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Research Article

Virtual reality in the treatment of anxiety and chronic neuropathic pain. Preliminary study

J Muriel-Fernández[1]*, C Muriel Villoria[1], MJ Sánchez Ledesma[1], JM Gonçalves Estella[1] and JM López Millán[2]

[1]Department of Surgery, University of Salamanca, Spain

[2]Department of Surgery, University of Sevilla, Spain

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***Corresponding author:** Jorge Muriel-Fernandez, Surgery Department, School of Medicine, University of Salamanca, C/ Alfonso X el Sabio, s/n, 37007, Salamanca, Spain, Tel: +34 619045000; E-mail: murimuriel@gmail.com

ORCiD: https://orcid.org/0000-0003-1497-3316

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Abstract

Background: Pain and anxiety caused by prolonged treatment of neuropathic pain can result in discomfort for patients. Virtual Reality (VR) is a technology that is capable of entertaining and distracting the user. Among its many applications, we find the improvement of pain management and the reduction of anxiety in patients undergoing medical treatment.

Objective: We aim to publish the protocol of a clinical trial for the reduction of pain and anxiety after a couple of VR sessions in patients with neuropathic pain that is difficult to treat.

Methods: An observational, analytical, and prospective study was conducted. Virtual Reality (VR) was employed as a technique aimed at reducing pain and anxiety, twice a week for 30 days, as a complement to pharmacological treatment. Pain was assessed using the 'Pain Detect' questionnaire and the Visual Analog Scale (VAS), while anxiety was evaluated through the Goldberg Scale.

Results: The preliminary results indicate that immersive virtual reality therapy is a promising alternative treatment for challenging-to-treat neuropathic pain. Without side effects, an appealing feature of VR therapy.

Conclusion: Virtual reality can be a useful tool for patients who present with neuropathic pain that is resistant to conventional treatments that generate pain and anxiety.

Introduction

Pain is defined as a complex and multidimensional sensory experience that comprises cognitive, behavioral, and psychological elements it is usually associated with unpleasant and subjective experiences and involves an adaptive function that allows for the initiation of protective responses [1].

Neuropathic pain is a condition that is frequently associated with affective symptoms and negative emotions (anxiety, depression, fear, etc.). In fact, it has been estimated that 20% - 30% of patients suffering from chronic pain also experience anxiety and depressive symptoms [2], specifically estimating that 50% of chronic pain patients will experience major depression at some point (34% in the case of neuropathic pain) [3]. Thus, the comorbidity of chronic pain and affective disorders is closely linked to a higher degree of pain severity, greater disability, and a substantial decline in the patient's quality of life [4], a situation that significantly complicates its treatment [5]. In this regard, the persistence of long-term pain and the sustained associated suffering appear to be determining factors in the development of affective and emotional disturbances secondary to the pain process. Specifically, it has been demonstrated that long-term neuropathic pain results in the

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hyperactivation of the LC-BLA pathway, which is responsible for anxious symptoms secondary to the pain process [6].

The development of an innovative technique within the broad spectrum of cognitive-behavioral techniques for pain management, whether acute or chronic, is known as Virtual Reality (VR). Over the past 10 years, there has been a growing interest in the use of VR technology as a method for pain reduction. In VR, users interact with a computer-generated three-dimensional environment. VR technology provides multi-sensory information (visual, auditory, tactile, and olfactory stimuli) that helps individuals interact in the simulated world. Virtual reality has proven to be useful in reducing chronic pain and related issues such as anxiety, hopelessness, time spent thinking about pain, and perceived time spent in a procedure [7].

Virtual Reality has become commonplace in most societies worldwide, as interacting with smartphones or computers has become a common occurrence. The concept of "Virtual Reality" lacks a single, homogeneous definition among authors who have worked on the subject. Virtual Reality can be defined as a synthetic or virtual context that provides a person with a sense of reality [8]. Virtual reality is an advanced communication interface based on interactive three-dimensional visualization, capable of collecting and integrating different sets of data into a single realistic experience [9]. The user interacts, through certain technological devices, with immersive simulations that replace sensory information from the real world with digitally generated alternatives, creating a sensation of effectively being in a different place than the current one.

The objective of this article is to evaluate the results obtained in terms of pain and anxiety relief with the application of Virtual Reality in this group of patients with persistent neuropathic pain.

Materials and methods

Trial design

An observational, analytical, and prospective study was conducted, including patients who, despite undergoing treatment for persistent neuropathic pain, continued to experience it despite the utilization of various treatment techniques and methods.

Participants inclusion criteria

All patients received conventional medical treatment with antidepressants, anticonvulsants, and opioids. Consequently, various interventional techniques were employed, including peripheral blocks, infiltration with botulinum toxin and radiofrequency techniques (Table 1).

Inclusion criteria comprised patients who were adults, possessed sufficient physical and mental capacity to undergo the planned procedures, demonstrated proficiency in using VR and validated scales, had a diagnosis of persistent neuropathic pain with moderate to severe intensity despite correct treatment, had received treatment for at least the preceding 3 months, and had provided informed consent to participate in a clinical study.

Participants exclusion criteria

As exclusion criteria, we considered the presence of unstable or poorly controlled hypertension or a history of recent cardiovascular events (within the last 6 months) before initiating treatment. Additionally, patients with cognitive deficits, where understanding and/or application of the scales, as well as correct responses to related questions, could not be achieved, were also excluded.

Data collection, sources of information, and intervention

The pain intensity was measured using the Pain Detect questionnaire [10], which is self-administered and consists of 9 descriptors. It detects neuropathic pain intensity and discriminates between possible neuropathic pain (scores between 12 and 19) and certain neuropathic pain (scores above 19). The Visual Analog Scale (VAS) was also employed, which is a quantitative one-dimensional scale that is effective and easily reproducible. Patients mark on a 100 mm segment with endpoints classified as no pain (0 mm) and maximum pain (100 mm); the measurement from point 0 to the marked point indicates the pain intensity. A change of 20 mm (or 2 points

Table 1: Patient characteristics and treatments.

Patient No	Gender	Diagnosis	Pharmacological Treatment	Interventional techniques	Topic Treatment
1	Male	postherpetic neuralgia	Pregabalin, duloxtin, baclofen, amitriptiline		Ketamine 3%, amitriptiline 5%, lidocaine 5%
2	Male	post-surgical cervicalgia	Pregabalin, tramadol, baclofen	Interscalenic block & ropivacaine at 0,2%	
3	Female	post-surgical causalgia	Amitriptiline, gabapentine		
4	Male	diabetic neuropathy	Gabapentine		
5	Male	postherpetic neuralgia	Lidocaine patch, ketamine	Intercostal block	Ketamine 3%, lidocaine 5%
6	Male	postherpetic neuralgia	Capsaicine patch	Intercostal block, radiofrequency	
7	Female	reflex sympathetic dystrophy radial fracture	Amitriptyline, gabapentine		
8	Female	lumbosacral radiculopathy	Amitriptyline, gabapentine	radiofrequency	
9	Male	trigeminal neuralgia	Carbamacepine, tramadol, gabapentine		

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on a 10-point pain intensity scale) is considered clinically significant.

Statistical analysis

The design of the study meant that the included patients could also act as "controls" since they had already required treatment for neuropathic pain in the previous 3 months and could compare their experience of the current session with the last one.

Anxiety was measured using the Goldberg Scale [11], a test that not only guides diagnosis but also quantifies intensity. It contains two subscales with nine questions each: anxiety subscale (questions 1–9). The first four questions of each subscale (questions 1–4) act as a precondition to determine whether the remaining questions should be attempted. Specifically, if a minimum of 2 questions among questions 1–4 are not answered affirmatively, the remaining questions of the first subscale should not be answered. In the case of the second subscale, answering affirmatively to one question among questions 10–13 is sufficient to proceed to answer the remaining questions.

The perception of time passage was analyzed as an attempt to indirectly measure if patients were distracted, had lower attention to pain, higher pain tolerance, and perhaps an early sense of having completed the scheduled treatment time (or programmed time).

Upon completion of the virtual reality application time (30 to 35 minutes), just before its removal, patients were asked about the approximate time they believed was remaining. This was termed "perceived time" (Perceived Time) and was recorded in 10 - 15 minute intervals based on their responses.

A difference in time (Scheduled Time - Perceived Time) ≥ 10 minutes was considered "significant," and if it was < 10 minutes, it was considered "unchanged." For patients who requested removal before completing the scheduled time, their "perceived time" was recorded by adding the time remaining for the treatment to the total scheduled time [Perceived Time = (Scheduled Time - Actual Time) + Scheduled Time].

Immersive VR treatment took place outside the hospital setting in the laboratory of the Department twice a week for five weeks.

Given the ineffectiveness of previous treatments, the application of Virtual Reality was proposed, using the Oculus Go VR 32GB model. The patients wore a head-mounted display, creating a stereo visual image that provides a sense of space and depth. A motion tracker on the display screen measured the head position and adjusted the visual image accordingly. As a result, users perceived their surroundings and could move within the simulated environment. The headset typically included headphones that provided sounds to further immerse the person in the virtual world. Other input devices allowed users to navigate the simulated environment and interact with virtual objects.

Results

A total of 9 cases were recorded, including 6 males and 3 females, with a mean age of approximately 60 years (median 59.5, interquartile range 28 - 84 years). All patients suffered from Localized Peripheral Neuropathic Pain (DNPL), as detailed in Table 1.

All patients agreed to participate in the study, except for one who decided not to continue after the initial contact with the VR system.

The distraction chosen by each patient succeeded in reducing pain (considered significant for a decrease in VAS ≥ 2 compared to their previous experience) in 3 patients, while 5 patients did not notice any changes (VAS difference of 0 or 1 point compared to their previous experience), and 1 patient had an even worse experience, choosing not to continue.

The evaluation of the "Pain Detect" questionnaire showed a significant decrease in the final score (at 30 days) in a total of 3 patients (more than 10 points) and in 5 patients (less than 10 points) (Table 2).

Regarding anxiety measured by the Goldberg Scale, during the session, it decreased in 4 cases (considered "significant anxiety" for a score greater than 2 points) (Table 3).

Regarding the perception of the passage of time (Table 3), 30 days after the end of the treatment, 50% of the patients

Table 2: Data referring to VAS (Visual Analog Scale) and Pain Detect Questionary.

VAS			"Pain Detect" Questionary	
Patient No	previous	30 days	previous	30 days
1	8	5	29	7
2	7	5	28	24
3	9	8	24	14
4	10	3	24	23
5	8	8	19	18
6	8		15	
7	9	8	27	23
8	7	7	14	8
9	8	8	18	1

Table 3: Data corresponding to the state of anxiety and time perception.

Goldberg Anxiety Subscale			Time Perception
Patient No	Previous	30 days	
1	2	0	30 min
2	3	3	60 min
3	3	1	35 min
4	2	2	40 min
5	2	1	30 min
6	2		20 min
7	2	1	35 min
8	3	0	35 min
9	4	0	30 min

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experienced a time difference greater than the real-time, considered "significant" (considering a treatment time of 30 minutes).

It is important to note that in some cases, even though there were no differences in the VAS, there was a significant decrease in the perception of time, indirectly suggesting a certain level of abstraction from the painful experience during the use of VR.

In all patients who were in a state of chronic neuropathic this preliminary work, our VR therapy was able to provide successful analgesic efficacy: 80% of the patients showed a reduction of more than 50% in pain intensity after ten consecutive treatment sessions. It is worth noting that pain, is known to be difficult to treat with conventional therapy. In two patients, the analgesic effect continued even after discontinuation of treatment. Additionally, none of the five patients in this study reported experiencing any related side effects.

Discussion and limitations

Our results indicate that immersive VR therapy is a promising alternative treatment for challenging neuropathic pain situations. Virtual reality technology is used in various fields, and its potential medical applications are of great interest. Its application as an analgesic modality is particularly noteworthy. Hoffman et al. developed an immersive virtual reality system for wound care in burn patients [12]. VR is interactive and maintains the patient's attention even during painful wound care. Virtual reality technology holds promise as an analgesic modality in various ways. The results of this new therapy are encouraging and consistent with the limited existing studies in the scientific literature [13]. We used virtual reality technology similar to that employed by Hoffman; most of the analgesia is derived from distraction [12]. Distraction is a possible underlying mechanism of the analgesia provided by our VR system.

Distraction can reduce pain intensity and its associated effects, typically only during the intervention. Two types of pain intensity reduction were derived from our results: immediate reduction after each session and lasting reduction at 30 days. In the case of immediate pain reduction, there was a possibility that the analgesic effect primarily originated from distraction. Distraction is a potential analgesic mechanism, and anxiety reduction is also a potential candidate for the underlying mechanism of analgesia provided by our VR system [13]. Since this was a pilot study to assess the analgesic efficacy of VR therapy for patients with treatment-resistant chronic neuropathic pain, the effective course, frequency, and duration of therapy have not been established. Our VR system needs to be installed in a research unit of a university hospital. According to McCabe's studies [14], it is reasonable to assume that therapy needs to be repeated on consecutive days to reverse maladaptive organization in patients with chronic neuropathic pain. However, our initial case showed a remarkable reduction in pain intensity from the first week. Thus, for the subsequent VR therapy sessions, the frequency was set at twice a week; however, the duration of each session was fixed at a time between 30 and 35 minutes, limited by time constraints. An important limitation of the present study is the design, as it involves an open case series without control conditions. Further studies with and without VR for patients with neuropathic pain are needed, and it is also necessary to determine the optimal time course of our VR therapy. Perhaps the most obvious and therefore promising advantage of using virtual reality is the ability to provide patients with a pain-free environment that distracts them from acute pain during painful medical procedures but also acts as an escape for patients with chronic pain [15]. We can highlight the main limitation of this study that it is an observational study, in which patients have not been randomized into various groups. This was decided in part because it is described in the literature that the possibility of choice by the patient can reduce the degree of pain derived indirectly to a greater extent by increasing personal satisfaction with the choice made.

Conclusion

Our preliminary results indicate that immersive virtual reality therapy is a promising alternative treatment for challenging-to-solve neuropathic pain. In addition to the lack of side effects, an attractive feature of VR therapy is that it allows subjects to undergo repetitive training with intensity, which is crucial for restoring neuronal plasticity and leads to a virtuous circle of therapeutic action. The cortical pain perception network changes in neuropathic pain.

Further studies are needed before concluding that analgesia provided by immersive virtual reality therapy is acquired as a result of modulating underlying changes in pain perception and anxiety. A promising advantage of using virtual reality is in the ability to provide patients with a pain-free environment distracting them from acute pain during medical procedures but also acting as an escape for patients with chronic pain.

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