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Molecules in focus

Virtual Reality interventions for acute and chronic pain management

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A R T I C L E I N F O

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A B S T R A C T

Virtual Reality (VR) is now consumer ready and nearing ubiquity. In terms of clinical applications, several studies suggest that VR can be effective as a complementary adjunct or alternative non-pharmacologic analgesic in a range of pain-inducing procedures and in management of chronic pain. The increasing affordability and quality of portable VR headsets and the ongoing utility of pain therapy signals an exciting future for the use of VR for analgesia. However, further research is needed to establish its long-term benefits if VR is to be adopted into mainstream protocols for analgesia management. This research requires a range of study designs with collection of patient self-report and clinical data together to develop bespoke interventions for different cohorts.

1. Introduction

Over the past two decades, non-pharmcological interventions for managing pain through Virtual Reality (VR) technologies have gained traction. VR allows the user to view, interact with and be immersed in a multisensory experience of a simulated 3D virtual world (e.g. videos or games) via consumer-ready head mounted displays such as the newly relaeased Oculus Quest ($400 USD). When effective, these interventions represent pain therapy proxies at lower costs of administration that can be even used by patients in the home (Chirico et al., 2016). VR pain therapy was first popularized when Hoffman and colleagues created *SnowWorld*; a VR game of throwing snowballs at animated characters. Used adjunct to opioids during burn wound care, the intervention was effective in alleviating pain in both adolescent (Hoffman et al., 2000) and adult patients (Hoffman et al., 2000). Interestingly, VR pain therapy remained effective even after repeated exposure during burn care treatment (Hoffman et al., 2001) and was comparable to opioid analgesic effect (Hoffman et al., 2007) based on subjective pain reports and objective results from Functional Magnetic Resonance Imaging (FMRI).

Because it is consumer ready, VR provides new affordances as a holistic care device, complementary to existing methods at all levels of healthcare. In this paper we outline current trends and describe the underlying mechanisms for managing acute and chronic pain through VR as a multi-diciplinary solution. We then highlight potential areas of further research and implementation. This is by no means a comprehensive review of existing evidence, rather we aim to provide a reflection on the current trends in implementation of what we will refer to herein as VR analgesia.

2. VR analgesia: areas of application and underpinning mechanisms

Current evidence on VR analgesia is dominated, to a great extent, by studies on acute and procedural pain. A review by Garrett et al. (2014) reported that although there was evidence to show VR effective for relieving immediate or short-term pain, there was a lack of evidence on long-term 'benefits' of using VR analgesia. It is important to note that the relative paucity of research in the area may well reflect the fact that cost-effective VR only became available around 2013 with the Oculus Rift. Here we highlight recent advances in VR analgesia in acute and chronic pain therapy.

2.1. VR analgesia for acute pain management

Indovina et al. (2018) classified a growing number of VR analgesia applications for acute pain management extending into areas such as (1) wound care and physical therapy, (2) pre- and post-surgical procedures, e.g. mitigating pain under local anaesthesia, (3) dental treatment, (4) transurethral microwave thermotherapy, and (5)

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venepuncture in paediatric patients. Frey et al. (2018) applied VR analgesia for managing labour pain (n = 28) in early stages of unmedicated contraction. In this study, participants watching VR videos of underwater scenes with relaxing music, reported significant decreases (up to 95%) in sensory, affective, and cognitive pain and reduced anxiety levels.

The virtual environments for medical purposes may span the entire gamut of immersion, from a 360 ° immersive video tour of a hospital (O'Sullivan et al., 2018) to interactive games such as *SnowWorld* (Hoffman et al., 2000) that allow interaction with the virtual environment with feedback. While in immersive virtual environments one perceives a sense of *presence*, i.e. feeling as though one is actually there. The extent of presence depends on features of VR afforded to the users. For instance seeing one's body parts such as hands manifested in the virtual world (i.e. embodiment) and blocking out noises from the physical world, may lead to a strong psychological experience that one inhabits the virtual world rather than the physical world where painful procedure is present (Persky and Lewis, 2019). This sense of presence can be very overpowering and diminish a persons ability to respond to noxiouis stimuli and attend to nociceptive neural signals which results in perceiving less pain (Pourmand et al., 2018). This mechanism is described as **distraction** and any strategy used to modulate pain in VR builds typically on a level of distraction. However, other mechanisms for VR analgesia include **focus shifting** and **skill-building** (Fig. 1). Those correspond to different levels of patient engagement with pain regulation and therefore agency, as discussed below.

Distraction analgesia (Hoffman et al., 2007), is the most well known mechanism attributed to the impact of VR on pain. Distraction is aimed at diverting a patient's attention from painful stimuli while immersed in a virtual environment. At the heart of distraction therapy is Melzack's (2001) Neuromatrix Theory of Pain, which postulates that inputs such as cognition, sensation and affect (as well as factors influencing these inputs, such as attention) can alter pain output (Fig. 2). This mechanism is linked to the perception of pain and fundamentally different to many analgesics that disrupt pathways that transmit nociceptive signals to central nervous system (Pourmand et al., 2018). This is because in cognition, attentional resources are limited and sensory distraction leaves fewer resources for pain processing. Thus it is thought that incorporation of diverse sensory modalities offers less opportunity for the subject to 'appreciate' pain (McCaul and Malott, 1984). VR as distraction is grounded in research showing efficacy in many forms of distraction, from relaxation through to cognitive tasks (Triberti et al., 2014). Pain can also be modulated via affect. An attentional shift from unpleasant circumstances such as disease symptoms, towards appealing or pleasant stimuli can obviate negative affects like stress and anxiety (Schneider and Hood, 2007). Indeed, the addition of 'fun' and positive emotions have been correlated with analgesia (Sharar et al., 2016). This is consistent with the circumplex model of pain, whereby negative affect actually worsens reported pain by activating the insula cortex, the region largely thought responsible for affect (Sharar et al., 2016).

Focus shifting is explored in an array of VR applications that assign more agency to the user. While distraction and feeling of presence in a virtual environment is an important characteristic of all VR analgesia interventions, focus shifting paradigms such as Multiple Object Tracking (MOT) can guide user interaction, set priorities for cognition and shift player attention from one virtual object to another. For instance Piskorz and Czub (2018) minimized pain and stress during a venipuncture procedure by engaging patients in specific tasks of tracking moving targets while requiring them to recall certain information. Gold and Mahrer (2018) used *Bear Blast,* an interactive VR application for reducing procedural pain in paediatric phlebotomy in a randomized controlled trial (n = 143) that was equally efficacious as standard care. Active engagement with game and user agency is an important factor for efficacy of this type of intervention. Jeffs et al. (2014) conducted a randomized control study (n = 30 adolescents) and found burn patients who actively engaged with a VR game experienced significantly less pain during wound care compared to patients who received passive distraction through watching TV.

Finally, **skill-building** through VR can help patients build capacities necessary to regulate their reponse to painful stimuli and be agents in their own care. For instance Grishchenko et al. (2016) designed *Voxel Bay*, an audio command interactive game to encourage pediatric patients exhale deeply to avoid hyperventilation durng painful procedures. In a scoping review, Gupta et al. (2018) found six VR studies that used skill-building techniques for reducing experimental or treatment pain (e.g. fibromyalgia, burn wound care, paediatric chronic headache). Enhancing patient's sense of control and agency was found an important goal for this type of VR analgesia. For instance controlling the unpleasant audio-visual aspects of a virtual object (linked to biosensor feedback) to make it more pleasant was shown to help patients self-regulate pain in an implicit way (Loreto-Quijada et al., 2014). Skill-building techniques, while more complicated to implement, highlight a less investigated area of medical VR research. Further exploration of sensory augmentation and neurophysiologic changes in VR could reveal new potentials for improving patient self-efficacy in pain management, particularly for those suffering from chronic pain.

2.2. VR analgesia for managing chronic pain

VR applications have been explored for managing chronic pain, i.e. persistent pain lasting beyond the healing period or over 3 months (Pourmand et al., 2018). Chronic pain can be of unknown origin (e.g fibromyalgia), or can arise from injuries (trauma, surgery, stroke), diseases (e.g. diabetes, multiple sclerosis and cancer) and drugs (e.g. anti-cancer drugs) (Jensen et al., 2011). Chronic pain is poorly served by current drugs and the economic, social and health consequences are of critical importance on both national and global levels. For example, this is highlighted by the current 'opioid crisis' where there has been a substantial rise in prescriptions for opioid analgesics in Australia resulting in 1 million Australians mis-using this class of drugs (Autstralian Institute of Health and Welfare, 2017). A VR alternative to analgesic drugs can reduce pain and save lives. While the mechanisms underlying the transition from acute to chronic pain remain unclear, it is thought to arise from interactions between the immune and neuronal systems at the site of injury (Glare et al., 2019). This leads to not only alterations in ascending pain transmission systems, but also modifications in the neurochemicals and wiring of brain systems involved in the sensory and affective components of pain. Like other non-pharmacological interventions, VR has the potential to target these brain systems.

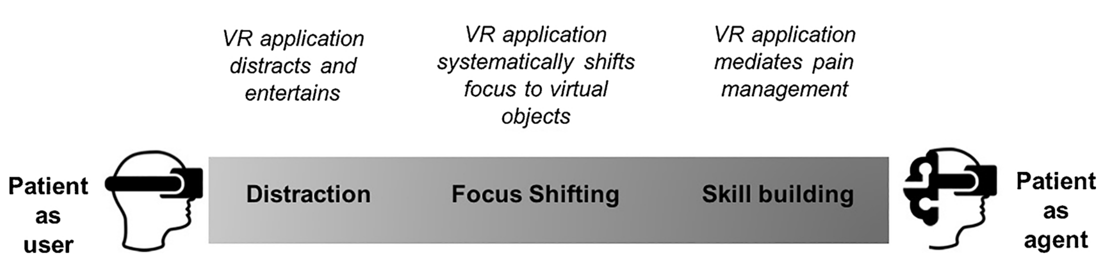

Fig. 1. Mechanisms by which VR analgesia alters pain output, ranging from simple distraction to skill-building via interaction.

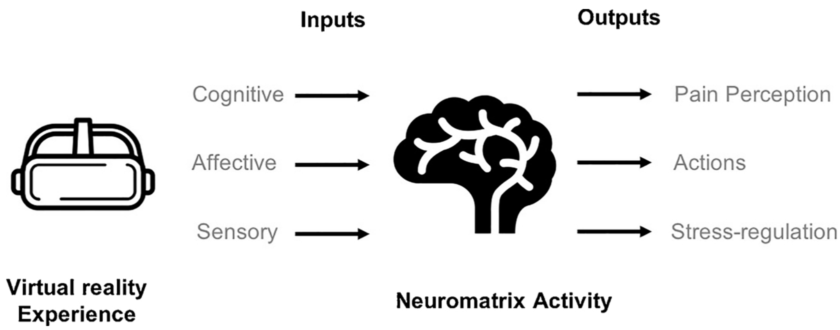

Fig. 2. The mechanisms through which Virtual Reality (VR) distraction operates is explained by the Neuromatrix theory of pain, stipulating that a pattern of activity is generated by an individual's neuromatrix (i.e. network of neurons) which can be manipulated through cognitive, affective and sensory inputs from VR and can alter the pain perception, as well as actions and stress regulation.

Through stimulating the visual, auditory, and proprioception senses, VR provides patients the capacity to manage chronic pain through distraction, focus shifting and/or building skills to modulate the processing of pain sensation. All of these mechanisms are represented in the nine studies (published 2013–2017) reviewed by Pourmand et al. (2018). Distraction and focus shifting therapy was administered via commercial games for a range of conditions including Subacrominal Impimgiment Syndrome (SIAS) (Pekyavas and Ergun, 2017) and in trials with variety of conditions such as cervical spine pain, lumbar spine pain, hip pain and more (Jones et al., 2016). Skill building was described as practicing relaxation in VR to overcome fibromyalgia (Botella et al., 2013), and paediatric chronic headache (Shiri et al., 2013). In the latter, biofeedback captured through galvanic skin response was incorporated in VR to allow patients to concentrate on their heartrate to change an image of their own facial expressions from an emotional state of agony to calm. The study was however limited in terms of analgesic effects beyond the VR session; a common limitation in studies of VR for chronic pain. The skill of controlling one's respiration through meditative acts is typical of many VR applications for chronic pain management (Li et al., 2011), but can be enhanced by using VR paired with biofeedback to imitate the experience of a virtual meditative walk (Gromala et al., 2015).

An area of growing interest in building pain management skills through VR is Phantom Limb Pain (PLP). PLP is linked to dysfunctional alterations in amputee's representations of their body, which results in neuroplastic changes in the central nervous system due to mismatch between motor signals and distorted visual feedback from the missing limb (Rothgangel and Bekrater-Bodmann, 2019). A VR intervention can create an effect of the amputated limb through 3D simulation, similar to mirror therapy. A comprehensive literature review by Dunn et al. (2017) found eight studies (published 2009–2017) that allowed patients gain agency of a virtual limb simulated in VR to perform assigned tasks, with or without tactile feedback to patients. Results revealed great potential for VR intervention as patients achieved reduced pain intensity although this evidence was limited to PLP case studies.

To achieve pain management in long term, patients with chronic conditions need to be empowered by learning sustainable strategies they can use without the constraint of a VR headset. Indeed some patients might avoid a VR experience due to fear that it might trigger the pain (Mertz, 2019). This highlights the importance of customization/personalization of VR analgesia in the success of the intervention (Pourmand et al., 2018). Further research is required not only into the different types of pain, but also individual responsiveness and the user experience in the VR environment. There is, at present, a significant gap in meaningful applications VR analgesia as such, which can only be addressed by putting design at the heart of the product development (Freeman et al., 2017) and in a cross-disciplinary collaboration with medical research.

3. Feasibility, challenges and future of using VR analgesia

"Every feeling person knows from personal experience what pain is", stated Livingston (1953) in his landmark article "*What is Pain?*" Pain is coined as our fifth vital sign that needs to be recorded and assessed in conjunction with the other vital signs (Rowbotham, 2001), but medicine is constantly searching for innovative solutions that could diminish patient perception of pain. Acute pain is considered a risk factor for a number of chronic pain syndromes such as phantom pain and chronic back pain (Dworkin, 1997) which are in turn linked to an alarming rise in use of prescription pain relief drugs that cause dependency (Gupta et al., 2018). In recent times, clear distinctions between anxiolytic and analgesic effects of pain management strategies have been debated, owing to an intrinsic neurological connection between physical pain and negative emotional response (Gaskin et al., 1992). Therefore, it is imperative that a broad suite of care strategies be available for vulnerable patients.

There is little doubt today that VR can be an effective (Indovina et al., 2018) and safe (Tashjian et al., 2017) adjunctive pain therapy. However several issues must be addressed before VR is widely accepted as a routine intervention in pain states. The feasibility of implementing and maintaining VR technology is a challenge for hospitals. More significantly, there is currently limited availability of viable and validated VR content, particularly those using non-distractive mechanisms. Additionally, one might ask "What is a meaningful reduction in pain in VR?" Meaningful changes in pain intensity is described in the literature and variation in individual pain sensitivity is established before devising therapies and trials (Rowbotham, 2001), but in terms of VR, the question remains elusive because we still do not know the limits of this technology.

There are a number of directions that future research on VR analgesia could take. Chirco et al. (2015) called for interdisciplinary investigations to create standardized procedures. This is important for identifying VR interventions suitable for different demographics. Spiegel (2018) reported that younger patients are more open to using VR while older patients find it intrusive, uncomfortable or confusing and suggested a "*VR pharmacy*" inclusive of various patient demographies. Several researchers urge more longitudinal trials with larger sample sizes (Austin and Siddall, 2019) and confirming intervention efficacy by combining patient self-report with bio-physiological parameters (e.g. for assessing stress) to better demonstrate VR capabilities for treating chronic pain and building patients resilience (Indovina et al., 2018; Chirico et al., 2016).

In summary, VR has moved through the hype-cycle and is now here to stay. The increasing affordability and quality of portable VR headsets and the ever present need for exploring new mechanisms for building resilience to pain through VR signals an exciting future for this area of research and practice. A number of considerations can improve the efficacy of VR analgesia interventions. For instance, enhance sense of presence in virtual environment particularly through embodiment, personalization and tailoring of VR to individual differences in preferences and usability to cater difference demographics, and facilitating interpersonal interactions through VR games can enhance its effectiveness (Pourmand et al., 2018; Spiegel, 2018). Taking the idea of a 'tailored experience' one step further to diversify sensory modalities through which patients interact with VR, such as haptic aids to conventional visual and auditory VR cues may be helpful in improving engagement, while simultaneously introducing opportunities of VR application in those with visual impairment. However, to be truly effective, much work needs to be done around strengthening the evidence base for the adoption of VR into mainstream protocols for analgesia management.

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