Ready Patient One: the role of therapeutic virtual reality in the future management of chronic pain

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Virtual Reality (VR) is commonly perceived as 'futuristic', a view that perhaps stems from Hollywood movies from over 20 years ago such as "Tron" and "The Matrix" featuring interactive, computer-generated virtual environments. Yet in 2021, science fiction has become reality with affordable, technologically advanced VR head mounted displays (HMDs) with motion tracking. There is increasing focus on the utility of VR for therapeutics, with pain management emerging as a key area in which VR shows great potential.

Pain is complex and multidimensional, including sensory and emotional components. Attention is an important aspect known to modulate pain, with multiple studies demonstrating reduced pain reporting with 'cognitive distraction'. This was classically illustrated by Bantick et al [1] who studied individuals receiving experimental painful stimuli whilst undertaking the modified Stroop task; a word-colour conflict task aimed at modulating attention. Reduced activation in the thalamus, insula and anterior cingulate cortex was observed on fMRI, correlating with reduced subjective pain intensity.

Modulation of neural activity during acute painful stimuli has similarly been shown to occur during VR experiences. Full audio-visual immersion with VR is thought to lift 'cognitive distraction' to a new level, eliciting self-transcendent feelings of "awe", refocussing attention away from pain and promoting positive mood changes [2-3]. Hoffman et al [4] conducted one of the first fMRI studies evaluating the neurophysiological influence of interactive VR for healthy participants undergoing experimental thermal pain stimuli. Participants were transported to an alternative, virtual reality filled with falling snow, ice caverns and winter creatures with use of VR. Significantly reduced activity within the pain neuromatrix was seen on fMRI, with the suggestion that VR influences modulation of sensory and emotional aspects of pain processing. A further randomised cross-over study by Lier et al [5] investigated changes in electroencephalography (EEG) evoked by 'active' VR, 'passive' VR and control conditions in healthy participants during acute experimental pain. During the 'active VR' intervention, participants travelled along a calm, naturalistic river whilst also being challenged to shoot objects in the distance. When compared with passive and control interventions, 'active' VR significantly reduced the amplitudes of early and late evoked potentials thought to be related to pre-perceptual and late-perceptual pain processing.

There is consistent evidence from clinical trials that VR significantly reduces subjective experiences of acute pain. A commonly cited example demonstrating VR's analgesic efficacy was published by Spiegel et al [6]. This randomised comparative effectiveness clinical trial compared efficacy of VR versus health and wellness video on a television screen. Hospitalised patients with pain of any type, but with an average severity of >3 on a 10-point VAS scale were included. Participants randomised to the VR arm were given a choice of immersive experiences from swimming with dolphins to playing an interactive VR game. The study demonstrated significant reductions in pain immediately post-VR compared to controls ($p<0.04$). Significant effects persisted for up to 72-hours post-intervention ($P=0.04$) with greater analgesia seen in those with severe pain.

Caution is needed in extrapolating these findings to chronic pain. The biopsychosocial model of chronic pain describes its multi-layered nature with dynamic interactions among physiological, psychological, and social factors. Conditions such as Fibromyalgia Syndrome (FMS) are thought to be caused by a variety of processes, with central sensitisation

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characterised by dysregulation of nociceptive pathways and maladaptive neuroplasticity. Despite differences with acute pain, attention modulation strategies have also shown efficacy in chronic pain [7]. Therefore, VR might also be expected to show benefit.

Despite growing numbers of feasibility studies assessing the impact of VR on chronic pain, robust evidence is still lacking. Clinical trials feature heterogenous VR delivery strategies and small sample sizes. One of the earlier studies by Jones et al evaluated the effects of an interactive 'rail shooter' VR game, similar to those used by Hoffman and Lier, on patients with a variety of chronic pain conditions (n=30) [8]. Participants were transported to a nature landscape filled with trees, hills, caves, snow and otters. Interactivity was encouraged with participants shooting fish at the otters. During the VR experience, a 60% reduction in subjective pain ratings were reported, with a 33% reduction persisting when removing the HMD ($p<0.001$). Some participants reported analgesia lasting for hours or even days following the 5-minute VR experience, although formal follow-up was not conducted.

VR has also been investigated as an alternative delivery tool for traditional non-pharmacological treatments such as cognitive behavioural therapy (CBT), biofeedback and mindfulness. Darnall et al [9] conducted a randomised controlled pilot study comparing a self-administered skills-based VR program to an audio-only comparator in patients with chronic low back pain and FMS. Over a 21-day period, participants in the VR group underwent daily CBT, biofeedback or mindfulness conducted within an immersive setting. The audio group received the same guided instruction, without the immersive visual elements. Significant reductions in average pain intensity and improvements in sleep, mood and stress were found in the VR group. Freeman et al [10] also demonstrated large beneficial effect sizes associated with a VR-based automated avatar-led CBT program in a cohort of patients with height phobias.

In the US, the FDA has formally recognised the emerging field of immersive therapeutics as "Medical Extended Reality" (MXR) [11]. Therapeutic VR is now used in hundreds of medical centres in the US for a wide variety of indications including chronic musculoskeletal pain. This has largely been facilitated by the FDA's breakthrough device program. Under the regulatory framework for medical devices currently in place in the UK and EU, substantive feasibility work followed by larger clinical trials are needed to drive future use of MXR in medical institutions. These trials should continue to evaluate the acceptability, feasibility, tolerability and efficacy of VR in specific chronic pain conditions such as FMS [12]. Emphasis should be placed on investigating the short-term and long-term impact of evolving VR technologies, virtual environments, control mechanisms, VR activities and embodiment; as well as robustly evaluating safety. A greater understanding of the underlying mechanisms by which VR influences pain pathways is needed through neuroimaging and physiological studies, investigating the influence on neuroplasticity and salience networks.

Non-pharmacological treatments are now embedded in standard recommendations for the management of chronic pain. There is no doubt that VR has enormous potential to revolutionise management given its unique ability to deliver immersive, individualised treatments remotely. This technology is set to become increasingly widespread and accessible over the coming years, but one for which there is also an urgent need for robust evaluation to guard against false claims of effectiveness and unregulated use.

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