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REVIEW ARTICLE

Utilising Virtual Reality in Pain Management: A Systematic Review

FAIZ D[1*], NOR RUMAIZAH MN[1], PUTERI SOFIA NADIRA MK[1], MOHD SHAHIR A[2]

[1]Department of Community Health, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia
[2]Pain Unit, Avisenna Hospital, Shah Alam, Malaysia

ABSTRAK

Realiti maya (VR) menawarkan pesakit dengan suplemen bebas ubat, terapi alternatif atau pelengkap untuk pengurusan kesakitan tradisional. Teknologi VR membenarkan penggunaannya dalam pelbagai tetapan dalam dunia perubatan. Oleh itu kami ingin menilai bukti yang ada sehingga kini yang menyokong VR dalam pengurusan kesakitan. Kami melakukan tinjauan sistematik terhadap kajian intervensi dan pemerhatian yang meneliti aplikasi VR dalam pengurusan kesakitan antara tahun 2010 dan 2019. Kami menggunakan pangkalan data Scopus, PubMed, Web of Science, Ovid MEDLINE dan EBSCOhost untuk mengenal pasti kajian menggunakan kata kunci pesakit, VR, perubatan dan pengurusan kesakitan. Data diperoleh oleh dua penyiasat dan persetujuan dicapai dengan penglibatan penyelidik ketiga dan keempat. Sintesis naratif untuk semua kajian telah dilakukan. Sebanyak 451 petikan dikenal pasti, dan di antaranya 12 kajian telah memenuhi kriteria. Kajian melibatkan pelbagai negara dengan usia peserta antara 6 hingga 75 tahun. Kajian adalah kecil dan menggunakan reka bentuk, instrumen dan ukuran yang berbeza untuk hasil. Kajian menangani kesakitan eksperimental, akut dan kronik dengan empat kategori keadaan iaitu kecederaan terbakar, penyakit ortopedik dan sakit kepala kronik. Penggunaan VR adalah berkesan semasa menangani kesakitan eksperimental dan pengurusan kesakitan akut. Sebahagian besar kajian yang melibatkan VR semasa rehabilitasi fizikal yang menyakitkan menemukan bahawa VR berkesan mengurangkan kesakitan kronik dan sebahagian kecil kajian menunjukkan kesan jangka panjang analgesia VR selepas terapi. Penggunaan VR untuk kesakitan kronik dari segi psikologi dan terapi kelakuan kognitif (CBT) menunjukkan penambahbaikan dari sudut kelakuan, emosi dan motivasi yang dapat memberi penambahbaikan kepada kualiti kehidupan.

Address for correspondence and reprint requests: Dr. Faiz bin Daud. Department of Community Health, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Jalan Yaacob Latiff, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia. Tel: +603-91458794 Email: faizdaud@ppukm.ukm.edu.my

VR adalah teknologi yang boleh digunapakai dalam menangani kesakitan kronik dan akut. Penyelidikan menunjukkan penggunaan VR mampu memberikan kesan analgesia yang berkekalan walaupun telah selesai sesi VR. Walau bagaimanapun kajian jangka panjang, sampel yang lebih besar serta kajian lebih menyeluruh diperlukan bagi membukti keberkesanan dari sudut klinikal serta kos dalam penggunaan teknologi ini.

Kata kunci: keberkesanan rawatan, pemulihan, pengurusan kesakitan, rawatan luka, realiti maya, terapi

ABSTRACT

Virtual reality (VR) offers patient with a drug free supplement, an alternative or complementary therapy to traditional pain management. VR technology allowing its use in a wide variety of settings in the medicine world. So, we would like to evaluate the current existing evidence supporting VR in pain management. We conducted a systematic review of interventional and observational studies that examined VR applications in pain management between 2010 and 2019. We used Scopus databases, PubMed, Web of Science, Ovid MEDLINE and EBSCOhost to identify the studies using keywords "patient", "virtual reality", "medicine" and "pain management". Data was obtained by two investigators and agreement was reached with the involvement of a third and fourth investigator. Narrative synthesis for all research was done. A total of 451 citations were identified, among which 12 studies met the criteria for inclusion. Studies involve various countries with participant age ranging from 6 to 75 years old. Studies were small, employed different design, instrument and measure for outcome. Studies addressed experimental, acute and chronic pain with four categories of condition which are burn injury, orthopedic diseases and chronic headache. VR was effective during the procedure in experimental and acute pain management. Majority of studies involving VR in painful physical rehabilitation therapy found VR reduced chronic pain and some provide evidence of lasting analgesia effect of VR after therapy. The usage of VR in chronic pain in term of psychological and cognitive behavioral therapy (CBT) showed improvement of positive mood, emotional and motivation that could lead to improvement of quality of life. VR also useful to elicit findings during painful cervical kinematics assessment in chronic neck pain. VR is a promising technology to be applied in managing chronic and acute pain. Some research showed that VR usage is able to provide lasting effect of analgesia even after VR session. However, there is a need for long term, larger sample sizes and well controlled studies to show clinical and cost-effectiveness for this technology to be used in clinical settings.

Keywords: pain management, rehabilitation, therapy, treatment efficacy, virtual reality, wound care

INTRODUCTION

Pain management as suggested by World Health Organization Analgesic Ladder (WHO 2020), encourage the usage with or without adjuvant therapy at every step of pain stage. Conventional pain management largely involve opioid particularly in chronic pain, but there are negative side effects associated with opioid use in regard to resistance, dependency, misuse, hyperalgesia, and even mortality (Hser et al. 2015; Trang et al. 2015; Vowles et al. 2015). The mixture and the ongoing need to relieve pain, on top of existing traditional forms of care require new therapeutic approaches to help alleviate or control pain.

From science fiction to a modality in pain management. Virtual reality (VR) has had promising application in science and medicine, including intervention delivery since the 1990s. Its usage has been studied in wide range of medical conditions (Gupta et al. 2018; Li et al. 2011; Malloy & Milling 2010; Meijer et al. 2018; Pourmand et al. 2017; Sulea et al. 2014) with a growing evidence of VR as an alternative strategy for pain. Experiments demonstrated that VR have positive effect in pain during a variety of medical procedures and also as an adjunct to pain medication which due to the fact that VR consist of interactions between individual and a computer generate environment stimulating multiple sensory modalities, include visual, auditory, or haptic experiences (Hoffman et al. 2011; Li et al. 2011; Mahrer & Gold 2009). This immersive, entertaining effects are useful for redirecting the patient's attention away from painful treatment experiences and reducing anxiety, discomfort, or unpleasantness (Hoffman et al. 2011; Li et al. 2011).

The most recent systematic review on VR was done 8 years ago, and with the update or advancement of VR technology such as portable head mounted displays (HMD) that has made VR more practical and feasible we would like to study on new emerging evidence on the effectiveness of VR in pain management.

MATERIALS AND METHODS

A comprehensive search, documentation and review was conducted in accordance with the guidelines for Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Liberati et al. 2009) (Figure 1).

Eligibility Criteria

Interventional and observational studies pertaining to VR as a technique for pain management were included. Interventional studies are consisting of randomised and non-randomised controlled trials with or without crossover study designs that evaluated VR usage for acute and chronic pain. We excluded experimental pain. We also include case series as observational studies. We excluded reviews, animal experiments, in vivo/ in vitro, qualitative research (i.e. interviews, surveys) and abstracts of the conference. We included studies in English language over the last 9 years.

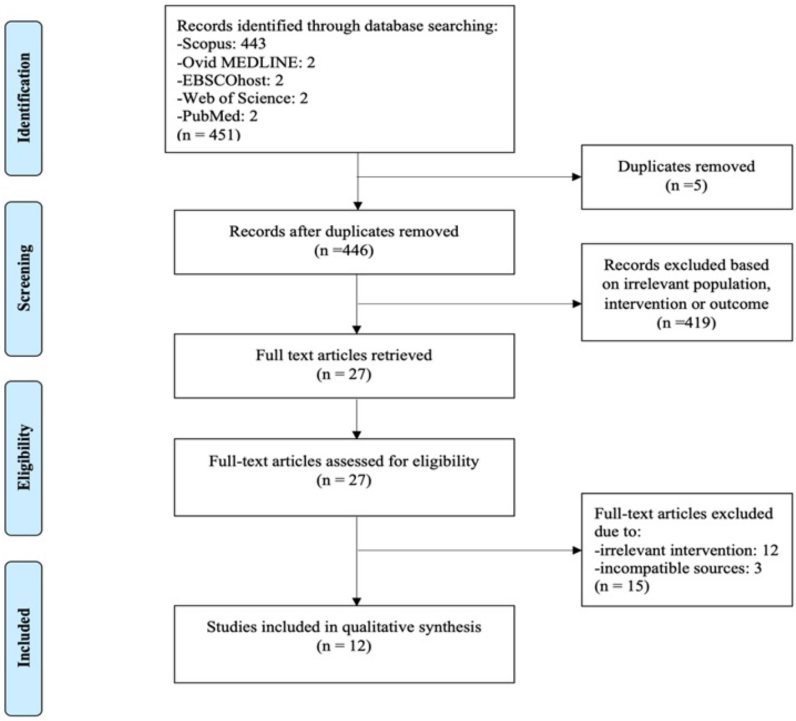

Figure 1: PRISMA flowchart of virtual reality as pain management modality

Sources of Data and Search Strategy

We utilised PubMed, Ovid MEDLINE, EBSCOhost, Web of Science (WOS), and Scopus databases to identify studies from 2010 to 2019 in English language. The literature search strategy was carried out using distinct keywords of "patient", "virtual reality", "medicine" and "pain management" with its respective Medical Subject Heading (MeSH) terms from PubMed and synonyms were used and all search stopped on 27th February 2020. The search strategy and keywords combination with Boolean Operators ('AND' and 'OR') employed are as tabulated in Table 1.

Selection of Studies

Two researchers screened the title and abstracts of each article independently using a planned search strategy to further determine inclusion or exclusion. Any ambiguity in the evaluation were overcome by discussion leading to consensus, with a third-party functioning as an arbitrator, where appropriate. We excluded articles that did not meet the inclusion criteria. In preliminary screening, when the decision to include or exclude was not clear, we discussed and flagged article as 'inclusion' or 'unclear' in which we retrieved the full review of the studies for further evaluation. Eligible studies were defined according to the requirements for inclusion.

Extraction of Data

Table 1: Search strategy and keywords

Patient AND	Virtual reality AND	Medicine AND	Pain management
TITLE-ABS ("patient" OR "patients" OR "patient outcome assessment" OR "patient safety" OR "patient preference" OR "patient-centered care" OR "patient selection" OR "patient participation" OR "patient compliance" OR "patient care team" OR "patient care planning" OR "patient care" OR "patient acceptance of health care" OR "patient care" OR "continuity of patient care" OR "patient comfort" OR "outpatients" OR "inpatients")	TITLE-ABS ("virtual reality" OR "virtual reality exposure therapy" OR "computer simulation" OR "patient-specific modeling" OR "computer graphics" OR "technology" OR "technologies" OR "metaverse" OR "artificial intelligence" OR "cyberspace" OR "simulated 3-D environment" OR "second life" OR "virtual world" OR "virtual life" OR "virtual environment" OR "multiverse" OR "computer simulated environment" OR "user-computer interface")	TITLE-ABS ("medicine" OR "palliative medicine" OR "hospital medicine" OR "molecular medicine" OR "precision medicine" OR "travel medicine" OR "evidence-based emergency medicine" OR "integrative medicine" OR "evidence-based medicine" OR "clinical medicine" OR "state medicine" OR "social medicine" OR "preventive medicine" OR "physical and rehabilitation medicine" OR "holistic health" OR "behavioural medicine" OR "behavioral medicine" OR "community medicine" OR "medicine in the arts" OR "complementary therapies" OR "complimentary therapies" OR "translational medical research" OR "mind-body therapies" OR "public health" OR "one health")	TITLE-ABS ("pain management" OR "Pain, Burning" OR "Burning Pain" OR "Burning Pains" OR "Pains, Burning" OR "Suffering, Physical" OR "Physical Suffering" OR "Physical Sufferings" OR "Sufferings, Physical" OR "Pain, Migratory" OR "Migratory Pain" OR "Migratory Pains" OR "Pains, Migratory" OR "Pain, Radiating" OR "Pains, Radiating" OR "Radiating Pain" OR "Radiating Pains" OR "Pain, Splitting" OR "Pains, Splitting" OR "Splitting Pain" OR "Splitting Pains" OR "Ache" OR "Aches" OR "Pain, Crushing" OR "Crushing Pain" OR "Crushing Pains" OR "Pains, Crushing" OR "palliative care" OR "pain" OR "analgesia" OR "analgesic" OR "distraction" OR "discomfort")

A pre-designed data extraction form were used to insert details on data extraction after researchers did narrative analysis and critical evaluation of the included articles. We extracted the following data i.e. study characteristics (type of study design, method of participant selection, study duration, sample size, amount of intervention and control group participants, baseline features of the studied population, objectives and outcomes measured), participant characteristics (country, study setting, inclusion criteria, exclusion criteria and age), and analysis of results (type of pain, stage of pain condition, duration of VR or dosage, situation of using VR, VR software, device and type being used and endpoints of study).

RESULTS

Overview

In the effort to determine the pain relief results of VR, we collected 451 unique citations through the use of our online database analysis. Leading up to reviewing the titles and abstracts, five overlapping papers were removed. A total of 446 titles and abstracts were screened on the basis of eligibility criteria which then 419 were omitted due to the irrelevant population studied, aspects of intervention or outcomes. Afterwards, 27 full text articles were further filtered according to eligibility, 15 of which had been excluded for the following reasons i.e. 12 for irrelevant intervention and 3 unsuited sources (conference abstracts and review). Eventually, 12 publications were included in the review. PRISMA search flowchart is as shown in Figure 1. Articles selected were conducted in quite diverse countries such as, United States of America (USA) (Jeffs et al. 2014; Law et al. 2010; Maani et al. 2011; Schmitt et al. 2011), Slovenia (Ortiz-Catalan et al. 2016), Israel (Sarig-Bahat et al. 2010; Shiri et al. 2013), Japan (Osumi et al. 2019; Sano et al. 2016; Sato et al. 2010), and Spain (Garcia-Palacios et al. 2015; Herrero et al. 2014). The age of participants ranges from between 4 and 75 years of age. Four studies are randomised controlled trial (one of which is crossover design), six are non-randomised clinical trial (one with comparison group), one case series and one pilot study. Further, most studies were single armed (nine studies) and others are two-armed (three studies) but with unequal number of participants assigned for intervention and control. Various VR equipment were used, whereby five studies utilised a complete immersive VR environment via head mounted displays (HMD) which equipped with integrated sound system and head motion tracking, two studies used VR goggles or helmet on a mounted device to held it in place near patient's eyes, three studies with VR and augmented reality displayed on a desktop computer screen achieving mirror visual feedback system via biofeedback device or surface electrodes such as Cyberglove, Galvanic Skin Response and Myoelectric Pattern Recognition. Another two studies displayed the Engaging Media for Mental Health Applications (EMMA's) World via projector to a large screen. The type of pain can be identified as experimental pain on healthy individual (Law et al. 2010), acute pain (Jeffs et al. 2014; Maani et al. 2011) and chronic pain (Garcia-Palacios et al. 2015; Herrero et al. 2014; Ortiz-Catalan et al. 2016; Osumi et al. 2019; Sano et al. 2016; Sarig-Bahat et al. 2010; Sato et al. 2010; Schmitt et al. 2011; Shiri et al. 2013). Experimental pain explores induced pain by a cold pressor while acute pain is consist of two research on thermal burn injury. On the other hand, chronic pain investigates the chronic musculoskeletal, neuropathic and headache pain. Included studies description as stated in Table 2. Although the participants experienced various types of pain, the findings of all these studies were compiled to estimate the effects. In this review, the findings and conclusions reported by the authors are influenced by prognostic factors such as comorbid conditions and the pain tolerance of individuals as possible potential confounders that either underestimate or overestimate the actual effects of the association.

Experimental Induced Pain

A randomised controlled trial (RCT) in a suburban community among 79 children at the age of 6 to 15 years old, used immersive VR with HMD helmet for children to play game using their voice as an interactive distraction while being induced with cold pressor

Table 2: Characteristics of the 13 included studies reporting virtual reality as pain management modality

Type of Pain	Author (Year)	Study Design	Study Setting	Pain Condition	Situation of using VR	VR duration/ dosage per session	Sample size: intervention/ control	VR software, device and type	Result	Conclusion
Experimental pain	Law et al. 2010	RCT	Suburban community, Age 6-15 years old	Cold-pressor induced	Voluntary cold-pressor pain by submerging non-dominant hand in the cold water up to the wrist	4 minutes	79/-	HMD helmet with Fifth Dimension Technologies, 3D stereoscopic with colour display and headphones incorporated. Nintendo WiiTM game system were used.	Children demonstrated significantly greater improvement in pain tolerance during interactive distraction (playing VR game using their voice via VR helmet with integrated headphones) compared to passive distraction (watch video displayed via VR helmet with integrated headphones), t(78)=6.85, p=0.001	Increasing the demand for central cognitive processing, enhanced the pain attenuating effects of VR technology assisted distraction
Acute pain	Maani et al. 2011	Non RCT with crossover	Army Institute of Surgical Research Burn Center, 20 -27 years old	Burn wound in the army (explosive)	Wound cleaning or debridement	6 minutes	12/-	VR goggles (rockwell Collins SR-80A) were used. Googles were held in place near patient's eyes by robot like arm goggle holding system ((to avoid exclusion of participant with burn to the head or face area). 3D virtual world of SnowWorld via Voodoo Envy laptop. Noise cancelling earphones block outside sounds, substitute calming music and sound effects.	Patients reported significantly less pain when distracted with VR. Pain intensity dropped from 6.25 of 10 to 4.50 of 10. "Pain unpleasantness" ratings dropped from "moderate" (6.25 of 10) to "mild" (2.83 of 10). "Time spent thinking about pain" dropped from 76% during no VR to 22% during VR. Patients rated "no VR" as "no fun at all" (<1 of 10) and rated VR as "pretty fun" (7.5 of 10). Follow-up analyses showed VR was especially effective for the six patients who scored 7 of 10 or higher (severe to excruciating) on the "worst pain" (pain intensity) ratings.	This controlled study showed that immersive VR able to reduced pain experiences by patient with combat related burn injuries during severe burn wound debridement. The greatest reduction was seen among patients with the highest pain during no VR session. These patients were the first to use a VR goggle system mounted on unique custom robot-like arm.

Type of Pain	Author (Year)	Study Design	Study Setting	Pain Condition	Situation of using VR	VR duration/ dosage per session	Sample size: intervention/ control	VR software, device and type	Result	Conclusion
Acute pain	Jeffs et al. 2014	RCT	Burn outpatient clinic, 10-17 years old	Burn injury	Wound care	5 to 100 minutes	8/20	VR helmet on mounted devices (to avoid exclusion of participant with burn to the head or face area). 3D virtual world of SnowWorld via desktop VR analgesia workstation Falcon NW Fragbox, with interactivity using Kensington orbit trackball and music through Bose quiet comfort 3 headphones.	The VR group (Snow World) reported less pain during wound care than either the passive distraction (watch movie) or standard care group as determined by multivariable linear regression adjusted for age, sex, pre-procedure pain, state anxiety, opiate use, and treatment length. The VR group was the only group to have an estimated decrease in pain perception from pre-procedure pain to procedural pain reported. Adolescents pre-treated with opiate analgesics and female adolescents reported more pain during wound care.	Interactive and high technology VR is a powerful, engaging distraction in lessening pain perception during burn wound care in the adolescent population in the ambulatory setting even without HMD helmet. Further studies with larger sample sizes are warranted to replicate findings and extend to other populations including inpatient settings and other types of procedures.
Chronic pain	Sarig-Bahat 2010	Non RCT	Departments of Physical Therapy and Occupational Therapy and outpatient physical therapy clinic, Mean age 39 years old	Neck pain	Cervical kinematics assessment	Nil	25/42	HMD and electromagnetic tracker for motion sensor (placed at the back of HMD to track neck motion). Virtual Environment by Game Maker software.	Velocity and smoothness of cervical motion were more restricted in patient with chronic neck pain.	Researcher were actually attempting to do study the effect of neck pain on cervical kinematics during an activity that simulates functional movements and thus VR environment has been chosen, due to the fact that it has been demonstrated to enhance the effectiveness of exercise interventions in various applications as well as to reduce the pain and anxiety experienced.

Type of Pain	Author (Year)	Study Design	Study Setting	Pain Condition	Situation of using VR	VR duration/ dosage per session	Sample size: intervention/ control	VR software, device and type	Result	Conclusion
Chronic pain	Schmitt et al. 2011	RCT with crossover design	Department of Anaesthesiology, age 6-19 years old	Paediatric burn	Rehabilitation therapy	6-20 minutes	54/-	HMD (nVisor SX, VR 1280, ProView XL 50, ProView Sr 80). 3D virtual world of SnowWorld on Windows OS.	Subjects reported significant decreases (27–44%) in pain ratings during virtual reality. They also reported improved affect ("fun") during virtual reality. The analgesia and affect improvements were maintained with repeated virtual reality use over multiple therapy sessions.	Immersive virtual reality is an effective non-pharmacologic, adjunctive pain reduction technique in the pediatric burn population undergoing painful rehabilitation therapy. The magnitude of the analgesic effect is clinically meaningful and is maintained with repeated use.
Chronic pain	Sato et al. 2010	Case series	Outpatient pain clinic, age 46-74 years old	Complex Regional Pain Syndrome	Motor control therapy	No time limit	5/-	No HMD/goggles. AutoDesk 3DS Max virtual reality system on personal computer desktop, cyberglove as a hand input device, FASTRAK as a real time position and motion tracker. It is a mirror visual feedback system.	Four of the five patients whom received virtual reality mirror visual feedback therapy showed >50% reduction in pain intensity. Two of these patients ended their visits to our pain clinic after five sessions.	Virtual reality mirror visual feedback therapy is a promising alter-native treatment for complex regional pain syndrome. Further studies are necessary before concluding that analgesia provided from virtual reality mirror visual feedback therapy is the result of reversing maladaptive changes in pain perception.

Type of Pain	Author (Year)	Study Design	Study Setting	Pain Condition	Situation of using VR	VR duration/ dosage per session	Sample size: intervention/ control	VR software, device and type	Result	Conclusion
Chronic pain	Shiri et al. 2013	Single arm pilot study	Outpatient Paediatric neurology clinic, age 12-17.5 years old	Paediatric headache	Relaxation therapy	30 minutes	10/-	No HMD/goggles. ProComp Infiniti system via a desktop computer. Two electrodes tracking Galvanic Skin Response which was used as Biofeedback device (ability to relax/sensitivity for headache). It displays virtual representation of patient and their pain. Patient watch their image on screen and try to relax.	Nine patients completed the 10-session intervention. Ratings of pain, daily functioning, and quality of life improved significantly at 1 and at 3 months posttreatment. Most patients reported applying their newly acquired relaxation and imagery skills to relieve headache outside the lab	It is a novel system, combining biofeedback and virtual reality, and it is found be feasible for pediatric use. Randomized controlled studies in larger populations are needed in order to determine the utility of the system in reducing headache, improving daily functioning, and elevating quality of life.
Chronic pain	Herrero et al. 2014	Non RCT	Rheumatology outpatient clinic, age 27-66 years old	FMS	Psychological therapy	20 minutes	40/-	No HMD/goggles. VR environment via Adaptive display software called Engaging Media for Mental Health Applications (EMMA's) World, displayed using two projectors on 3x4 meter screen, Dolby 7.1 surrounding sound audio system.	Significant increases in general mood state, positive emotions, motivation, and self-efficacy due to VR environment which could enhance activity management among chronic pain patient with FMS	Preliminary findings show the potential of VR as an adjunct to the psychological treatment of such an important health problem as chronic pain

Type of Pain	Author (Year)	Study Design	Study Setting	Pain Condition	Situation of using VR	VR duration/ dosage per session	Sample size: intervention/ control	VR software, device and type	Result	Conclusion
Chronic pain	Garcia-Palacios et al. 2014	RCT with repeated measures	Rheumatology Service of public hospital, age 23-70 years old	FMS	Cognitive-behaviour therapy	60 minutes	31/30	No HMD/goggles. VR environment via Adaptive display (EMMA's World) displayed using two projectors on 4x1.5 meters horizontal screen, a speaker system. EMMA is mood induction procedure using 5 scenarios.	Significant improvements in the primary outcome: disability measured with the Fibromyalgia Impact Questionnaire (FIQ) and in secondary outcomes, such as perceived quality of life and some of the coping strategies included in the Chronic Pain Coping Inventory: task persistence and exercise. There were no differences in other secondary outcome measures like pain intensity and interference and depression. Participants reported high satisfaction with the VR component.	VR treatment had positive effects in reducing the impact of FMS on the life of the participants (measured by the FIQ) and significant improvement in perceived quality of life. These findings show that the VR component could be useful in the Cognitive-behaviour therapy (CBT) treatment of FMS. Encourage the need to continue exploring the use of integrating VR with CBT interventions for the treatment of FMS.

Type of Pain	Author (Year)	Study Design	Study Setting	Pain Condition	Situation of using VR	VR duration/ dosage per session	Sample size: intervention/ control	VR software, device and type	Result	Conclusion
Chronic pain	Ortiz-Catalan et al. 2016	Non RCT	Rehabilitation, age 26-74 years old	Intractable PLP	Rehabilitation for the lost limb	2 hours	14/-	No HMD/Goggles. Augmented and Virtual reality combined displayed on a computer screen. Motor phantom execution using myoelectric pattern recognition (via surface electrodes). Patient playing a racing game in which car is driven by phantom movements.	After 12 sessions, patients showed statistically and clinically significant improvements in all metrics of phantom limb pain. Phantom limb pain decreased from pre-treatment to the last treatment session by 47% for weighted pain distribution, 32% for the numeric rating scale, and 51% for the pain rating index. The numeric rating scale score for intrusion of phantom limb pain in activities of daily living and sleep was reduced by 43% and 61%, respectively. Two of four patients who were on medication reduced their intake by 81% (absolute reduction 1300 mg, gabapentin) and 33% (absolute reduction 75 mg, pregabalin). Improvements remained 6 months after the last treatment.	Potential value in motor execution of the phantom limb as a treatment for phantom limb pain. Promotion of phantom motor execution assisted by machine learning, augmented and virtual reality, and gaming is a non-invasive, non-pharmacological, and engaging treatment with no identified side effects at present.

Type of Pain	Author (Year)	Study Design	Study Setting	Pain Condition	Situation of using VR	VR duration/ dosage per session	Sample size: intervention/ control	VR software, device and type	Result	Conclusion
Chronic pain	Sano et al. 2016	Non RCT	Pain and Palliative Medicine Department, age 46-75 years old	Deafferentation pain caused by brachial plexus avulsion or arm amputation / PLP	Rehabilitation	Nil	7/-	Head Mounted Display (Oculus Rift, Oculus VR), Human motion detection system (KinectTM, Microsoft), Data glove (CyberGlove® II, CyberGlove Systems) for detecting finger flexion, 3D world by Unity	Task with the tactile feedback reduced deafferentation pain more (41.8 ± 19.8%) than the task without the tactile feedback (28.2 ± 29.5%), which was supported by a Wilcoxon signed-rank test result ($p < 0.05$).	Tactile feedback strengthens the pain reduction effect of the task in the virtual reality system.
Chronic pain	Osumi et al. 2019	Non RCT	Outpatient hospital, age 23-71 years old	PLP	Rehabilitation	20 minutes	19/-	Head Mounted Display (Oculus Rift, Oculus VR), virtual world via 3D CG software, producing mirror-reversed computer graphic images of the intact arm a virtual phantom limb, infra-red video cameras (kinetic for Winds v2, Microsoft) to detect movement of intact arm and hand/fingers.	VR rehabilitation significantly restored movement representation ($P<0.0001$) quantified using the bimanual coupling effect and significantly alleviated PLP intensity ($P<0.0001$). PLP alleviation via VR rehabilitation was significantly correlated with "kinesthesia-related pain characteristics" but not "somatosensory-related pain characteristics"	VR rehabilitation may be particularly effective for PLP associated with distorted phantom limb movement and body representations (e.g., clamping, gnawing), compared with typical neuropathic sensations (e.g., shooting, burning, dysesthesia).

Abbreviations: VR=Virtual Reality; USA=United States of America; RCT=Randomised controlled trial; HMD=Head Mounted Display; CROM=Cervical Range of Motion; PLP=Phantom Limb Pain; 3D=Three-dimensional; EMMA=Engaging Media for Mental Health Applications; FMS=Fibromyalgia Syndrom pain by keeping their hands submerged in the water for not more than four minutes. When compared with only watching the video via the VR helmet as a passive distraction, it proves that pain tolerance that was defined as the amount of time (in seconds) that the participant can kept their hand in the cold water significantly improve with interactive distraction. Thus, increasing the demand for central cognitive processing, enhanced the analgesia effect of VR environment in the form of distraction (Law et al. 2010).

Acute Pain

Two studies involving burn wound injury participants investigated the used of immersive VR during wound care (cleaning, debridement) procedure to reduce the pain experienced by the patients. Both used VR goggles or helmet that were mounted on a holding device in which it will be held in place near to the patient's eyes but not fully touching the head or face area to avoid exclusion of patient with burn injury to the particular area. Furthermore, both studies used the same 3D virtual world of 'Snow World'. The controlled study done among 12 army personnel with combat related burn injuries, age between 20 to 27 years old (Maani et al. 2011) showed that using immersive VR has dropped the pain intensity, pain unpleasantness and time spent thinking about the pain significantly compare to when procedure done without VR experience. The procedure done under VR was fixed at six minutes and it is found to be particularly effective among patient who has initially severe to excruciating pain intensity rating. The other study done among 10 to 17 years old outpatient burn injury patients (Jeffs et al. 2014), post procedure questionnaire revealed that the VR group that consist of eight patient reported less pain than either passive distraction (10 patients) or standard care (10 patients) during wound care procedure (ranging from five to 100 minutes) as determined by multivariable linear regression adjusted for age, sex, preprocedural pain, state anxiety, opiate use and treatment length. Using adolescent pediatric pain tool, it was found that the VR group to have an estimated decrease in pain perception from baseline pre-procedure pain to procedural pain. Even without fully HMD helmet, both study showed that participant still able to engage in an interactive distraction thus lessening pain perception or intensity.

Chronic Pain

There were three studies that involves patient with chronic phantom limb pain (PLP). One study using non-immersive VR and the other two utilise immersive VR. The non-immersive did not use HMD or VR goggles, instead augmented and VR were combined and displayed on a computer screen with surface electrode attached over stump to record synergistic muscle activation during motor volition of the phantom limb (phantom motor execution). 14 patients played a racing game in which the car is driven by phantom movements. After 12 sessions, patients showed statistically and clinically significant improvements in all metrics of phantom limb pain. Phantom limb pain decreased from pre-treatment to the last treatment session by 47% for weighted pain distribution, 32% for the numeric rating scale and 51% for the pain rating index. The numeric rating scale score for intrusion of phantom limb pain in activities of daily living and sleep was reduced by 43% and 61%, respectively. Two of four patients who were on medication reduced their intake by 81% (absolute reduction 1300 mg, gabapentin) and 33% (absolute reduction 75 mg, pregabalin). Improvements remained 6 months after the last treatment (Ortiz-Catalan et al. 2016). The other two studies used immersive VR via HMD. Immersive VR were used with tactile feedback (via CyberGlove) to detect finger flexion, in which the patients executed a reaching task using the virtual phantom limb manipulated by their real intact limb (mirror reversed conversion). It showed that adding tactile feedback on the intact hand further enhanced the pain reduction effect among the seven patient during carrying out the task in the VR system (Sano et al. 2016). Osumi et. al (2019) subjected 19 PLP patients to perform VR rehabilitation protocol for 20 minutes in which during the VR rehabilitation, mirror-reversed computer graphic images of an intact arm (the virtual phantom limb) were presented to patients via a head-mounted display, inducing the perception of voluntary execution of movements of their phantom limb when intending bimanual movements. VR rehabilitation significantly restored movement representation ($P<0.001$) quantified using the bi-manual coupling effect and significantly alleviated PLP intensity ($P<0.001$). PLP alleviation via VR rehabilitation was significantly correlated with "kinesthesia-related pain characteristics" but not "somatosensory-related pain characteristics" (Osumi et al. 2019). In a case series study involving complex regional pain syndrome (Sato et al. 2010), no HMD or VR goggles were used, only using VR system and environment displayed on computer desktop for motor control therapy procedure. However, it has cyber-glove as a hand input device, FASTRAK as a real time position and motion tracker with a mirror visual feedback system. Four of the five patients who received VR mirror visual feedback therapy once a week for five to eight sessions showed more than 50% reduction in pain intensity with two of the patients ended their visits to the pain clinic after five sessions. Another rehabilitation or physical therapy that use immersive VR is among the pediatric patient with chronic burn injury. Fifty-four subjects (6 to 19 years old) performed range-of-motion exercises under a therapist's direction for one to five days. During each session, subjects spent equivalent time in both the VR and the control conditions (treatment order randomised and counter balanced). Subjects reported significant decreases (27 to 44%) in pain ratings during VR. They also reported improved affect ("fun") during VR. The analgesia and affect improvements were maintained with repeated VR use over multiple therapy sessions (Schmitt et al. 2011).

Other than using VR during

physical rehabilitation in chronic pain, there were three studies that uses VR technology or environment in psychological, cognitive behavior and relaxation therapy to improves pain or quality of life. A study on ten children with pediatric chronic headache, aimed at using VR system combined with biofeedback for the treatment. With VR and biofeedback, they effectively practiced relaxation and learned to associate successful relaxation with positive pain-free images of themselves. Nine patients completed the 10-session intervention. Ratings of pain, daily functioning, and quality of life improved significantly at 1 and at 3 months post-treatment. Most patients reported applying their newly acquired relaxation and imagery skills to relieve headache outside the lab (Shiri et al. 2013). Two studies on patients with fibromyalgia syndrome (FMS) used non-immersive VR in psychological therapy and cognitive-behavioural therapy (CBT). Both studies used adaptive display software called Engaging Media for Mental Health Applications (EMMA's) World in which it is a mood induction procedure. Herrero et al. (2014) showed that there are significant increases in general mood state, positive emotions, motivation, and self-efficacy due to VR environment which could enhance activity management among chronic pain patient with FMS. This is important because the main difficulty found in FMS patient is unwillingness to start significant daily activities due to the pain. It shows that VR has the potential to assist in psychological treatment in chronic pain. A study on 61 women diagnosed with FMS, randomly allocated into two group i.e. VR treatment and treatment as usual showed that there are significant improvements in disability measured with the Fibromyalgia Impact Questionnaire (FIQ) and in perceived quality of life. However, there were no differences in pain intensity (Garcia-Palacios et al. 2015).

Lastly, due to the fact that VR environment has been demonstrated to enhance the effectiveness of exercise interventions in various applications as well as to reduce the pain and anxiety experienced, VR were used in cervical kinematics assessment and it effectively showed that velocity and smoothness of cervical motion were more restricted in patient with chronic neck pain compared to asymptomatic participants (Sarig-Bahat et al. 2010).

DISCUSSION

In this review, we attempt to describe the use of VR in pain management in term of experimental pain, acute pain and chronic pain. In experimental and acute pain, the studies showed that VR is an effective tool in reducing acute pain experienced during the procedures which are voluntary cold pressor pain and during wound care that involves wound cleaning and debridement lasting from four to 100 minutes in duration. It is found that fully and non-immersive VR still able to allow greater level of immersion that it can effectively function as distraction and alleviate pain during the procedures, whereby in both studies involving wound care in burn injury patients, a complete HMD set were not used instead VR goggle were mounted on devices to held it closes to the eyes only. Our findings are consistent with previous systematic reviews, which have found VR to be effective in reducing pain (Chan et al. 2018; Malloy & Milling 2010; Shahrbanian et al. 2009; Witmer & Singer 1998). However, we were unable to find and compare with acute pain studies that looked into effect of VR towards pain experienced after the medical procedures and also exploring other various medical procedures which could offer more solid evidence of the effectiveness on the usage of VR in acute pain management. Nevertheless, a study on VR as a distraction to alleviate pain among patients during flexible cystoscopy found that there was no benefit of VR in mitigating pain during the procedure. For acute pain, we managed to find studies involving the younger generation from 6 to 27 years old, not involving the older age. The relationship of age with VR efficacy on pain or anxiety could be significant as younger children are often more engaged in magical thinking and captivated by imaginative play (Bolton et al. 2002; Lillard 1993). Thus, there is a need to focus on applicability to adults and elderly. There were no significant heterogenicity in study population and pain conditions, which poses a limitation for the acute pain section for this systematic review.

It is important to also review the efficacy of VR in chronic pain because in chronic pain multiple variable are involve with the sensation of pain which include various psychological factors and central nervous system processes (Grichnik & Ferrante 1991), thus it is possible that despite VR effectively reduced pain in acute pain, it will be ineffective in chronic pain because of these factors. Our review found that there are multiple research involving chronic pain and the findings of VR use in chronic pain are consistent. This is particularly true when VR is directly used during undergoing painful physical rehabilitation therapy in pediatric burn, complex regional pain syndrome and phantom limb pain in which VR significantly reduce pain intensity. Two studies showed that there is a possibility of lasting analgesics effect in patient with chronic pain conditions in which two out of five patient with complex regional pain syndrome that received VR mirror feedback therapy ended their visits to pain clinic after five sessions with VR as they are able to cope without pain medication (Sato et al. 2010). Furthermore, in intractable PLP patients, improvement of pain and reduction of pain medication remained for six months after last rehabilitation treatment with VR (Ortiz-Catalan et al. 2016). More studies with larger sample size is needed to further prove that VR can have long-lasting effect even after the session ended in order to improve quality of life of patient with chronic pain condition. The other end of VR used in chronic pain is in term of psychological therapy and CBT to alleviate pain and quality of life. Combining biofeedback and VR, paediatric patient with chronic headache able to acquire relaxation and imagery skills to relieve headache even without VR (Shiri et al. 2013). VR were showed to have potential as an adjunct to the psychological treatment of chronic pain in term of positive mood, emotion and motivation in initiating daily activities and new outlook on their disability, even though not directly reducing pain intensity. Other than that, due to its flexibility and distraction ability to reduce pain, VR can also utilise to assess cervical kinematics in patient with chronic neck pain (Sarig-Bahat et al. 2010). In this review, studies involving chronic pain is consisted of younger to elderly generation, however, most of the pain condition revolves around orthopedic disorder.

As VR continues to be proven effective as an alternative or adjunct to pain management, it is crucial to consider the cost, feasibility and accessibility of VR equipment. Ensuring VR to not becoming obstacle in term of cost could benefit more to the healthcare. Further studies are needed in term of cost-effectiveness of VR as a pain management tool. This review also highlights the need for higher quality randomised clinical trials in both acute and chronic pain conditions. Studies should compare between the usage of VR and other analgesia therapies, recommended dosage of VR, long term efficacy even after VR and in efficacy in different settings such as in intensive care. There is also need for standardisation in the definition of immersive and non-immersive VR experience as this could affect the outcome differently, due to the fact that there is still limited evidence of immersive versus non immersive VR for pain management (Shahrbanian et al. 2012). Immersive and non-immersive could differ greatly in term of the cost of equipment needed.

CONCLUSION

VR is a promising technology to be applied in managing chronic and acute pain. Some research showed that VR able to provide lasting effect of analgesia even after VR session, however there is a need for long term, larger sample sizes and well controlled studies to show clinical and cost-effectiveness for this technology to be used in clinical settings.

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