

ACUTE & PERIOPERATIVE PAIN SECTION

Special Article

Innovative Technology Using Virtual Reality in the Treatment of Pain: Does It Reduce Pain via Distraction, or Is There More to It?

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Abstract

Objective. Virtual reality (VR) is an exciting new technology with almost endless possible uses in medicine. One area it has shown promise is pain management. This selective review focused on studies that gave evidence to the distraction or non-distraction mechanisms by which VR leads to the treatment of pain.

Methods. The review looked at articles from 2000 to July 29, 2016, focusing on studies concerning mechanisms by which virtual reality can augment pain relief. The data was collected through a search of MEDLINE and Web of Science using the key words of “virtual reality” and “pain” or “distraction.”

Results. Six studies were identified: four small randomized controlled studies and two prospective/pilot studies. The search results provided evidence

that distraction is a technique by which VR can have benefits in the treatment of pain. Both adult and pediatric populations were included in these studies. In addition to acute pain, several studies looked at chronic pain states such as headaches or fibromyalgia. These studies also combined VR with other treatment modalities such as biofeedback mechanisms and cognitive behavioral therapy.

Conclusions. These results demonstrate that in addition to distraction, there are novel mechanisms for VR treatment in pain, such as producing neuro-physiologic changes related to conditioning and exposure therapies. If these new mechanisms can lead to new treatment options for patients with chronic pain, VR may have the ability to help reduce opioid use and misuse among chronic pain patients. More studies are needed to reproduce results from prospective/pilot studies in large randomized control studies.

Key Words. Virtual Reality; Chronic Pain; Acute Pain; Distraction; Technology

Introduction

Virtual reality (VR) is a powerful technology, with just the name itself evoking infinite possibilities. It has quickly grown from a science fiction dream to a multibillion dollar industry, with mass-produced and widely available wide field-of-view VR devices requiring no more than an advanced smartphone and adaptor headsets available at a fraction of the previous price. In the field of pain management, research has shown VR to be promising in multiple treatment modalities. These include wound care, physical therapy [1], dental pain [2], burns [3], and ischemic pain [4].

While VR technology has been around for more than a few decades, it took its current form very recently. Its prominence grew when the military found use for it in aviation simulators [5]. At first, the hardware required to support VR technology would fill an entire room. As

technology has advanced, the delivery systems have become smaller. Currently there are versions that are desktop screen based, projectors, helmets, or goggles. Each of these devices is designed to provide a screen for the delivery of immersive VR. For devices such as goggles and helmets, the VR screens are mounted close to the user's eyes and can restrict the field of view to only the VR screen. The development of advanced VR helmets, those that are "high tech" vs "low tech" in terms of field of view, blocking out reality, and higher number of pixels, has led to greater analgesic effects. Two words often used with VR are "immersion" and "presence." Defining these terms can help explain how VR functions. "Immersion" is an objective term that describes the amount of sensory input the VR system creates. "Presence" is a subjective value of the illusion one experiences when using the system. While separate values, an increase in immersion often leads to an increase in presence felt by the user [6,7].

Treatment of pain has made some strides in recent years, but there is still room for improvement. Currently acute pain, such as pain experienced postoperatively, is treated with pharmacologic regimens that include non-steroidal anti-inflammatory drugs, acetaminophen, opioids, and gabapentin, which can be combined with local anesthetics and nerve blocks to produce proper pain relief [8]. One situation where current therapies are not sufficient for acute pain control is burn injuries, which require additional levels of care including multiple dressing changes and wound debridements. The combination of the continuous need for pain relief, the long course of recovery, and the severity of pain refractory to current treatment modalities prompts the need for novel treatment strategies to replace or act as adjunctive options to further relieve pain [9–11].

Treatment of chronic pain has recently shifted away from the use of opioids. There are multiple reasons for this change, ranging from the side effects of chronic use to the incidence of tolerance, dependence, and even cases of hyperalgesia [12]. Rates of misuse of opioids in chronic pain have been estimated to be around 21% to 29%, and risk of addiction to opioids has been estimated to be 8% to 12% [13]. For those addicted, mortality rates are increased to up to 20 times the rate of the general population [14]. The limited efficacy in treating certain types of pain and the long-term side effects of the pharmacologic treatment options have put a premium on novel nonpharmacologic treatment options for chronic pain.

The capability of VR to reduce pain has mostly been attributed to active distraction. One main rationale is that attention is required for pain and exists in limited supply; therefore, diverting attention can reduce the resources available for processing pain [15,16]. This distraction mechanism of pain reduction was used long before VR technology. VR is thought to be more effective than traditional methods of distraction because of its immersive property, encompassing a patient's visual processing,

auditory processing, and even physical actions, which in theory demand more attention [17]. The theory of distraction can explain why past studies have demonstrated decreased pain during VR treatment in the setting of acute pain. However, this requires the VR equipment to be active in order to provide relief, which could be complicated, expensive, and unrealistic in treating anything beyond acute pain in a clinic or hospital setting [17]. If new mechanisms for the impact of VR on pain were supported, such as altered coping or neurophysiologic changes, it could open the door and provide a rationale for extended use of VR in pain outside the acute setting. In order to expand the use of VR for the treatment of pain, other mechanisms of pain relief besides distraction should be explored and utilized. Although VR technology is becoming more accessible to the average consumer, there are still barriers of cost, equipment, technical competence, and effective VR programs. The ultimate goal of alternate mechanisms (beyond distraction) should be to produce lasting benefits on pain control even when the patient is not actively using a VR device. In this selective review, we focus on studies that support, detract, or give evidence to mechanisms other than distraction by which VR leads to pain relief.

Methods

This paper looked at articles from 2000 to the present, July 29, 2016, focusing on studies concerning mechanisms by which virtual reality can augment pain relief. The data was collected through a search of MEDLINE and Web of Science using the key words of "virtual reality" and "pain" or "distraction." Specific articles were chosen based upon their ability to address factors that improve distraction with virtual reality or give insight into other mechanisms by which VR may interact with pain. Overall six studies were identified, four small randomized controlled studies and two prospective/pilot studies (studies listed in Table 1). The search results provided evidence that distraction, as expected, is a technique by which VR can have beneficial effects when used in the treatment of pain. These articles focused on acute pain in both adult and pediatric populations. There were also articles showing evidence of new mechanisms by which VR may interact with pain.

Mechanisms

Distraction

Distraction is a well-studied mechanism in VR and is the prevailing belief in explaining how VR reduces acute pain [17,20,22,23]. Studies continue to look at distraction as a mechanism for VR technology's effectiveness in treating pain, with these studies advancing knowledge of the factors that can be manipulated to maximize this treatment effect [6,11,17,24–28]. Many of these studies look at the ability to increase user immersion, which leads to increased presence. This increase in immersion can be influenced by increasing the quality

Table 1 Studies included in review

Reference, Year	Study Type	Number of Participant	Age Range, y	VR and Control	Outcome Measured	Results	Limitations
Garcia-Palacios et al. 2015 [18]	RCT	61	23 to 70	Group screen projected VR vs treatment by rheumatologist	Fibromyalgia Impact Questionnaire (FIQ), Brief Pain Inventory, Chronic Pain Coping Inventory, Beck Depression Inventory II, Quality of Life Index (QLI-Sp)	Significant decrease in FIQ and increase in QLI-Sp, no change in other variables	Lack of control consisting of current standard of care, low education level of participants
Morris et al. 2015 [19]	Pilot	21	18 to 78	No VR used, fibromyalgia subjects matched with nonfibromyalgia subjects	fMRI	Increased activation of areas associated with pain catastrophization in patients with fibromyalgia	Small sample size, no use of VR, proof of concept only
Jeffs et al. 2014 [20]	RCT	30	10 to 17	Tripod-mounted VR helmet vs movie on screen vs standard care	Adolescent Pediatric Pain Tool Word Graphic Rating Scale	Significantly less procedural pain in VR group vs passive distraction, no significant difference between VR and standard of care	Small sample size, lack of generalizability beyond ambulatory setting for burns
Loretta-Quijada 2014 [16]	RCT	77	20 to 56	Screen projected VR with distraction or control software vs blank screen control	Pain threshold, pain tolerance, pain sensitivity range, strongest pain intensity, estimation of time, pain catastrophizing scale, pain self-efficacy	VR distraction significantly increased pain threshold and increased pain tolerance vs No VR; no significant decrease in pain intensity; VR control significantly increased pain tolerance, increased pain sensitivity, lowered time estimation, increased self-efficacy tolerance, and decreased helplessness vs No VR	Unbalanced female to male ratio (70:7), use of nonimmersive VR

(continued)

Table 1 Continued

Reference, Year	Study Type	Number of Participant	Age Range, y	VR and Control	Outcome Measured	Results	Limitations
Shiri et al. 2013 [21]	Prospective single arm pilot study	10	10 to 17	Screen projected VR combined with biofeedback	Pain visual analog scale, Pediatric Quality of Life Inventory	Decreased headache severity and increased quality of life	Small sample size, lack of controlled or randomized design, mixture of headache types
Law et al. 2011 [22]	RCT	79	6 to 15	Virtual reality helmet with interactive or passive distraction video-game vs helmet without distraction, crossover control	Pain tolerance	Significant increase in tolerance for interactive vs passive distraction; older children demonstrated larger response	No control for speech used in interactive VR, no assessment of specific cognitive functions being used

FIQ = Fibromyalgia Impact Questionnaire; fMRI = functional magnetic resonance imaging; QLI-sp = Quality of Life Index; RCT = randomized controlled trial; VR = virtual reality.

of the VR system [6] or through the addition of sound or tactile feedback [25,29].

Pain secondary to burn wounds is one area where the current standard of care for pain control is often ineffective in delivering adequate relief. This severe pain is often resistant to opioid and nonopioid analgesics [30,31]. In order to obtain sufficient pain control, large doses are often necessary, which creates unwanted side effects such as nausea, constipation, and drowsiness [31]. Jeffs et al. [23] used a single blinded, randomized controlled study with 30 adolescents age 10 to 17 years to compare the effects of standard care (including unscripted communication from nurses), passive distraction (movie on a small screen TV at the bedside with noise-canceling headphones) and VR distraction (SnowWorld pain control virtual environment, www.vrpain.com) during burn wound care. Patients in this active VR group were able to control a character moving through the SnowWorld environment using a trackball controller and could interact with the virtual world in several ways, including by throwing snowballs. These patients also received noise-canceling headphones that limited their audio input to that generated by the VR experience. The VR distraction used a tripod-mounted helmet device to avoid using a head-mounted display helmet, which enabled patients with facial burns to be included. The tripod-mounted device allowed for close immersion and a restricted view of reality without relying on a head-mounted display, such as goggles, helmets, or masks. Patients completed either the passive distraction or the active VR for the duration of their burn care procedure. Pain scores were measured using the Adolescent Pediatric Pain Tool word graphic rating scale (APPT-WGRS), which includes a 100 millimeter line word graphic scale to rate pain intensity and has proven efficacious in previous studies [32]. The results showed significantly less procedural pain in the VR group vs the passive distraction group (95% CI = 2.4–45.0, $P=0.029$). For VR vs standard of care, there was a decrease in pain intensity, but this was not statistically significant (95% CI = –9.5 to 28.9, $P=0.32$). The VR treatment group was reported as the only group to have a decrease in pain perception from preprocedural pain to wound care procedural pain. The pain perception statistical significance, or lack of significance, was not shown in the results [23]. In summary, the results of this study support the use of VR as an effective pain control method during wound care procedures for burn wounds. Beyond this, the distraction created by VR was greater than with passive distraction, and this correlated with increased pain reduction. Limitations of this study include it being a single-center study with small group sizes. There was also a difference in time from injury for the passive distraction group, which had less total time from injury. Although this was not statistically significant, it could have had some effect on the results as this group had a higher mean pain score [23].

In Jeffs et al. [23], the passive and VR-based distractions differed in the fact that the VR distraction was

delivered via a tripod-mounted helmet while a small screen was used for the passive distraction. Law et al. [33] used passive and interactive distractions both delivered via the same helmet, even using the same game (Nights: Journey of Dreams, Aqua Garden level) for both groups. The only difference between the two distractions was the passive group only watched and listened to prerecorded sights and sounds within the videogame, while the interactive group allowed the user to control the game themselves. The design was a randomized controlled trial of 79 children age six to 15 years examining whether increased demand on central cognitive processing through distraction tasks would increase a child's tolerance for cold pressor pain. Each patient underwent a baseline trial with a VR helmet but no distraction followed by two counter-balanced trials of passive and interactive distraction. Pain tolerance was measured by the time, in seconds, a child could keep their hand in cold water (7°C). The results showed a significant increase from baseline in pain tolerance for both passive and interactive distraction ($P=0.001$). There was also a significant increase in tolerance during interactive distraction when compared with passive distraction ($P=0.001$). There was no significant order effect. As a secondary analysis, this study evaluated age differences of six to nine years vs 10 to 15 years and their response to distraction. There was no significant difference for passive distraction, but in the interactive distraction trials there was a significant increase in response for the older group [33]. In summary, this article provides evidence for pain tolerance increasing with either passive or interactive VR distraction. When compared with each other, interactive distraction provides a greater increase in pain tolerance. This fits with models of the role of attention and pain where pain engages central attention resources [34]. Therefore, engaging central cognitive resources with tasks can produce an interference with pain processing [21]. This study has a few limitations. First, the study population is restricted to children and adolescents, making generalization to other populations difficult without further studies. There was also no assessment of the cognitive processes involved in the distraction tasks to ensure that they were, in fact, increased with the distraction methods. Lastly, the interactive task required the child to speak, making it hard to rule out the possibility that speaking, independent of VR activity, influenced the increased pain tolerance [33].

Neurophysiologic Changes

In addition to looking at the evidence supporting distraction as a mechanism for the reduction in pain seen with VR technology, this selective review also looked at articles that may provide evidence for other mechanisms. Loreto-Quijada et al. [17] used a randomized controlled trial of 77 psychology students age 20 to 56 years to compare two virtual environments. One treatment group looked at distraction, while the other looked at active participation in VR to improve perception of control over pain, and a third control group incorporated a control

non-VR group utilizing a static screen. The VR distraction treatment consisted of an interactive virtual environment (surreal world). The VR Control Enhancement Condition (VRC) group involved manipulation of an irregularly shaped and sharp polygon (representing pain) to a sphere representing calm with no pain. Sounds were used along with the shape, starting with an unpleasant sound that could be manipulated to a pleasant sound. Unlike the previously mentioned study by Law et al. [33], this study went beyond measuring pain tolerance. Measured values included pain threshold, pain tolerance, pain sensitivity range, strongest pain intensity, estimation of time, pain catastrophizing, and pain self-efficacy (perceived ability to tolerate and decrease pain). The significant results for the VR Distraction group were increased pain threshold vs No VR ($P<0.05$) and increased pain tolerance vs No VR ($P<0.05$), which agrees with the results from a previous study on pain distraction [22]. This study found no significant decrease in pain intensity for the VR Distraction group. The effect of VR distraction on decreasing pain intensity has had mixed results in previous studies [3,4,10,11]. The VRC group showed significant results for increased pain tolerance vs No VR ($P<0.001$), increased pain sensitivity vs No VR ($P<0.05$), and lower time estimation ($P<0.05$). In cognitive measures, significant results were found for increased self-efficacy tolerance vs No VR ($P<0.05$) and decreased helplessness vs No VR ($P<0.001$). For the VR Distraction group, there were no significant differences in the cognitive variables (pain catastrophizing and pain self-efficacy) [20]. In summary, this article provides evidence that VR can have an effect on decreasing pain by mechanisms other than distraction. Limitations of this study include an uneven female to male ratio (70:7) and the use of a nonimmersive VR system.

Shiri et al. [35] is a prospective, single-armed, open-label pilot study of 10 patients designed to present the rationale and feasibility of a novel system combining VR and biofeedback as a treatment option for pediatric chronic headaches. The study enrolled six patients with migraines and four with tension headaches. This study used a similar approach for the VR system as Loreto-Quijada et al. [20]. Instead of using shapes and sounds, however, this study utilized pictures of each patient with a spectrum of emotional states from agony to happiness. The authors then utilized Galvanic Skin Response (GSR) readings to integrate the facial expression being seen in VR by the patient. Patients were asked to look at the screen and attempt to relax, and when the GSR hit a prespecified cutoff point, the shown facial expression would change and in theory lead the patient to a more relaxed state. Results showed a significant improvement in the extent to which headaches limited daily function at one month and three months post-therapy. Quality of life was also significantly increased during treatment and on follow-up at one and three months. On free response sections of the follow-up survey, it was reported that the majority of the patients reported times when they were able to relax

during a headache to the point where the pain was relieved [35]. The limitations of this study include that it is a pilot study with only 10 patients, it had two different types of headaches in the study (migraine and tension), it was not randomized, and it had more males than females. In summary, while this study is very limited it provides an indication that VR combined with biofeedback has the potential to be used in treatment of chronic pain caused by headaches in the pediatric population utilizing a mechanism different from VR distraction.

Morris et al. looked at pain catastrophization in patients with and without fibromyalgia using functional magnetic resonance imaging (fMRI) to compare levels of activity in areas associated with pain catastrophization. The premise was based on a pilot study showing the possible efficacy of imaginary exposure therapy for fibromyalgia [36], and previous studies showing success of VR in exposure therapy for treatment of other medical issues such as anxiety and phobias [19,37]. Using VR images of active and passive activities, the study showed significantly more activation of the regions associated with pain catastrophization in patients with fibromyalgia being shown active images. Based on this, the proof-of-concept study concluded that there is reason to further investigate the use of VR exposure therapy for the treatment of fibromyalgia [38].

While the direct reduction of pain via distraction or other mechanisms is one option, it is not the only way VR may help in the treatment of pain. Studies looking into the use of VR in the treatment of fibromyalgia have suggested that VR may be used to help patients live with the pain [18,38,39]. Garcia-Palacios et al. used a single blinded, randomized controlled trial of fibromyalgia patients to compare treatment as usual (via medications prescribed by a rheumatologist) to cognitive behavioral therapy (CBT) treatment using VR as an adjunct. The results showed a significant decrease in impact of fibromyalgia as measured by the Fibromyalgia Impact Questionnaire for the VR-assisted CBT group. It also reported significant increases in perceived quality of life while no significant changes were found in pain intensity and pain interference [39]. While this study is limited by the control group not including CBT without VR, its stated goals were limited to showing feasibility and preliminary efficacy of VR in combination with CBT for treatment of fibromyalgia.

Discussion

Recent studies continue to provide support for the existing evidence for the ability of VR technology to reduce acute pain through a distraction mechanism in both adult and pediatric populations [20,23,33]. Strong evidence has also shown that the quality of VR and the amount of immersion delivered by the VR technology directly correlates with the measured quantity of analgesic effect [6,11,25]. VR technology is advancing rapidly, with endless imaginable prospective applications. Medicine has the opportunity to benefit immensely from

these advances and also has the potential to contribute to the progression of VR technology through research.

While there is a large body of evidence supporting distraction as the mechanism by which VR can lead to pain relief, studies have recently focused on other mechanisms by which VR may affect pain. In this selective review, multiple studies suggested that there are other mechanisms, beyond simple distraction, by which VR may be able to reduce pain [20,35,38,39]. The studies looking at these alternate mechanisms tend to focus on chronic pain rather than acute pain.

One of the main techniques used to explore nondistracting mechanisms is the utilization of VR programs that differ from the programs used in distraction-based VR technology.

Loreto-Quijada et al. [20] and Shiri et al. [35] both used techniques that transitioned from visuals representing feelings of pain to visuals representing feelings of calm and comfort or happiness. Loreto-Quijada et al. used shapes and sounds to depict the change while Shiri et al. showed that each subject previously obtained visuals of themselves making faces to represent different feelings. Shiri et al. also incorporated biofeedback mechanisms to trigger when the images would change. This was reported to promote awareness of the pain and the bodily reaction to it. Several patients also self-reported the ability to stop headaches by thinking about the VR experience or by attempting to be calm [35]. Garcia-Palacios et al. [39] used VR in a group setting with the goal of promoting emotions and motivations to get patients with fibromyalgia active as part of their treatment regimen. It is a strategy not meant to treat pain directly, but instead to overcome one of the obstacles that can hurt the treatment effectiveness of patients with chronic pain syndromes. The ability to change behavior or provide new behavior strategies for patients suffering from chronic pain can provide lasting benefits even when the VR device is removed.

If these results could be replicated in larger studies, the implications would be far reaching. Current treatment modalities for acute and chronic pain are not ideal or optimal for every patient. Currently, opioid abuse is a huge national problem, with many patients falling victim to substance abuse beginning from an opioid prescribed for legitimate pain [12]. In addition to the risk for dependence, in many situations of chronic pain, opioids do not provide sufficient relief. Even in situations where opioids do provide initial relief, tolerance can build and reduce this effect. Alternative or adjunctive treatment options are necessary for a great number of patients [40].

VR technology provides incredible flexibility, allowing virtual worlds to be created that are only limited by the creativity of their creators. Our continually expanding understanding of how pain is created, interpreted, and acted upon by the nervous system may complement

the improvements in VR to be one of the solutions to the problems facing acute and chronic pain treatment. In this selective review, we discussed evidence that shows that VR is capable of reducing acute pain. If acute pain can be more adequately controlled, patients may require fewer opioids and fewer patients would be likely to become opioid dependent. Chronic pain patients are at increased risk for opioid dependence and misuse because of the persistent nature of their pain. If VR can help relieve chronic pain, this would also have a huge impact on the number of people at risk of becoming dependent.

Beyond the ability to reduce opioid abuse, VR may be able to help patients once they are opioid dependent. Morris et al. [38] suggested that VR could help as part of exposure therapy in patients with fibromyalgia to reduce pain catastrophization, augmenting the cognitive reaction of these patients to their chronic pain. VR has been studied similarly for use in drug dependence. Many studies have looked at the ability of VR to elicit and reduce cravings in chronic alcohol and tobacco use disorder patients, reporting good results [41–47]. Studies have also demonstrated early promise in opioid use [48,49]. An additional study looked into the ability to predict risk of future opioid misuse based upon an attentional bias elicited during VR testing [50]. This suggests that VR may have the ability to influence the opioid abuse crisis from multiple mechanisms.

In summary, this selective review discussed evidence of more than one mechanism by which VR could be used effectively in pain management. Distraction is most suitable for acute pain management and has been well studied. In terms of further research for distraction techniques, larger studies are needed to show which situations call for VR and how it can be logistically integrated into treatment plans. Evidence was also found for neurophysiologic changes caused by VR, which were most evident in the treatment of chronic pain. The evidence for these mechanisms is not as strong as the distraction method for the treatment of acute pain. Blinded, randomized controlled studies are needed to compare these nondistraction methods to no treatment and current treatment options. The VR technology for these goals exists and continues to improve. This may be one of those rare situations where we do not have to wait for technology to catch up to our knowledge. We have the technology—we just need to know how to use it.

References

- 1 Carrougher GJ, Hoffman HG, Nakamura D, et al. The effect of virtual reality on pain and range of motion in adults with burn injuries. *J Burn Care Res* 2009;30:785–91.
- 2 Furman E, Jasinevicius TR, Bissada NF, et al. Virtual reality distraction for pain control during periodontal

- scaling and root planing procedures. *J Am Dent Assoc* 2009;140:1508–16.
- 3 Kipping B, Rodger S, Miller K, Kimble RM. Virtual reality for acute pain reduction in adolescents undergoing burn wound care: A prospective randomized controlled trial. *Burns* 2012;38:650–7.
- 4 Magora F, Cohen S, Shochina M, Dayan E. Virtual reality immersion method of distraction to control experimental ischemic pain. *Isr Med Assoc J* 2006;8:261–5.
- 5 Schmitt PJ, Agarwal N, Prestigiacomo CJ. From planes to brains: Parallels between military development of virtual reality environments and virtual neurological surgery. *World Neurosurg* 2012;78:214–9.
- 6 Hoffman HG, Seibel EJ, Richards TL, et al. Virtual reality helmet display quality influences the magnitude of virtual reality analgesia. *J Pain* 2006;7:843–50.
- 7 Slater M, Wilbur S. A framework for immersive virtual environments (FIVE): Speculations on the role of presence in virtual environments. *Presence Teleoper Virtual Environ* 1997;6:603–16.
- 8 Chou R, Gordon DB, de Leon-Casasola OA, et al. Management of postoperative pain: A clinical practice guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. *J Pain* 2016;17:131–57.
- 9 Schmitt YS, Hoffman HG, Blough DK, et al. A randomized, controlled trial of immersive virtual reality analgesia, during physical therapy for pediatric burns. *Burns* 2011;37:61–8.
- 10 Maani CV, Hoffman HG, Morrow M, et al. Virtual reality pain control during burn wound debridement of combat-related burn injuries using robot-like arm mounted VR goggles. *J Trauma* 2011;71:S125–30.
- 11 Gutierrez-Maldonado J, Gutierrez-Martinez O, Cabas-Hoyos K. Interactive and passive virtual reality distraction: Effects on presence and pain intensity. *Stud Health Technol Inform* 2011;167:69–73.
- 12 Trang T, Al-Hasani R, Salvemini D, et al. Pain and poppies: The good, the bad, and the ugly of opioid analgesics. *J Neurosci* 2015;35:13879–88.
- 13 Vowles KE, McEntee ML, Julnes PS, et al. Rates of opioid misuse, abuse, and addiction in chronic pain: A systematic review and data synthesis. *Pain* 2015; 156:569–76.

- 14 Hser YI, Evans E, Grella C, Ling W, Anglin D. Long-term course of opioid addiction. *Harv Rev Psychiatry* 2015;23:76–89.
- 15 Hoffman HG, Chambers GT, Meyer WJ 3rd, et al. Virtual reality as an adjunctive non-pharmacologic analgesic for acute burn pain during medical procedures. *Ann Behav Med* 2011;41:183–91.
- 16 Li A, Montano Z, Chen VJ, Gold JI. Virtual reality and pain management: Current trends and future directions. *Pain Manag* 2011;1:147–57.
- 17 Mahrer NE, Gold JI. The use of virtual reality for pain control: A review. *Curr Pain Headache Rep* 2009;13:100–9.
- 18 Herrero R, Garcia-Palacios A, Castilla D, Molinari G, Botella C. Virtual reality for the induction of positive emotions in the treatment of fibromyalgia: A pilot study over acceptability, satisfaction, and the effect of virtual reality on mood. *Cyberpsychol Behav Soc Netw* 2014;17:379–84.
- 19 Parsons TD, Rizzo AA. Affective outcomes of virtual reality exposure therapy for anxiety and specific phobias: A meta-analysis. *J Behav Ther Exp Psychiatry* 2008;39:250–61.
- 20 Loreto-Quijada D, Gutierrez-Maldonado J, Nieto R, et al. Differential effects of two virtual reality interventions: Distraction versus pain control. *Cyberpsychol Behav Soc Netw* 2014;17:353–8.
- 21 Legrain V, Damme SV, Eccleston C, et al. A neuro-cognitive model of attention to pain: Behavioral and neuroimaging evidence. *Pain* 2009;144:230–2.
- 22 Dahlquist LM, McKenna KD, Jones KK, et al. Active and passive distraction using a head-mounted display helmet: Effects on cold pressor pain in children. *Health Psychol* 2007;26:794–801.
- 23 Jeffs D, Dorman D, Brown S, et al. Effect of virtual reality on adolescent pain during burn wound care. *J Burn Care Res* 2014;35:395–408.
- 24 Hoffman HG, Richards TL, Coda B, et al. Modulation of thermal pain-related brain activity with virtual reality: Evidence from fMRI. *Neuroreport* 2004;15:1245–8.
- 25 Johnson S, Coxon M. Sound can enhance the analgesic effect of virtual reality. *R Soc Open Sci* 2016;3:150567.
- 26 Lee M, Pyun SB, Chung J, et al. A further step to develop patient-friendly implementation strategies for virtual reality-based rehabilitation in patients with acute stroke. *Phys Ther* 2016;96(10):1554–64.
- 27 Tong X, Gromala D, Gupta D, Squire P. Usability comparisons of head-mounted vs. stereoscopic desktop displays in a virtual reality environment with pain patients. *Stud Health Technol Inform* 2016;220:424–31.
- 28 Triberti S, Repetto C, Riva G. Psychological factors influencing the effectiveness of virtual reality-based analgesia: A systematic review. *Cyberpsychol Behav Soc Netw* 2014;17:335–45.
- 29 Sano Y, Wake N, Ichinose A, et al. Tactile feedback for relief of deafferentation pain using virtual reality system: A pilot study. *J Neuroeng Rehabil* 2016;13:61.
- 30 Patterson DR, Hoffman HG, Weichman SA, Jensen MP, Sharar SR. Optimizing control of pain from severe burns: A literature review. *Am J Clin Hypn* 2004;47:43–54.
- 31 Summer GJ, Puntillo KA, Miaskowski C, Green PG, Levine JD. Burn injury pain: The continuing challenge. *J Pain* 2007;8:533–48.
- 32 Wilkie DJ, Holzemer WL, Tesler MD, et al. Measuring pain quality: Validity and reliability of children's and adolescents' pain language. *Pain* 1990;41:151–9.
- 33 Law EF, Dahlquist LM, Sil S, et al. Videogame distraction using virtual reality technology for children experiencing cold pressor pain: The role of cognitive processing. *J Pediatr Psychol* 2011;36:84–94.
- 34 Eccleston C, Crombez G. Pain demands attention: A cognitive-affective model of the interruptive function of pain. *Psychol Bull* 1999;125:356–66.
- 35 Shiri S, Feintuch U, Weiss N, et al. A virtual reality system combined with biofeedback for treating pediatric chronic headache—a pilot study. *Pain Med* 2013;14:621–7.
- 36 Rodero B, Garcia J, Casanueva B, Sobradie N. Imagined exposure as treatment of catastrophizing in fibromyalgia: A pilot study. *Actas Esp Psiquiatr* 2008;36:223–6.
- 37 Powers MB, Emmelkamp PM. Virtual reality exposure therapy for anxiety disorders: A meta-analysis. *J Anxiety Disord* 2008;22:561–9.
- 38 Morris LD, Louw QA, Grimmer KA, Meintjes E. Targeting pain catastrophization in patients with fibromyalgia using virtual reality exposure therapy: A proof-of-concept study. *J Phys Ther Sci* 2015;27:3461–7.

- 39 Garcia-Palacios A, Herrero R, Vizcaino Y, et al. Integrating virtual reality with activity management for the treatment of fibromyalgia: Acceptability and preliminary efficacy. *Clin J Pain* 2015;31:564–72.
- 40 Stempniak M. The opioid epidemic. *Hosp Health Netw* 2016;90:22–4, 6–9.
- 41 Vollstadt-Klein S, Loeber S, Kirsch M, et al. Effects of cue-exposure treatment on neural cue reactivity in alcohol dependence: A randomized trial. *Biol Psychiatry* 2011;69:1060–6.
- 42 Traylor AC, Parrish DE, Copp HL, Bordnick PS. Using virtual reality to investigate complex and contextual cue reactivity in nicotine dependent problem drinkers. *Addict Behav* 2011;36:1068–75.
- 43 Thewissen R, Snijders SJ, Havermans RC, van den Hout M, Jansen A. Renewal of cue-elicited urge to smoke: Implications for cue exposure treatment. *Behav Res Ther* 2006;44:1441–9.
- 44 Son JH, Lee SH, Seok JW, et al. Virtual reality therapy for the treatment of alcohol dependence: A preliminary investigation with positron emission tomography/computerized tomography. *J Stud Alcohol Drugs* 2015;76:620–7.
- 45 Pericot-Valverde I, Secades-Villa R, Gutierrez-Maldonado J, Garcia-Rodriguez O. Effects of systematic cue exposure through virtual reality on cigarette craving. *Nicotine Tob Res* 2014;16:1470–7.
- 46 Lee JH, Kwon H, Choi J, Yang BH. Cue-exposure therapy to decrease alcohol craving in virtual environment. *Cyberpsychol Behav* 2007;10:617–23.
- 47 Bordnick PS, Traylor AC, Carter BL, Graap KM. A feasibility study of virtual reality-based coping skills training for nicotine dependence. *Res Soc Work Pract* 2012;22:293–300.
- 48 McHugh RK, Park S, Weiss RD. Cue-induced craving in dependence upon prescription opioids and heroin. *Am J Addict* 2014;23:453–8.
- 49 McHugh RK, Fulciniti F, Mashhoon Y, Weiss RD. Cue-induced craving to paraphernalia and drug images in opioid dependence. *Am J Addict* 2016;25:105–9.
- 50 Garland EL, Howard MO. Opioid attentional bias and cue-elicited craving predict future risk of prescription opioid misuse among chronic pain patients. *Drug Alcohol Depend* 2014;144:283–7.