividing the 25-ft (or 7.62-m) distance by the time (in seconds) required to cover the distance.

Cognitive Function

Besides the PASAT-3" for assessing processing speed and working memory, 2 other instruments were used to evaluate each participant's cognition: the Buschke Selective Reminding Test (SRT) and the Behavior Rating Inventory of Executive Function-Adult (BRIEF-A).

The SRT is a verbal learning test that consists of 12 memorization trials, which has been used in individuals with MS.¹⁸ In the first trial, the participants listened to a list of 12 unrelated words, then repeated as many words as they could recall. On each subsequent trial, participants were reminded selectively of the words that were not recalled on the preceding trial. This process was repeated until the participant could recall all the words or reached 12 trials. Fifteen minutes later, participants were asked to recall as many words as possible again. The number of the recollected words on this delayed recall trial was chosen to assess the ability of verbal learning and memory. The higher the number, the stronger the verbal learning ability.

The BRIEF-A is a standardized rating scale to assess the everyday behaviors associated with specific domains

TABLE 1. Demographic and Disease Information for Both Groups of Participants With MS

Characteristic	Training group (n = 9)	Control group (n = 9)	P value
Age, y	53.9 ± 4.9	48.8 ± 11.7	.123
Female sex	8	9	.50 ^a
Height, cm	165.5 ± 7.9	165.6 ± 3.9	.488
Mass, kg	76.4 ± 12.0	73.3 ± 17.4	.336
PDDS scale score	3.1 ± 2.1	4.1 ± 1.5	.104
Duration of MS, y	14.1 ± 7.3	16.7 ± 10.1	.269
MS type, RR/SP	8/1	9/0	.50 ^a

MS, multiple sclerosis; PDDS, Patient Determined Disease Steps; RR, relapsing-remitting; SP, secondary progressive.

Note: Values are presented as mean ± SD or number.

^aFisher exact test was used.

of the executive functions in adults.¹⁹ It comprises 3 main index scores: Global Executive Composite (GEC) and its 2 components, the Behavioral Regulation Index (BRI) and the Metacognition Index (MI). The BRI assesses behaviors that require abilities of inhibition, emotional control, and self-monitoring, and the MI assesses behaviors that entail initiation, working memory, planning, and organizing. Lower scores indicate a better level of executive function.

Quality of Life

The 36-item Short Form Health Survey (SF-36) was used to assess participant QOL.²⁰ This instrument taps health concepts that are relevant to individuals with MS from their own perspective. It generates 8 subscales, based on which 2 summary scores are created: the Physical Component Summary (PCS) and the Mental Component Summary (MCS). In addition, the physical activity level of each participant was monitored by using the Godin Leisure-Time Exercise Questionnaire.²¹

Vibration Training

A side-alternating vibration platform (Galileo; Novotec Medical GmbH) was used (FIGURE S2A). While holding the handlebar for balance, participants stood barefoot over clearly marked positions on the platform during training. Participants were required to maintain stance on the platform with knees at 20° flexion and the trunk held upright. Each training session consisted of 5 bouts of vibration exposure, each followed by a 1-minute rest (FIGURE S2B). The training session was repeated 3 times weekly over 6 weeks for a total of 18 sessions. The vibration frequency was 20 Hz throughout the training course. The peak-to-peak amplitude and the bout duration, respectively, were gradually increased over the training course: 2 mm and 1 minute for the first 2 weeks, 4 mm and 1 minute for the following 2 weeks, and 4 mm and 1.5 minutes for the last 2 weeks. Participants were closely monitored and asked to report any adverse effects or reactions. Participants in the control group

received no vibration exposure but were told to maintain their usual lifestyle.

Statistical Analysis

As mentioned, 3 categories of outcome measurements were collected: disability level (PDDS scale, MSFC, and gait speed), cognitive function (PASAT-3", SRT, and BRIEF-A, including the BRI, MI, and GEC), and QOL (SF-36, consisting of the PCS and the MCS). In addition, the physical activity level was assessed. Each outcome measurement category was analyzed by using generalized estimating equation (GEE) analysis. Each outcome variable (Y) was formulated by the following model: $Y = \beta_0 + \beta_1 G + \beta_2 S + \beta_3 G \cdot S$, where G indicates the group assignment (training vs control), S represents the assessment session (pretraining vs posttraining), and β_{0-3} denote the coefficients. Group and session were 2 main factors in the model. If a significant group \times session interaction was observed (ie, the P value for the coefficient β_3 was significant), post hoc tests followed to interpret the interaction. Paired t tests were used to compare the outcome measures between sessions within the group, and independent t tests were executed to compare the outcome measures between groups within the session. All statistical analyses were performed using SPSS Statistics for Windows, version 24.0 (IBM), with a significance level of $P < .05$.

RESULTS

We screened 30 potential participants, and 27 (90%) passed the screening. Eventually, 18 participants (60%) were enrolled and evenly randomized into either the training or control group (FIGURE S1). The demographic and disease characteristics were comparable between groups (TABLE 1). Participants in the training group underwent the 18 training sessions and all participants attended the 2 assessments for a retention rate of 100%.

No major discomfort or adverse reactions to vibration were reported during the study. Itching of legs, which is typical for vibration intervention, was reported

TABLE 2. Between-Group Comparisons of Outcome Measures During Pretraining and Posttraining Sessions

Outcome measure (total possible score)	Training group		Control group		P values ^a		
	Pretraining	Posttraining	Pretraining	Posttraining	Group	Session	Group × session
PDDS scale score (/8) ↓	3.06 ± 2.08	2.33 ± 2.29	4.17 ± 1.46	4.33 ± 1.94	.062	.287	.088
MSFC score							
Overall ↑	0.25 ± 1.82	1.10 ± 2.03	-0.25 ± 1.92	-0.25 ± 1.72	.600	.007	.006
Speed, m/s ↑	0.89 ± 0.35	1.08 ± 0.35	0.93 ± 0.44	0.90 ± 0.45	.689	.025	.003
PASAT-3" (/64) ↑	33.2 ± 10.6	37.8 ± 10.8	26.9 ± 13.5	27.4 ± 12.0	.102	.035	.100
NHPT, s ↓ ^b	33.1 ± 12.0	31.4 ± 14.1	37.5 ± 19.0	36.3 ± 18.0	.655	.422	.766
BRIEF-A score							
GEC (/210) ↓	113.3 ± 25.6	104.2 ± 23.6	131.2 ± 36.2	133.2 ± 34.8	.073	.330	.128
BRI (/90) ↓	45.3 ± 10.7	41.9 ± 9.9	52.8 ± 16.4	52.7 ± 15.3	.109	.309	.341
MI (/120) ↓	68.8 ± 15.5	62.3 ± 14.8	78.4 ± 20.4	80.6 ± 20.6	.061	.412	.049
SRT score (/12) ↑	5.89 ± 1.90	8.22 ± 2.64	7.56 ± 3.84	7.44 ± 3.05	.712	.030	.017
SF-36 score							
PCS (/100) ↑	58.6 ± 15.7	69.0 ± 16.1	41.5 ± 16.1	34.3 ± 11.5	<.001	.644	.013
MCS (/100) ↑	74.9 ± 19.6	76.2 ± 21.7	48.9 ± 22.8	48.2 ± 17.1	<.001	.965	.867
Physical activity level ↑ ^c	20.5 ± 18.2	22.8 ± 19.5	19.7 ± 20.7	24.5 ± 22.1	.961	.089	.553

BRI, Behavioral Regulation Index; BRIEF-A, Behavior Rating Inventory of Executive Function-Adult; GEC, Global Executive Composite; GEE, generalized estimating equation; MCS, Mental Component Summary; MI, Metacognition Index; MSFC, Multiple Sclerosis Functional Composite; NHPT, 9-Hole Peg Test; PASAT-3", Paced Auditory Serial Addition Test-3"; PCS, Physical Component Summary; PDDS, Patient Determined Disease Steps; SF-36, 36-item Short Form Health Survey; SRT, Selective Reminding Test; ↑ or ↓, desired direction of improvement for the respective variable.

Note: Values are presented as mean ± SD. All outcome measurements were analyzed using the GEE approach.

^aP values are for coefficients (β_{1-3}) in GEE models.

^bTime of NHPT was average time of both dominant and nondominant sides.

^cPhysical activity level is monitored by the Godin Leisure-Time Exercise Questionnaire.

by 1 participant. This effect was mild and diminished after approximately 5 training sessions. The training protocol was well accepted by all the participants in the training group, and they did not consider vibration training difficult. The physical activity level was comparable between groups ($P = .961$) and sessions ($P = .089$), and the group × session interaction effect was not significant ($P = .553$) (TABLE 2).

Disability Status

The GEE analysis did not reveal a significant difference in PDDS scale scores for group ($P = .062$), session ($P = .287$), and group × session interaction ($P = .088$) (Table 2). The MSFC score demonstrated no main effect for group ($P = .600$), a significant main effect for session ($P = .007$), and a significant group × session interaction ($P = .006$) (Table 2). Post hoc analyses showed that the training group ($P = .006$), but not the control group, exhibited a significant increase in MSFC score from the pretraining to posttraining session. A similar trend was observed with the gait speed. The gait speed showed no significant main effect for group ($P = .689$), a significant main effect for session ($P = .025$), and an interaction effect for group × session ($P = .003$). Follow-up analyses found that the training group walked faster during the posttraining than the pretraining assessment ($P = .003$). However, the control group showed no improvement

in gait speed between assessments. The PASAT-3" score displayed no main effect for group ($P = .102$) or interaction effect for group × session ($P = .100$) and a significant main effect for session ($P = .035$). The 9-Hole Peg Test score did not show any significant main or interaction effects.

Executive Function in Daily Living

The GEE model did not indicate any significant effects of the BRI for group, session, or their interaction (Table 2). Similar results were found with the GEC score (Table 2). The MI score exhibited a nonsignificant main effect for group ($P = .061$) and session ($P = .412$). In contrast, the group × session interaction was significant ($P = .049$). Post hoc analysis indicated that at posttraining assessment, the training group showed a significantly lower MI value than the control group ($P = .021$), and the training group, not the controls, demonstrated a significant reduction in MI score from the pretraining to the posttraining session ($P = .045$).

Verbal Learning and Memory

We observed a nonsignificant main effect for group ($P = .712$) but a significant main effect for session ($P = .030$) and group × session interaction ($P = .017$) in the SRT (TABLE 2). The significant interaction effect was caused by the substantial improvement in the SRT

score in the training group ($P < .001$), but not the control group ($P = .456$), from pretraining to posttraining.

Quality of Life

The PCS of the SF-36 test showed significant effects for the main factor of group ($P < .001$) and group \times session interaction ($P = .013$) (Table 2). Post hoc comparison indicated that the training group, but not the control group, experienced a significant training-induced improvement in the PCS score ($P = .050$). The training group displayed a higher PCS value than the control group at the pretraining test ($P = .018$). The between-group difference in the PCS value further increased at the posttraining session ($P < .001$). The MCS of the SF-36 showed a significant main effect for group ($P < .001$) but no significant effects for the main factor of session ($P = .965$) or the group \times session interaction ($P = .867$) (TABLE 2). At both assessments, the training group exhibited higher MCS values than did the control group ($P < .001$ for pretraining and $P = .004$ for posttraining).

DISCUSSION

These results indicate that the 6-week progressive vibration program is safe, feasible, and tolerable to individuals with MS. This training program could be effective in improving cognitive function, QOL, and disability status in individuals with MS. The results also demonstrate our ability to recruit and retain individuals with MS for this study successfully. The attrition rate was 0% across the 6 weeks, and no major adverse events were reported during the training period in the present study.

The hypothesis that the 6-week vibration training course induced improvements in cognition and QOL in individuals with MS was supported by the results. First, the results indicate that the 6-week vibration training intervention, relative to the controls, significantly increases the MSFC score in individuals with MS. As previously reported, MSFC¹⁷ score is closely correlated to the Expanded Disability Status Scale score, a clinically accepted assessment of the disability status of individuals with MS. Thus, the present findings support the notion that vibration improves the disability status in individuals with MS. The results reinforce the conclusion from a previous study, which was based on a single-group design.¹³

It has been suggested that vibration training could be an effective training modality, producing effects similar to resistance (ie, strengthening muscles) and aerobic exercise (ie, enhancing cardiorespiratory fitness).²² Increasing evidence confirms that physical activity delays disease progression in individuals with MS.²³ Previous studies documented that both resistance and aerobic training have the potential to mitigate disability level in individuals with MS.²⁴ Because vibration training is a physical exercise modality, it could alter the level of disability in individuals with MS. The present

findings augment our understanding of the effect of exercise-based training, in particular vibration training, on improving the disability level in individuals with MS.

The T25FW test score is primarily based on ambulatory capability. Gait speed is closely related to lower-limb muscle strength, body balance, and the plantar sensation level in individuals with MS.²⁵ Previous studies demonstrated that vibration training improves these factors.¹² Therefore, the increased gait speed could be attributed to the vibration-related improvements in these factors. The positive impact of vibration training on gait speed is practically important for individuals with MS, because the preservation of mobility is critical for them to maintain independence, work, and social participation.²⁶

Second, the present results indicate that the 6-week training course improves cognitive function in individuals with MS. Specifically, the training group, but not the control group, demonstrated a significant improvement in the PASAT-3" score (Table 2). The PASAT-3" was established to assess auditory information processing flexibility and speed, sustained and divided attention, and calculation ability. The significant increase in PASAT-3" score from pretraining to posttraining sessions suggests an improvement in these cognitive domains in the training group.

Although all 3 components of the BRIEF-A test showed a trend that the scores were improved more in the training group than in the control group, only the MI component showed a significant group \times session interaction (TABLE 2). The present results signify that vibration training could enhance executive function, particularly the MI component, in individuals with MS. Although previous studies applying vibration to adults in a healthy condition or with attention-deficit/hyperactivity disorder found an acute effect on inhibitory control,⁹ we did not find significant changes in the BRI, which measures components such as inhibition and emotional control. The present findings could suggest that vibration training is more beneficial in organization and working memory components of processing speed, as measured by the MI of the BRIEF-A and the PASAT-3".

The SRT score displayed a significant group \times session interaction (Table 2). From the pretraining to posttraining tests, participants in the training group showed a significant increase in the number of words recalled during the delayed recall trial. However, the control group demonstrated a slight reduction in the number of recalled words. This result suggested that individuals with MS may benefit from the 6-week vibration training program to improve their verbal learning and memory capacity.

Third, health-related QOL, particularly the PCS, showed a significant group \times session interaction (Table 2). The PCS score was significantly improved for the

training group from the pretraining to posttraining tests. The same measurement slightly declined between the tests for the control group. This finding indicates that the 6-week vibration training has the potential to enhance the physical domain of QOL for individuals with MS.

Similar to gait speed, the improvement in the disability status and the physical component of the QOL in individuals with MS after the vibration training course can be linked to increased lower-limb strength, improved body balance, and enhanced sensation. However, the mechanism of vibration training improving cognitive functions remains to be determined. One possibility is that long-term vibration training may lead to the alteration of the brain structure and function. Traditional exercise training has been proved to improve cognitive function in older adults²⁷ and individuals with MS,²³ perhaps through alteration in the brain structure and function. Vibration training as a type of exercise may have the potential to modify brain structure. This notion could be supported by a previous study that reported enhanced brain activity during vibration training in mice and humans.²⁸ Nevertheless, more studies are needed to explore the underlying mechanisms of vibration training that improve cognition in individuals with MS.

Currently, no agreement exists about choosing vibration parameters. The vibration frequency of 20 Hz, initial vibration amplitude of 2 mm, and initial bout duration of 1 minute were selected based on previous studies, which adopted similar parameters and reported positive results in individuals with MS.^{13,14} The tilting movement of the side-alternating vibration induces rotation at the hip and lumbosacral joints.²⁹ This extra degree of freedom lowers the body's mechanical impedance, prompts the energy transfer to the human body, and facilitates neuromuscular adaptations.³⁰ Thus, the side-alternating vibration platform was used in the present study. The progressive training protocol has been implemented in previous studies concerning individuals with MS and documented promising results, as it complies with the progressive overload training principle.¹² However, the present vibration training protocol was just 1 of the countless sets of possible protocols. Different protocols could deliver various vibration dosages, and thus the training effects.¹⁵ More research is needed to identify the optimal vibration parameters that can maximize the training effect in individuals with MS.

The present study has limitations. First, the sample size was small, the disease type was mainly relapsing-remitting MS, and the disability level was limited between mild and moderate. The lack of the norms of the outcome measurements further prevents us from testing the representativeness of the sample size, which affects the generalizability of the findings to

PRACTICE POINTS

- » Vibration training can be well accepted and tolerated by individuals with MS.
- » Vibration training could be an effective means to improve physical and cognitive functions and quality of life in individuals with MS.

the overall MS population, but sets the basis for future studies in this area. Second, the control group did not receive any particular training pertaining to this study but maintained their usual lifestyle. This could have created biases in the results, because participants in the training group had more opportunities to communicate with investigators and travel to the laboratory than the control group. Lastly, some important clinical information, such as spasticity, fatigue, and vision, and the use of medications were not collected from the participants. The footwear was not standardized for the walking test. These factors could have introduced biases into the results. All these issues should be further examined by involving other technologies, such as functional magnetic resonance imaging of the brain, to explore such mechanisms based on larger sample sizes.

Despite the limitations, this study—as the first of its kind, to our knowledge—suggests a 6-week vibration training course could improve cognitive functions and QOL among individuals with MS. Approximately 40% to 60%² and more than 90%²⁶ of individuals with MS experience cognitive impairment and restricted mobility, respectively. The goal of rehabilitation in individuals with MS is to decrease the impact of MS on personal activity, function, and social participation to allow individuals with MS the highest possible independence and QOL. With the high adherence rate, vibration training could be a nonpharmacologic and inexpensive alternative or adjunctive therapy in MS rehabilitation. Having a proven program to help manage MS-related disability and cognitive impairment is essential to optimize health-related QOL for individuals with MS. □

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