Effects of Sensory Interventions on Fatigue in People With Multiple Sclerosis: A Systematic Review

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Background: Fatigue is 1 of the most common and annoying symptoms in patients with multiple sclerosis (MS). The purpose of this study was to investigate the effect of sensory interventions on fatigue in people with MS based on a systematic review of sensory evidence.

Methods: The Google Scholar, PubMed, Scopus, and Cochrane Library databases were searched from January 1990 to July 2020. Studies with nonpharmacologic sensory interventions as a main or secondary intervention according to the assessment of fatigue as the primary or secondary therapy outcome in patients with MS were included.

Results: Nine articles were reviewed by examining the inclusion and exclusion criteria. Four types of interventions were related to exercises, including sensory integration exercises, vestibular rehabilitation, Frenkel exercises, and exercises with or without vibration; and 2 types were performed using robots and 1 type using vibration only. Vestibular rehabilitation therapies, exercise-based sensory integration interventions, and the use of vibration have shown significant effects in relieving fatigue in patients with MS.

Conclusions: The evidence in this study is insufficient to show a dramatic effect of sensory integration therapy in various forms. However, despite the studies, sensory integration therapy can be considered a potential treatment for fatigue in patients with MS. Further studies with stronger methods are needed to make this treatment a reality. *Int J MS Care. 2022;24:29-34. doi:10.7224/1537-2073.2020-123*

Multiple sclerosis (MS) is a lesser-known degenerative disease that occurs in early adulthood.[1] A wide range of symptoms, including visual impairment, muscle weakness, sensory impairment, and pain, are reported in these individuals.[2] Fatigue is 1 of the most common and annoying symptoms of this disease, which has been reported in 50% to 92% of people with MS.[3,4] Fatigue is defined as the lack of mental or physical energy that is perceived by sufferers or caregivers to affect a person's normal and desirable activities. Patients with MS can distinguish between physical fatigue and other physical symptoms of the disease, such as weakness in certain muscle groups, neurologic defects in the production of insufficient muscle strength, and physical tiredness, as well as between mental fatigue and emotional and mental symptoms of depression such as decreased motivation, decreased mood, inability to complete tasks, and lack of concentration.[5] The possibility of fatigue in people with MS increases with recurrence of the disease, increased disability, lack of mobility, and the experience of heat and decreases with cold.[5] All kinds of activities in a person's daily life, including finding and keeping a job, home management, child care, and leisure, can be affected by fatigue.[6] Damage to sensory and motor patterns and to functional communication of nerve cells has been known

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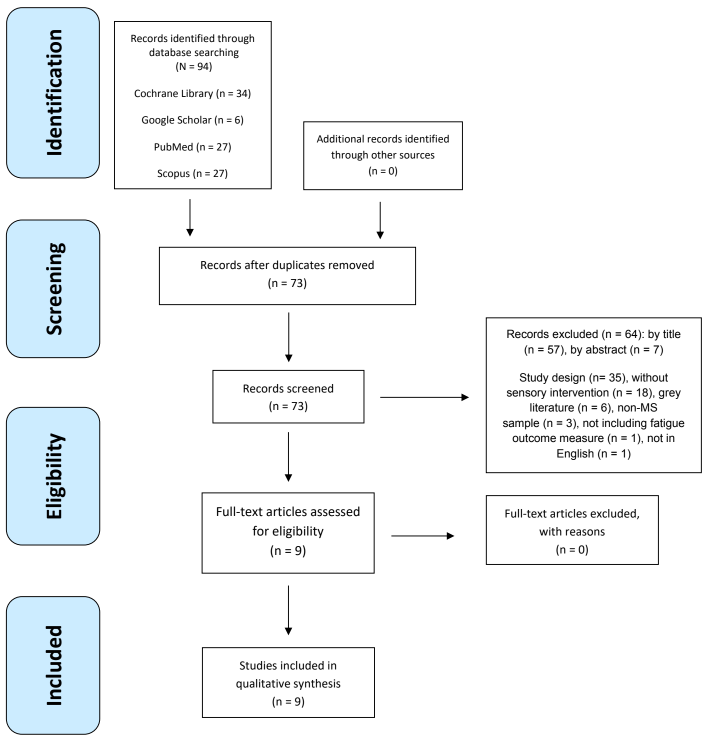
***Figure 1.* PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Flow Diagram[26]**



as the central cause of MS-related fatigue.[7] In topography by electroencephalopathy, it has been shown that there is a decrease in the amount of excitability in the primary sensory area and an increase in the amount of excitability in the primary motor area.[8]

Therefore, it seems that by affecting these areas, sensory interventions such as transcranial direct current stimulation can be effective in reducing fatigue in patients with MS.[9] The vestibular rehabilitation protocol, which aims to increase balance in people with MS, has also had a significant effect on reducing fatigue.[10] Therefore, to investigate the effect of sensory interventions on fatigue in people with MS, this study aimed to identify and review studies that use sensory approaches to reduce fatigue in people with MS.

Methods

The study was conducted based on PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.

Identification

To identify studies related to the effect of sensory interventions on fatigue in people with MS, the Google Scholar, PubMed, Scopus, and Cochrane Library databases were searched for English-language articles published between January 1990 and July 2020 using the keywords *multiple sclerosis, MS, fatigue, touch, proprioceptive*, and *vestibular*. Articles both with and without open access were searched.

Inclusion and Exclusion Criteria

Two experts (M.M. and M.S.) independently examined the studies in terms of compliance of the title or summary with the inclusion criteria. The inclusion criteria for this review are studies with sensory interventions as a main or secondary intervention in people with MS, considering the effect on fatigue as a main or secondary outcome. Only English-language studies are included in this review.

Data Extraction

Data extraction from studies was performed using a standardized form of data extraction based on CONSORT (Consolidated Standards of Reporting Trials).[11]

Quality Assessment

The quality of evidence of the studies included in this review was evaluated by the Downs and Black checklist.[12,13] The checklist is a 32-point scale that was developed by Downs and Black[12] to assess the methodological quality of randomized controlled trials and nonrandomized studies. It consists of 27 items distributed across 5 subscales: (1) reporting (10 items); (2) external validity (3 items); (3) bias (7 items); (4) confounding (6 items); and (5) power (1 item). This checklist provides a profile of the methodological strengths and weaknesses of studies. Each item scores 0 or 1, except for item 5 (in the reporting subscale), which scores 0 to 2, and item 27 (in the power subscale), which scores 0 to 5. Item 27 of the checklist was modified based on the presence (score 1) or absence (score 0) of sample size calculation, resulting in a total possible score of 28. The quality of the studies was classified into 4 levels based on the following score ranges: excellent (26-28), good (20-25), fair (15-19), and poor (≤14). This modification was done in 3 systematic review studies related to MS.[14-16] Studies were evaluated independently by 2 of us (M.M. and G.J.).

Results

Of the 94 studies obtained from the search, 21 were omitted due to duplication in the first stage. In the next step, 57 studies were omitted based on the title and another 7 based on the study abstract. Nine studies were entered for full-text screening, and all nine[17-25] were submitted to a review of the entire text and had inclusion criteria and did not have exclusion criteria (**Figure 1**).

Quality and Design of the Studies

The quality of the studies based on the Downs and Black checklist is summarized in **Table S1**, which is published in the online version of this article at ijmsc.org.

Of the studies included in this systematic review, 8 are randomized controlled trials[17-23,25] and 1 is a pretest/posttest quasi-experimental study.[24] The treatment period in the studies ranged from 5 days to 12 weeks and consisted of 5 to 60 sessions. The duration of the sessions varied from 10 to 75 minutes. Only 3 articles were accompanied by follow-up: 4 weeks in 2 studies[18,25] and 8 weeks in the other study[22] (**Table S2**).

Sample Characteristics

The articles included in this study had variable sample sizes of 17 to 80 people. In total, these studies included 357 people: 223 who received a research-related intervention and 134 in the control group or on the waiting list. The dropout percentage also varied from 2.66% to 47.05%.

Outcome Measures

In the 9 studied articles, 3 fatigue-related assessments were used to measure the severity and extent of the effect of fatigue. The Fatigue Severity Scale (FSS) was used in 5 studies[18-20,22,23] and the Modified Fatigue Impact Scale (MFIS) in 4 studies,[21,23-25] 1 of which was also associated with the FSS.[23] The Fatigue Impact Scale (FIS) was also used in an independent study.[17]

Intervention Type

The types of interventions performed in the articles were divided into 3 categories: those related to exercises (n = 4),[17,18,20-25] those performed with the help of robots (n = 2),[18,23] and those performed only by vibration (n = 1).[19] Among the 4 types of interventions related to exercises, 6 studies examined sensory integration exercises,[18,20,21,23-25] 3 examined vestibular intervention,[17,22,25] and 1 assessed Frenkel exercise.[17] Also, 1 study investigated performing exercises with and without whole-body vibration.[24] Exercises related to these studies were in the intervention or control groups. Exercises in these studies were designed to integrate multiple sensory inputs while evoking a postural equilibrium response. Another study performed therapeutic exercises in 1 group on a vibrating platform and in another group without vibration. The exercises were the same in the intervention groups, and the difference was in being on or off the platform. In the study by Brichetto et al,[21] balance exercises were performed in various positions using a biofeedback plate, on the floor, and in front of a mirror. Gandolfi et al[20] used sensory integration exercises in 3 levels of open eyes, closed eyes, and with visual conflict (to create wrong inputs) and also on 2 levels of floor and foam mat. Both static and dynamic exercises were used in their study to further simulate daily life activities. Protocols of 3 vestibular rehabilitation studies[17,22,25] were reviewed. They all had 2 training sections: position and eye movements. Of the exercises performed, only 1 study in 1 of the intervention groups used Frenkel exercises.[17] These exercises were performed in 3 positions: lying down, sitting, and standing. In both robotics articles[18,23] the robot was used as a gait aid and taught how to gait correctly. In both studies, assisted devices such as a harness supported the body weight so that it could use these robots more safely. Alguacil Diego et al[19] used vibration only in semi-squat mode in which the patient was balanced by the handles of the Zeptoring vibrating platform (Scisen GmbH), and external support was used if necessary. No exercise was used in this intervention, and the total vibration and rest for each treatment session were recorded for 10 minutes.

Effectiveness of Interventions

Exercise-Based Interventions

Comparing 2 types of interventions based on walking robots with sensorimotor exercises, Saggini et al[23] found that the group based on FSS exercise therapy showed a decrease in fatigue, but this decrease was not significant ($P = .2058$). However, not only was there a decrease in fatigue on the MFIS in this treatment group, but this decrease was significant ($P = .0353$). In another study, Gandolfi et al[18] examined the effect of integration interventions using the FSS and showed that participants had a significant reduction in fatigue on the FSS ($P = .052$). In a study with 2 intervention groups, Uszynski et al[24] tested a series of movement exercises with the same dose and duration with the difference of standing or not standing on the vibrating platform to obtain the most effective method. In this study, it was shown that a significant reduction in fatigue is observed only in the group of exercises without standing on the platform ($P = .012$). Brichetto et al[21] compared the effect of sensory integration exercises in the 3 senses (visual sense, somatosensory and vestibular systems) and conventional rehabilitation exercises; no significant change in fatigue was achieved using the MFIS ($P > .05$). Gandolfi et al,[20] comparing conventional rehabilitation exercises and balance exercises of sensory integration using the FSS, showed a significant improvement in the intervention group ($P < .002$). In a study considering 2 types of exercises, Karami et al[17] found that both Frenkel exercises and vestibular rehabilitation can lead to a significant reduction in fatigue and FIS score, and there was a significant difference between the two intervention groups. Vestibular rehabilitation intervention with a significant difference compared with the Frenkel exercise intervention group led to a decrease in fatigue scores (P = .007). Examining these 2 interventions, they found that the difference between the 2 intervention groups was not in the cognitive subtest (P = .1) but in the physical (P = .001) and psychosocial (P = .01) subtests. Tramontano et al,[22] in their study by Mann-Whitney U test, showed that in the vestibular rehabilitation group there was a significant increase in FSS function, but this increase was not observed in the control group. Hebert et al[25] showed that there was a significant difference in recovery based on MFIS score in the intervention group with vestibular rehabilitation compared with the control group (P = .024) and the wait-list group (P = .005). However, no difference was observed between the control group and the wait-list group ($P > .99$).

Robot-Assisted Interventions

Among the 2 studies using gait robot interventions, Gandolfi et al[18] did not observe a significant change in the target group in the FSS assessment before and after the intervention. Also, in the study by Saggini et al,[23] a decrease in mean FSS scores was observed in the whole sample and in the intervention groups, but this change was not statistically significant. In this study, the change in MFIS scores in the whole sample was statistically significant, but there was no significant difference between the intervention groups with robots and the training group.

Vibrotherapy Intervention

Of the studies included in this article, only 1 used vibration as the sole intervention without performing any other exercises or interventions. The study by Alguacil Diego et al[19] did not show a significant change in the reduction of fatigue on the FSS for the intervention group.

Discussion

The aim of this study was to systematically review past studies that have examined the effectiveness of sensory integration–based interventions on fatigue in patients with MS. The results of these studies showed that sensory integration interventions based on exercise therapy techniques had significant positive effects on survival in patients with MS, which ultimately led to improved balance and quality of life in these patients.[17,18,20-22,25] Studies have also shown that approaches based on assisted therapies and robotics, as well as the use of vibration, which are used to improve sensory integration, reduce fatigue.[18,19,23] In the present study, 9 articles were reviewed on the effectiveness of sensory integration-based approaches on fatigue in patients with MS.[26] The evidence for the effect of fatigue is discussed in the following subsection.

Confirmatory Evidence of Effect on Fatigue

Exercise-Based Sensory Integration Interventions

Exercise therapy is a nonpharmacologic approach that affects the symptoms of MS.[27,28] Changes and improvements in fatigue based on exercise therapy have been shown in several studies.[29-31] There are different forms of exercise therapy, including exercises based on sensory integration and a range of vestibular exercises. These exercises improve the functions of the visual and cerebellar systems and balance by compensating for the defects of the vestibular system, and also reduce fatigue by improving balance.[32] In the present study, 7 studies examined the effect of exercise-based sensory integration interventions on fatigue recovery.[17,18,20-23,25] The results of these studies showed that vestibular exercises, exercise therapy interventions, and sensory integration have beneficial effects on reducing the severity and effects of fatigue in people with MS. Also, it can help to improve other symptoms of the disease. However, in a study by Brichetto et al,[21] no significant positive effect was found in patients' MFIS scores. Reduction of fatigue was demonstrated after various types of exercise therapy, including aerobics and treadmills. In all the studies, the mechanism of the effect of exercise on fatigue is still unknown, and different mechanisms have been proposed for this effect. Exercise is thought to have a protective role and helps regenerate nerves by modulating the growth of central nervous system neurons functionally and structurally.[33] On the other hand, it seems that this change may occur by affecting and correcting the symptoms of secondary fatigue in patients. Past studies have shown that exercise therapy can reduce fatigue by improving symptoms such as depression, anxiety, and sleep disorders.[34] However, the effect of factors such as duration of illness, Expanded Disability Status Scale (EDSS) score, or cognitive impairment on people with MS cannot be ignored, and the severity and weakness of these factors can change the outcome of the intervention. However, exercise therapy programs, even with a small number of participants in these groups, have shown improvement in mild fatigue.

Robot-Assisted Sensory Integration Interventions

Therapies using robotic devices have advanced a lot in the past 2 decades; they can use frequent, specific, and intense exercises with a wide range of active and active assistive exercises in patients.[35] There are different types of robotic aids that can be used in a variety of ways. In 2 studies by Gandolfi et al[18] and Sagini et al,[23] the effect of training and application of robotic devices on balance disorders and fatigue in patients with MS were examined. The results of these studies in the groups that used exercises based on robotic devices compared with exercise therapy did not show a statistically significant difference in the change and improvement of fatigue and helped only in items such as walking speed. Sagini et al[23] chose a double proprioceptive rehabilitation training that could have a clear positive spillover on a patient's impairment and sense of fatigue and gait and balance impairment; however, Sagini et al point to the role and logical relationship between EDSS and fatigue scores, but that is an aspect that has not yet been adequately investigated in the literature. On the other hand, Gandolfi et al,[18] with a larger sample, could stratify patients by EDSS score, which would allow us to better understand the robot-assisted approach. In most previous studies, robotic devices have been used to improve balance and gait.[36,37] In recent years, the use of this approach has shown positive effects on gait status and balance in chronic diseases such as stroke and Parkinson disease.[38,39] In all these studies, patients' balance was reported to be improved by motivating patients through the use of a new robotic approach and the application of deep sense stimuli. Because only 2 studies of robot-assisted sensory integration interventions were included in this review, it is not possible to reach any conclusions regarding their effectiveness in reducing the severity or impact of fatigue. In any case, it seems that more studies are needed in this area to evaluate the impact of the use of new technologies on the symptoms of MS, especially fatigue.

Vibration-Based Sensory Integration Interventions

The use of vibration and whole-body vibration technology is now proposed as a complementary technique in the treatment and rehabilitation of neurologic patients. In the present study, 2 of the 9 studies used these techniques to evaluate the effect of recovery and control of MS symptoms such as fatigue.[19,24] The results of these studies showed that the application of these techniques with or without exercise therapy has beneficial effects in the treatment of fatigue in patients with MS. Although in the study by Alguacil Diego et al[19] there was no significant difference between the 2 groups in the fatigue score, the authors reported a positive change and suggested factors such as the use of more reliable tools such as the MFIS to more accurately assess fatigue. Uszynski et al[24] were the first to examine the effect of whole-body vibration on fatigue, and they reported a greater reduction in fatigue than the group that used exercise therapy alone. The true mechanism of recovery through vibration was not known in neurologic patients and is still under investigation, but some have suggested that vibration improves muscle contraction by stimulating muscle spindles and increases muscle strength.[40,41] Numerous studies have shown the beneficial effects of vibration on muscle strength, pain, balance, and quality of life in patients with neurologic disease.[42-44] Uszynski et al[24] suggested using the vibration effects at a tolerable frequency dose in patients with MS. However, factors such as a patient's type of MS, EDSS score, and cognitive status that may affect the vibration therapy dose should be considered.

Limitations of the Evidence and Review

In this review study, we tried to show the significant effects of sensory integration approaches on reducing fatigue in people with MS, but the important point to note is that there is not sufficient evidence to determine which approach or technique is more effective. And items such as the primary outcome of fatigue in the studies, tools used to assess fatigue and their validity and reliability, and the number of participants in the intervention groups were the limitations of these studies.

Despite the existing limitations in the reviewed studies and the insufficient evidence, reviewing past studies and reviewing effective techniques in this area can provide a clear perspective on the rehabilitation and treatment of patients with MS. Future studies can complement this review and area of research. ☐

PRACTICE POINTS

- Use of a vestibular rehabilitation protocol has a positive effect on reducing fatigue and increasing performance in patients with MS with fatigue symptoms.
- Evidence from this study suggests that sensory integration exercises can have a positive effect on reducing fatigue. However, more studies are needed to determine the dose of exercise and to evaluate the dimensions of the effect.
- The use of vibrotherapy and robot-assisted gait has no significant effect on reducing fatigue in patients with MS.

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