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Can a virtual reality-based rehabilitation program have a positive impact on the quality of life of adults with Multiple Sclerosis (MS)?

Megan Leise, PA-S

A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree Of Master of Science

In

Health Sciences – Physician Assistant

Department of Physician Assistant Studies
Philadelphia College of Osteopathic Medicine

Philadelphia, Pennsylvania

December 15, 2017
Abstract

OBJECTIVE: The objective of this selective EBM review is to determine whether or not virtual reality based rehabilitation programs have a positive impact on the quality of life of people with MS.

STUDY DESIGN: Review of 2 randomized control trials (RCTs) and one randomized control cross over pilot study written in English, two of which were published in 2013 and one in 2016.

DATA SOURCES: Two randomized control trials (RCTs) and one randomized control cross over pilot study, all three non-blind, published in peer-reviewed journals found via PubMed.

OUTCOME MEASURED: Quality of life was measured via Falls Efficacy Scale- International, Modified Fatigue Impact Scale, and MS Impact Scale- 29 (MSIS-29).

RESULTS: All three studies showed a significant improvement quality of life in MS patients with virtual reality based training compared to conventional therapy or no physical therapy.

CONCLUSION: All three studies showed that there was an increase in the quality of life in patients with MS with use of VR based training. However, further studies with larger sample sizes that examine a uniform specialized MS VR program will be needed to reinforce the conclusion that virtual reality based training is effective in improving quality of life in adults with MS.

KEY WORDS: Virtual reality, Multiple Sclerosis, rehabilitation, Wii, video game
INTRODUCTION

Multiple Sclerosis (MS) is a frustrating and devastating disease that negatively impacts one’s quality of life. MS, the most prevalent type of demyelinating disorder, is an autoimmune condition that primarily affects the central nervous system. Patients must deal with physical, emotional, and psychological obstacles as the disease progresses. MS is a chronic disease process that requires multiple management methods to deal with the aforementioned issues.

This topic is relevant to patients and the physician assistant (PA) practice. A patient’s quality of life is one of the most important aspects to patients and their health care providers. Optimizing quality of life is always one of the primary goals of any disease management. PAs will come across MS patients whether working in psychology, neurology, radiology, physical therapy, emergency medicine, family medicine, urology, and other areas of internal medicine. Therefore, management affecting the quality of life of MS patients is a very relevant topic in the PA profession.

The annual cost for the treatment and management of MS is 11,540.92 ±2701.08 € which equals about $13,559.43 ±3,173.50. Cost is only second to congestive heart failure. Because the disease is chronic, this annual cost will likely increase as a patient develops other comorbid conditions associated with aging. The amount of healthcare visits each year depends on the patient and their course of disease. Depending on numbers of relapses, an increased amount of visits to the emergency room or primary care office will have to occur. Additionally, some patients may see a neurologist every 6 months, a nutritionist every 6 months, physical therapist twice a week, urologist every year, psychiatrist once a week, etc. The number of specialists and visits varies per patient, but nonetheless, the list of medical visits is often lengthy.
The underlying cause of MS is not fully understood. However, cigarette smoking, vitamin D deficiency, history of EBV exposure after childhood is said to increase one’s risk of developing MS. Females and Caucasians are also known to be at a higher risk. There are known to be 4 different courses: relapsing/remitting (the most common), secondary progressive, primary progressive, and progressive/relapsing. Magnetic resonance imaging (MRI) is known to be the best tool for diagnosing and assessing the management of MS. Residual deficits from acute exacerbations of MS generally cannot be predicted.

Goal of MS treatment is mainly to prevent relapses. For acute episodes or relapses, methylprednisolone 1 mg IV for 2-3 days followed by prednisone 60-80 mg PO for one week is standard treatment. For relapse prevention and first line treatment, the options include: interferon beta-1a 40 mcg subcutaneous three times a week or intramuscularly once a week, glatiramer acetate, Fingolimod, teriflunomide, or dimethyl fumarate. Other relapse preventing methods to add to first line treatment include natalizumab, mitoxantrone, and alemtuzumab. Plasmaphoresis is used in patients who relapse is refractory to corticosteroid use.

Symptoms experienced by MS patients include muscle spasms and spasticity, decreased mobility and strength, ataxia, tremor, balance issues, fatigue, bladder dysfunction, sexual dysfunction, cognitive impairment, and pain. Therefore, symptomatic treatment is very important for these patients. There are numerous pharmacologic and non-pharmacologic options for each symptom. Choosing the different treatment methods varies for each patient and depends on interactions with the other medications they are taking. This reinforces why a healthcare team, rather than an individual healthcare provider, is necessary for each MS patient.

The symptomatic treatment of these patients can easily lead to a myriad of medications and pharmacy bills. For fatigue, modafinil, amantadine, or cognitive behavioral therapy may be
Antimuscarinic drugs are often prescribed for bladder dysfunction management. For neuropathic pain, first line options include pregabalin, gabapentin, and amitriptyline. Other options include tramadol, opioids, cannabinoids. Treatment of depression maybe warranted as well with an antipsychotic or antidepressant medication. Drugs can also be utilized to improve ataxia, balance issues, muscle strength and mobility. For example, baclofen or gabapentin are used for spasticity and muscle spasm management. Dalfampridine can be administered to help coordination and steady one’s gait. Physical therapy, occupational therapy, and speech therapy are non-pharmacological modes of MS management that help with these symptoms. Similar to these physical modalities of therapy, virtual reality (VR) will aid in the management of MS without needing to add yet another drug to their regimen.

Unfortunately, patients are not always compliant with pharmacological or physical therapy treatments. For physical therapy especially, patients may attend a few sessions but later discontinue therapy. MS being a chronic disease, management modalities, especially physical therapy, can be very disheartening when improvements are not seen right away or the therapy is difficult. Because of reasons like these, usage of VR based training in the treatment of MS has been proposed. Introducing VR based training may increase consistency and continuing of treatment by providing a more interesting and fun method. VR modalities also stimulate real life movements and scenarios, which will translate to everyday life. That way, even if the activities are difficult, patients will be encouraged to continue therapy. Also, if the therapy mirrors everyday activities, patients can become more confident when performing activities outside of therapy.

OBJECTIVE
The objective of this selective EBM review is to determine whether or not virtual reality based rehabilitation programs have a positive impact on quality of life of people with MS.

SEARCH STRATEGY

METHODS

The population included in each study was adults with Multiple Sclerosis. VR based activities were utilized in treatment for experimental groups. In two of the studies, the Nintendo Wii Balance Board was the VR mode for the experimental group. In the remaining study Computer Assisted Rehabilitation Environment (CAREN) system was implemented.

The types of studies included are 2 randomized control trials and one randomized controlled crossover pilot study. The demographics of each study are described in Table 1. Conventional balance and physical therapy exercises were prescribed to the control group in the 2 randomized control trials. The remaining study controlled crossover pilot study compared VR to a 12-week period of no specific treatment or physical therapy plan. Different questionnaires measuring quality of life were used to measure outcomes in each study.

The studies examined were collected from *Neurorehabilitation and Neural Repair* (2013), *Multiple Sclerosis Journal* (2013), and *Journal of Neuroengineering and Rehabilitation* (2016). To find these articles, key words such as, virtual reality, treatment, Multiple sclerosis, Wii, and video game, were used on PubMed search engine. Each article includes published data and was published in English. Articles were selected based on similar subject demographics as well as similar analysis strategies of VR based training on the quality of life of MS patients. Articles were selected through PubMed searches from accredited journal articles published within the past 5 years.

The inclusion criteria were studies published from 2013-2018 with subjects that were 18 years or older with a relapsing- remitting or secondary progressive multiple sclerosis (MS)
course. Each study had to have a control group that either refrained from a special exercise-training program or completed traditional physical therapy exercise. The studies also needed to include an experimental group that implemented a virtual reality based exercise-training program to compare to the control. The outcome compared between groups had to measure the effect of the exercise program on the quality of life of the subjects.

Exclusion criteria were studies published prior to 2013 that subjects under 18 and utilized physical therapy techniques without incorporation of virtual reality or video games. Studies that did not assess the treatment’s effect on quality of life were excluded from searches.

Table 1: Demographics and Criteria for all three studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th>Number of Patients</th>
<th>Age (yrs)</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
<th>Withdraw</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prosperini</td>
<td>Randomized Controlled Crossover Pilot Study</td>
<td>36</td>
<td>26.7-45.9</td>
<td>18 or older, Relapsing- remitting or secondary progressive MS course, Expanded Disability Status Scale (EDSS) score less than or equal to 5.5, Able to walk without resting for 100 meters, Have ataxia, inability to walk in a straight line, positive Romberg test, Willingness to not change or start new medication during study</td>
<td>Use of a device for assistance or foot ankle orthosis, Relapse within the past 6 months, Inception of new treatment within the past 3 months, Presence of seizures, blurred vision, Vestibular disease (non-MS related), Cardiovascular or respiratory disease, Psychiatric disease, Cognitive impairment</td>
<td>2</td>
<td>12 weeks of daily sessions of home- based training with Wii Balance Board system</td>
</tr>
<tr>
<td>Brichtto</td>
<td>Randomized Control Trial</td>
<td>36</td>
<td>28.8-53.8</td>
<td>Adult with MS without relapse/ worsening of disease in past 3 months, Able to walk without aid of cane or crutch, EDSS less than or equal to 6, Ambulation Index less than or equal to 4</td>
<td>Psychiatric disorders, blurred vision, severe cognitive impairment</td>
<td>0</td>
<td>60 minutes of Nintendo Wii balance board for 3 x week for 4 weeks</td>
</tr>
<tr>
<td>Kalron</td>
<td>Randomized Control Trial</td>
<td>33</td>
<td>33.3-56.6</td>
<td>Adult with diagnosis of relapsing-remitting and MS, Score between 3-6 on expanded disability status scale indicating moderate neurological disability</td>
<td>Relapse of corticosteroid treatment within the past 6 months, Severed depression or deficit in cognition, Orthopedic issues affecting balance,</td>
<td>2</td>
<td>30 minute sessions with CAREN system for 2 x week for 6 weeks</td>
</tr>
</tbody>
</table>
OUTCOMES MEASURED

An outcome measured in all three studies was quality of life.

RESULTS

Two of the studies are randomized control experiments and one is a randomized controlled crossover pilot study, all of which assess the effects of VR based training on the quality of life in patients with MS. All patients included in the studies were men and women over 18 years old with MS. The two randomized control studies compared an experimental group using VR based training to a control group using conventional physical therapy treatment. The randomized controlled crossover pilot study included patients who completed a trial of virtual reality based training and period of observation. All three studies used change in mean from baseline, ANOVA F score, and/or t-test for independent samples for continuous data.

In the study by Prosperini et al., 36 adults with MS were randomly divided into two groups, Group A and Group B. All patients performed various tests at baseline (T0) including a MSIS-29 questionnaire. The MSIS-29 questionnaire included 29 questions aimed to assess the mental and physical impact of MS on the daily life of the patient from their perspective. The MSIS-29 was readministered after week 12 (T1) and week 24 (T2) of the study. For the first 12 weeks of the study, Group A completed daily 30 minute session of home-based therapy using the Nintendo Wii Balance Board while Group B was observed, receiving no specific intervention. During the second 12 weeks of the study, Group B completed home based VR therapy while Group A received no intervention. No time effect in either groups’ MSIS-29 score was seen. However a significant time by treatment interaction effect was seen (F=4.282, p=0.023). This demonstrated significant between group differences over time in subjective improvement in
quality of life with use of Wii Balance Board training. Regardless of the order in intervention, both groups showed improvements in MSIS-29 score at T2 compared to T0.

Twenty-four of the subjects reported at least one adverse event during the course of the study. Five of these reports were said to be due to the Wii Balance Board system, most commonly after the initial introduction of the high level and more difficult programs. Only one subject needed technical assistance in the set up of the Wii system. Five subjects reported low back or knee pain during the course of the intervention. Lastly, one subject from each group withdrew from the study, resulting in 17 subjects in each group to be analyzed.

Table 2. Group descriptions and results of Prosperini et al

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Change, T1-T0, Mean (SD)</td>
<td>-12% (27)</td>
<td>+2% (15)</td>
</tr>
<tr>
<td>% Change, T2-T0, Mean (SD)</td>
<td>-2% (15)</td>
<td>-10% (22)</td>
</tr>
<tr>
<td>Time Effect</td>
<td></td>
<td>F=0.668, p=0.520</td>
</tr>
<tr>
<td>Time x treatment effect</td>
<td></td>
<td>F=4.282, p=0.023</td>
</tr>
</tbody>
</table>

In the study by Brichetto et al., 36 subjects were randomly divided into 2 groups, Wii group and control group. Subjects completed a series of tests including the Modified Fatigue Impact Scale (MFIS) at baseline (T0) and at the conclusion of the intervention (T1). A blinded physician completed the tests and observed the outcomes. While the primary outcome assessed the effects of Wii Balance Board training on balance of MS patients, quality of life was also assessed with the MFIS. The intervention included three 60-minute sessions a week for 12 weeks. For the Wii group, these sessions utilized the Wii Balance Board. In the control group, the subjects completed an hour of static and dynamic exercises similar to a conventional physical therapy based exercise regimen. While both groups saw improvement in MFIS scores at T1 compared to T0, and larger difference was seen in the Wii group. SPSS 18 for Windows was
used for statistical analysis and a repeated measure ANOVA was used to compare group and time data \( p<0.05 \).

<table>
<thead>
<tr>
<th>Table 3: Group descriptions and results for Brichetto et al</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Group</td>
</tr>
<tr>
<td>MFIS Total score T0</td>
</tr>
<tr>
<td>MFIS Total score T1</td>
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</tbody>
</table>

In the study by Kalron et al, 32 subjects were randomly divided into 2 equal groups. Outcome variables were collected at baseline and after the 6-week intervention period. Both groups completed two 30-minute sessions for 6 weeks. The experimental group utilized virtual reality system training via the CAREN Integrated Reality System. CAREN creates a virtual reality environment with 3D imaging, sound, and proprioceptive factors. The control group completed stretching, postural control and stability exercises that were traditional for MS therapy. One subject from each group dropped out within the first 3 weeks of the study due to transportation issues getting to the MS centers.

The Fall Efficacy Scale International (FES-I) was a self-reporting questionnaire used to measure the fear of falling as well as the impact of this fear on the quality of life of a MS patient. A higher score, 64 being the highest, represents a higher fear of falling. IBM SPSS statistic software was used for analysis. Both groups were compared at baseline using the t-test for independent samples for continuous variables and the chi-square test for categorical data. ANOVA was used to observe effects of both groups and one’s outcomes versus the other. \( P \) value \(<0.05 \) was considered significant. A significant difference was seen in time factor as well as group by time factor between both groups. The group that utilized the CAREN virtual reality system had significantly lower FES-I scores compared to baseline and to the control group, indicating an improvement in quality of life and lesser fear of falling.


<table>
<thead>
<tr>
<th>Table 4: Group descriptions and results for Kalron et al</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FES-1 Questionnaire mean difference from pre and post intervention (SD)</strong></td>
</tr>
<tr>
<td>FES-1 Questionnaire mean difference from pre and post intervention (SD)</td>
</tr>
<tr>
<td>F (p value) for time factor</td>
</tr>
<tr>
<td>F (p value) for group x time factor</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Limitations are evident in the three mentioned studies. In all three, the sample size was very small. A larger number of participants would prove a more significant effect of the experimental therapy method. Also, in the Prosperini crossover pilot study there was no blindness. Therefore, the subjects were aware of both the experimental and control period. No blindness was used in the Kalron study as well. Furthermore, in the Prosperini study, there was no wash out period for the subjects in between the control and experimental trials. Lastly, Brichetto et al. and Kalron et al. mention that they did not follow up with the subjects to evaluate the effects of VR based training overtime.

Due to the age of the subjects in each study, a number of them were not familiar with the technology utilized in the experimental groups. Therefore, many had to be taught how to properly use the technology. The current generation, however, sees VR and Wii gaming systems more as commonplace. Therefore, as the current generations ages, those who develop MS can readily begin such treatment options at the inception of the disease process and forgo the need of instructions and teaching how to use the technology. As mentioned, drop-outs occurred strictly due to difficulties with the gaming system. In the future, this issue will likely not exist.

As mentioned, the cost of care and treatment of a patient with MS is significant. Physical therapy is often prescribed for management to preserve function and strength for these individuals. Insurance plans may approve and pay for a certain number of total sessions or a
certain number of sessions per week. The number of sessions covered by insurance, if not adequate, may limit the benefits for the patient. Paying for more sessions or sessions without any insurance coverage may certainly deter patients from doing the necessary therapy. Despite the necessity of physical therapy, these patients often discontinue sessions, do not complete enough, or do not keep of with the programs prescribed. While VR based training aims to encourage continuity and compliance, the issue of insurance coverage is very real. Especially if a uniform technology is not used, insurance companies will be hesitant to approve coverage. Therefore, while usage of a Nintendo Wii provided benefit for subjects in the Brichetto and Kalron studies, Nintendo Wiis are expensive game systems. Because they are originally sold as gaming systems and not used for medicinal purposes the majority of the time, insurance will likely not cover the purchase of it. This issue may resolve if a specific system is designed solely for the purpose of MS rehabilitation or if treatment centers house such programs and patients train as outpatients. A uniform usage of a system similar to the CAREN system may help with this issue. However the CAREN system would be located at an office that patients would have to travel to rather than be able to use the VR therapy in their own home.

All studies measured the quality of life of the MS patients via questionnaires. However, other variables were also focused on in each study including improvements in balance or postural control. To truly evaluate improvement in quality of life of MS patients, future studies should exclude the evaluation of other variables.

CONCLUSION

All three studies reported significant positive impact on VR based training programs on the quality of life of MS patients at the conclusion of the trials. Because this thought of incorporating new technologies with traditional physical therapy for MS patients is relatively
new, there is not extensive research on the matter. These three studies provide the potential, however, for this thought to be further investigated. Video games or VR programs may start to be specifically made and catered to the purpose of MS rehabilitation. This will allow for a more uniform method of treatment. With a uniform experimental protocol, the results can be more reliable in comparison.

In future studies aimed to evaluate VR based training for MS patients, they should be double blinded, include larger sample sizes, and use a uniform VR program. Future studies should also include multiple follow up questionnaires to track the progress of the subjects after the study has been completed.
References


