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Clinical Studies

Remote cognitive behavioral therapy utilizing an in-home virtual reality toolkit (Vx Therapy) reduces pain, anxiety, and depression in patients with chronic cervical and lumbar spondylytic pain: A potential alternative to opioids in multimodal pain management

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ABSTRACT

Background Context: Virtual reality (VR) reduces pain through visual and auditory distraction without narcotic-related side effects or dependency. Cognitive behavioral therapy (CBT) improves pain-related disability and quality of life, but patient access remains a challenge. We hypothesized that in-home weekly CBT coordinated with daily use of a proprietary VR toolkit will reduce pain, anxiety, and depression for patients with non-operative chronic cervical and lumbar spondylitic pain with and without radiculopathy.

Methods: A total of 145 patients with chronic spondylitic pain (63 cervical, 46 noradicular lumbar, 36 radicular lumbar) were enrolled into a guided 14-week VR+CBT program (Vx Therapy) consisting of weekly encounters with a trained therapist and 50 modules. Pain/anxiety severity scores and time to pain recurrence were recorded prospectively by patients. PROMIS measures of overall daily pain intensity, behavior, interference, anxiety, and depression were recorded at baseline and conclusion of the program.

Results: A total of 52% of the 145 patients were male. The average (SD) age of the cohort was 51 (10.7) years (range: 24–76 years). Mean score for all PROMIS domains were significantly improved after 14 weeks of Vx Therapy (pain intensity 36±24 vs. 28±21, interference 39±25 vs. 24±21, behavior 35±21 vs. 25±16, anxiety 51±28 vs. 41±26, depression 58±32 vs. 48±32) for the entire cohort and each diagnosis group. Virtual reality acutely reduced pain on average by 33% (4.5±2.5 vs. 6.7±2.2, $p<.05$) across all 14 weeks, lasting a mean 2.8 hours after use. Duration of pain relief increased by the final vs. first month (4.5 hours vs. 2.5 hours, $p<.05$). Virtual reality acutely reduced anxiety on average by 46% (3.5±3 vs. 6.4±2, $p<.05$) across all 14 weeks lasting a mean 2.7 hours after use. The effect was similar for all 3 groups.

Conclusions: Fourteen weeks of a remote CBT guided in-home VR toolkit provided effective and sustained pain, anxiety, and depression relief in patients with chronic degenerative neck/back pain with and without radiculopathy. The non-invasive, non-pharmacological nature of Vx Therapy makes it an ideal option for pain management in the post-opioid epidemic era.

FDA device/drug status: Approved, Class I.

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Introduction

Virtual reality (VR) is a rapidly developing technology that creates a fully immersive experience for the user in a 3-dimensional computer-generated environment. A head mounted display worn by the user integrates visual and auditory stimuli to create an immersive virtual world. Initially, VR technology was developed by the US Military for training, and quickly gained favor within the gaming industry. It has subsequently been developed as a tool for training in clinical settings such as surgical education in orthopedic and neurosurgical procedural training [1,2]. The clinical applications of VR are expanding as well; its use has been demonstrated in the treatment of pain and psychiatric disorders, as well as for physical rehabilitation [3–6]. Recent examples include VR use for patients with both acute and chronic pain, cancer pain, and during painful medical procedures [7–17].

Pain and psychiatric health conditions represent a major health burden demanding substantial resource utilization and frequent healthcare encounters. Approximately 100 million people in the United States (US) are affected by chronic pain [18]. The economic burden of chronic pain through both direct costs and lost productivity has been estimated to be as high as $600 billion dollars, greater than the costs of diabetes, heart disease, and cancer [18].

Medication and invasive procedures have long been a cornerstone of pain management. As our understanding of the science of chronic pain has evolved, however, in addition to the opioid epidemic of the last decade, it has become clear that non-invasive, non-pharmacologic treatment options are desperately needed. Most major guidelines now recommend treating chronic pain from a multidisciplinary, multimodal approach that emphasizes non-pharmacologic treatments [19]. Examples of multimodal treatments include physical therapy and exercise, lifestyle and behavioral modifications, and psychological therapies [20,21].

Cognitive behavioral therapy (CBT) is the gold standard psychological therapy with evidence supporting its use for chronic pain and associated anxiety, depression, and physical disability [22]. The positive effects of CBT and other psychological therapies on improving chronic pain including chronic back pain are well validated [23–25]. However, access to CBT remains a challenge in most care communities as it relies on the presence of trained care providers and adequate transportation is necessary for in-person encounters. Furthermore, poor engagement with these trained providers limits not only access but programmatic success.

Harvard MedTech Vx Pain Relief Program (Vx Therapy) is a remote CBT that utilizes an in-home VR toolkit that connects the patient with virtual reality programing and directed guidance through the program by a behavioral health clinician. This system obviates the need for in-person health visits by generating a patient-specific virtual world in the patient's own home thus representing a paradigm-shifting modality for patients with pain. In a cohort of patients with non-operative degenerative neck/back pain, we hypothesized that in-home, weekly CBT delivered through a proprietary VR toolkit would reduce pain, anxiety, and depression over a 3-month treatment period.

Methods

Vx Therapy

The Harvard MedTech Vx Pain Relief Program (Vx Therapy) is a physician prescribed 3-month therapeutic curriculum that consists of home-based virtual reality therapy (VRT). This program includes weekly telephonic visits to direct cognitive-behavioral intervention therapies (CBT) with a masters-level behavioral health clinician (Vx Navigator) who is assigned to each patient after completion of an initial clinical intake. The virtual reality headset is mailed to the patient's home. Therapeutic interventions are individualized for each patient during their weekly telephonic calls based upon their symptoms in order to attain optimal patient outcomes. All patients consented to undergo Vx Therapy.

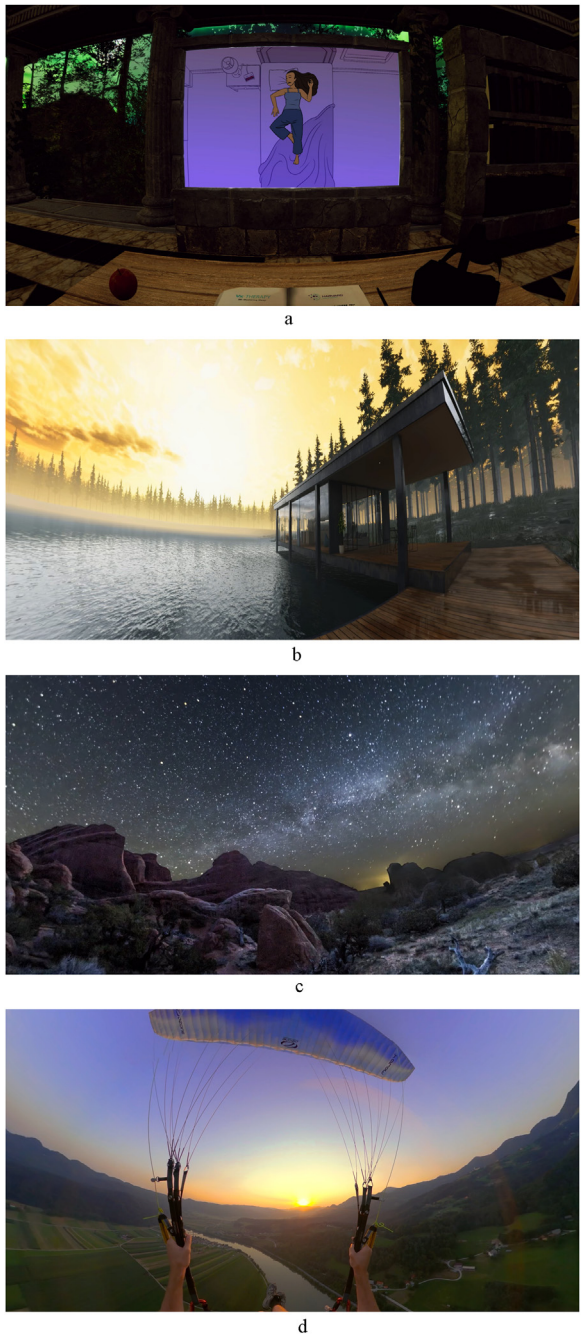

Fig. 1. Example content across the 4 categories of immersive audiovisual virtual reality modules: education, meditation, distraction, escape/entertainment. (A) Educational courses are included to increase patient understanding of their underlying pathophysiology as well as to promote dialogue with their care team. (B) Guided meditations are successful because of the limited distractions that occur within the virtual environment. (C) Distraction content is designed to be both immersive and engaging to decrease thalamic activity. (D) Escape modalities are highly immersive from an experiential perspective but allow patients the freedom and self-actualization to control what and where they are escaping for their own entertainment.

Virtual reality therapy hardware is a PICO headset pre-programmed with proprietary software designed and curated by Harvard MedTech. While wearing the headset and earphones, patients are fully immersed through visual and auditory stimuli in a non-internet connected environment. The VRT program includes 20 hours of content, organized as 3 to 20 minutes immersive audio-visual modules in 4 categories: education, meditation, distraction, and escape/entertainment (Fig. 1). To

maximize the benefit of the Vx platform, patients (with guidance from their Vx Navigator) can select their environments, settings, and educational content to optimize their immersion. The curated content is delivered to the patient in an organized manner by their Vx Navigator to move the patient into the VRT with personalized goals based upon their individual needs. In addition to helping patients understand their symptoms, the navigator directs the patients to specific content and suggests when they should watch it to best use the program to facilitate their recovery. As such the amount of content that is viewed varies based on the individual patient's programmatic needs. The content is designed to minimize vertigo, but patients are instructed to participate in the program while seated at a desk or table and to remove the Vx Therapy platform should they experience vertigo or associated symptoms.

Outcome measurement and analysis

From August 2020 to March 2022, patients insured under a variety of worker's compensation plans were eligible to be prescribed Vx Therapy as a noninvasive, nonpharmacologic treatment for chronic or subacute pain syndromes of any etiology. As a part of the standard of care of Vx Therapy, pain, and anxiety severity scores (0 best, 10 worst) were recorded prospectively by patients before and immediately after VRT use, as was time to pain recurrence. This data was communicated to their Vx Navigator during weekly sessions. The Patient-Reported Outcome Measurement Information system (PROMIS) item banks are a validated method of obtaining and reporting patient-reported outcomes [26]. PROMIS measures (100 best, 0 worst) across 5 domains (overall daily pain intensity, pain behavior, pain interference, anxiety, and depression) were also recorded in weekly telephone interviews from baseline through the conclusion of 14 weeks of Vx Therapy.

For the current study, the de-identified digital records of all patients undergoing Vx Therapy for a primary diagnosis of degenerative neck or back pain due to spondylosis with and without radiculopathy were retrospectively reviewed. This study met ethical approval as no protected health information was used. Acute pain and anxiety scores before and immediately after in-home VRT were compared to determine the acute efficacy of VRT use. PROMIS measures at baseline and at conclusion of the 14 weeks Vx Therapy program were compared to determine the effectiveness of Vx Therapy at improving overall daily pain, anxiety, and depression associated with their degenerative spinal conditions. PROMIS outcomes data were determined to be in a normal parametric distribution. Univariate parametric data are reported as mean ± SD. Bivariate comparative analyses were conducted using a paired t-test. Statistical significance was defined as $p<.050$.

Results

A total of 145 consecutive patients were prescribed Vx Therapy for chronic cervical or lumbar pain over a 18-month period. Patients were referred from orthopedics, neurosurgery, psychiatry, and interventional pain clinicians. The patients were 52% male with an average (SD) age of 51 (10.7) years (range: 24–76 years). The majority of patients (70%) reported neck or back pain lasting greater than 2 years, while the remaining patients had symptom durations of less than 2 years.

Primary diagnosis was cervical spondylosis with neck pain in 63 patients (44%), lumbar spondylosis with axial back pain in 46 patients (32%), and lumbar spondylolysis with radiculopathy in 36 patients (25%). For each diagnosis group, baseline pain scores (range: 0–10) were 7.5, 5.8, and 5.0, respectively. Mean baseline pain-related anxiety scores (range: 0–10) were 6.8, 6.1, and 7.3 respectively. All patients completed their 14-week course of Vx Therapy.

Mean score for all PROMIS domains (range: 0–100) were significantly improved after 14 weeks of VRT vs baseline (pain intensity 36±24 vs. 28±21, pain interference 39±25 vs. 24±21, pain behavior 35±21 vs. 25±16, anxiety 51±28 vs. 41±26, depression 58±32 vs. 48±32) for the entire cohort and for each diagnosis group, Table. VRT acutely reduced pain during use on average by 33% (4.5±2.5 vs. 6.7±2.2, $p<.05$) across all 14 weeks (Fig. 2A) lasting a mean 2.8 hours after use (Fig. 2B). The duration of pain relief increased significantly when comparing the final (4.5 hours) vs. first month (2.5 hours) of VR use ($p<.05$). VR use acutely reduced anxiety during use on average by 46% (3.5±3 vs. 6.4±2, $p<.05$) across all 14 weeks (Fig. 3A) lasting a mean 2.7 hours after use (Fig. 3B). Steady improvements in weekly pain and anxiety scores were seen across the interval (Figs. 2–3). These effects on pain and anxiety were similar for all three diagnosis groups.

Table
Overall PROMIS (0 worst, 100 best) pain, pain behavior, pain interference, anxiety, and depression scores recorded at entry into and at 14 weeks conclusion of the in-home Vx Therapy program

	Neck pain	Back pain	Lumbar radicular pain
Cohort population size	63	46	36
	Mean±SD	**Mean±SD**	**Mean±SD**
PROMIS pain intensity			
First week	29.0±21.9	28.9±21.2	26.6±21.5
Last week	34.8±27.2	36.4±22.9	35.3±24.6
PROMIS pain behavior			
First week	24.7±14.7	24.4±15.3	26.7±18.2
Last week	32.4±22.3	34.2±21.1	37.0±19.7
PROMIS pain interference			
First week	25.2±21.6	24.4±21.4	22.9±21.3
Last week	39.7±27.0	38.6±26.6	38.9±25.5
PROMIS anxiety			
First week	41.4±27.5	38.7±27.8	44.1±25.4
Last week	52.7±27.6	48.9±30.2	52.3±31.0
PROMIS depression			
First week	50.8±30.3	44.3±34.2	49.9±33.9
Last week	57.7±30.4	57.8±32.0	60.3±34.0

A significant improvement ($p<.05$) was observed across all diagnosis groups.

Discussion

Virtual reality is an evolving technology with expanding applications in gaming, military and medical training, and clinical care. While some early studies have supported the use of VR in the treatment of acute and chronic pain, the efficacy in treating neck and back pain resulting from degenerative spondylosis is unclear. The present study adds to the currently sparse body of literature demonstrating the efficacy of VRT in both subacute and chronic pain syndromes [3,17]. VR is thought to reduce pain through visual and auditory distraction, as well as alterations in brain neurobiology in several brain regions involved in the principle pain pathways. These effects are similar to those observed with opioid use, but without narcotic-related side effects or dependency [3,27–33].

The opioid epidemic in the US is a national crisis resulting in skyrocketing mortality. In 2015, over 33,000 people died from opioid misuse and overdose [34]. Prescription opioid misuse has been reported in up to 4% of the adult US population [35]. Alternative nonpharmacologic treatment options are desperately needed to combat this trend. Cognitive behavioral therapy is one such non-invasive treatment option and is considered the gold standard psychotherapy that improves pain-related anxiety, depression, physical disability, resiliency and quality of life [22,36]. However, access to CBT is a significant challenge for many patients given the shortage of trained behavioral health professionals and the costs of care. Moreover, patients are often unable to attend appointments due to physical, social or financial constraints, further limiting access to care.

The Vx Pain Relief Program (Vx Therapy) is a novel treatment paradigm that allows for remote CBT to be delivered in the patient's home via a VR device with specifically curated content. Vx Therapy utilizes a VR toolkit to connect patients with a behavioral health clinician who develops a patient-specific treatment plan. The 4 domains of content that are included (Education, Meditation, Distraction, and Escape/Entertainment) are based on Level 1 data demonstrating their

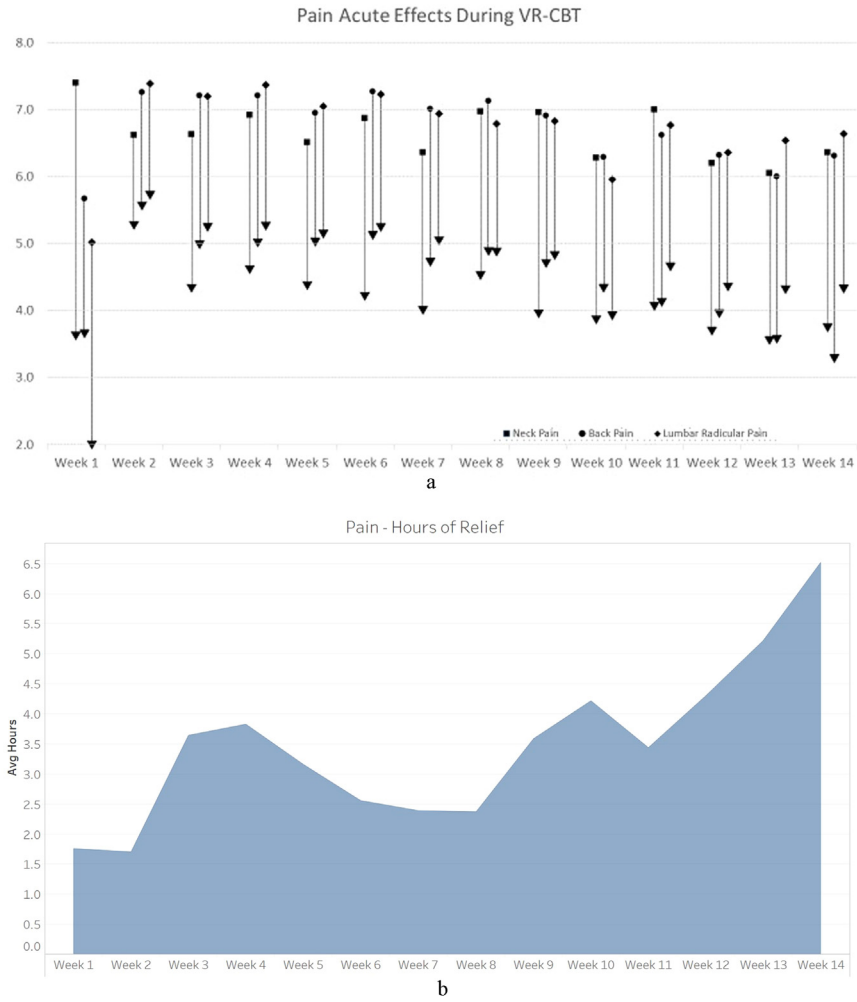

Fig. 2. (A) Average acute effects on pain severity immediately before and after using the Vx therapy virtual reality toolkit each day over the 14 weeks Vx therapy program for all patients. The use of Vx therapy modules via virtual reality headset resulted in acute reduction in pain (scale: 0-10). This effect persisted throughout 14 weeks. (B) Mean length of pain relief in hours after using the Vx therapy virtual reality toolkit. Duration of pain relief after using the virtual reality toolkit increased throughout the 14 weeks program.

benefit in patients with chronic back pain [23–25]. In this study, we evaluated the efficacy of this non-invasive, non-pharmacological treatment for patients with treatment-refractory chronic degenerative cervical and lumbar pain. We found that this therapy significantly improved pain and anxiety scores for patients with neck and low back pain, as well as patients with lumbar radiculopathy. Pain and anxiety during Vx Therapy sessions were significantly decreased by an average of 33% and 46%, respectively across the study interval. These results were durable across the entire 14-week study period with steady weekly improvement in the acute effects of therapy on pain and anxiety. The duration of these effects increased over the course of the program, as well (Figs. 2–3).

While the underlying neural mechanisms of pain control continue to be studied, one of the main functions of VR-based pain treatment is distraction such that the painful stimulus no longer receives the patient's attention. It is the immersive nature of the VR system that is able to effectively capture and maintain the patient's focus. The virtual world is able to compete with external painful stimuli and therefore decrease pain perception [37]. As such, a VR-based system is well poised to achieve the goals of traditional CBT to distract and decondition patients to negative stimuli to improve coping skills and overall function [38]. Vx Therapy delivers CBT remotely to patients in their own home and without the need for internet access such that they may undergo treatment even in resource-limited settings. Previous authors have expressed concern with the risk of habituation to VRT, as repeated exposures to treatment may lead to diminishing effects [3]. However, in the current study no habituation occurred, with treatment effects lasting and even improving across the study interval.

There is limited literature regarding VR-based treatments for patients with spinal disorders. Sarig-Bahat et al. [15] have previously shown that the addition of VR can increase cervical range of motion and improve pain scores in patients with neck pain [39,40]. Another report of 2 patients with chronic low back pain found that VRT improved patient symptoms [41]. In comparison, the present study includes a larger patient population that demonstrated continued improvement in both pain and anxiety during treatments and included validated patient reported outcome measures. The patients in our cohort-maintained benefit throughout the program and demonstrated, on average, increased duration of treatment effect with continued therapy.

This study is not without limitations. We performed a retrospective review of patients treated for chronic lumbar and cervical pain, and thus this methodology inherently limits the extent of analysis. However, all patient score data was collected in a prospective fashion as part of standard of care treatment. Patients were prescribed this therapy based on the discretion of the treating provider and did not undergo randomization. Moreover, while we demonstrated improved pain and anxiety scores up to 14 weeks with treatment, it will be important to assess the effects of VRT at longer term follow-up after the con-

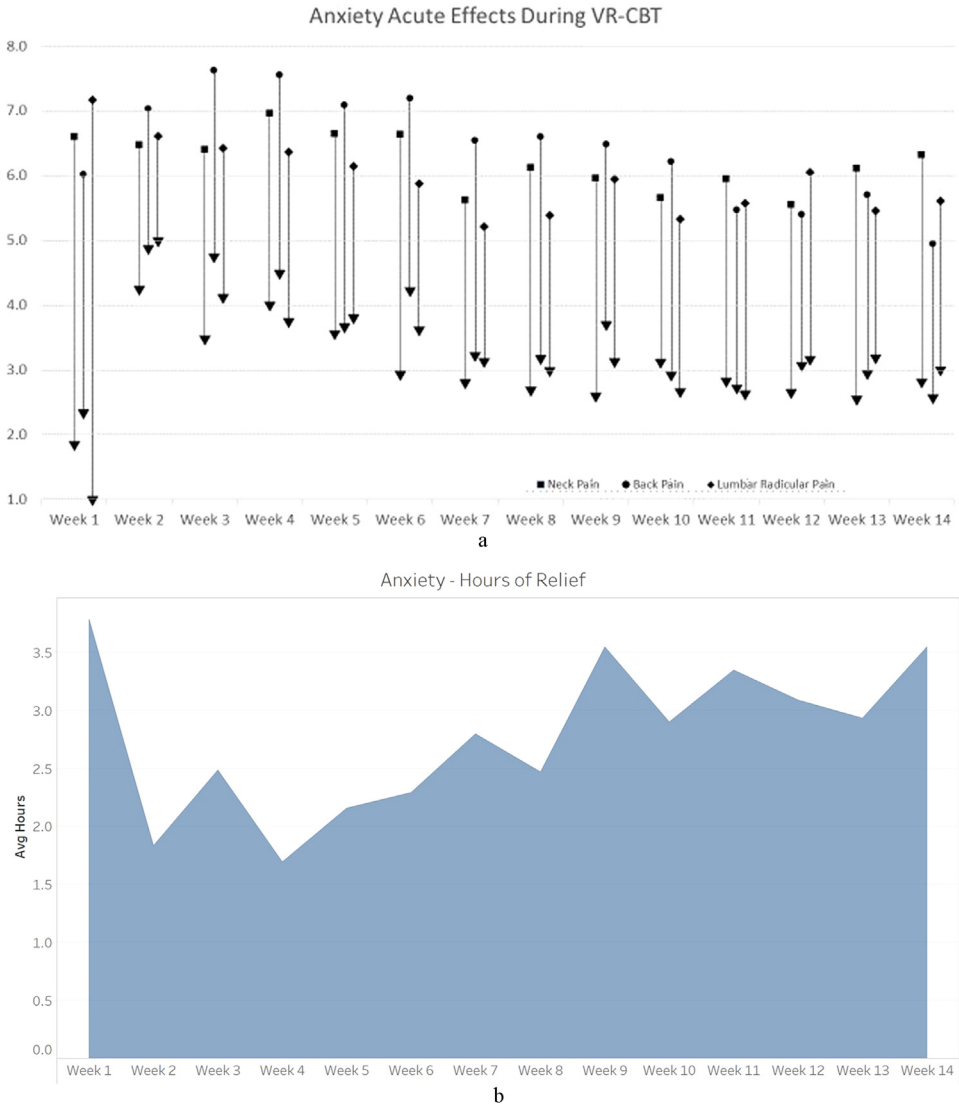

Fig. 3. (A) Average acute effects on anxiety immediately before and after using Vx therapy virtual reality toolkit each day over the 14 weeks Vx therapy program. The use of Vx therapy modules via virtual reality headset resulted in acute reduction in anxiety (scale: 0–10). This effect persisted throughout the 14 weeks. (B) Mean length of anxiety relief in hours after using Vx therapy virtual reality toolkit. Pain relief lasted an average of 3.5 hours after virtual reality toolkit use by week 14 of Vx therapy.

clusion of the 14 weeks therapy program to determine if these effects are maintained. Finally, there was no comparison arm in the current study. Direct comparison of Vx Therapy to other modalities of pain treatment for degenerative cervical and lumbar pain including opioid and non-opioid medication, standard rehabilitation regimens, and invasive treatments such as injections will be important areas of future investigation.

Conclusion

Use of a remote CBT guided in-home VR toolkit (Vx Therapy) provided effective and multi-hour sustained pain relief in patients with chronic degenerative neck and back pain with and without radiculopathy. Fourteen weeks of Vx Therapy resulted in significant improvement in overall pain, anxiety, and depression and reduced pain interference with physical and recreational activities. The effective, noninvasive, nonpharmacological nature of VR Therapy makes it an ideal option to improve outcomes and resiliency in the modern landscape of pain management.

Declaration of Competing Interest

MJM, SHF, and NT are shareholders in Harvard Medtech, LLC. GS is an employee of Harvard Medtech, LLC. The other authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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References

[1] McKnight RR, Pean CA, Buck JS, Hwang JS, Hsu JR, Pierrie SN. Virtual reality and augmented reality-translating surgical training into surgical technique. Curr Rev Musculoskelet Med 2020;13(6):663–74.
[2] Godzik J, Farber SH, Urakov T, et al. "Disruptive Technology" in spine surgery and education: virtual and augmented reality. Oper Neurosurg (Hagerstown) 2021;21(Suppl 1):S85–93.
[3] Li A, Montano Z, Chen VJ, Gold JI. Virtual reality and pain management: current trends and future directions. Pain Manag 2011;1(2):147–57.

[4] Rothbaum BO, Hodges L, Kooper R. Virtual reality exposure therapy. J Psychother Pract Res 1997;6(3):219–26.
[5] Rizzo AA, Difede J, Rothbaum BO, et al. VR PTSD exposure therapy results with active duty OIF/OEF combatants. Stud Health Technol Inform 2009;142:277–82.
[6] Carl E, Stein AT, Levihn-Coon A, et al. Virtual reality exposure therapy for anxiety and related disorders: a meta-analysis of randomized controlled trials. J Anxiety Disord 2019;61:27–36.
[7] Morris LD, Louw QA. Grimmer-Somers K. The effectiveness of virtual reality on reducing pain and anxiety in burn injury patients: a systematic review. Clin J Pain 2009;25(9):815–26.
[8] Chan E, Hovenden M, Ramage E, et al. Virtual reality for pediatric needle procedural pain: two randomized clinical trials. J Pediatr 2019;209:160–7 e164.
[9] Schneider SM, Kisby CK, Flint EP. Effect of virtual reality on time perception in patients receiving chemotherapy. Support Care Cancer 2011;19(4):555–64.
[10] Furman E, Jasinevicius TR, Bissada NF, Victoroff KZ, Skillicorn R, Buchner M. Virtual reality distraction for pain control during periodontal scaling and root planing procedures. J Am Dent Assoc 2009;140(12):1508–16.
[11] Gold JI, Kim SH, Kant AJ, Joseph MH, Rizzo AS. Effectiveness of virtual reality for pediatric pain distraction during i.v. placement. Cyberpsychol Behav 2006;9(2):207–12.
[12] Schneider SM, Workman ML. Virtual reality as a distraction intervention for older children receiving chemotherapy. Pediatr Nurs 2000;26(6):593–7.
[13] Schneider SM, Prince-Paul M, Allen MJ, Silverman P, Talaba D. Virtual reality as a distraction intervention for women receiving chemotherapy. Oncol Nurs Forum 2004;31(1):81–8.
[14] Sato K, Fukumori S, Matsusaki T, et al. Nonimmersive virtual reality mirror visual feedback therapy and its application for the treatment of complex regional pain syndrome: an open-label pilot study. Pain Med 2010;11(4):622–9.
[15] Sarig-Bahat H, Weiss PL, Laufer Y. Neck pain assessment in a virtual environment. Spine (Phila Pa 1976) 2010;35(4):E105–12.
[16] Gershon J, Zimand E, Pickering M, Rothbaum BO, Hodges L. A pilot and feasibility study of virtual reality as a distraction for children with cancer. J Am Acad Child Adolesc Psychiatry 2004;43(10):1243–9.
[17] Goudman L, Jansen J, Billot M, et al. Virtual reality applications in chronic pain management: systematic review and meta-analysis. JMIR Serious Games 2022;10(2):e34402.
[18] Gaskin DJ, Richard P. The economic costs of pain in the United States. J Pain 2012;13(8):715–24.
[19] Qaseem A, Wilt TJ, McLean RM, et al. Noninvasive treatments for acute, subacute, and chronic low back pain: a clinical practice guideline from the american college of physicians. Ann Intern Med 2017;166(7):514–30.
[20] Dale R, Stacey B. Multimodal treatment of chronic pain. Med Clin North Am 2016;100(1):55–64.
[21] Dey S, Vrooman BM. Alternatives to Opioids for Managing Pain. StatPearls. Hanover: Treasure Island (FL) ineligible companies; 2023.
[22] Thoma N, Pilecki B, McKay D. Contemporary cognitive behavior therapy: a review of theory, history, and evidence. Psychodyn Psychiatry 2015;43(3):423–61.
[23] Hilton L, Hempel S, Ewing BA, et al. Mindfulness meditation for chronic pain: systematic review and meta-analysis. Ann Behav Med 2017;51(2):199–213.
[24] Cherkin DC, Sherman KJ, Balderson BH, et al. Effect of mindfulness-based stress reduction vs cognitive behavioral therapy or usual care on back pain and functional limitations in adults with chronic low back pain: a randomized clinical trial. JAMA 2016;315(12):1240–9.
[25] Ashar YK, Gordon A, Schubiner H, et al. Effect of pain reprocessing therapy vs placebo and usual care for patients with chronic back pain: a randomized clinical trial. JAMA Psychiatry 2022;79(1):13–23.
[26] Rothrock NE, Amtmann D, Cook KF. Development and validation of an interpretive guide for PROMIS scores. J Patient Rep Outcomes 2020;4(1):16.
[27] Coghill RC, Sang CN, Maisog JM, Iadarola MJ. Pain intensity processing within the human brain: a bilateral, distributed mechanism. J Neurophysiol 1999;82(4):1934–43.
[28] Coghill RC, Talbot JD, Evans AC, et al. Distributed processing of pain and vibration by the human brain. J Neurosci 1994;14(7):4095–108.
[29] Craig AD, Chen K, Bandy D, Reiman EM. Thermosensory activation of insular cortex. Nat Neurosci 2000;3(2):184–90.
[30] Hofbauer RK, Rainville P, Duncan GH, Bushnell MC. Cortical representation of the sensory dimension of pain. J Neurophysiol 2001;86(1):402–11.
[31] Iadarola MJ, Berman KF, Zeffiro TA, et al. Neural activation during acute capsaicin-evoked pain and allodynia assessed with PET. Brain 1998;121(Pt 5):931–47.
[32] Duncan GH, Bushnell MC, Talbot JD, Evans AC, Meyer E, Marrett S. Pain and activation in the thalamus. Trends Neurosci 1992;15(7):252–3.
[33] Hoffman HG, Richards TL, Van Oostrom T, et al. The analgesic effects of opioids and immersive virtual reality distraction: evidence from subjective and functional brain imaging assessments. Anesth Analg 2007;105(6):1776–83.
[34] Skolnick P. The opioid epidemic: crisis and solutions. Annu Rev Pharmacol Toxicol 2018;58:143–59.
[35] Saha TD, Kerridge BT, Goldstein RB, et al. Nonmedical prescription opioid use and DSM-5 nonmedical prescription opioid use disorder in the United States. J Clin Psychiatry 2016;77(6):772–80.
[36] Knoerl R, Lavoie Smith EM, Weisberg J. Chronic pain and cognitive behavioral therapy: an integrative review. West J Nurs Res 2016;38(5):596–628.
[37] Rutter CE, Dahlquist LM, Weiss KE. Sustained efficacy of virtual reality distraction. J Pain 2009;10(4):391–7.
[38] Hylands-White N, Duarte RV, Raphael JH. An overview of treatment approaches for chronic pain management. Rheumatol Int 2017;37(1):29–42.
[39] Sarig Bahat H, Takasaki H, Chen X, Bet-Or Y, Treleaven J. Cervical kinematic training with and without interactive VR training for chronic neck pain - a randomized clinical trial. Man Ther 2015;20(1):68–78.
[40] Sarig Bahat H, Croft K, Carter C, Hoddinott A, Sprecher E, Treleaven J. Remote kinematic training for patients with chronic neck pain: a randomised controlled trial. Eur Spine J 2018;27(6):1309–23.
[41] Trujillo MS, Alvarez AF, Nguyen L, Petros J. Embodiment in virtual reality for the treatment of chronic low back pain: a case series. J Pain Res 2020;13:3131–7.