Reports on Global Health Research
Louw A, et al. Rep Glob Health Res 6: 157.
https://www.doi.org/10.29011/2690-9480.100157
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Research Article

Pain Neuroscience Education Delivered Through Virtual Reality for Common Musculoskeletal Conditions Seen in Physical Therapy: An Exploratory Study

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Citation: Louw A, Zimney K, Stopher D, Saldanha KG, Shockley J, et al. (2023) Pain Neuroscience Education Delivered Through Virtual Reality for Common Musculoskeletal Conditions Seen in Physical Therapy: An Exploratory Study. Rep Glob Health Res 6: 157. DOI: 10.29011/2690-9480.100157.

Received Date: 28 April, 2023; **Accepted Date:** 03 May, 2023; **Published Date:** 05 May, 2023

Abstract

Treating persistent musculoskeletal pain in healthcare and globally is clinically challenging and emerging digital therapeutic treatments such as augmented and virtual reality may help ease this burden. Current best evidence supports pain neuroscience education (PNE) as a viable strategy to ease pain and disability of patients attending physical therapy with persistent musculoskeletal pain. The objective of this exploratory study was to determine what, if any, positive effects PNE delivered via virtual reality may yield on the four largest patient groups seen in physical therapy and healthcare in general – low back, neck, knee, and shoulder pain. Forty patients (10 patients each with low back, neck, knee, and shoulder pain) underwent a 12-minute PNE session following an in-person physical therapy session. Prior to and immediately following treatment, heart rate, self-reported pain ratings (numeric pain rating scale – NPRS), pain catastrophizing (pain catastrophization scale – PCS), fear-avoidance (fear-avoidance beliefs questionnaire – FABQ) and active range of motion was measured. Additionally, the global rating of change (GROC) scale was used following treatment to assess the patient experience. No significant changes were found in heart rate and blood pressure. FABQ-PA (physical activity) improved significantly in patients with neck, shoulder, and back pain, with large effect sizes. PCS improved significantly ($p = 0.034$) for patients with low back pain, while only patients with shoulder pain showed a significant change in self-reported pain ($p = 0.04$). Active range of motion improved significantly in both peripheral joint patient populations (knee flexion [$p = 0.003$], knee extension [$p = 0.002$] and shoulder flexion [$p = 0.023$]), but not spinal patients (back and neck). Mean GROC scores for patients with shoulder (3.0) and knee pain (3.4) were above the minimal clinically important difference. This is the first study to explore PNE-VR for different body regions in patients with persistent pain attending PT. The largest positive shifts were seen for fear of physical activity. Patients with shoulder pain and disability received the greatest benefit from PNE-VR, followed by patients with LBP and knee pain. Future research is needed to develop, test and implement larger scale, controlled trails of virtual reality for patients seeking care for musculoskeletal pain in healthcare.

Keywords: Pain Neuroscience Education; Musculoskeletal Pain; Virtual Reality; Rehabilitation; Digital Therapeutics

Introduction

IIt is well-known that the financial impact of the treatment of musculoskeletal pain in healthcare is significant in the United States (US) and continues to rise [1, 2]. The lifetime prevalence of musculoskeletal pain is reported to be between 40 – 80%, with a reoccurrence rate of nearly 80% [2-5]. With reoccurring episodes of pain and disability, patients are often referred to physical therapy (PT) [6]. Collectively, low back pain (LBP), neck pain, shoulder pain, and knee pain accounts for 80% of outpatient PT visits in the US [6-8]. Persistent musculoskeletal pain creates a significant clinical challenge for healthcare providers, warranting further exploration into evidence-based biopsychosocial approaches [9].

For persistent musculoskeletal pain, it is well-understood that a multi-model approach is needed [9-11]. Current best-evidence treatment for persistent musculoskeletal pain calls for an approach that contains three key elements - cognitive (education), movement, and strategies to calm down a sensitized central and peripheral nervous system [11-13]. Of the three proposed treatments, it is easily argued that PT is most familiar with, and uses movement as a mainstay of its treatment [14, 15]. Within this mandate, therapists can use various forms of movement considering comorbid issues, patient preferences, current best evidence, safety, etc [16]. In the last decade, the pharmaceutical industry has spent considerable time and resources developing ways to calm down the nervous system, i.e., membrane stabilizers, selective-serotonin reuptake inhibitors, etc [17]. In rehabilitation, attention has also shifted to non-pharmacological treatment strategies to calm the central nervous system without the potential side effects of pharmaceuticals [18]. Emerging treatments and evidence supports the use of mindfulness-based stress reduction, breathing, sleep hygiene, relaxation, etc [18-20]. These treatments are now gaining more research and clinical interest from PT, thus fulfilling another one of the three key elements of a program aimed at persistent musculoskeletal pain and disability.

The third component, often used first to set the framework for movement and strategies to calm the nervous system, is education. The objective of the educational component is to change cognitions associated with pain, including high levels of fear-avoidance, pain catastrophizing, anxiety, poor or faulty beliefs about pain, trauma, etc [21, 22]. Most of these educational approaches in PT are borrowed from psychotherapy and may include cognitive behavioral therapy, trauma-informed care, acceptance and commitment therapy, motivational interviewing, positive psychology, etc [21, 23]. In recent years, pain neuroscience education (PNE) emerged from within PT to teach patients more about the biology and physiology of their underlying pain experience, explicitly aiming at persistent musculoskeletal pain [13, 21, 22]. Various systematic reviews and meta-analyses have shown strong evidence that PNE positively influences self-rated pain scores, disability, fear-avoidance, and pain catastrophization [22, 24]. Furthermore, evidence indicates that PNE allows for improved movement and, when combined with movement, is superior to PNE-alone [13, 22, 24]. Additionally, the evidence shows PNE can also yield a calming effect on the nervous system as seen by increased pressure pain thresholds and improved neurodynamic tests of mechanosensitivity of the nervous system [22]. From a PT perspective, it is thus argued that PNE, along with various forms of movement and strategies to calm the nervous system, is in line with the current best evidence to treat persistent musculoskeletal pain.

The best-evidence approach for movement, education, and calming of the nervous system is exciting, yet a significant clinical barrier remains – clinical time to incorporate these approaches. In US PT clinics, most visits average around 30 minutes; thus, time is limited to provide reassessment, treatment, instruction, and review of home exercise programs [25-27]. This presents a clinical dilemma in delivering best-evidence multimodal approaches in limited clinical time, especially for more complex clinical cases such as persistent musculoskeletal pain. One possible emerging strategy is digital therapeutics. Digital therapeutics is a subset of digital health and aims to use digital technologies, including Internet-based health technologies, to treat patients [28]. Emerging digital therapeutics include applications, virtual and augmented reality, wearable technology, etc. [19, 29-31]. Because of the limited time in which clinicians have to treat patients with persistent musculoskeletal pain, digital therapeutics could potentially be utilized to help drive these evidence-based multimodal approaches [19, 31, 32]. In lieu of time constraints, it is argued that some treatments can be delivered in-person by the PT in the available time, i.e., exercise and hands-on therapies.

In contrast, some treatments can be added to a clinical setting via digital therapeutics, i.e., mindfulness, meditation, breathing, education, and more. In this model, a patient may receive a more comprehensive approach to treating their persistent pain and, at the same time, alleviate a clinical burden for the clinician. Recently, a PNE virtual reality (VR) program (PNE-VR) (BehaVR™) was developed to educate patients more about pain and early data showed similar positive changes compared to therapist-led treatment in self-reported pain ratings, fear-avoidance, and patient satisfaction [32]. Additionally, the platform adds other best-evidence strategies such as mindfulness and relaxation. To date, very little is known about the potential benefits of PNE-VR in PT practice. The primary aim of this exploratory case series was to determine what positive effects PNE-VR may yield on the four largest patient groups seen in PT – those with LBP, neck pain, knee pain, and shoulder pain. The secondary aim was to look for differences between diagnosis groups using PNE-VR.

Methods

Patients

A convenience sample of forty consecutive patients attending outpatient PT were invited to participate in the study (Figure 1). This included 10 patients with LBP, 10 with neck pain, 10 with knee pain, and 10 with shoulder pain. Data collection was performed at 4 PT clinics in 4 different states (OK, KY, NC and RI) for 3 months. Each of these clinics have been using a recently developed PNE-VR program, which has been tested in some preliminary research [32]. Institutional Review Board approval was obtained for this study at Southwest Baptist University. After an appropriate explanation of the study and obtaining informed written consent, patient demographic data were collected. Inclusion criteria were that patients be proficient in the English language, no precautions or contraindications specific for VR (i.e., pre-existing binocular vision abnormalities or seizures), be over the age of 18, present with pain and limited range of motion, and not pregnant at the time of the study. The study was designed as an exploratory case series with pre-and post-PNE-VR measurements.

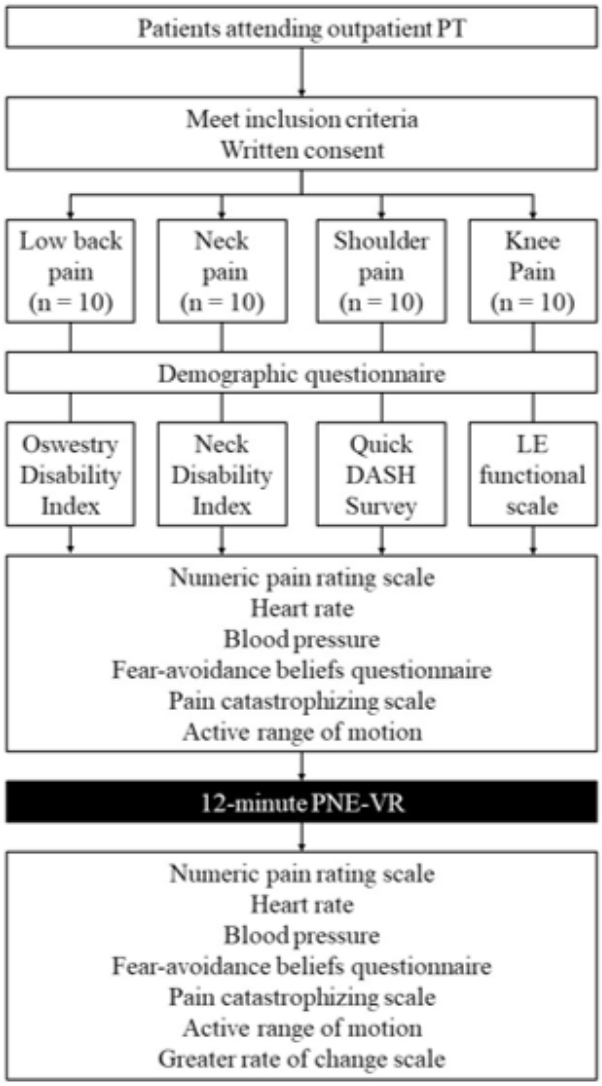

Figure 1: Study Flow Chart (DASH = Disabilities of Arm, Shoulder, and Hand; LE = Lower extremity).

Intervention

The PNE-VR session was designed to be delivered after a patient's planned PT session, thus not interfering with their current treatment plan. At the completion of their normal one-on-one session with the attending PT, patients were placed in a private treatment room for the PNE-VR session. The PNE-VR was delivered using a headset and earphones while a patient was seated in a comfortable chair (Figure 2). Patients were familiarized with the VR headset, navigating the VR dashboard the subject sees in the headset, and how to access each of the sessions utilizing a hand-held activator. The PNE-VR sessions were uploaded via a wireless signal to the headset and the subject used a hand-held activator to start, navigate and end their PNE session. The PT was not in the room during the PNE-VR. The software tracked the subject throughout the sessions, ensuring they fully complete each session. The VR system provides a total 360-degree immersion, including sound, as a means to provide a true sensory virtual environment. The total of the PNE-VR treatment session was 12 minutes to limit prolonged VR exposure and mimic typical in-person therapist-led PNE [25, 33]. The content of the PNE-VR is in line with current one-on-one, clinician-led PNE research [22, 25]. The PNE-VR session included an introduction to PNE (1 minute), an introduction to the nervous system (3 minutes), a metaphor of the sensitive alarm system to educate patients on hyperalgesia and allodynia (2 minutes) [25]. A metaphor of the "nosy" neighbor to educate patients about spreading pain as a consequence of a sensitized nervous system (2 minutes), and strategies used to calm down a sensitized nervous system non-pharmacologically (4 minutes).

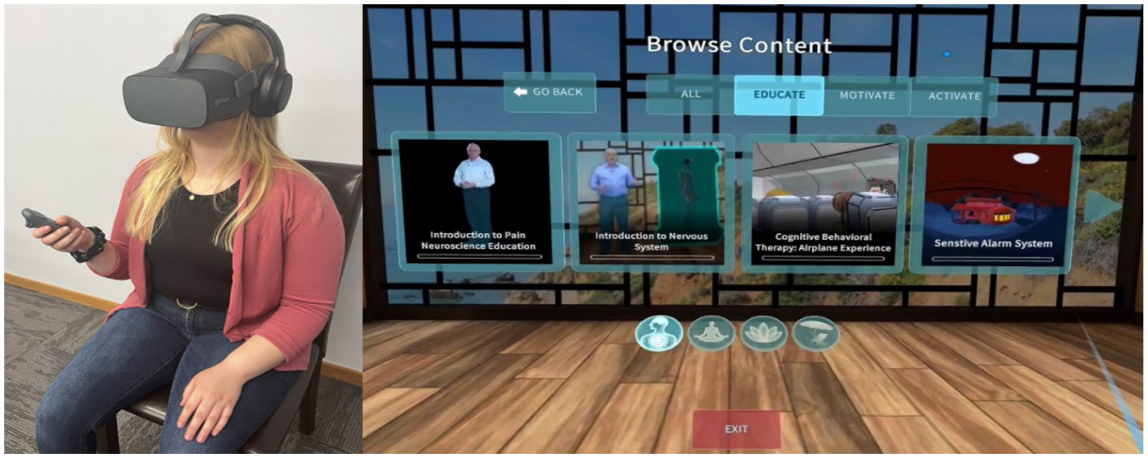

Figure 2: PNE-VR

Measurements

Before PNE-VR, patients completed a demographic survey including age, gender, duration of pain, race, level of education, employment status, past history of pain, previous surgery on the affected body area, the body part being treated, and family history of joint pain. For each of the four body regions, a disability score was obtained to describe further the cohort of patients in the study (Figure 1):

LBP (Oswestry Disability Index – ODI): The ODI is a validated, extensively utilized questionnaire for people who suffer from LBP. It consists of 10 items representing different health constructs (i.e., pain intensity, physical functioning, sleep functioning, social functioning). Each section is scored on a 0 to 5 rating scale, where zero means 'No pain' and 5 means 'Worst imaginable pain'. The total score of the ODI is calculated by adding all scores of applicable items, dividing the obtained score by the maximal total score, and by multiplying the result by 100 to get a percentage score [34]. The higher the score, the higher the patient-determined disability [34, 35].

Neck Pain (Neck Disability Index – NDI): The NDI is a modification of the ODI questionnaire. It consists of a patient-completed, condition-specific, functional-status questionnaire with 10 items: pain, personal care, lifting, reading, headaches, concentration, work, driving, sleeping, and recreation. The NDI has sufficient support and usefulness to retain its current status as the most commonly used self-report measure for neck pain [36]. It is calculated the same way as the ODI. Each section is scored on a 0 to 5 rating scale, where zero means 'No pain' and 5 means 'Worst imaginable pain'. The total score of the NDI is calculated by adding all scores of applicable items (total of 50 or 100% activity limitation) [37].

Knee Pain (Lower Extremity Functional Scale - LEFS): The LEFS is a 20-item valid patient-rated outcome measure for measuring lower extremity function for adults [38]. The LEFS has shown reliability and validity in measuring disability in lower extremity musculoskeletal conditions [39]. The questionnaire rates several functional tasks from "Extreme Difficulty" to "No Difficulty." The maximum score is 80 points. The higher the score, the higher the function [38, 39].

Shoulder Pain (Quick Disabilities of the Arm, Shoulder and Hand questionnaire - QuickDASH): The QuickDASH is a validated, abbreviated version of the original DASH outcome measure. It is an 11-item questionnaire measuring the ability to perform functional tasks, absorb forces, and current symptoms. It uses a 1-5 rating scale. This questionnaire is used with anyone with upper extremity (shoulder, elbow, hand) pain or symptoms [40]. The higher the score, the greater the patient-rated disability [40].

Before and immediately following PNE-VR, a series of measurements were performed to assess the efficacy of the PNE-VR session. Measurements were a blend of psychometric measures, patient self-report measures, and physical measures (Figure 1):

Self-Reported Pain Rating (Numeric Pain Rating Scale – NPRS): The NPRS is a standard self-reported pain rating scale for numerous musculoskeletal conditions [41-43]. For each body part or condition, a separate minimal detectable change (MDC) and minimal clinically important difference (MCID) have been established. In line with the patient population of this study and covering various musculoskeletal conditions, the MCID for chronic musculoskeletal pain of 1 point by Salaffi, et al was used to measure clinical efficacy [44].

Blood Pressure (Millimeters of Mercury – mmHg): Patient blood pressure was measured using an automatic blood pressure cuff.

Heart Rate (Beats per Minute – bpm): Patient heart rate was measured using an automatic blood pressure cuff.

Fear-Avoidance (Fear-avoidance beliefs questionnaire - FABQ): The FABQ is a 16-item questionnaire that was designed to quantify fear and avoidance beliefs in individuals with LBP, but have since been adapted to musculoskeletal pain. The FABQ has two subscales: 1) a 4-item scale to measure fear-avoidance beliefs about physical activity (FABQ-PA) and 2) a 7-item scale to measure fear-avoidance beliefs about work (FABQ-WS). Each item is scored from 0 to 6, with possible scores ranging between 0 and 24 and 0 and 42 for the physical activity and work subscales, respectively, with higher scores representing an increase in fear-avoidance beliefs. The FABQ has demonstrated acceptable levels of reliability and validity in previous studies [45, 46]. Presence of avoidance behavior is associated with an increased risk of prolonged disability and work loss. It is proposed that FABQ-PA >14 and FABQ-WS > 34 are associated with a higher likelihood of not returning to work or activities of daily living [47]. The MCID for the FABQ has been reported as 13.0 [48].

Pain Catastrophizing (Pain Catastrophization Scale – PCS): The PCS is a self-report questionnaire that assesses inappropriate coping strategies and catastrophic thinking about pain and injury. The PCS has been used in previous musculoskeletal studies [49, 50] and demonstrated strong construct validity, reliability, and stability [51]. The PCS utilizes a 13-item, 5-point Likert scale with higher scores indicating elevated levels of catastrophizing. Previous studies using the PCS have shown a median score of 18 in healthy individuals, and a score over 30 is reported as a high level of pain catastrophization [51]. In patients with musculoskeletal pain, the PCS's minimal detectable change (MDC) is reported to be 9.1 [52], and the MCID has not been established.

Active Range of Motion:

Low Back:

Active trunk flexion: Active trunk forward flexion, measured from the longest finger on the dominant hand to the floor in centimeters (cm) [53-55]. The MDC for active trunk forward flexion has been reported as 4.5 cm [56].

Straight leg raise (SLR): SLR was used as a neurodynamic measurement rather than a test of hamstring length. SLR was measured with an inclinometer placed on the tibial crest 5cm distal to the inferior border of the patella on the most affected leg [53-55]. SLR for this study kept the ankle in neutral (90 degrees) with no added dorsiflexion or plantar flexion, per previous studies [53-55]. MDC for SLR has been reported as a 5.7 degree difference [56].

Neck:

Neck active range of motion for flexion, extension, and left and right rotation was measured using an inclinometer as used in past studies on neck pain [57, 58]. Cervical spine range of motion measures with a goniometer have been shown to be reliable in all directions [59] and the MDC values for lateral bending have been reported as 2.89°, 6.78° for extension, and 3.81° for flexion [60].

Shoulder:

Active shoulder flexion of each patient's *affected* arm was assessed with a goniometer with the patient seated. Skin marks were placed for the goniometric measurements to allow consistency of pre- and post-PNE-VR measurements. There is good reliability and validity of goniometric shoulder AROM measurements [61-63]. The MDC for shoulder flexion has been reported as 8 degrees, and the calculation of the MCID is dependent on patient pathology [62, 64].

Knee:

Active knee flexion and extension range of motion was assessed with a standard goniometer with the patient in a supine

position. To ensure consistency of pre- and post-treatment measurements, skin marks are placed for the goniometric measurements. There is good evidence for the reliability and validity of goniometric knee range of motion measurements [65]. The MDC for knee pain varies between 3-5 degrees, while the minimal clinically important difference (MCID) is reported at 10 degrees [66, 67].

Patient self-reported experience following the PNE-VR was measured only post-intervention, using the global rate of change (GROC) scale. The GROC is a scale that measures self-perceived change in health status. The primary purpose is to qualify the extent to which a patient has improved or deteriorated over time. The GROC scale involves a single question for the patient to rate their change concerning a particular condition over a specified period. The patient then rates on a scale to score the magnitude of this change. The scale used goes from -7 (a very great deal worse) to 7 (A very great deal better). The MCID for the GROC for chronic musculoskeletal pain has been reported as a change of 2.0 [68].

Statistical Analysis

All statistics were performed using IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, N.Y., USA) using the significance threshold of $\alpha<0.05$. Descriptive statistics of frequencies, means and standard deviations were calculated for the entire sample population and each body region group. Patient characteristics of age, pain duration, and GROC scores were evaluated between each body region for differences utilizing a one-way ANOVA. In addition, a test for homogeneity of variance was performed on each analysis. Bonferroni correction was used during post-hoc analysis to look for individual differences between the groups. Paired sample t-test was done on individual range of motion, blood pressure, and heart rate changes for each body region before and after the intervention. Reporting of mean differences and standard deviation for each and Hedges' *g* calculation for effect size analysis is reported. Interpretation of effect size for Hedges' *g* was 0.15 for small effects, 0.40 for medium effects, and large effects at 0.75 [69]. The ordinal data of FABQ-PA, FABQ-WS, PCS, and NPRS were compared pre and post-intervention using Wilcoxon matched-pairs signed-rank test. The effect size was calculated through the formula $r = z/\sqrt{N_1+N_2}$. Reporting of magnitude utilized Cohen's criteria [70] of .10 for small effects, .03 or greater for medium effects, and large effects with *r* greater than .50.

Results

Patients

Forty consecutive patients' data were collected, with 10 patients collected for each body part region of the neck, shoulder, back, and knee. The average age was 53.3 (SD = 15.1) years for the whole group, with each body part region demographics listed in Table 1. There was a significant difference between the shoulder and back groups with age, $F(3,36) = 3.90$, $p = .016$. No differences between pain duration were found between groups, and the mean duration of the cohort (82.9 months), indicates a population of patients with persistent pain. Even though four different disability scales were used, the overall cohort exhibited moderate disability associated with their joint pain.

	All (n=40)	Neck (n=10)	Shoulder (n=10)	Back (n=10)	Knee (n=10)
Mean Age (years) (SD)	53.3 (15.1)	54.2 (13.4)	60.0 (8.5)	41.0 (15.3)	57.8 (15.9)
Mean Pain Duration (months) (SD)	82.9 (112.6)	64.7 (85.9)	82.1 (103.3)	56.8 (67.8)	128.2 (169.9)
Gender (female) (%)	25 (62.5)	6 (60)	8 (80)	6 (60)	5 (50)
Race (%)					
African American	8 (20)	2 (20)	2 (20)	1 (10)	3 (30)
Hispanic	3 (7.5)	0 (0)	1 (10)	2 (20)	0 (0)
White	24 (60)	7 (70)	7 (70)	3 (30)	7 (70)
Asian	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Other	5 (12.5)	1 (10)	0 (0)	4 (40)	0 (0)
Mean NDI (SD)		21.9 (9.4)			
Mean DASH (SD)			40.4 (16.5)		
Mean ODI (SD)				12.9 (7.8)	
Mean LEFS (SD)					36.0 (14.1)

NDI = Neck Disability Index, DASH = Disability Arm, Shoulder, Hand, ODI = Oswestry Disability Index, LEFS = Lower Extremity Functional Scale

Table 1: Patient Demographics

Blood Pressure and Heart Rate

Heart rate and blood pressure measurements pre-and post-intervention showed no significant differences for any body region groups.

Self-reported pain and psychometric measures

A few significant differences were found when comparing changes for FABQ-PA, FABQ-WS, PCS, and NPRS after the intervention. FABQ-PA changes were found to be significant, with a decreasing score for all the body regions, except for the knee. (Figure 3) The changes for neck, shoulder, and back FABQ-PA scores demonstrated large effect sizes, r = -.54, -.54, and -.56, respectively. Interestingly, only the FABQ-WS showed a significant change for patients with back pain, z = -2.2, p = .029, r = -.49. All the other body parts did not have significant changes. A similar finding was also found when looking at changes in the PCS score for each body region. Only the patients with back pain had a significant change after the treatment in regard to PCS score moving from 10.1 (SD = 8.0) pre-treatment to 8.0 (SD = 6.9) post-treatment, z = -2.1, p = .034, r = -.47. A change post-treatment for NPRS score was only found in the patients in the shoulder pain group, with a change of 1.4 points reduction in pain, z = -2.1, p =.040, r = -.47, exceeding the MCID.

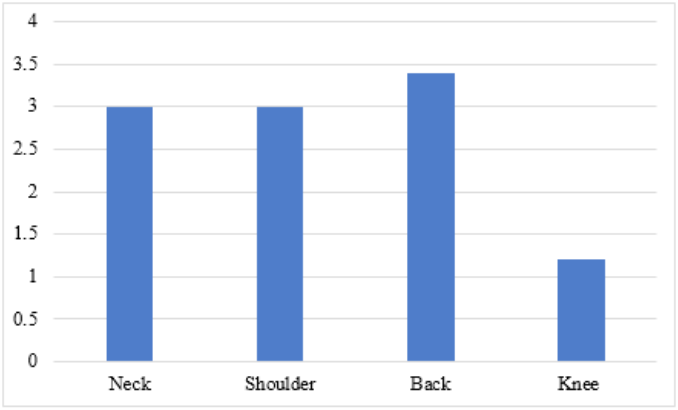

Figure 3: Reduction in FABQ-PA Score after PNE-VR Intervention

Physical Measures

Some significant differences were found when looking at ROM changes between some of the body regions (Table 2). Shoulder flexion changed 5.7 degrees (SD = 6.6) pre-and post-treatment, demonstrating a small effect size. Knee flexion and extension also had significant changes, 4.6 (SD = 3.6) and 4.7 (SD = 3.6) degrees of improvement, respectively, exceeding MDC. This demonstrated a small effect on knee flexion and a medium effect on knee extension. Patients with neck and back pain showed no significant changes in ROM scores after the intervention.

	Mean Difference (SD)	95% Confidence Interval	*p*-value	Effect Size (Hedges' *g*)
Neck flexion	0.7 (7.1)	-4.4 to 5.8	0.762	0.06
Neck extension	4.7 (8.7)	-1.5 to 10.9	0.121	0.42
Neck left rotation	2.3 (7.0)	-2.7 to 7.3	0.329	0.14
Neck right rotation	1.6 (11.8)	-6.9 to 10.1	0.679	0.09
Shoulder flexion	5.7 (6.6)	1.0 to 10.4	0.023*	0.12
Trunk Flexion	-4.4 (7.7)	-9.9 to 1.1	0.101	-0.25
Straight leg raise	4.4 (10.3)	-3.0 to 11.8	0.210	0.17
Knee flexion	4.6 (3.6)	2.0 to 7.2	.003*	0.38
Knee extension	4.7 (3.6)	2.2 to 7.2	.002*	0.61
* Denotes significant difference				

Table 2: Paired Sample t-Test Pre-Post Treatment ROM changes for Each Body Region

Global Rate of Change

There were significant differences in GROC scores after treatment for the groups (Figure 4). The neck group's mean GROC scores differed from shoulder and knee mean scores, F (3,36) = 4.37, p = .010. Individual GROC scores for shoulder and knee (3.0 and 3.4, respectively) were above the minimally clinically important change of 2.0 [68]. However, there was no change in the GROC score for patients with neck pain and minimal change (1.4 points) on the GROC score for patients with LBP.

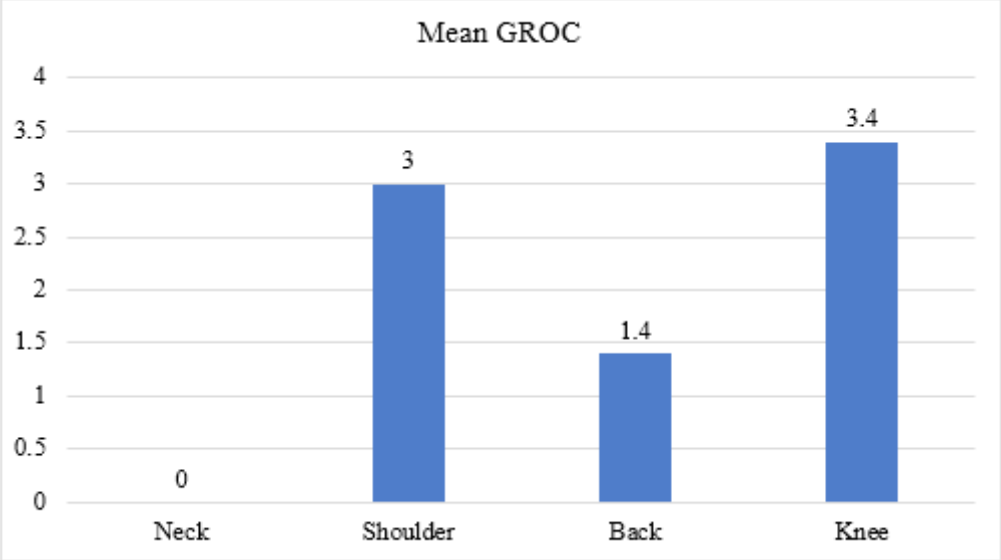

Figure 4: Mean GROC Scores Following PNE-VR

Different Body Regions

Table 3 showcases the comparative and cumulative results of the various outcome measures per body region after PNE-VR. The most positively influenced factor by PNE-VR was fear of physical activity. At the same time, the shoulder joint yielded the most positive shifts of all the body regions, with the neck least influenced.

	Blood pressure	Heart rate	NPRS	FABQ-PA	FABQ-WS	PCS	ROM	GROC
Neck				✓				
Shoulder			✓	✓			✓	✓
Back				✓	✓	✓		
Knee							✓	✓

NPRS = Numeric Pain Rating Scale, FABQ-PA = Fear Avoidance Belief Questionnaire – Physical Activity, FABQ-WS = Fear Avoidance Belief Questionaire – Work Scale, PCS = Pain Catastrophizing Scale, ROM = Range of Motion, GROC = Global Rating of Change

Table 3: Comparative and Cumulative Results of PNE-VR for Musculoskeletal Pain in PT

Discussion

This initial study explored PNE-VR for different body regions in patients with persistent pain attending PT. The most significant positive shifts were seen in fear of physical activity. Patients with shoulder pain and disability received some of the greatest benefits from PNE-VR, followed by patients with LBP and knee pain.

Following PNE-VR, all patient groups, except for neck pain, had a significant shift in FABQ-PA. Fear-avoidance is a powerful driver of persistent pain, and in recent years many treatments in PT have focused on strategies to influence fear-avoidance positively [33, 48, 71]. Interestingly, current PNE research shows a reduction of fear-avoidance and pain catastrophization as the potential primary underlying mechanism behind the success with PNE [12, 13, 21, 22, 24]. A reduction in fear-avoidance allows patients to move more and benefit more from movement-based therapies such as exercise [71]. Reductions in pain catastrophizing have been tied to improved endogenous pain modulation [72]. This study showed that a brief PNE-VR session yields changes in FABQ-PA and PCS comparable to in-person PT-delivered PNE [22]. This finding is key since it demonstrates that a PNE-VR session may add additional benefit to a patient when added after in-person therapy. Additionally, the 12-minute session did not add a significant additional burden to patients from a time perspective. In addition, as seen in GROC scores, the patients' global change rate was positive, especially in patients with shoulder and knee pain. Furthermore, the patient population in this cohort represented a patient sample with years of pain and moderate disability, which often pose significant clinical challenges for clinicians and is the ideal patient group that may benefit from this more robust, add-on, additional treatment [73].

PNE research originated with studies on persistent LBP and to-date, the vast number of clinical studies on PNE has focused on persistent LBP [22, 24]. In this study PNE-VR yielded a positive shift in the persistent LBP cohort shifting FABQ-PA, FABQ-WS, and PCS, concurring with current PNE evidence. Surprisingly, PNE-VR produced most of its benefits for shoulder pain. To date, only one PNE study has been published looking at preoperative PNE in patients preparing for shoulder surgery, which showed that PNE was able to positively influence fear-avoidance, active shoulder flexion, and pressure pain thresholds [74]. The results from this PNE-VR study concur with similar results, indicating that PNE may be a valuable tool in treating patients with shoulder pain and disability and should be further studied. Likewise, the PNE-VR session yielded positive shifts in the patients with knee pain, concurring with previous preoperative PNE studies for knee replacements [75, 76]. Of particular note is that PNE delivered a change in active range of motion in both peripheral joints, which may be of some potential clinical benefit.

Interestingly, PNE-VR had little benefit for patients attending PT with neck pain and disability. This finding is in contrast to a case study using PNE-VR on a patient with persistent neck pain that showed positive effects on pain ratings, PCS, and disability [32]. In a non-VR study, Meeus, et al. showed PNE to increase pain knowledge and alter PCS, which is in contrast to this study. Therefore, additional investigation should explore if PNE-VR has a role in persistent neck pain.

This study contains various limitations. First, by design as an exploratory case series, the lack of control subjects warrants cautious interpretation of the results. Future studies should test a sample of patients undergoing PT with or without the addition of PNE-VR, to truly study the impact of PNE-VR versus traditional therapy. This study also did not explore any follow-up or lasting results, limiting its findings to short-term with no long-term outcomes. Finally, the sample size of this study is small, adding to the limited interpretation of the results. The patient sample used in this study was a convenience sample of patients opting into the study. A patient selection bias may be present, with those opting into the study being more suitable for this intervention, thus showing improved outcomes.

Conclusion

This is the first study to explore PNE-VR for different body regions in patients with persistent pain attending PT. The most significant positive shifts were seen for fear of physical activity. Patients presenting with shoulder pain and disability received the greatest benefit from PNE-VR, followed by patients with LBP and then knee pain. Patients with neck pain demonstrated the least benefit from the PNE-VR treatment used in this study. Future studies should explore larger scale, multi-center clinical trials with comtrol groups what may benefit from VR. The ability to develop such programs plus the ever-expanding research and technology into VR may allow for scalable treatments that may benefit many seeking care from healthcare providers on a regional, national and even global scale.

Author Contributions: AL, DS, KZ and GS developed the research protocol. TC submitted IRB. TC and KZ completed the statistical analysis. Data collection was undertaken by DS, GS, DM, JS and LE. AL and KZ drafted the original manuscript. All authors helped with editing and preparing final manuscript. All authors have read and agreed to the published version of the manuscript.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of Southwest Baptist University, Bolivar MO.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Conflicts of Interest: Authors AL and KZ do provide scietific consultation for BehaVR™ - the virtual reality platform used for the study, but did not gather data for the study. None of the other authors declare any conflict of interest.

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