

Virtual Reality Impact on Fatigue, Quality of Life, Gait and Balance in Patients with Multiple Sclerosis: A Narrative Review

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Abstract: ***Background:** VR technology provides an opportunity for high-intensity, task-oriented multisensory feedback training, which has the potential to enhance motor learning and training. The aim of this review was to explore the potential advantages of VR in addressing key aspects such as fatigue, quality of life, gait, and balance in individuals diagnosed with multiple sclerosis (MS). **Methods:** This review followed the guidelines of PRISMA. A comprehensive search on the following electronic databases was conducted: PubMed, Google scholar and PEDro. The inclusion criteria involved studies presenting original research data focused on individuals diagnosed with MS, assessing outcomes pertaining to fatigue, quality of life, gait, or balance, and published in English or other languages with an available English version. **Results:** 7 articles were included in the review. Most of the studies (n=5) included were clinical trials, (n=1) case study and (n=1) review. As far as the clinical trials, three studies (n=3) compared VR with usual care, one (n=1) with the use of robotics and (n=1) had no control group. **Conclusion:** VR ensures an enhanced experience for patients, yielding positive outcomes in their rehabilitation journey. The integration of VR alongside conventional balance exercises has demonstrated a significant improvement in balance. Tele-rehabilitation utilizing VR has proven to be notably superior to conventional rehabilitation in terms of balance, postural control, gait, and compliance.*

Keywords: multiple sclerosis, MS, virtual reality, VR, fatigue, quality of life, balance, gait

1. Introduction

Multiple sclerosis (MS) is an immune mediated disease of the Central Nervous System (CNS) with prevalence 1 million people in the US and 2.5 million people worldwide. Specifically in MS turns against the tissues of the CNS by destroying the myelin, the protective covering of the nerve (Baird et al., 2018).

Virtual reality is a computer-based system of either 2D or 3D environments and its user can interact with these environments through additional electronic tools-equipment. VR provides sensory feedback, which stimulates brain activity and improves neuroplasticity (Virtual Reality Treatment for Multiple Sclerosis - Physiopedia, n.d.). VR enables high-intensity, task-oriented multisensory feedback training and can enhance motor learning and training by combining motor and cognitive demands in an attractive and interactive way, motivating participants to deal with the game's demands and not just the movements (Casuso-Holgado et al., 2018).

Many studies have been founding possible benefits on the use of VR in people with MS (Moreno-Verdu et al., 2019; Casuso-Holgado et al., 2018). Motor disability is one of the most widespread and impactful consequences of MS. Problems such as balance, quality of life, gait and weakness are very common. A total of 90% of patients report motor disability within ten years after the onset of the disease. This motor disability is related to broad aspects of the patient

including emotional and mental health, daily activities, quality of life and autonomy (Baird et al., 2018).

VR technology provides an opportunity for high-intensity, task-oriented multisensory feedback training, which has the potential to enhance motor learning and training. By integrating both motor and cognitive demands in an engaging and interactive manner, VR motivates participants to address the challenges presented by the virtual environment, extending beyond mere physical movements. Against this backdrop, the aim of this review was to explore the potential advantages of VR in addressing key aspects such as fatigue, quality of life, gait, and balance in individuals diagnosed with multiple sclerosis (MS). By examining the existing literature, this review sought to shed light on the potential benefits of utilizing VR as a therapeutic tool in the management of MS-related impairments.

2. Methods

Review strategy: This review followed the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher d et al., 2009).

Data sources: A comprehensive search on the following electronic databases was conducted: PubMed, Google scholar and PEDro using medical subject headings related to multiple sclerosis 'multiple sclerosis', 'virtual reality', 'fatigue', 'quality of life', 'gait' and 'balance'.

Inclusion criteria: To ensure the inclusion of all relevant studies, the following criteria were applied: (a) studies reporting original research data on individuals diagnosed with multiple sclerosis; (b) studies evaluating outcomes related to fatigue, quality of life, gait or balance; (c) studies with full-text availability; and (d) studies published in either English or other languages but with an English version.

Study selection: Two independent reviewers (A.C.) and (Ev.T.) conducted the eligibility screening of the studies in a standardized and blinded manner. The screening involved the assessment of titles and abstracts, and the exclusion of duplicate articles. Following this, full paper copies were retrieved, and a blinded full-text screening was carried out by the same reviewer (A.C.). In case of any disagreements between the authors during any stage of the screening process, a third reviewer (Em.T.) was consulted for resolution.

3. Results

Calabrò et al. study examined the effects of the combination of VR with robotics (Lokomat) in gait, balance and coordination in non-ambulatory patients (Calabrò et al., 2017). A total of 40 participants-patients with MS, aged 18-65 years, with a walking disability were included and underwent 40 sessions of 8 weeks. These patients were evaluated before and after the intervention. The experimental group was subjected to VR and robotics, while the control group only to robotics. Both groups underwent general exercises. The results of the present research show that the integration of VR in robotics can activate different areas of the brain involved in motor learning. It is a promising method in terms of spasticity, balance, gait and even depression as there is interactivity and the patient is easier to comply.

A similar research process investigating the use of Lokomat in combination with classical conventional exercises was conducted by Russo et al. (Russo et al., 2018). Forty-two patients were included and divided into the following groups: the experimental group in which two-dimensional VR robotic training was applied for 6 weeks, a program used 12 weeks before the start of classical rehabilitation, and the control group in which traditional classical rehabilitation exercises were applied. The measurement parameters were independence-gait, balance, TUG and depression. Patients were evaluated 6 weeks later, at the end of training and 1 month later. The results of the research reveal that robotic training in combination with two-dimensional VR can be a valuable tool and enhance simple traditional rehabilitation in the motor reintegration of these patients.

The research of Peruzzi et al. compared the integration of VR on the treadmill with the use of a treadmill in terms of gait improvement (Peruzzi et al., 2016). Eight patients were included, and underwent a 6-week program of 45 min in both single and dual activity to assess gait endurance and obstacle negotiation. The patient undergoes a treatment that included a treadmill, a safety belt, and the use of VR with either an LCD screen or an HMD. There was an attachment to the shoes in order to achieve real time, as well as a unit is placed on the head to perceive the rotations in the horizontal

plane. The VR presents a path with obstacles, audio-visual stimuli, various distractions, etc. The results of the present research indicate that the speed and walking length during the dual task are improved. In addition, obstacle negotiation is also improved for patients with moderate disabilities. In single activities on the more affected side no significant change in hip extension was found during the terminal phase. Plantar flexion on the less affected side showed improvement during the pre-swing phase. However, in dual activities a significant increase in both hip and ankle joint strength was observed, while ankle strength also increased.

Ozkul et al. conducted a more extensive investigation of Immersive VR (IVR) effects on balance, mobility and fatigue compared to simple balance exercises (Ozkul et al., 2020). A total of 51 patients with MS were included, and they were divided into three groups: the IVRG, n:17, the balance training group (BTG), n:17 and the control group (CG, n:17). The experimental IVR group underwent a program of 2 p/week for 8 weeks. These are augmented reality applications in rehabilitation and were designed by Silikon Bilisim Company, a company that develops game software. RAGU requires Microsoft's Kinect to analyze the image as well as Oculus VR glasses to provide the three-dimensional (3D) image. Progressively the parameters become more difficult. Finally, there is an audio stimulus during which the patient receives information about the correct or incorrect performance (clap, etc., group with balance training exercises, underwent a program 2 p/week, for 8 weeks, and performed exercises similar to those of the experimental group, and a control group, where they underwent relaxation exercises at home. The patients were evaluated both before the beginning of the programs and at the end, at 8 weeks. The Berg Balance Scale (BBS) was used for the evaluation. The results showed that IVR presented the same, if not similar, results as classical walking training in terms of balance, mobility and fatigue.

An up-to-date study compared the results of a simple conventional rehabilitation and a rehabilitation based on VR at home (tele-rehabilitation) (Pagliari et al., 2021). 70 patients were included and divided into the groups: 35 patients received remote VR therapy for 30 sessions, and 35 patients received conventional home rehabilitation for 30 sessions. In both groups motor and cognitive evaluations were conducted pre-treatment and after 6 weeks after the treatment. The results show that 63.3% of the patients in the experimental group had a significant improvement in the physical domain as well as in their quality of life. In addition, remote VR presented to be significantly superior in terms of balance, postural control, dynamic gait as well as patient compliance to receive and perform the treatment systematically than conventional home rehabilitation.

At Costa et al. case study a combined treatment of tDCS and VR was reported (Costa et al., 2019). The patient was 51 years old and reported muscle weakness in the left lower extremity since the age of 37. He underwent a treatment with tDCS and VR (Nintendo's commercial game). In this clinical case, no statistically significant results were noted regarding the patient's fatigue, balance and quality of life.

A systematic review studied the effectiveness of VR compared to conventional exercise or no intervention, in patients with MS and motor disorders (Nascimento et al., 2021). The parameters covered in this review were functional mobility, fatigue, quality of life and balance. A total of 9 clinical trials published between 2012-2020 were included. The total sample includes 424 participants and was divided into an experimental group, in which patients underwent VR, and a control group, in which patients underwent conventional exercises or no intervention. The results showed that the functional mobility of the patients in

the experimental group had no significant difference compared to the control group. Specifically, the effects of functional mobility were either similar or negligible compared to conventional exercise. In addition, the remaining parameters, those of balance, fatigue and quality of life, showed that VR is equal to or superior to conventional exercises or no intervention, with the possibility of approaching superior improvement. Finally, no additional benefits were found regarding VR in combination or not with conventional exercise, while better methodology and further research are needed.

Table 1: Studies included in the review

Author (s)	Method	Results
Nascimento et al., 2021	VRvsConventional physiotherapy	VR>or equal from conventional or non-intervention to balance/fatigue/p.g VR = or insignificant > in functional mobility Combined VR+ conventional therapy no additional benefits found
Calabro et al., 2017	VR+ robot (Locomat)	Valuable for spasticity/balance/gait/depression/patient compliance Activates different areas of the brain
Russo et al., 2018	VR (robot+Locomat) 2D+ conventional physiotherapy	Gait/balance/mobility/depression is enhanced comparatively superior to simple traditional rehabilitation
Peruzzi et al., 2016	VR + treadmill vs treadmill	VR + treadmill > hip and ankle during gait cycle
Okzul et al., 2020	IVR (HMD +VR) vs conventional balance exercises	Similar results occur. It is recommended to incorporate it into conventional exercises for a holistic treatment
Pagliari et al., 2021	Tele-VRvsconventional physiotherapy	Statistically significant results (VR>) in balance / orthostatic control / gait / compliance
Costa et al., 2019	VR + tDCS	This is an isolated clinical case with no results. However, it is a very promising method.

4. Discussion

The evaluation of the existing literature yielded a total of 7 articles that were included in the review. These articles examined the effects of virtual reality (VR) on fatigue, quality of life, gait, and balance in patients with multiple sclerosis (MS). The majority of the studies (n=5) were clinical trials, while one was a case study and another was a review. Among the clinical trials, three studies compared VR with usual care, one compared it with the use of robotics, and one did not include a control group.

The research conducted by Nascimento et al. and Okzul et al., both involving the use of head-mounted display (HMD) with VR, appear to converge on the conclusion that integrating VR into simple conventional rehabilitation is important. They observed improved results in functional mobility, balance, and other aspects. Calabro et al. concluded that adding the Lokomat device to the treatment process enhances outcomes related to symptoms such as depression, balance, and patient compliance. Russo et al. supported these findings while also emphasizing the integration of VR with simple conventional treatment.

Furthermore, it appears that combining VR therapy with another medium yields better results. Perruzzi et al. found that the combination of VR and treadmill therapy was superior to treadmill therapy alone in terms of the gait cycle. Pagliari et al. highlighted the superiority of tele-rehabilitation with VR compared to standalone VR application in terms of postural control, balance, and other factors. Finally, the research conducted by Costa et al. indicated that the addition of transcranial direct current stimulation (tDCS) resulted in statistically better outcomes.

Overall, these findings suggest that integrating VR into conventional rehabilitation approaches, combining VR with other modalities, and utilizing tele-rehabilitation with VR can lead to improved outcomes in terms of fatigue, quality of life, gait, balance, and patient compliance in individuals with MS.

5. Conclusion

In conclusion, the integration of VR alongside conventional balance exercises has demonstrated a significant improvement in balance. The inclusion of VR in the therapeutic approach offers a more comprehensive outcome. Moreover, tele-rehabilitation utilizing VR has proven to be notably superior to conventional rehabilitation in terms of balance, postural control, gait, and compliance. When considering patients with MS, remote treatment provides numerous additional benefits. Patients have the ability to tailor their treatment schedule, taking into account the fluctuating effects of the disease throughout the day, under the guidance of their healthcare professional. Furthermore, receiving treatment in a familiar and supportive environment alleviates the patient's emotional burden and promotes comfort, tranquility, and compliance. Overall, this method of treatment ensures an enhanced experience for patients, yielding positive outcomes in their rehabilitation journey.

Future research in the field of VR for patients with MS should build upon the existing literature to further explore the potential benefits and optimize the application of VR in clinical practice. Firstly, there is a need for more randomized controlled trials comparing VR interventions with standard care or other rehabilitation modalities, in order to establish the effectiveness of VR across various outcomes such as fatigue, quality of life, gait, and balance. Additionally, future

studies should investigate the long-term effects of VR interventions and determine the optimal duration, frequency, and intensity of VR sessions to maximize therapeutic benefits. Moreover, the inclusion of larger sample sizes and diverse patient populations would enhance the generalizability of the findings. Finally, exploring the cost-effectiveness of implementing VR technology in clinical settings and addressing potential barriers to widespread adoption are important considerations for future research. By addressing these research gaps, we can further advance our understanding of the potential of VR as an innovative and effective therapeutic tool for individuals with MS.

Conflict of interest

The authors declare no conflict of interest

References

- [1] Baird JF, Sandroff BM, Motl RW. Therapies for mobility disability in persons with multiple sclerosis. *Expert Rev Neurother.* 2018 Jun;18(6):493-502. doi: 10.1080/14737175.2018.1478289. Epub 2018 May 30. PMID: 29772185; PMCID: PMC6291756
- [2] Calabrò, R. S., Russo, M., Naro, A., de Luca, R., Leo, A., Tomasello, P., Molonia, F., Dattola, V., Bramanti, A., & Bramanti, P. (2017). Robotic gait training in multiple sclerosis rehabilitation: Can virtual reality make the difference? Findings from a randomized controlled trial. *Journal of the Neurological Sciences*, 377, 25–30. <https://doi.org/10.1016/J.JNS.2017.03.047>
- [3] Casuso-Holgado MJ, Martín-Valero R, Carazo AF, Medrano-Sánchez EM, Cortés-Vega MD, Montero-Bancalero FJ. Effectiveness of virtual reality training for balance and gait rehabilitation in people with multiple sclerosis: a systematic review and meta-analysis. *Clin Rehabil.* 2018 Sep;32(9):1220-1234.
- [4] Costa, G. C., Kunitake, A. I., Fonseca Junior, P. R., Ledur, Â. C., Elord Júlio, C., Pereira, G. S., Corrêa, J. C. F., & Correa, F. I. (2019). Effect of transcranial direct current stimulation combined with a virtual reality exercise on balance in a patient with multiple sclerosis: a case report: <https://doi.org/10.1177/1059712319873912>, 28(4), 307–313. <https://doi.org/10.1177/1059712319873912>
- [5] Moher d, Liberati A, Tetzlaff J, Altman G. (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ.* 2009; 339: b2535.
- [6] Moreno-Verdu M, Ferreira-Sanchez MR, Cano-de-la-Cuerda R, Jimenez-Antona C. Eficacia de la realidad virtual sobre el equilibrio y la marcha en esclerosis múltiple. *Revision sistematica de ensayos controlados aleatorizados [Efficacy of virtual reality on balance and gait in multiple sclerosis. Systematic review of randomized controlled trials].* *Rev Neurol.* 2019 May 1;68(9):357-368. Spanish.
- [7] Nascimento, A. S., Fagundes, C. V., Mendes, F. A. dos S., & Leal, J. C. (2021). Effectiveness of Virtual Reality Rehabilitation in Persons with Multiple Sclerosis: A Systematic Review and Meta-analysis of Randomized Controlled Trials. *Multiple Sclerosis and Related Disorders*, 54, 103128. <https://doi.org/10.1016/J.JMSARD.2021.103128>
- [8] Ozkul, C., Guclu-Gunduz, A., Yazici, G., Atalay Guzel, N., & Irkeç, C. (2020). Effect of immersive virtual reality on balance, mobility, and fatigue in patients with multiple sclerosis: A single-blinded randomized controlled trial. *European Journal of Integrative Medicine*, 35, 101092. <https://doi.org/10.1016/J.EUJIM.2020.101092>
- [9] Pagliari, C., di Tella, S., Jonsdottir, J., Mendozzi, L., Rovaris, M., de Icco, R., Milanese, T., Federico, S., Agostini, M., Goffredo, M., Pellicciari, L., Franceschini, M., Cimino, V., Bramanti, P., & Baglio, F. (2021). Effects of home-based virtual reality telerehabilitation system in people with multiple sclerosis: A randomized controlled trial: <https://doi.org/10.1177/1357633X211054839>. <https://doi.org/10.1177/1357633X211054839>
- [10] Peruzzi, A., Cereatti, A., della Croce, U., & Mirelman, A. (2016). Effects of a virtual reality and treadmill training on gait of subjects with multiple sclerosis: a pilot study. *Multiple Sclerosis and Related Disorders*, 5, 91–96. <https://doi.org/10.1016/J.JMSARD.2015.11.002>
- [11] Russo, M., Dattola, V., de Cola, M. C., Logiudice, A. L., Porcari, B., Cannavò, A., Sciarrone, F., de Luca, R., Molonia, F., Sessa, E., Bramanti, P., & Calabrò, R. S. (2018). The role of robotic gait training coupled with virtual reality in boosting the rehabilitative outcomes in patients with multiple sclerosis. *International Journal of Rehabilitation Research*, 41(2), 166–172. <https://doi.org/10.1097/MRR.0000000000000270>