Virtual reality in multiple sclerosis – A systematic review

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ABSTRACT

Introduction: Multiple sclerosis (MS) is an inflammatory disease in which the insulating cover of nerve cells in the brain and spinal cord are damaged. The methods used for motor rehabilitation of patients with neurological problems require the performance of several rehabilitation exercises. Recently, studies related to the use of video game consoles have proliferated in the field of motor rehabilitation. Virtual reality (VR) has been proposed as a potentially useful tool for motor assessment and rehabilitation.

Objective: The purpose of this study was to investigate the results shown in previous studies on “Multiple Sclerosis” and “Virtual Reality”.

Method: A bibliographic review was performed without time limitations. The research was carried out using PubMed and BVS databases. Considering keywords, we included articles that showed the terms “Multiple Sclerosis” and “Virtual Reality”. The review was according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines

Results: The initial search yielded 41 articles. After the duplicates were removed, two authors independently evaluated the title and abstract of each of the articles with the study inclusion criteria. From these, 31 articles were excluded based on the title and abstract. Finally, 10 articles were isolated that met the inclusion criteria.

Conclusion: VR represents a motivational and effective alternative to traditional motor rehabilitation for MS patients. The results showed that VR programs could be an effective method of patients with MS rehabilitation in multiple cognitive and / or motor deficits. Additional research is needed to support the rehabilitation protocols with VR and increase the effects of treatment.

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1. Introduction

Multiple sclerosis (MS) is an inflammatory disease in which the insulating cover of nerve cells in the brain and spinal cord are damaged (Lozano-Quilis et al., 2014). At present, approximately 3 million people suffer from MS in the world; the disease begins between the ages of 20 and 50, and it is twice as common in women as in men (Leocani et al., 2007; Lozano-Quilis et al., 2014). There is no known cure for MS, but there are several therapies focused on improving functioning after an attack, preventing new attacks, and preventing disability (Turekca et al., 2014). Therapies, including medication and neurorehabilitation, improve some symptoms, but cannot change the development of the disease (Lozano-Quilis et al., 2014).

The progressive nature of MS is highly variable and can cause deterioration in physical capabilities requiring human and/or technological assistance to patients performing activities of daily living (Mahajan et al., 2014). Many neurological diseases sequelae are treated on an outpatient basis in hospitals and specialized centers (Ortiz-Gutierrez et al., 2013). In addition, most patients with MS have difficulties related to mobility, geographical location, or both, which prevent them from receiving treatment at a rehabilitation center. Therefore, there is an increasing interest in the development of health projects for the rehabilitation of MS patients (Ortiz-Gutierrez et al., 2013).

The methods used in motor rehabilitation for patients with neurological problems require the performance of several rehabilitation exercises. These methods present two important problems. Firstly, the motor skills exercises are proposed in an insistent and repetitive way, which is not motivating and decreases the patient’s interest in performing them, thus affecting their treatment adherence. Secondly, these methods require the patients to be at specific centers under the supervision of qualified professionals to ensure correct performance (Lozano-Quilis et al., 2014).

Taking into account those difficulties, there has been an increased number of studies using video game consoles in the motor rehabilitation field (Ortiz-Gutierrez et al., 2013). Virtual reality (VR) has been proposed as a potentially useful tool in motor assessment and rehabilitation (Leocani et al., 2007), as VR-based training provides repetitive practice, feedback information and motivation for endurance practice, and could promote visual, auditory and tactile input, and motor learning (Laver et al., 2011; Lehrer et al., 2011).

Considering the above deliberations, the purpose of this study is to investigate the results shown in previous studies about VR used in MS. The presentation of existing knowledge about the technological modernity provoked by VR tasks in MS will aid in the organization of treatment programs and benefits for the functional improvement of patients.

2. Methods

This review was based on a systematic search conducted in April 2015 of published articles available on PubMed (Medline) and Virtual Health Library Search Portal databases (BVS). The review was according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Hutton et al., 2015). The use of checklists, e.g. PRISMA, improves the reporting quality of systematic reviews and provides substantial transparency in the article selection process (Knobloch et al., 2011; Panic et al., 2013). The search occurred using the keywords “Multiple Sclerosis” AND “Virtual Reality”.

To select the articles, we used three steps. The first step was looking for articles in databases, and reading the titles and abstracts. The second step was the exclusion of works using the title or abstract, and inclusion criteria analysis. The third and final step was to analyze the full-text of the eligible works (Massetti et al., 2014; Menezes et al., 2015) (Fig. 1).

2.1. Study selection

Studies published in English were eligible if they met the following criteria: (1) Study population with a diagnosis of MS, and (2) VR analysis in this population. There were no restrictions regarding sample size. Articles were excluded if they: (1) were not databased (e.g. books, theoretical papers, or secondary reviews), (2) were not in the English language, (3) used populations not explicitly identified with an MS diagnosis, or (4) did not include a VR analysis. We planned to pool statistical data from quantitative studies within meta-analyses.

After the removal of duplicates, three authors evaluated titles, abstracts and the inclusion criteria independently. All identified studies were collected in EndNote Web (Thomson Reuters).

3. Results

Initially, the search identified 41 articles. Then, 30 articles were kept after exclusion of duplicates, and the remaining 30 articles were analyzed.
excluded by title and abstract. Finally, 10 articles met the inclusion criteria (Fig. 2).

Flowchart of selected articles adapted from (Moher et al., 2010). The 10 eligible studies in this review are summarized in Table 1 regarding sample, intervention and VR description. Table 2 presents the main outcomes. A range of outcome measures were used and, consequently, we were unable to pool data within meta-analyses.

4. Discussion

Neurorehabilitation programs are one of the most popular therapies aimed at reducing disabilities and social disadvantages resulting from MS (Ortiz-Gutierrez et al., 2013). The performance of motor rehabilitation exercises in the rehabilitation process is important to patients with MS, even more so if the patients still have satisfactory motor skills (Mahajan et al., 2014). MS patients could begin a rehabilitation process through virtual rehabilitation exercises using games with easy and intuitive interaction (i.e., using Natural User Interfaces (NUI) that are similar to the ones in game consoles) (Lozano-Quilis et al., 2014).

VR technology can provide an interactive environment for the assessment and training of motor abilities (Leocani et al., 2007). VR is an innovative tool for the disabled population and has also been studied in other populations, such as those with Cerebral Palsy (Baram and Lenger, 2012; Barton et al., 2013; de Mello Monteiro et al., 2014), Parkinson’s Disease (Baram et al., 2002; dos Santos Mendes et al., 2012; Pompeu et al., 2012), Down syndrome (Berg et al., 2012; Courbois et al., 2013), Stroke (Baram et al., 2010; Doud et al., 2013) and Autism (Kandalaft et al., 2013; Mitchell et al., 2007). In addition, different types of VR have been used in studies, e.g. Xbox 360® and Kinect (Ortiz-Gutierrez et al., 2013), Xbox 360® (Gutierrez et al., 2013) or even authors’ own Software (Leocani et al., 2007).

Results from the selected studies in this review showed that VR interventions in MS patients improved arm movement and control (Sampson et al., 2015), balance (Eftekharsadat et al., 2015) and walking abilities (Baram and Miller, 2006). The results also showed that VR interventions optimized sensory information processing and integration systems (Ortiz-Gutierrez et al., 2013), enabling anticipatory postural control and response mechanisms (Gutierrez et al., 2013), and improving gait parameters (Baram and Miller, 2010; Fulk, 2005). The authors suggested that VR interventions might serve as a successful therapeutic alternative (Gutierrez et al., 2013; Ortiz-Gutierrez et al., 2013) and as a motivational and effective alternative to traditional motor rehabilitation (Lozano-Quilis et al., 2014). Moreover, VR was an effective input interface for wheelchairs (Mahajan et al., 2014).

Sampson et al. (2015) demonstrated the feasibility of using advanced control approaches combined with Functional Electrical Stimulation (FES) and robotic support to improve arm movement for people with MS. There was excellent MS patient adherence to the intervention, and no side effects were reported. The intervention resulted in improvements in reaching accuracy with and without FES and reduced impairment in the proximal arm. The development of these technologies will allow increased rehabilitation intensity with minimal therapist mediation. The resulting improvements and positive feedback of all study participants regarding improved arm movement and control should not be ignored (Sampson et al., 2015).

In Eftekharsadat et al. (2015), MS patients underwent VR-based training using the Biodex Balance System SD and presented significant improvements in balance and fall risk. In VR-based
<table>
<thead>
<tr>
<th>Citation</th>
<th>Sample</th>
<th>Experimental/Control intervention</th>
<th>Frequency, duration of intervention</th>
<th>VR description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sampson et al. (2015)</td>
<td>Five people with MS</td>
<td>The system assists patients in following a specified trajectory path, employing an advanced model-based paradigm termed ILC to adjust the FES to improve accuracy and maximize voluntary effort. Reaching tasks were repeated six times with ILC learning the optimum control action from previous attempts</td>
<td>Eighteen one-hour training sessions over 10 weeks</td>
<td>Stimulation Assisted by Iterative Learning system (FES hardware, a VR task display, and a graphical user interface)</td>
</tr>
<tr>
<td>Eftekharsadat et al. (2015)</td>
<td>Thirty patients with relapsing-remitting or secondary-progressive MS</td>
<td>The intervention of two sessions per week consisted of a balance training program (postural stability training program) using the Biodex Balance System SD</td>
<td>At baseline and after 12 weeks</td>
<td>Biodex Balance System SD</td>
</tr>
<tr>
<td>Mahajan et al. (2014)</td>
<td>Eleven participants with MS</td>
<td>During each visit, subjects performed virtual wheelchair driving trials using the joystick mode they were assigned and two algorithms. During every visit, participants first used the standard algorithm followed by either of the two specialized algorithms: MSPFA or MSPFA, FA</td>
<td>Two visits were scheduled at least two days and no more than 10 days apart</td>
<td>Joystick-tuning software</td>
</tr>
<tr>
<td>Lozano-Quilis et al. (2014)</td>
<td>Eleven patients with MS</td>
<td>The control group (n=5) performed standard balance and gait rehabilitation exercises. The patients belonging to the experimental group (n=6) spent 45 min performing the same exercises, and during the last 15 min of the session, they performed the virtual rehabilitation exercises</td>
<td>Ten one-hour sessions of rehabilitation, completed once per week.</td>
<td>Kinect-Software RevoEM has three motor rehabilitation exercises: TouchBall, TakeBall, and StepBall</td>
</tr>
<tr>
<td>Ortiz-Gutierrez et al. (2013)</td>
<td>Fifty patients with MS</td>
<td>The control group (n=25) received physiotherapy treatment 2x/week (40 min per session). The experimental group (n=25) received monitored telerehabilitation treatment via videconference (40 sessions, 4x/week, 20 min per session)</td>
<td>Ten weeks for both groups. Evaluation at baseline and at the end of the treatment protocol</td>
<td>Xbox 360&lt;sup&gt;®&lt;/sup&gt; and Kinect</td>
</tr>
<tr>
<td>Gutierrez et al. (2013)</td>
<td>Fifty patients with MS</td>
<td>The control group (n=25) received physiotherapy treatment twice a week (40 min per session). The experimental group (n=25) received telerehabilitation treatment using the Xbox 360&lt;sup&gt;®&lt;/sup&gt; console monitored via videconference. (40 sessions, four sessions per week, 20 min per session)</td>
<td>Ten weeks for both groups</td>
<td>Xbox 360&lt;sup&gt;®&lt;/sup&gt;</td>
</tr>
<tr>
<td>Baram and Miller (2010)</td>
<td>Twenty-one patients with MS</td>
<td>Ten patients trained with transverse lines while 11 trained with checkerboard tiles, both provided by a wearable VR device</td>
<td>Baseline performance was measured before device use. Following 20 min training with the device and 10 min rest, performance without the device was measured again and compared to the baseline performance</td>
<td>Closed-loop augmented reality apparatus</td>
</tr>
<tr>
<td>Leocani et al. (2007)</td>
<td>Twenty-four patients with MS</td>
<td>Twelve right-handed MS patients and 12 control individuals performed a motor-tracking task with their right upper limb, following the trajectory of an object projected on a screen along with online visual feedback on hand position from a sensor on the index finger</td>
<td>Pre- and post- 12-trials training test</td>
<td>Software Khymeia SRL (Padova, Italy)</td>
</tr>
<tr>
<td>Baram and Miller (2006)</td>
<td>Sixteen randomly selected MS patients with gait disturbances predominantly due to cerebellar ataxia.</td>
<td>On-line (display-on) and residual short-term therapeutic effects on walking speed and stride length. Examination consisted of the patient walking a straight track of 10 m: baseline, online display off, online display on, and residual effects</td>
<td>One evaluation of four stages</td>
<td>Portable visual-feedback VR apparatus: a closed-loop, head-mounted device</td>
</tr>
<tr>
<td>Fulk (2005)</td>
<td>A 48-year-old female with a 10-year history of MS.</td>
<td>Locomotor training using both a BWS with TM and overground walking as well as a VR-based balance intervention</td>
<td>Two days a week for 12 weeks; two-month follow-up overground and VR-based balance</td>
<td>BWS/TM system and overground and VR-based balance</td>
</tr>
</tbody>
</table>

MSPPAs: MS personally fitted algorithms; MSPFA, FAs: MSPFAs with fatigue adaptation; FES: Functional electrical stimulation; BWS: body weight support; TM: treadmill; VR: virtual reality; ILC: iterative learning control; MS: Multiple Sclerosis.
balance training performance, there was no need for stabilized posture control, which reduces the rehabilitation difficulty and increases exercise safety. According to the findings, VR-based balance training programs seem to be effective and successful at improving balance performance in patients with MS according to the results of the fall risk and postural stability tests (Eftekharsadat et al., 2015).

The results from Baram and Miller (2006) indicate that it is possible to use VR cues superimposed on the real world in a closed-loop fashion to help patients with MS in gait control. The on-line and residual improvement was inversely related to baseline walking speed and stride length. These performance improvements seem particularly noteworthy compared to the control results, in which there was no meaningful improvement. The authors suggest that the findings regarding residual improvement are particularly encouraging: average short-term residual therapeutic improvement in walking speed was 24.49% in patients with baseline walking speed below the median and 9.09% in patients above the median (Baram and Miller, 2006).

Ortiz-Gutierrez et al. (2013) and Gutierrez et al. (2013) demonstrated that a telerehabilitation program based on a VR system allows MS patients to optimize the sensory information processing and integration systems necessary to maintain the balance and postural control of people with MS. Ortiz-Gutierrez et al. (2013) A telerehabilitation program based on a VR system allows one to optimize the sensory information processing and integration systems necessary to maintain the balance and postural control of people with MS.

The reviewed studies demonstrated satisfactory results using VR technology in these requirements, showing that VR can be a favorable method of motor learning in the MS population. A telehealth program based on a VR system allows one to optimize the sensory information processing and integration systems necessary to maintain the balance and postural control of people with MS.

### Table 2.
<table>
<thead>
<tr>
<th>Citation</th>
<th>Outcome measure(s)</th>
</tr>
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<tbody>
<tr>
<td>Sampson et al. (2015)</td>
<td>Improved accuracy of tracking performance both when assisted and unassisted by FES; reduction in maximum amount of FES needed to assist tracking; and less impairment in the proximal arm that was trained. The system was well tolerated by all participants with no increase in muscle fatigue reported. FES combined with passive robot assistance is viable as a potentially effective intervention to improve arm movement and control in pwMS and provides the basis for a follow-up study.</td>
</tr>
<tr>
<td>Eftekharsadat et al. (2015)</td>
<td>The TUG, FRI, and OSI were improved in the intervention group after 24 sessions of balance training. The changes in TUG, FRI, and OSI indices in the intervention group were higher than the control group. The VR-based balance training program could improve the balance ability of the patients with MS.</td>
</tr>
<tr>
<td>Mahajan et al. (2014)</td>
<td>Participants with MS showed better driving performance metrics while using the customized algorithms than while using the standard algorithm with the VCJ. Fatigue adaptation algorithms are especially beneficial in improving overall task performance while using the VCJ in isometric mode. The VCJ, along with the personally fitted algorithms and fatigue adaptation algorithms, has the potential to be an effective input interface for wheelchairs.</td>
</tr>
<tr>
<td>Lozano-Quilis et al. (2014)</td>
<td>The results obtained suggest that RemovEM represents a motivational and effective alternative to traditional motor rehabilitation for MS patients.</td>
</tr>
<tr>
<td>Ortiz-Gutierrez et al. (2013)</td>
<td>A telerehabilitation program based on a VR system allows one to optimize the sensory information processing and integration systems necessary to maintain the balance and postural control of people with MS.</td>
</tr>
<tr>
<td>Turekca et al. (2014)</td>
<td>HC’s driving speed varied more during the undistracted vs. distracted driving segment. Driving speed was not associated with any cognitive or physical measures. MS participants’ CL deviations were associated with fine motor movement during undistracted and distracted driving. In contrast, HC’s CL deviations were associated with working memory during undistracted and distracted driving. Fatigue severity was associated with undistracted driving in the MS group. Driving performance of MS individuals was affected by physical symptoms, and cognitive symptoms played a more important role in HC. In MS individuals, fatigue may be the moderating factor between driving and cognition.</td>
</tr>
<tr>
<td>Gutierrez et al. (2013)</td>
<td>The VR program enables anticipatory PC and response mechanisms and might serve as a successful therapeutic alternative in situations in which conventional therapy is not readily available.</td>
</tr>
<tr>
<td>Baram and Miller (2010)</td>
<td>Patients with gait disorders due to MS, training with a glide-symmetric visual feedback cue, showed a significantly higher improvement in their gait parameters than patients training with a visual feedback cue without distinct symmetry. Both groups performed worse in depth planes compared to the frontal plane. MS patients performed worse than control individuals in the frontal plane at both evaluations, whereas they had lower percent post training improvement in the depth planes only. The authors’ VR system detected impaired motor learning in MS patients, especially for task features requiring a complex integration of sensory information (movement in the depth planes).</td>
</tr>
<tr>
<td>Leocani et al. (2007)</td>
<td>Patients whose baseline walking speed was below the median showed an average on-line improvement of 13.46% in their walking speed, while patients whose baseline walking speed was above the median improved their speed by 1.47%. The average short-term residual therapeutic improvement in walking speed was 24.49% in patients with baseline walking speed below the median, and 9.09% in patients with BWS above the median. Similar results were obtained for improvements in stride length. Patients with MS showed improvements in walking abilities using VR visual-feedback cues.</td>
</tr>
<tr>
<td>Fulk (2005)</td>
<td>The client demonstrated improvements in gait speed, gait endurance, and balance post-intervention and maintained the improvements at a two-month follow-up. This case report is the first on the use of locomotor training with BWS/TM system and overground and VR-based balance interventions for a client with MS.</td>
</tr>
</tbody>
</table>

FES: Functional electrical stimulation; OSI: overall stability index; TUG: timed ‘up and go’; FRI: fall risk index; VCJ: variable compliance joystick; HC: healthy controls; CL: Center lane; PC: postural control; TR: telerehabilitation; VR: Virtual Reality; BWS: body weight support; TM: treadmill; MS: Multiple Sclerosis.
successful alternative in the MS rehabilitation process. This was also demonstrated in studies that used VR combined with other technology.

Considering some limitations, such as small sample size and no control group, the results must be carefully interpreted and further studies are needed. Factors associated with VR, such as excessive fatigue, game difficulty level, high physical requirements, spasticity and sensory loss, were cited by the reviewed studies. These factors should be evaluated in an effective treatment by experts in the rehabilitation exercise process and should be clinically evaluated.

Some technologies present bias relative to the cost and analysis of the evaluation strategy. The results showed promising results by using VR in rehabilitation, but follow-up studies are needed to enhance treatment effects in patients with MS.

5. Conclusion

VR represents a motivational and effective alternative to traditional motor rehabilitation for MS patients. The results showed that VR programs could be an effective method of MS rehabilitation in multiple cognitive and/or motor deficits. Additional research is needed to support the rehabilitation protocols with VR and increase the effects of treatment.

Authors’ contributions

All authors participated in the acquisition of data and revision of the manuscript. All authors determined the design, interpreted the data and drafted the manuscript. All authors read and gave final approval for the version submitted for publication.

Declaration of interest

The authors report no conflict of interest. All authors were responsible for the content and writing of this paper.

References