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REVIEW

Technology-Based Rehabilitation in People with Multiple Sclerosis: A Narrative Review

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Abstract

With the overall progress of technology, developing technological approaches has become an integral part of modern society, and using advanced technology in rehabilitation has gained increasing importance. This narrative review discusses the role of technology-based rehabilitation in people with multiple sclerosis by presenting the evidence, advantages, and disadvantages of robotic rehabilitation, virtual reality training applications, telerehabilitation, and movement analysis systems. Technological systems used in rehabilitation are based on motor learning principles by providing task-specific and highly repetitive activities. Current scientific evidence emphasizes that significant gains in ambulation and upper extremity function can be achieved with technological approaches. The use of technological approaches in multiple sclerosis rehabilitation, despite being challenging in terms of cost and accessibility, is promising and has enormous potential for the future. However, although the evidence supports the use of technological systems in multiple sclerosis rehabilitation, well-designed studies with a larger sample size are needed.

Keywords: Multiple sclerosis, biomedical technology, robotics, virtual reality, telerehabilitation, remote sensing technology

Introduction

Multiple sclerosis (MS) is an autoimmune disease of the central nervous system characterized by inflammatory demyelination and axonal damage (1). MS is typically diagnosed between the ages of 20 and 30 years (1). Since MS is a disease that can affect many regions of the central nervous system, it causes many symptoms such as motor, sensory, visual, and autonomic disorders, impairs physical and cognitive functions in people with MS (pwMS), and negatively affects the quality of life and employment (1,2). Rehabilitation practices, including physiotherapy, are one of the most frequently used treatment options for managing symptoms in pwMS. Technological advancement has created new possibilities for neurorehabilitation. As with other populations with a chronic disease, it is necessary to identify or develop new assessment and treatment methods for pwMS (3). Along with technological developments, current neurorehabilitation practices focus on the principle of motor learning with high-intensity, repetitive and task-specific exercises (4).

With the development of technological systems and their application to rehabilitation settings, technology-based devices have become usable in daily evaluation and treatment programs. The advantages of technology-based rehabilitation in pwMS are listed as follows:

- The training content provided in technology-based rehabilitation is similar to the tasks individuals frequently encounter in their daily lives. Therefore, technology-based rehabilitation applications are task-specific (4).
- Visual or auditory feedback given in technology-based rehabilitation allows patients to receive information about their task performance (4).

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- They increase the duration, intensity, and frequency of the treatments and hence allow them to perform a considerable number of movements (4).

- They increase motivation and enhance active participation in and compliance with the treatment regimen (5).

- This narrative review aims to discuss the role of technology-based rehabilitation in pwMS by presenting the evidence, advantages, and disadvantages of robotic rehabilitation, virtual reality (VR) training applications, telerehabilitation, and movement analysis systems. Table 1 provides an overview of the advantages and disadvantages of technology-based rehabilitation methods compared to traditional rehabilitation, their areas of use, and clinical efficacy.

Effects of Robotic Systems in Technology-Based Rehabilitation for pwMS

In recent years, robotic technology has considerably developed with the availability of new scientific approaches and extensive electro-mechanical components (6). With these developments, "robotic technology" has become usable in the field of rehabilitation (6).

A key feature of robotic rehabilitation is that it induces neuroplastic changes and motor recovery by providing increased functional activity within the sensory-motor network (7). Robotic rehabilitation helps reduce the therapist's physical fatigue. In addition, setting the rehabilitation program according to the patient's needs and providing visualized performance feedback increases patients' motivation. Offering an objective evaluation of the patient's physical performance by using computer-aided evaluation scales are other important advantages of robotic rehabilitation (4). However, robotic systems also have disadvantages such as being expensive and making it difficult to feel the differences during movement because of the decreased therapist-patient interaction.

A literature review was conducted on September 30, 2021, using MEDLINE via PubMed and Google Scholar using the related keywords including "robotic systems", "rehabilitation", "multiple sclerosis", and "randomized controlled trial". Table 2 provides an overview of some selected randomized controlled trials (RCTs) of robotic systems in MS rehabilitation.

In a majority of pwMS, balance and gait are affected. Gunn et al. (8) have reported that as many as 50-80% of pwMS experience

Table 1. Overview of advantages and disadvantages of technology-based rehabilitation methods compared to traditional rehabilitation, their areas of use and clinical efficacy

Advantages	Disadvantages	Area of use	Effectiveness in clinical practice
• Provides repetitive/intensive exercise training • Adaptable to patient condition • Usable in immobile patient • Movements similar to activities of daily living • Delivering engaging/motivating training • Increased safety • Provides rehabilitation at home • Induces neuroplastic changes • Induces motor recovery • Reduces the therapist's physical fatigue • Provides multisensory input and multisensory feedback • Facilitates adaption to different environmental • Saves time for the patients • Enables patients to receive rehabilitation services in an environment that they are comfortable • Close follow-up • Enable assessment in real-world unsupervised environments • Offers an objective assessment • Remote database access	• Expensive equipment • Difficult to feel the differences that occur during movement • Decreased therapist-patient interaction • Requires technical expertise • Difficult limb configuration • Lack of natural interfaces	• Impairment/Function • Balance • Walking functions • Upper extremity functionality • Lower extremity functionality • Quality of life • Fatigue • Disability • Functional mobility	• Improvement in cognitive/motor functions • Improvement in gait and balance performance • Improvement in brain connectivity • Improvement in the quality of life • Reduces in fatigue Offers an objective assessment • Improvement of functionality in daily life

Table 2. An overview of some selected randomized controlled trials of robotic systems in MS rehabilitation

Study	Sample size	Experimental intervention	Control intervention	Duration and frequency	Measured domains	Main results
Androwis et al. (2021) (21)	10 pwMS Robotic xoskeleton assisted exercise rehabilitation (REAER) group: 6 Conventional gait training (CGT) group:4	The exercise consisted of approximately 30 minutes of above-ground walking training using the recommended maximum allowable level of 100% robotic assistance/ session (week 1) at baseline. At the end of the training program, approximately 45 minutes of walking training was continued using the recommended maximum allowable level of 40% robotic assistance/session (week 4).	Focused on mobility, gait, balance, and lower extremity function. Sessions included training on elements of stretching, strengthening, ambulation training, balance training, weight support, transfer training, stepping length and width and weight shift during ambulation.	4 weeks 2 times/ week	Functional mobility, walking endurance, cognitive processing speed, brain connectivity (thalamocortical resting-state functional connectivity based on fMRI)	Compared with CGT, 4-weeks of REAER was associated with large improvements in functional mobility, cognitive processing speed and brain connectivity between the thalamus and ventromedial prefrontal cortex, but not walking endurance. However, increased thalamocortical brain connectivity was associated with improved functional mobility, walking endurance, and cognitive processing speed.
Sconza et al. (2021) (22)	17 pwMS Experimental Group: 8 Control Group: 9	Each training session on the Lokomat lasted 30 min. All participants started with 40% body weight support and an initial treadmill speed of 1.5 km/h. In the following sessions, the training was standardized by increasing the speed of the training and then removing the body weight support. After each Lokomat session, participants performed a 60-minute physiotherapy program that included a general exercise program and gait training.	Each training session was carried on 1 hour and a half. The conventional physiotherapy treatment consisted of a general exercise program and gait training. It consisted of cardiovascular warm-up exercises, muscle stretching exercises, active-assisted or active isometric and isotonic exercises for the main muscles of the trunk and limbs, relaxation exercises, coordination, and static/dynamic balance exercises. Conventional gait therapy included the concept of proprioceptive neuromuscular facilitation, training to walk on different surfaces with or without appropriate walking aids, exercises to restore a correct gait pattern, implementation of residual compensatory strategies, and progressive increase in walking resistance.	5 weeks 5 times/ week	Gait speed, lower limb motor and function skills, gait and balance skills, instrumental kinematic parameters, disability and quality of life	In both groups, it was observed that RAGT was more beneficial than the control treatment on the improvement of activities of daily living, gait parameters, motor abilities and autonomy.

Straudi et al. (2020) (23)	72 PwMS Robot-assisted gait training (RAGT) group: 36 PwMS Conventional therapy (CT) group: 36 PwMS	Robot-assisted walking training, which lasted for about 40 minutes, was performed on the Lokomat treadmill. As the training progressed, adjustments (10% each) in these parameters were done according to the patient's performance.	A total of approximately 40 minutes of assisted walking was performed, placed between 10 -minute warm-up and cool-down periods. The patients walked 80 m without resting in the closed straight corridor with walking devices.	4 weeks 3 times/ week	Gait speed, mobility, balance, fatigue, quality of life	This study, performed in a PwMS population, failed to show a greater benefit of RAGT compared to gait training-based CT in terms of walking speed. Similarly, secondary outcomes, including fatigue, quality of life, balance, and mobility, were no more beneficial for RAGT compared to conventional treatment. However, significant improvements of gait speed, walking endurance, balance and quality of life were observed following both treatments.
Gandolfi et al. (2018) (12)	44 PwMS experimental group =23 control group =21.	Patients underwent robot-assisted hand training on an Amadeo. Three different training modes were performed: 1) passive flexion and extension of the fingers (10 min) with continuous passive movement (CPM); 2) active-assisted therapies with functional use of the hand (10 min); 3) interactive therapy via active training with specifically developed virtual therapy games (10 min).	The protocol for upper limb rehabilitation consisted of upper limb mobilization (shoulder girdle, elbow, wrist, and finger joints), facilitation of movements, and active tasks that were chosen out of 15 that are challenging for patients.	5 weeks 2 times/ week	Upper limb activity, Upper limb function, Upper limb performance, The EMG activity of 6 upper limb muscles (deltoid scapular, deltoid clavicular, triceps brachii, biceps brachii, flexor carpi radialis, and extensor carpi radialis), Quality of life, Patient satisfaction with daily activities or social roles	There were no significant between-group differences in outcomes. Electromyography showed relevant changes providing evidence of increased activity in the extensor carpi. The training effects on upper limb activity and function were comparable between the two groups. However, robot-assisted training demonstrated remarkable effects on upper limb use and muscle activity.

Feys et al. (2015) (13)	17 PwMS experimental group: 9 control group group: 8	Training sessions lasted 30 minutes by interacting with the HapticMaster robot in an individualized virtual learning environment. This virtual learning environment allows people to learn and train the skill components necessary during the activities of daily living related to the upper extremity.	Conventional rehabilitation programs consisted of 2 h multidisciplinary treatment per day including 30 min physiotherapy, 30 min occupational therapy, and 60 min group physiotherapy, speech therapy, or psychotherapy.	8 weeks 3 times/ week	Hand grip strength, upper limb activity, upper limb sensorimotor function, active range of motion, movement duration and speed	PwMS commented favorably on the robot-supported virtual learning environment and reported functional training effects in daily life. Robot-measured three-dimensional motion tasks were carried out to make transport and reach motion tasks more efficient in a shorter time. However, observational analyzes of the included cases showed great improvements in upper extremity sensorimotor function in subjects with more significant upper extremity dysfunction but no significant change for any clinical measure in the intervention and control group.

balance disorders and more than 50% of them fall at least once a year. Impaired balance and walking cause fear of falling and decreased dual-task performance in those concerned (8). Studies on robotic-assisted rehabilitation in pwMS primarily have explored its effects on the lower extremities concerning improving the balance and gait parameters. In 2021, 12 RCTs were included in a systematic review that evaluated the effects of robotic systems on balance and walking in pwMS (9). It was stated that wearable exoskeleton-type robots were the most frequently used to improve balance and gait patterns in pwMS (9). When the studies included in the review were examined, it was seen that the treatments applied included 2 to 5 sessions per week, i.e.; overall between 6 and 40 sessions, and the session duration ranged from 40 to 50 minutes (9). The review has reported an increase in walking speed, cadence, and stride length and a decrease in double support stance time in a clinically meaningful way (9). It has further reported improved balance parameters after the robotic rehabilitation and that this improvement was also maintained at a 3-month follow-up (9).

Tremor, coordination disorder, muscle weakness, sensory disorders, and spasticity in the upper extremities seen in pwMS have been found to limit the upper extremity activities (10). Holper et al. (11) reported that 56% of 205 pwMS had disorders in the upper extremity function, and 71% of them had limitations and restrictions in activities and participation requiring the use of hands and arms. Upper extremity rehabilitation includes practices to increase patients' independence in daily life and quality of life. At present, in pwMS, a limited number of robotic systems that are used for upper extremity rehabilitation exist. These devices improve hand and arm function with targeted tasks and reaching movements (12,13). Robots can assist movement in different ways. For example, robots may be chosen to achiev direct action movement or to passively move a limb; they can further provide the user with stimuli and feedback of different modalities used to facilitate a movement (14). Studies investigating the effectiveness of robot-assisted upper limb training in pwMS are scarce, and most of these studies have used a combination with VR (12,13). A systematic review including 30 studies investigated the effects of upper extremity rehabilitation in pwMS (15). Six of the included studies investigated the effectiveness of robot-assisted upper extremity exercises in pwMS (13,16-20). Two studies (17,20) compared the effects of different robot-assisted training. One study (13) compared the robotic rehabilitation group with the control group, which continued their routine treatment, and three studies (16,18,19) only investigated the effects of robotic rehabilitation without a control group. In the studies, the duration of treatment was between 1.5 and 10 weeks, the frequency was between 2 and 5 days a week, and the session duration was between 30 and 60 minutes. It was found that robot-assisted upper extremity training improved body functions and structures, and activity with effect sizes from low to high (15).

All the RCTs listed in Table 2 compare robotic rehabilitation with traditional rehabilitation methods. Robotic-assisted rehabilitation was applied for 8-25 sessions, and the duration of each session was between 30 and 40 minutes. Two studies found that robotic rehabilitation was more effective than conventional rehabilitation in functional mobility, cognitive processing speed, and brain connectivity improvement of activities of daily living, gait parameters, motor abilities, and autonomy walking speed (21,22). Three studies compared robotic rehabilitation with conventional rehabilitation and found no significant difference in the study outcomes, including gait speed, mobility, balance, fatigue, quality of life, and upper limb-related assessments (12,13,23). The difference between the studies might be due to the difference in the protocols.

Robotic-assisted upper and lower extremity rehabilitation methods effectively improve balance, walking functions, and lower extremity functionality in pwMS. Although these methods seem to have the potential to improve upper extremity functionality, more studies are needed.

Robotic systems should be used in the rehabilitation of pwMS in the clinic. However, the clinical condition of an individual is critical in the selection of the robotic system to be used. The contracted joint cannot complete normal joint movement, which can be problematic when robotic systems are used. Robotic systems used in patients with spasticity should have a mechanism to detect and direct it. The robotic system should provide active-assisted movement when the patient cannot complete the active movement and have active resistance exercise options.

Effects of VR in Technology-Based Rehabilitation for pwMS

VR is defined as a three-dimensional simulation system that allows interaction with an environment constructed by computerized systems, which gives the feeling of moving in the real world (24). The main principles of VR involve creating activity environments suitable for daily life (a), providing multisensory (i.e., visual, somatosensory, and auditory) input (b) and multisensory feedback (c) to facilitate adaption to different environmental conditions and enable learning (25). The advantages of VR rehabilitations are that they are innovative and enjoyable, suitable for different learning styles with realistic scenarios, and simplify complex movements. However, VR rehabilitation also has disadvantages. These disadvantages are often associated with immersive technologies created with head-mounted displays (26). The possible side effects and disadvantages of virtual reality therapy should be explained to the patient, and if any symptoms occur, the therapist should stop the therapy. The most significant disadvantages of virtual reality applications are examined in two categories (27). The first of these is seen as "cybersickness". The cybersickness is due to immersion during virtual reality therapy (28). Cybersickness symptoms include headache, pallor, sweating, dryness of mouth, stomach fullness, nausea, vomiting, eyestrain, disorientation, ataxia, and vertigo (29). The second disadvantageous category of VR is the 'after-effects'. The after-effects symptoms are usually seen due to the subject's adaptation to the sensory and motor needs of the virtual world and the need for time to return to the real world after the virtual reality application (30). Movement disorder, changes in postural control, perceptual-motor disturbances, lethargy, and fatigue are after-effect symptoms (30). In addition, the expensiveness of virtual reality applications and the fact that devices produced with virtual reality technology are not suitable for rehabilitation purposes are among the other disadvantages (26). The role of VR training approaches as a rehabilitation method in pwMS is discussed in the literature. Many studies have stated that interacting with a VR may significantly affect both motor and cognitive functions in pwMS (31-33).

A literature review was conducted to determine RCTs about VR on September 30, 2021, using MEDLINE via PubMed and Google Scholar using the related keywords including "virtual reality", "video-based exergaming", "rehabilitation", "multiple sclerosis", and "randomized controlled trial". Table 3 provides an overview of some selected RCTs that used VR in MS rehabilitation.

A recent systematic review and meta-analysis, including 9 RCTs (424 pwMS), investigated the effects of VR applications used with motor training (34). This review has shown that VR interventions involved a frequency of 8 to 25 sessions, with each session ranging between 10 and 60 minutes (34). It has further been found that virtual reality-based motor training increased balance and quality of life, reduced fatigue, and did not change functional mobility in pwMS compared to conventional rehabilitation programs and routine treatments (34). Ten studies (466 pwMS) were included in another systematic review and meta-analysis examining the effects of VR training applications on walking and balance in pwMS (35). It showed that motor training in VR increased balance, postural control, mobility, and walking ability compared to the control group without intervention (35). Further findings showed a reduction of symptoms such as fatigue and fear of falling (35). The total number of sessions of the included studies ranged from 8 to 48, and training frequency was between 1 and 4 sessions per week, and the training duration varied between 20 and 60 minutes per session (35). These studies concluded that VR training could be as effective as conventional training in improving balance, quality of life, and fatigue, and more effective than no intervention in improving balance and gait in pwMS.

A recent systematic review and meta-analysis including 10 studies investigated the effects of VR applications on upper extremity functions in pwMS (36). The review has confirmed the frequent use of Microsoft Kinect and Nintendo Wii VR programs for motor training interventions in pwMS (36). Results have shown a total duration of virtual reality-based training programs from 1 day to 6 months, and the duration of individual sessions was between 20 and 60 minutes (36). The training content comprised of upper extremity activities such

Table 3. Overview of some selected randomized controlled trials of virtual reality in MS rehabilitation

Study	Sample size	Experimental intervention	Control intervention	Duration and frequency	Measured domains	Main results
Molhemi et al. (2021) (38)	39 PwMS Virtual reality (VR)-based group: 19 Control group: 20	Progressive balance exercises were used using the Xbox360 with Microsoft's Kinect. (35 min.)	The standing exercise included multidirectional stepping and single- and double-leg standing; the walking exercise involved forward, backward, and side walking and weight-shifting exercise; consisted of the lunge, half-squat, leaning, and reaching.	6 weeks 3 times/ week	Limits of stability, balance, functional mobility, walking speed, dual task capacity, fall history	Both VR-based and conventional balance exercises improved balance and mobility in PwMS, while each acted better at improving certain aspects. VR-based training was more effective at improving cognitive-motor function and reducing falls, while conventional exercises provided better directional control.
Ozdogar et al. (2020) (41)	60 PwMS video-based exergaming group:21 conventional rehabilitation group: 19 control group:20	Video-based exergaming group: The video-based exergaming was implemented using a game console. In all games were required core stabilization, balance, and arm and leg function. Conventional rehabilitation group: This program included balance, arm and leg, and core stability exercises. (45 min.)	Control group: During the study period, participants were asked not to participate in a new exercise program if they did not have a previous exercise program.	8 weeks 1 times/ week	Upper extremity functions, cognitive functions, core stability, walking, depression, fatigue, quality of life	There was no significant difference in changes from baseline in study results at 8 weeks between video-based exergaming and conventional rehabilitation groups. Outcomes regarding arm function, cognitive function, most leg function, and balance were significantly improved in the video-based exercise and conventional rehabilitation groups.
Maggio et al. (2020) (39)	60 PwMS semi-immersive virtual reality (VR) training group (EG): 30 control group (CG): 30	The patient performed exercises in a virtual context to stimulate different cognitive areas through a widescreen dynamic interface that responded to the patient's movements with audiovisual feedback. (60 min.)	Conventional cognitive training consisted of a face-to-face approach between patient and therapist in individual sessions. The tasks were presented using a paper-and-pencil method and were designed to encourage specific cognitive skills.	8 weeks 3 times/ week	Cognitive/motor functions, visual perception, visuospatial abilities, short term visual memory, working memory and executive functions, speed of information processing, sustained attention, functional mobility, depression, and quality of life	CG and EG showed significant improvement in mood as well as various cognitive/ motor functions. In EG only, we observed a significant increase in visual perception, visuospatial abilities, short-term visual memory, working memory and executive functions, information processing speed and sustained attention, along with functional mobility.

Cuesta-Gómez et al. (2020) (40)	30 PwMS Experimental group (16) Control group (14)	Received the same conventional motor rehabilitation therapy (45 min) plus Leap Motion Controller (15 min)	Conventional motor rehabilitation based on functional task practice was applied. This practice included shoulder, elbow, wrist, and finger mobilization, strengthening of the upper extremity extensor muscles, and stretching exercises for the upper extremity flexor muscles.	10 weeks 2 times/ week	Upper limb grip muscle strength, coordination, speed of movements, fine and gross dexterity, fatigue, and quality of life.	Significant improvements were observed in the post-treatment assessment for coordination, speed of movement, and fine and coarse upper extremity dexterity in the experimental group compared to the control group. In addition, significant results were found in coordination, speed of movement, fine and coarse follow-up for the more affected side.
Yazgan et al. (2020) (42)	47 PwMS Group I:16 Group II:16 Group III:15	Group I (Nintendo Wii Fit) training protocol consisted of games such as Penguin Slide, Table Tilt, Ski Slalom, Heading and Balance Bubble selected from the Wii Fit Plus balance games section. The game levels and repetitions were determined by the therapists for each patient to standardize the progress of the exercises. (60 min.) The Group II (Balance Trainer) training protocol consisted of Collect Apples, Outline, Rowing Battle, and Motion Evaluation games included in the device software, which allowed patients to perform balance exercises in different directions. (60 min.)	Group III (control group) waitlisted	8 weeks 3 times/ week	Balance, functional mobility, walking speed, fatigue, quality of life	All parameters evaluated in groups I and II showed statistically significant improvement after treatment. Changes in all outcome measures were found to be superior in group I compared with group III. Similarly, all measures except the walking speed were found to be superior in group II compared with group III. Changes in balance and Quality of life were found to be superior in group I compared with group II. In comparison with no intervention, exergaming with Nintendo Wii Fit and Balance Trainer improves balance, increases functionality, reduces fatigue severity, and increases the quality of life in pwMS.

as reaching, grasping, carrying, and organizing the kitchen (36). The review has suggested that VR for the upper extremity in pwMS increased upper extremity muscle strength and function compared to conventional treatment and other upper extremity physiotherapy and rehabilitation approaches (36). Another systematic review has included 10 studies examining the effect of virtual reality-based rehabilitation on motor and cognitive parameters in pwMS and has found that VR reduced the risk of falling and improved balance, postural control, and gait parameters in pwMS (37). In addition, it has been stated that VR optimizes sensory information processing and integration in the brain, increases patients' motivation towards treatment, and facilitates motor learning (37).

VR rehabilitation programs were applied for 8-24 sessions, and each session lasted between 15 and 60 minutes (Table 3). In most studies, VR rehabilitation was compared with conventional rehabilitation (38-41). The results of these studies are different from each other. Molhemi et al. (38) found that VR-based training was more effective than conventional rehabilitation in improving cognitive-motor function and reducing falls, while conventional rehabilitation improved directional control. It can be thought that the reason for this is that VR-based rehabilitation consists of balance training, and conventional rehabilitation consists of training to move in different directions. Cuesta-Gómez et al. (40) found that VR rehabilitation was more effective than conventional training in improving coordination, speed of movement, and fine and coarse upper extremity dexterity parameters. However, Ozdogar et al. (41) found no significant difference in upper extremity functions, cognitive functions, core stability, walking, depression, fatigue, quality of life between VR and conventional rehabilitation. It can be thought that the differences are due to the different content, duration, and frequency of the applied VR and conventional rehabilitation methods. Yazgan et al. (42) compared the VR rehabilitation with the control group that received no rehabilitation and found that VR rehabilitation provided significant improvements in balance, functional mobility, walking speed, fatigue, and quality of life. Studies have shown that virtual reality-based rehabilitation improved motor and cognitive functions in pwMS, and patients had a positive attitude towards this type of training. Reviews have also reported that there is no consensus on the most effective VR application for rehabilitation in pwMS. In addition, the dose-response relationship of exercises in a VR and gains in motor and cognitive function is not clear. Therefore, more studies are needed to investigate VR applications for rehabilitation in pwMS.

VR applications are promising approaches used to improve rehabilitation processes. Physiotherapists should be informed of these systems and trained about using them to expand VR use in clinical settings. In VR rehabilitation, therapists should prefer games that can recover functional deficiencies and provide a clear and safe recovery to the patient. During rehabilitation, the patient should be constantly observed, and possible side effects should be evaluated throughout the treatment.

Effects of Telerehabilitation in pwMS

There is an increasing interest in developing innovative ways of providing patient-centered, technology-supported MS rehabilitation outside hospital settings, such as telerehabilitation (43,44). Telerehabilitation applications provide rehabilitation services to patients at home, especially exercise training and health behavior-changing approaches such as motivational interviews and social cognitive theory. Patients can access their treatments through video calls, software applications (apps), and online platforms (45,46).

Telerehabilitation provides rehabilitation opportunities for patients who cannot receive rehabilitation services due to the problems such as geographical remoteness, economic constraints, and physical disabilities. In addition, telerehabilitation enables to maintain the continuity of care for patients concerning rehabilitation services. Further advantages of telerehabilitation are that it helps overcome the barrier of patient transportation over long distances and saves time for the patients having to travel to the rehabilitation center or therapists to provide home visits. Finally, telerehabilitation enables patients to receive rehabilitation services in an environment where they are comfortable. However, telerehabilitation-based interventions also have some disadvantages, such as the difficulty of finding the appropriate digital platform and the decrease in the quality of the treatment because of the internet connection problems. In addition, patient-therapist interaction is reduced during telerehabilitation.

Various telerehabilitation systems have been developed and investigated in pwMS (47). A literature review was conducted on September 30, 2021, using the MEDLINE via PubMed and Google Scholar using the related keywords including “telerehabilitation”, “multiple sclerosis”, and “randomized controlled trial”. Table 4 provides an overview of some selected RCTs of telerehabilitation in MS.

A recent systematic review and meta-analysis including 9 studies with a total of 716 pwMS evaluated the effects of telerehabilitation applications on the motor, cognitive, and patient participation parameters (43). The duration of the studies ranged from 6 weeks to 6 months, and telerehabilitation training was delivered using a session duration of 30 minutes and a frequency of twice a week on average (43). The effect of telerehabilitation applications integrated with the patient was large for motor disability, medium for gait and balance, and small for cognitive outcomes (43). They also have a medium effect on depression (43).

Videoconference systems, VR applications, and sensor-based systems are often used for telerehabilitation-based training (33). Hoang et al. (48) provided step training together with a telerehabilitation-based VR application for 12 weeks at home. This study found that the telerehabilitation-based VR training program was usable and safe, and positively affected stepping, standing, balance, coordination, and functional performance (48).

Dennett et al. (5) have investigated the feasibility of a web-based exercise program twice a week for 6 months in pwMS. The patients reported that the applied exercise program increased their physical activity levels, and they felt more motivated and fit after exercises (5). Patients also reported that although it was easy to access the web-based exercises, they would prefer an application that they could download to their mobile devices instead of connecting via a link. They also added that an app would facilitate their access to the exercise program and increase their opportunities to exercise at different places and daytimes, which overall increased their compliance with the exercises (5).

Table 4 provides an overview of some RCTs investigating the effects of telerehabilitation-based intervention methods. Telerehabilitation-based interventions last for 16-52 sessions. Tarakci et al. (49) compared the effects of supervised exercise and telerehabilitation and they found that telerehabilitation can improve health-related quality of life and activities of daily living, yet, supervised exercises can be more beneficial regarding

Table 4. Overview of some selected randomized controlled trials of telerehabilitation in MS rehabilitation

Study	Sample size	Experimental intervention	Control intervention	Duration and frequency	Measured domains	Main results
Tarakci et al. (2021) (49)	30 PwMS Group 1 (Controlled Exercise Group): 15 Group 2 (Telerehabilitation Group): 15	2nd Group (Telerehabilitation Group): The exercises given to Group 1 were given as prescribed for the patients to practice at home.	1st group (Controlled Exercise Group): Warming up, cooling down, stretching, strengthening, gait, balance and coordination exercises were given under the supervision of a physiotherapist.	12 weeks 3 times/ week	Functional independence, fatigue, quality of life	Significant improvements were found in all outcome measures in both groups after treatment. It was found that the quality of life of the patients in the 1st group increased more than the patients in the 2nd group, while their fatigue levels decreased more than the patients in the 2nd group. It was emphasized that a structured home-based exercise program could be an alternative to supervised exercises in patients with multiple sclerosis.
Kahraman et al. (2020) (50)	33 PwMS Experimental Group: 19 Control Group: 14	The participants in the experimental group were given motor imagery training by the physiotherapist via video conferencing. (20 min.)	The control group was a waiting list group that did not receive any additional specific treatment.	8 weeks 2 times/ week	Dynamic balance during walking, walking speed, endurance and perceived ability, balance performance assessed by a computerized posturography device, balance confidence, cognitive functions, fatigue, anxiety, depression, and quality of life.	Telerehabilitation-based motor imagery training is an effective method in improving walking, balance performance and cognitive functions in pwMS, reducing fatigue, anxiety, and depression levels, and increasing their quality of life compared to the control group who continue their routine treatment
Donkers et al. (2020) (51)	48 PwMS Telerehabilitation Group: 32 Control Group: 16	The website includes exercises (videos, text, and audio descriptions) that are individually prescribed by a physical therapist at the initial assessment. These exercises focused on core and upper-extremity strength. Participants in the web-based intervention arm were informed that every 2 weeks during the 6-month intervention period, the treating physical therapist would review their online exercise diaries and remotely change the difficulty level and/or a number of repetitions of the exercise programs.	Participants in the usual care exercise group were given a written, home-based exercise program consistent with the most common method for exercise prescription practice for outpatient physiotherapy services at the website.	26 weeks 2 times/ week	Number of exercise sessions over the study period of 26 weeks, dynamic grip strength and fatigability, functional mobility, fall history, anxiety, and depression	Nearly 50% of participants (23 of 48) exercised at least twice per week for at least 13 of the 26 weeks. There was no difference in exercise compliance between the web-based and control groups. There were no problems with the safety of web-based physiotherapy.

Novotna et al. (2019) (52)	39 PwMS Experimental group: 23 Control Group: 16	Patients in the treatment group performed home-based balance exercises using a portable tablet-based game platform. (at least 15 min.)	Control group continued their routine treatment.	7 weeks 7 times/ week	Balance, functional mobility, spatio-temporal gait parameter, falls efficacy	It was found that the patients in the treatment group had good compliance with game-based balance exercises. After the completion of the home-based balance exercise program, although the balance performance of the patients in the treatment group improved significantly compared to the patients in the control group, no significant differences were found between the gait parameters of the two groups.
Fjeldstad-Pardo et al. (2018) (53)	30 PwMS Group 1: (customized unsupervised home-based exercise program): 10 Group 2 (remote PT supervised via audio/ visual real-time telecommunication): 10 Group 3 (in-person PT at the medical facility): 10	2nd Group: Exercises consisting of visual and auditory feedback were given by videoconference method 2 days a week. 3rd Group: Exercise training was given 2 days a week in a clinical setting under the supervision of a physiotherapist.	1st Group: home exercises to be done 5 days a week are given.	8 weeks 1st Group: 5 times / week. 2nd Group: 2 times/ week 3rd Group: 2 times/ week	Gait and balance performed with a computerized system, functional gait assessment, quality of life, fatigue, disability	The functional gait assessment outcome measure improved significantly in all groups. No significant difference was found between the 2nd and 3rd groups in various outcome measures. Telerehabilitation training is a feasible treatment modality comparable to face-to-face treatment in improving gait and balance in people with MS.

fatigue and health profile compared to telerehabilitation. Kahraman et al. (50) found that telerehabilitation-based motor imagery training was an effective method to improve dynamic balance during walking, walking speed, perceived walking ability, balance confidence, most cognitive functions, fatigue, anxiety, depression, and quality of life compared to the control group who continued their routine treatment. Donkers et al. (51) investigated the effects of web-based exercise training given asynchronously and exercise programs given as home exercise prescriptions. As a result of the study, no significant difference was found between the groups regarding dynamic grip strength and fatigability, functional mobility, fall history, anxiety, and depression (51). Novotna et al. (52) compared asynchronous balance training with the control group that did not receive rehabilitation training. They found that asynchronous telerehabilitation-based balance training significantly increased balance in pwMS (52). Fjeldstad-Pardo et al. (53) formed two experimental groups in their study; one was given synchronous telerehabilitation-based exercise training, the other was given exercise training under the supervision of a physiotherapist in a clinical setting, and the control group was given an exercise prescription to apply at home (53). It was found that there were improvements in the functional gait, quality of life, fatigue, and disability in all three groups, and there was no significant difference between the synchronous telerehabilitation group and the face-to-face rehabilitation group (53). Based on the existing evidence, it is suggested that telerehabilitation-based interventions are as much effective as face-to-face methods in pwMS. In addition, pwMS are satisfied with their telerehabilitation-based interventions. However, it needs to be pointed out that thus far, the number of studies that have investigated the effects of telerehabilitation interventions on activities of daily living, fatigue, quality of life, pain, and self-efficacy in pwMS is limited.

Due to the progressive nature of the MS, long-term follow-up and rehabilitation are particularly important. This method is advantageous for providing long-term follow-up and rehabilitation in patients with geographical distance, economic restrictions, and physical disabilities. Telerehabilitation-based interventions may be a viable alternative rehabilitation method for pwMS, but there is still insufficient evidence of the most effective type of telerehabilitation and its setting. Therefore, there is a need for further high-quality telerehabilitation research in pwMS.

Effects of Movement Analysis Systems in Technology-Based Rehabilitation for pwMS

Several approaches for assessing mobility and balance in pwMS include subjective assessment scales, self-reported measures, performance-based measures, and laboratory-based movement analysis measures. The significant disadvantages of subjective assessment methods, self-report scales, and performance-based measures are that they are insensitive to minor changes in mobility and balance impairments and they only provide information at a single time point. In addition, subjective measures have many systematic biases such as order, scale, and halo effects, which can be affected by psychological factors (54). Mobility and balance impairment in pwMS show fluctuations daily and even within one day (45). Therefore, easy-to-use, objective and inexpensive assessment tools are required to detect changes in balance and mobility and be used in pwMS.

Smart wearable devices have been developed rapidly in recent years with new technologies (55). These devices are mainly used in monitoring, management, diagnosis, medical treatment, and rehabilitation (55). They can be used on all human body parts, including the head, limbs, and torso. Sensors are mainly inserted into glasses, helmets, headbands, hearing aids, earrings, headphones for head wearable devices (55). Torso wearable devices are frequently inserted to underwear, belts, and suits (56). Upper extremity accessories (i.e., watch, bracelet) can be used in movement analysis and monitor physiological parameters such as body temperature and heart rate (57). Lower limb wearable devices are frequently inserted into shoes and socks (58). Wearable devices directly measure acceleration and angular velocity of body parts, respectively. Inertial measurement units (IMUs) are typically used for this purpose and include an accelerometer and a gyroscope. Accelerometers measure non-gravitational acceleration, and gyroscopes use the earth's gravity to help determine the orientation and angular velocity.

Some studies have investigated the concurrent validity and accuracy of sensor-based assessment systems in MS and found that they showed high accuracy and concurrent validity against the commonly used method (59-65). Sun et al. (66) have included a total of 33 studies involving 1292 pwMS in their systematic review evaluating the effects of technological approaches used for mobility and balance monitoring in pwMS. Results from this review and other studies have shown that wearable sensor systems were most frequently used to evaluate gait and balance in pwMS (59-66). Upper extremity dysfunction affects the quality of life, daily living activities, employment status of individuals, and the ability to use walking aids. On the other hand, evaluating upper extremity movements with sensors has received less attention in pwMS for many years. This may be due to the lack of understanding of the importance of upper extremity dysfunction compared to balance and gait disorders, which are prominent symptoms of MS (67). In order to reduce this deficiency, studies investigating upper extremity dysfunction in pwMS and the effects of these disorders on the functionality of patients should be increased. The importance of upper extremity dysfunction and objective assessment in MS rehabilitation should be emphasized. Elsworth-Edelsten et al. (68) have analyzed arm movements during walking in pwMS using a 12-camera movement analysis system (VICON Mx3+; ViconPeak® 101, Oxford, UK) and have found an increased mean elbow flexion and decreased overall arm movements during walking in pwMS compared to a healthy control group. Since the upper extremity function is also important for pwMS, more studies are needed to develop valid and accurate systems to evaluate it.

Close follow-up of patient is critical in chronic diseases (69). One of the most significant advantages of these systems is that they enable collecting and monitoring users' data during the day and provide a dynamic, intelligent, and comprehensive analysis of various indicators (55). Remote treatment planning and lifestyle management are other significant advantages of movement analysis systems. In addition, due to their lightweight and wearable properties, mobile movement analysis systems (e.g., IMUs) have a good potential for mobility assessment in real-world unsupervised environments. In contrast, cameras and other environment sensing technologies have limitations in their capture range and hardware portability and are better suited for controlled environments (e.g., laboratories, clinics, nursing homes). Some of the disadvantages of these systems are their limitations in evaluating movement analysis in social life, high costs, overly complex analysis requiring a trained team, and difficult calibration. Movement analysis systems to be used should be selected in line with the needs of the patient and the user's clinical and technological experience.

Conclusion and Recommendations

Technological systems provide various benefits to pwMS with features facilitating the realization of movement, providing task-specific training content, relying on motor learning principles, supporting treatment planning, minimizing obstacles (e.g., distance, time), and enabling objective evaluation of functional performance. These relatively new and promising systems are thought to complement conventional treatment and assessment methods. As the cost of technological systems decreases and their accessibility and usability increase, the potential of the systems is suggested to be further explored in pwMS. However, it is recommended that professionals with appropriate clinical backgrounds apply these technologies and seek them for the sake of the patients and their caregivers. In addition, it appears helpful to involve and engage patients and their caregivers in the further development and evaluation of technology for rehabilitation in MS.

Ethics

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: H.K., B.S., T.K., Design: H.K., B.S., T.K., Data Collection or Processing: H.K., B.S., T.K., Analysis or Interpretation: H.K., B.S., T.K., Literature Search: H.K., B.S., T.K., Writing: H.K., B.S., T.K.

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