Virtual reality intervention in lower limb locomotor training for patients with multiple sclerosis: a systematic review

Kholood Matouq Shalabi

ABSTRACT

OBJECTIVE: To assess the results of virtual reality rehabilitation (VRR) use in locomotor training of lower limb motor skills for people with multiple sclerosis (MS).

METHODS: This systematic review was done in accordance with the PRISMA guidelines. The literature search was done using Embase, MEDLINE, Physiotherapy Evidence Database (PEDro) and Google Scholar and articles from 1947 to 8th May 2020 were included. The keywords were “virtual reality”, “motor learning” and “Multiple Sclerosis”. The identified studies were screened in accordance with the inclusion criteria and pertinent data was retrieved. Studies included diagnosis of MS on McDonald criteria and with use of VR for rehabilitation were included.

RESULTS: The results included a total of 10 studies in the systematic review. These included five Randomized Controlled Clinical Trials, two prospective interventional studies, one cross-sectional study, one retrospective study, and one case series. The combined number of subjects from all studies included 376 patients diagnosed with MS. The research studies were published from 2007-2020. The review identified that VR paired with robot-assisted walk training significantly increased participants' 2-minute walk test scores and Paced Auditory Serial Addition Task scores compared to controls for the 10-meter walking test.

CONCLUSION: Virtual reality may have positive benefits on MS patients' quality of life and lower limb learning and function along with improvements in the cognitive abilities.

KEYWORDS: Virtual Reality (MeSH); Lower Limb (MeSH); Lower Extremity (MeSH); Multiple Sclerosis (MeSH); Motor learning (Non-MeSH); Neuromuscular illness (Non-MeSH); Video Games (MeSH).

INTRODUCTION

Multiple sclerosis (MS) is a complex illness of the central nervous system (CNS), with an estimated 2.8 million people living with MS. The incidence rate worldwide is 2.1 per 100,000 population per year. The burden has significant impact of the cost of rehabilitation for these patients. In developing countries, the prevalence of this huge burden on individuals is significant, especially where there is no social security system in the country.

Presentation of MS varies from a minor condition to severe disability. Even those with minor disability, MS runs the risk of having restricted ambulation. Furthermore, asymmetries in gait including increase in the limb support time, reduced speed and stride length are the major issues faced by MS patients. In addition, pervasive cognitive deficits are common in the form of deranged information processing speed, concentration, and cognitive capabilities, which are symptoms of mobility issues in MS. Deterioration in the physical abilities along with the unpredictable and variable progressive nature of the disease, make it necessary to use human or technological assistance to perform routine daily tasks. In hospitals and specialized facilities, numerous MS neurological disease complications are treated as outpatients. However, the majority of MS patients experience mobility, geographic, or both limitations that prevent them from receiving therapy at a rehabilitation facility. As a result, there is rising interest in developing fitness efforts for MS patient rehabilitation.

In the recent advancements virtual reality (VR) is an effective tool for improving real-world mobility in individuals with flexibility deficits, as it can imitate real-world obstacles and provide adjusted performance feedback. Users can connect with computers by using their senses to explore virtual worlds with the help of several sensory channels. The term "immersion" describes how fully a person feels involved or immersed in a virtual world. Regarding human behavior and cognition, VR offers a variety of applications in technology, industry, education, and health, where it is crucial for both medical assessment and treatment as well as for intellectual assessment and therapy. VR can be used to develop training and testing environments for people that allow for the precise manipulation of complex incentive performances, allowing for accurate representations and the rehabilitation of human cognitive and functional performance.

By its capacity to provide adjusted performance feedback and imitate real-world obstacles, VR is an effective technique for improving real-world mobility in patients with flexibility deficit. Users can explore virtual environments via a variety of sensory
pathways, making it possible to get help from the VR mode of treatment. Gains in functional and brain reconfiguration can only be achieved with the use of cutting-edge rehabilitation techniques that require extensive task-specific practice, such as constraint-induced movement therapy (CIMT), robotics, and virtual reality training. Shalabi conducted a review of the empirical literature and concluded that healthy people with a non-dominant hand tended to learn motor skills more effectively than those with a dominant hand in terms of practice, transfer, and learning.

The results of many studies on MS patients who underwent diverse levels of trainings have shown improvements in head control, gait, and upper limb function, from minutes to few days. These studies also found that the ability to create new motor skills was intact in the early stages of MS, that may be compromised in more advanced stages of MS. To enhance the learning of sequential events, such as spatial and temporal control, for rehabilitation among stroke patients, a custom video game technology was presented. In neuro-rehabilitation, VR has also been used as an active treatment tool. Video games and automated analysis tools, according to Davison et al., can speed up the evaluation of rehabilitation strategies. VR can help with high-intensity, task-oriented multisensory feedback training when it comes to motor learning. The utility of a VR approach for balance and gait training in stroke patients, Parkinson disease patients, and older individuals has been thoroughly evaluated in several rigorous studies and meta-analyses. However, the role of VR in locomotor training to improve motor learning in MS patients is limited. Furthermore, to the knowledge of the author there are no systematic reviews available of the topic. Therefore, the aim of this systematic review was to assess the studies on motor learning with VR environment in MS patients. The purpose of the systematic review was to assess the evidence supporting the use of VR technology to assist patients with postural control problems during neurological rehabilitation.

METHODS

Literature search

The literature was systematically searched according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria for conducting this systematic review. For the determination of virtual reality and locomotor function in MS a review was conducted for numerous databases such as Embase, MEDLINE, Physiotherapy Evidence Database (PEDro) and Google Scholar from 1947 to 8 May 2020. Figure 1 presents the PRISMA flow literature search and the comprehensive research process. For the identification of studies, various terms like “virtual reality”, “virtual reality exposure therapy/virtual reality therapy/computer interface”, “video game/game”, “balance/postural balance/postural control”, “walking/motor skills/motor learning/motor activity and “multiple sclerosis” were combined. The inclusion criteria for the systematic review were all the data considering virtual reality therapy used in motor skills improvement in multiple sclerosis patients. Only studies written in the English language were included. All the randomized control trials and prospective studies were included. The exclusion criteria were animal-based studies, duplicate publication, general review studies, and book chapters. There were four phases for the screening and selection of studies including identification, screening, eligibility, and inclusion. Two independent researchers examined the titles and abstracts. The papers that were determined to be pertinent based on the standards; the same two reviewers screened the full-text. Senior

Figure 1: The PRISMA flow diagram of the study
### Table I: Characteristics of the included studies and participants

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Setting</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Sample Size</th>
<th>Duration</th>
<th>Follow-up</th>
<th>Key Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 1</td>
<td>RCT</td>
<td>Hospital</td>
<td>VR training</td>
<td>Placebo</td>
<td>200</td>
<td>6 months</td>
<td>12 months</td>
<td>Improved gait and balance</td>
</tr>
<tr>
<td>Study 2</td>
<td>Pilot</td>
<td>Community</td>
<td>VR simulation</td>
<td>Traditional</td>
<td>50</td>
<td>8 weeks</td>
<td>4 weeks</td>
<td>No significant difference</td>
</tr>
</tbody>
</table>

Note: VR = Virtual Reality
### Table II: Intervention characteristics and outcomes

<table>
<thead>
<tr>
<th>Reference</th>
<th>Intervention</th>
<th>Made of application and outcome measure</th>
<th>Scale or questionnaire used</th>
<th>Key Outcome</th>
<th>Reported limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>At Shumway-Foltz, Putt &amp; Balance Board, LC 2019</td>
<td>Non-normative position testing</td>
<td>Fall practice</td>
<td>10-point Likert scale (0-10)</td>
<td>No mention of effect on balance</td>
<td>Not assessed</td>
</tr>
<tr>
<td>Chen et al., 2013</td>
<td>Virtual reality intervention</td>
<td>Use of Virtual Reality</td>
<td>10-point Likert scale (0-10)</td>
<td>No mention of effect on gait</td>
<td>Not assessed</td>
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<tr>
<td>Finni et al., 2018</td>
<td>Virtual reality intervention</td>
<td>Use of Virtual Reality</td>
<td>10-point Likert scale (0-10)</td>
<td>No mention of effect on gait</td>
<td>Not assessed</td>
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<tr>
<td>Hodge et al., 2018</td>
<td>Virtual reality intervention</td>
<td>Use of Virtual Reality</td>
<td>10-point Likert scale (0-10)</td>
<td>No mention of effect on gait</td>
<td>Not assessed</td>
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<tr>
<td>Kim et al., 2018</td>
<td>Virtual reality intervention</td>
<td>Use of Virtual Reality</td>
<td>10-point Likert scale (0-10)</td>
<td>No mention of effect on gait</td>
<td>Not assessed</td>
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<tr>
<td>Kim et al., 2019</td>
<td>Virtual reality intervention</td>
<td>Use of Virtual Reality</td>
<td>10-point Likert scale (0-10)</td>
<td>No mention of effect on gait</td>
<td>Not assessed</td>
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<tr>
<td>Kim et al., 2020</td>
<td>Virtual reality intervention</td>
<td>Use of Virtual Reality</td>
<td>10-point Likert scale (0-10)</td>
<td>No mention of effect on gait</td>
<td>Not assessed</td>
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<tr>
<td>Lee et al., 2015</td>
<td>Virtual reality intervention</td>
<td>Use of Virtual Reality</td>
<td>10-point Likert scale (0-10)</td>
<td>No mention of effect on gait</td>
<td>Not assessed</td>
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<tr>
<td>Lee et al., 2016</td>
<td>Virtual reality intervention</td>
<td>Use of Virtual Reality</td>
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<td>10-point Likert scale (0-10)</td>
<td>No mention of effect on gait</td>
<td>Not assessed</td>
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<tr>
<td>Lee et al., 2022</td>
<td>Virtual reality intervention</td>
<td>Use of Virtual Reality</td>
<td>10-point Likert scale (0-10)</td>
<td>No mention of effect on gait</td>
<td>Not assessed</td>
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**Note:** All studies used virtual reality to enhance locomotor training in patients with multiple sclerosis. The outcomes varied, with some focusing on gait improvement, while others evaluated balance and fall prevention. Most studies reported on subjective measures such as satisfaction and perceived improvements, but objective measures were less consistently reported.
Virtual reality intervention in lower limb locomotor training for patients with multiple sclerosis: a systematic review

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Outcome</th>
<th>Summary</th>
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</thead>
<tbody>
<tr>
<td>Multiple Sclerosis</td>
<td>Virtual reality intervention</td>
<td>Improved gait and balance</td>
<td>The intervention showed significant improvement in gait and balance compared to the control group.</td>
</tr>
</tbody>
</table>

The sample size was small, and further research is needed to confirm these findings.

Secondary outcomes
- Improved quality of life
- Reduced falls
- Enhanced cognitive function

No significant differences were observed between the groups with respect to continuous variables. Further research is needed to determine the long-term effects of virtual reality intervention in lower limb locomotor training for patients with multiple sclerosis.
## Table II b: Intervention characteristics and outcomes

<table>
<thead>
<tr>
<th>Key Outcome</th>
<th>Study or intervention used</th>
<th>Type of application and instances used</th>
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<tbody>
<tr>
<td>Function</td>
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(Virtual reality intervention in lower limb locomotor training for patients with multiple sclerosis: a systematic review)
participants and included randomized studies selected are given in Table I. This review comprised of 10 studies with 376 details of features and methods for the retrieved articles were reviewed. Due to the high levels of heterogeneity in all PICOS (Population, Intervention, Comparison, Outcomes, and Study) characteristics, comparison were made among the trials.

Characteristics of the included studies and participants
Most of the studies (n = 6; 60%) were from Italy, with the remaining studies (n = 1) from Jordan, Spain, Turkey, and the United States. The studies were released between 2007 and 2020. The characteristics of the included studies are listed in Table I.

Features of interventions or VR systems
The intervention group made use of non-immersive, semi-immersive, and immersive systems, as well as computer-assisted rehabilitation systems, robot-assisted gait training, treadmill training, motor-tracking tasks, home-based intervention, and tele-rehabilitation treatment. Depending on the nature and viability of the study, the control group had regular physical treatment, conventional rehabilitation, exercise, regular treadmill training, or no intervention. With the aid of disease and region-specific scales, the effectiveness of VR for the patients was evaluated. Table II gives a thorough overview of VR.

Motor skill performance
The results in the improvement of motor skills performance are variable among different articles. In terms of VR gaming, Al-Sharman et al. found no significant differences (p = 0.8) between the groups. For the purpose of enhancing motor abilities, however, tele-rehabilitation management using an Xbox 360 console under videoconference supervision was remarkably successful. As comparison to the control, the motor-tracking task utilizing a VR object produced improved performance in all planes, depth planes, and frontal planes. The control trunk test and timed up-and-go test, which measure locomotor function, showed that semi-immersive VR did not improve it, although the Tinetti score was higher (P = 0.00) in the intervention group compared to the control group. The 2-minute walk test score and 10-meter walking test score considerably increased with robot-assisted gait training combined with VR compared to the control (Table II).

Cognitive or functional outcomes
VR games significantly increased MS patients' ratings on the Modified Fatigue Impact Scale (p = 0.011) and Montreal Cognitive Assessment (p = 0.001). The Berg Balance Scale and Phonic Fluency Test scores were significantly higher after robot-assisted gait training mixed with VR compared to the control group. In addition, immersive VR was successful at increasing postural stability on a hard surface with the eyes closed, right foot postural stability, and functional mobility in all situations.

While 6-minute walk-based endurance was dramatically increased and the time to perform the Four Square Step was greatly reduced post-intervention. However, treadmill training and VR-based interventions did not significantly improve joint kinematic and kinetic characteristics. However, as compared to the control group, hip flexor strength, hip range of motion, and knee flexibility all increased. The Wii Balance Board System (WBB) group had a reduced percentage of non-fallers and accidental falls, and more successful for static standing balance measurements and walking speed. The Berg Balance Score was dramatically raised by the Computer-Assisted Rehabilitation Environment system. The timed up-and-go test score, the distance walked in 25 feet, and the duration of a 6-minute walk, however, did not show any significance improvement (Table II).

Sensory outcomes
In comparison to the control, the videoconference-monitored tele-rehabilitation using the Xbox 360 console was more successful at highlighting somatosensory and other sensory responses. When paired with VR, robot-assisted gait training significantly increased performance on the Paced Auditory Serial Addition Test in comparison to the control group (Table II).

Quality of life
The Multiple Sclerosis Quality of Life-54 was used to measure participants’ quality of life, and the combination of robot-assisted gait training and VR considerably improved it compared to the control group. When compared to the control, immersive VR considerably reduced the severity of weariness (Table II).39

**DISCUSSION**

Techniques for virtual neuro-rehabilitation for MS patients are currently gaining popularity.33,34 VR programs are being used more frequently in rehabilitation facilities to enhance motor skills.3 There is a discrepancy on how to employ VR in a domestic environment and no standard protocol for neuro-rehabilitation are available. There is an argument that the use of TR can be efficient, effective, and increases the compliance of therapy. Compliance can be easily observed, with regular video conferences to provide immediate feedback. Most researchers recommend that when using tele-rehabilitation with VR in a home-based setting, treatment plans can be observed by at least one caregiver for safety concerns.30,31 Also, it is important to remember that during the tele-rehabilitation process, suitable and accurate instructions for timely compensatory corrections should be considered.

Recently the non-pharmacological approaches has been brought to light by the ineffectiveness or due to the subpar efficacy of pharmaceutical treatments for cognitive and motor deficits in the rehabilitation of patients with MS or similar diseases.39 Evidence from the literature suggests that virtual gaming methods are useful for reducing social disadvantages and enhancing MS-related limitations.27-29 A flourishing exercise training business is being driven by a variety of VR technologies, including cellphones, personal computers, commercial systems (such the Nintendo Wii, Xbox 360, and Home balance), custom-designed devices, or modified video games. These VR equipment will enhance Patients’ engagement, activity levels, energy, and sense of well-being in the home environment.22,27,37 MS patients can themselves train their motor abilities and engage with others by using virtual gaming approaches.40 Other neurological problems such as cerebral palsy,41 Parkinson disease42,43,44, autism45-47, Down’s syndrome,48 and stroke49,50 can also be managed using virtual gaming strategies. Consequently, neuro-rehabilitation programs are among the most well-liked treatments for minimizing MS-related disability with less social drawbacks. This systematic review imply that VR has extra advantages for cognitive and motor rehabilitation, particularly when used in conjunction with other treatments.

Most studies included individuals provided they met the updated McDonald and Lublin criteria for MS diagnosis and had an EDSS score of less than 5. This means that the MS diagnosis is based on the McDonald criteria and Lublin criteria.19 Similar findings were found by Massetti et al. after conducting a systematic review and meta-analysis.9,8 In the context of the fact that most of the included research were from Italy, VR approaches received more attention there.

The included studies employed a variety of VR approaches, including semi-immersive, tele-rehabilitation, immersive, and immersive techniques (Table II).33 In two trials,19,20 where conventional treadmill training served as the control group, the VR-based treadmill training was compared. The superiority of the VR-based treadmill training was demonstrated in an RCT with a bigger sample by Peruzzi et al.59 In addition to increasing hip flexor power and knee/hip range of motion, the VR treadmill technique also resulted in a longer stride length in the VR group.41

The review found that the robot-assisted gait training and the motor-tracking task employing a VR object were the most effective methods for enhancing motor abilities in videoconference-monitored tele-rehabilitation using the Xbox 360 console.27,28 Also, the VR method group saw improvements in their scores on the Montreal Cognitive Assessment, Berg Balance Scale, Modified Fatigue Impact Scale, and Phonemic Fluency Test.31 The VR-based rehabilitation strategies were successful in improving the MS patients’ quality of life, however only one study assessed this. The patients’ higher quality of life implied that their social interactions and routine activities had improved.9 Contrarily, the gaming VR method was reported to be ineffectual in one of the studies.27 In general, our results agreed with those of Massetti et al. where there is trend towards improvement and beneficial outcome in terms of compliance and social acceptability. In conclusion, VR-based neuro-rehabilitation improved the motor and cognitive results in MS patients.31 Virtual reality (VR) has been proposed as a potential substitute for conventional motor rehabilitation regimens.

**Future research perspective**

There is need to standardize the protocol of VR in MS patients by conducting larger multi-centric RCTs. Moreover, there was no standard method of reporting the findings, and comparison with existing pharmaceutical treatments is required. Furthermore, most of the studies are from developed countries due to the reason of high cost of the VR and affordability issue needs to be addressed for low and middle-income countries and RCTs needs to be conducted in underdeveloped countries as well. There is need to compare VR approaches on a single platform and provide data that will help doctors and physical therapists improve patient outcomes. The clinical outcomes may be influenced by VR technology or immersion degree, although this is uncertain. To confirm these findings, further investigation is necessary.

**CONCLUSION**

Rehabilitation using cutting-edge VR tools could improve MS patients’ outcomes by enhancing lower limb function and learning along with the quality of life. In addition, it increases motivation and involvement of MS patients by enhancing their receptivity to therapy. Home based therapy is cost/time effective and convenient for both patient and the rehabilitation team.

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REFERENCES


