

EFFICACY OF VIRTUAL REALITY AND VISUAL ILLUSION ON NEUROPATHIC PAIN IN SPINAL CORD INJURY: A SYSTEMATIC REVIEW

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ABSTRACT

Background: The international association for the study of pain defines neuropathic pain as "pain caused by a lesion or disease of the somatosensory nervous system." Neuropathic pain may affect 40-60% of patients with spinal cord injury and is often difficult to treat. Pharmacologic management is typically the first step in treatment, but medications frequently provide only 30-50% improvement in a limited subgroup of patients. Nonpharmacologic treatments are not yet well studied. Virtual reality (VR) and visual illusory (VI) training have been suggested in the management of neuropathic pain.

Methods: A search of PubMed, CINHAL, Scopus, and Embase databases conducted in April 2017, using identical search terms, yielded 38 total articles. Six articles remained following a duplication screen, title screen, and abstract screen, and application of inclusion and exclusion criteria. **Purpose:** The purpose of this systematic review was to assess the evidence concerning VR and VI training in the effective management of neuropathic pain in people with spinal cord injury. **Results:** Following the conclusion of the electronic search and screening process, six articles were chosen for review. Five of the six articles demonstrated that VR and VI had a positive effect on neuropathic pain intensity and quality. **Conclusion:** The inclusion of VR and VI in a rehabilitation protocol may lead to significant reduction in neuropathic pain in patients with spinal cord injury. VI or VR was shown to be a reasonable consideration for alternative neuropathic pain management when compared to the effectiveness of pharmacologic interventions. **Keywords:** neuropathic pain, spinal cord injury, virtual reality, visual illusion

INTRODUCTION

The International Association for the Study of Pain defines neuropathic pain as "pain caused by a lesion or disease of the somatosensory nervous system" at any level of the peripheral or central nervous system.[1] Neuropathic pain differs from nociceptive pain in that it can occur in the absence of a stimulus or with a normally innocuous stimulus, making the diagnosis process challenging. Neuropathic pain may be classified based on localization of the lesion or disease process, by etiology as either peripheral or central in origin, or by anatomical structure involved.[2] Causes of peripheral neuropathic pain include diabetic neuropathies, peripheral nerve injury, brachial plexus avulsion, and compressive neuropathies. Primary diagnoses that may result in the presence of central neuropathic pain include, but are not limited to, multiple sclerosis, stroke, spinal cord injury, syringomyelia, and Parkinson's Disease.[2]

Damage to the central nervous system is expected to result in sensory loss or negative symptoms, but in clinical practice some patients may present with pain and/or abnormal sensations known as positive symptoms.[2] These positive symptoms are separated as either unpleasant, named dysesthesias, or not unpleasant, termed paresthesias.[2] These positive symptoms can manifest as either stimulus-evoked or stimulus-independent pain. Stimulus-evoked pain is either considered as a hyperalgesia, an exaggerated response to a normally painful stimulus, or allodynia, pain produced by a typically non-painful stimulus.[2] Stimulus independent pain or "spontaneous pain" occurs without a clear provoking stimulus. Symptoms of stimulus-independent pain include both paresthesias, manifested as tingling or itching sensations, and dysesthesias, such as throbbing, shooting, stabbing, or burning sensations.[2]

It is estimated that nearly 3.75 million cases of chronic neuropathic pain exist in the United States alone.[2] Neuropathic pain can affect 40-60% of people with incomplete spinal cord injury and is often difficult to diagnose and treat secondary to its varied nature and complex underlying factors.[3,4] Diagnosis is often made based on physical examination and history to determine whether distribution of the pain and clinical characteristics are consistent with a relevant lesion of the nervous system. Additionally, diagnostic testing and imaging may assist in the diagnosis of neuropathic pain.[1,5] For example, an MRI of the brain may be used to document the area of the lesion in a person with suspected central neuropathic pain or a nerve conduction study may be used to demonstrate a sensory lesion in a patient with peripheral neuropathy.[1,5] There is no current gold standard test used for diagnosing neuropathic pain.[5]

Whereas pharmacologic management is typically the first step in treatment, medications shown to be most effective for managing neuropathic pain frequently provide only 30-50% improvement in a limited subgroup of patients.[1] Even with medication, patients often report continued or worsening pain over time.[2] The Federal Drug Administration (FDA) has approved a short list of medications for management of neuropathic pain such as anti-epileptics and antidepressants. Currently, no opioids have been approved for the management of neuropathic pain.[2] Nonpharmacologic treatments such as massage, ultrasound, neurostimulation, cognitive-behavioral therapy and therapeutic exercise are not yet well studied and their effectiveness in the treatment of neuropathic pain is still disputed.[1,2]

Virtual reality (VR) training is used to provide biofeedback in an interactive manner by incorporating multiple sensory systems.[4] Typical physical therapy management of chronic pain includes strength, flexibility, range of motion, and core or balance training programs in addition to yoga, Tai Chi, and pilates.[6] The quality of the evidence in regards to the effectiveness of physical activity and exercise for chronic pain is low.[6] There are some encouraging results in reduction of pain severity and improved physical function, but large inconsistencies exist between studies.[6]

VR training, including the use of Wii Fit™ and Kinect for Xbox®, has been studied within physical therapy for the management of balance and gait deficits in participants with stroke and ankle sprain, and in community dwelling elderly adults.[7,8,9,10] Studies have found that VR training in conjunction with traditional balance training has led to improvements on balance ability in participants with chronic stroke.[7] Additionally, VR training was seen effective in improving not only postural balance but also lower extremity strength in community-dwelling elderly adults.[9] A systematic review and meta-analysis of the effect of VR training on balance and gait in patients with stroke by de Rooij et al.[10] suggests that VR training is more effective than traditional balance or gait training without VR. However, the study reviewed articles with broad inclusion criteria and diversity as well as varying outcome measures leading to limitations in determining the true effectiveness of VR training.

Visual illusory (VI) training is based on the principle of disorganization in the primary somatosensory cortex and can be considered similar to VR training in the use of biofeedback and interactive training.[11] By including visual feedback in task specific training and creating a visual illusion through interventions such as mirror therapy or guided imagery, reorganization of the primary somatosensory cortex and activation of the cortical mechanisms associated with movement can occur with an absence of pain. VI training is often used in conjunction with VR to promote neuroplastic changes within the brain. A 2009 randomized control trial (RCT) by Cacchio et al.[12] used mirror therapy and visual feedback to decrease neuropathic pain in people affected by complex regional pain syndrome (CRPS) type 1 and people with stroke. The participants who received active mirror therapy reported reduced pain and improved function after 4 weeks of training in the experimental group. Similarly, Villiger et.al[4] and Moseley[13] conducted studies incorporating VI training with motor imagery and VR to achieve reduced pain levels in people with spinal cord injury.

The prevalence of neuropathic pain in persons with neurologic disorders and its complex medical management through pharmacologic interventions leaves researchers and medical professionals seeking novel treatments. VR and VI training have been suggested as beneficial in the management of neuropathic pain.[3] These treatment options seek to decrease pain through correcting the inconsistent transmission between sensory feedback and motor output, thus regulating the perturbations of the somatosensory system.[3,14] The purpose of this systematic review was to assess the evidence concerning VR and VI training in the effective management of neuropathic pain in people with spinal cord injury.

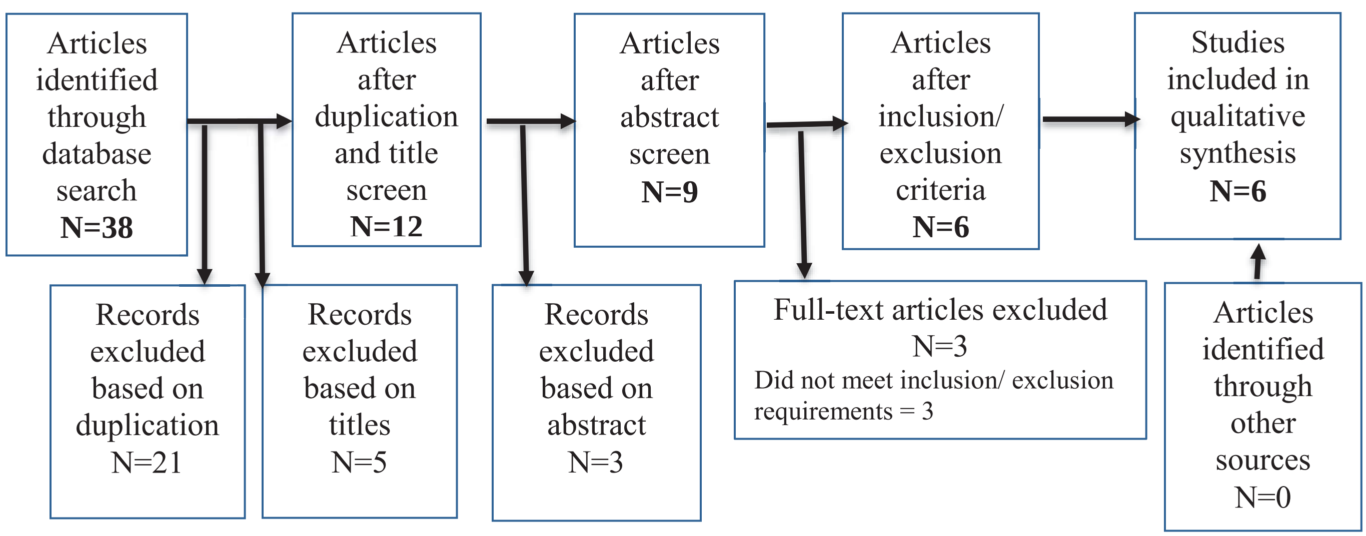
METHODS

An electronic search of PubMed, CINAHL, Scopus, and Embase databases was initially conducted in November 2016 using identical search terms including “spinal cord injury” OR “sci” OR “paraplegia”, “virtual reality” OR “visual illusion” AND "neuropathic pain." The search was limited to articles published in the last 10 years, and to those published in the English language. A more recent search conducted in April 2017 using the same parameters yielded no new results. The search yielded 38 total articles for consideration, and these were assessed through a screening process. The article screening included a duplication screen that eliminated 21 articles, a title screen eliminated five additional articles, and an abstract screen eliminated three articles. The screening process resulted in nine articles to be assessed via the inclusion criteria of spinal cord injury, neuropathic pain, and virtual reality. Following this final screening step, six articles remained for inclusion in the systematic review. The results of the search and screening processes are summarized in Table 1 Search Results and Figure 1 PRISMA Flow Diagram.

Table 1: Search Results

SEARCH STRATEGY	PubMed	CINAHL	Scopus	Embase	Total
(spinal cord injury OR sci) or paraplegia	1165898	20241	145916	1682763	3014818
(virtual reality OR visual illusion)	16699	3656	99499	6811	126665
((spinal cord injury) OR sci)) OR paraplegia)) AND ((virtual reality or visual illusion))	760	45	199	413	1417
((spinal cord injury) OR sci)) OR paraplegia)) AND ((virtual reality or visual illusion)) and neuropathic pain	8	8	12	12	40
Filters: published in the last 10 years; English	8	8	12	10	38

Figure 1: PRISMA Flow Diagram



The six articles were then assessed for quality using the Physiotherapy Evidence Database (PEDro) and 2011 Oxford Centre for Evidence-Based Medicine (CEBM). The PEDro is a ten-point scale used to measure the internal validity of physical therapy interventional studies, with 1 being the least valid and 10 being the highest score.[15] The average PEDro score of the reviewed articles was 4.67 with a range of 2-10. The level of evidence was rated using the 2011 Oxford Centre for Evidence-Based Medicine (CEBM) scale. The CEBM is a five-point scale used to assess the study quality based on the design, with a lower number indicating a stronger study.[16] Level 1 studies indicate systematic reviews. The highest level of study included in this review are level 2 studies indicating a randomized control trial. Included in this review are two level 2 studies, two level 3 studies, and two level 4 studies.

RESULTS

Five of the six articles demonstrated that VR and VI had a positive effect on neuropathic pain intensity and quality. In the highest level study, Soler et al.[17] found decreased pain levels in the experimental group as compared to the placebo group in 39 individuals with spinal cord injury (SCI). In this study, researchers explored the effectiveness of VI with and without transcranial direct current stimulation (TrDCS) to decrease neuropathic pain. The participants must have experienced neuropathic pain at an intensity of at least four out of ten on a Numeric Rating Scale (NRS) for longer than six months. Participants were randomized into four groups. The experimental group received TrDCS with the addition of VI in the form of virtual walking, the second group (TrDCS group) received TrDCS and a sham VI consisting of a movie with variations of faces and sceneries. The third group (VI group) received a sham TrDCS with VI, and the last group (placebo group) received sham TrDCS and the sham VI. Pain was rated using a NRS of 0 – 10 with ten being the greatest pain.

Soler et al.[17] found that the experimental group showed a significant reduction in pain compared to VI alone ($p = 0.008$) and compared to the placebo group ($p = 0.004$). At the first follow up assessment (day 24), the experimental group showed significant reduction in pain compared to all three groups as follows: TrDCS ($p = 0.05$), VI ($p = 0.008$), and placebo ($p = 0.009$). At the second follow up (day 38), there was no difference among the groups, however at 12 weeks post treatment, the experimental group had maintained greater pain reduction compared to TrDCS (Mann-Whitney U: $p = 0.052$) and VI (Mann-Whitney U: $p = 0.053$) at levels approaching significance. Overall, this study indicates the inclusion of VI with ancillary interventions can be considered effective in the lasting management of neuropathic pain.

In the second highest study included in this review, Ozkul et al.[14] conducted a crossover study in which all participants received transcutaneous electrical nerve stimulation (TENS) and VI. Twenty-four inpatient participants with traumatic SCI and neuropathic pain of at least four on the Douleur Neuropathique 4 Questionnaire (DN4) and a four or greater on a visual analog pain scale (VAS) were randomly assigned into two groups. Pain severity and quality were assessed using the VAS and Neuropathic Pain Scale (NPS) respectively. Each group received treatment over the course of 10 sessions consisting of five days per week for two weeks. The TENS intervention consisted of 30 minutes per day with four electrodes applied to the spinal region. Parameters for the TENS application included pulse frequency of 80 Hz and duration 180 μs at an intensity range of 0-100 mA per second. The VI intervention consisted of 15 minutes per day of virtual walking with reflection of the client's upper body superimposed on a video of lower body walking. One group began with the TENS intervention while the other group began with VI. Following completion of the first intervention, the groups switched interventions. Both groups received the same intervention but in opposite order. No significant between group differences were reported, indicating that the order of the intervention made no clinical difference. However, the TENS intervention led to significant within group decrease in pain as measured by the VAS ($p < 0.05$). VI led to a significant decrease in pain qualities as measured by the NPS ($p < 0.05$).

Jordan and Richardson[3] reviewed preliminary data from a larger ongoing study examining the effects of virtual walking on neuropathic pain in people with spinal cord injury. Thirty-five participants with traumatic spinal cord injury who received the virtual walking treatment or virtual wheeling treatment (control group) were included. The experimental group received walking stimuli consisting of a 20 minute video of an actor in first person view walking along a path. The participants were asked to imagine that they were performing the movements of the actor. The examiner was blinded to the condition until all testing had been completed. Results showed a significantly larger decrease in pain with virtual walking when compared to virtual wheeling ($p = 0.03$).

In study by Villiger et al.[4], 14 people with chronic spinal cord injury participated in an intensive VR augmented training program to improve lower limb function and decrease neuropathic pain. The participants used a VR system with a first person view of two lower limbs, controlled by sensors fitted to the participant. The study tasks engaged four different muscle groups (tibialis anterior, quadriceps, hip abductors, and hip adductors) and involved the participants through feedback of task success. Pain was measured through the use of the NPS four to six weeks before the intervention, at the start of the intervention, at completion of the study, and 12-16 weeks post intervention. The intervention protocol consisted of four weeks of training using clinically relevant activities developed in cooperation with physical therapists. These various activities to incorporate lower extremity movement included foot bag juggling in which the participant juggled a ball between the left and right feet using ankle dorsiflexion movements, "hamster splash" in which the participant used ankle dorsiflexion to achieve movement of the animal on screen, "star kick" in which the participant had to extend the knee in a kicking motion, and "planet drive" in which the participant had to avoid obstacles on the screen by tilting the lower leg sideways in both directions. A total of 16-20 sessions were performed lasting 45 minutes in duration. Following completion of the intervention protocol, researchers found a significant decrease in pain intensity at completion of the study ($p < 0.004$) and at 12-16 week follow up ($p < 0.031$). Results also indicated a significant decrease in "unpleasantness" of pain at completion of the study ($p < 0.004$) and at 12-16 week follow up ($p < 0.016$). This study supports the use of VR in the treatment of neuropathic pain in clients with active lower extremity movement.

Roosink et al.[18] explored the effect of virtual feedback on gait motor imagery and pain. Nine participants with a spinal cord injury of greater than three months in duration and an injury level of C4 and below were included in the study. Participants performed VR for gait, forward and backward, with either static visual input or interactive use of an avatar. Participants were asked to assess their level of pain using the Basic Pain Data Set on a 0-100 scale. The average change in pain intensity from pre to post intervention was -2 on a scale of 0-100. There was no significant difference indicated for neuropathic pain intensity during the experiment, however, the researchers reported minor adverse effects of the training. The researchers concluded that the study demonstrated interactive VR training is feasible and facilitated motor imagery performance and contribute to a decrease in pain intensity.

Moseley[13] conducted a two-part study which included five people with paraplegia. In the first part of the study, Moseley investigated three conditions: virtual walking, guided imagery, and watching a video. For the first part of the study, virtual walking consisted of participants seated in front of a screen and mirror. The participants watched a film of an actor walking on a treadmill and were instructed to line up their top half in the mirror so that the film and participant were aligned. The client moved their upper body and upper extremities in time with the video so it appeared as if they were watching themselves walk. In the second guided imagery condition, a psychologist led the participant through a scene in which he was pain-free and performing an enjoyable activity. The third condition consisted of watching an animated comedy video aimed to control for the effect of receiving visual input. Following participation in all three conditions, all participants experienced a mean (95% CI) decrease in pain (100 mm VAS) of 42 mm for virtual walking, 18 mm for guided imagery, and 4 mm for watching the comedy video. Participants experienced a mean time to return to pre-task pain of 34.9 minutes for virtual walking, 13.9 minutes for guided imagery, and 16.3 minutes for the video. The results of this study indicate virtual walking was superior to guided imagery or watching a video in the decrease of pain and the time required for pain to return to pre-task levels.

Moseley then performed a further investigation of the virtual walking condition to determine its clinical application. Four clients who completed the original study underwent virtual walking for 10 minutes per day for a total of 15 days in a three week period. Moseley utilized pain VAS (100 mm) as a primary outcome measure and duration of pain relief in minutes as a secondary outcome measure. Pain VAS (100 mm) was measured both before and after the virtual walking intervention, then every minute for 30 minutes, followed by every 10 minutes until pain returned to pre-task level or for three hours, whichever came sooner. Following completion of the study, participants experienced a mean (95% CI) decrease in pain of 53 mm at post training and 43 mm at three month follow up. Clients also experienced an increase in the duration of pain relief and a decrease in the area of pain when compared to baseline assessments.[13] Based on these results, virtual walking was successful in reducing pain in these participants.

Of the articles reviewed, five indicated that VR or VI training is beneficial for the decrease of neuropathic pain for people with spinal cord injury.

DISCUSSION

The aim of this systematic review was to assess the evidence concerning VR and VI training in the effective management of neuropathic pain in people with spinal cord injury. Five of the six articles selected for review demonstrated that VR and VI had a positive effect on neuropathic pain intensity and quality. The limited results reveal a lack of quality literature related to the management and treatment of neuropathic pain in this population, perhaps because of its highly variable nature. Further high quality randomized control trials are needed to determine the most effective duration, frequency, type of VR or VI training and patient population that would most benefit from this type of pain management and treatment.

The inclusion of VR or VI, specifically virtual walking, within a rehabilitation protocol may lead to significant reduction in neuropathic pain quality and intensity in participants with spinal cord injury. Additionally, some evidence indicated that virtual lower extremity exercises may also lead to reduced neuropathic pain. Currently it is unclear whether VR and VI in conjunction with additional therapeutic interventions such as electrical stimulation demonstrate greater benefit than simply VR or VI training alone. Several of the studies reviewed incorporated adjunct therapies to attenuate the benefits of VR or VI training.[14,17]

Additionally, programs that had the participants attempt movement or imagine attempted movements appeared to have a greater effect on the reduction of pain achieved.[3, 4,14,17,18] In the specific articles reviewed, VI or VR was shown to be a reasonable consideration for alternative neuropathic pain management. With the continued development of technology, the inclusion of VR or VI training into a rehabilitation protocol should be considered as treatment for patients who are not experiencing pain relief from other interventions. Due to the steadily decreasing cost of equipment and the existing research support, these interventions may be easily integrated into a physical therapy plan of care to address neuropathic pain in people with spinal cord injury.

CONCLUSIONS

The inclusion of VR and VI in a rehabilitation protocol may lead to significant reduction in neuropathic pain in people with SCI. VI or VR was shown to be a reasonable consideration for alternative neuropathic pain management when compared to the effectiveness of pharmacologic interventions.

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No use of animals was incorporated within this study.
IRB approval was not mandated since it is a review of published manuscripts.

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