



User Experience in Immersive Virtual Reality-Induced Hypoalgesia in Adults and Children Suffering from Pain Conditions

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Abstract: Pain is the most common reason for medical consultation and use of health care resources. The high socio-economic burden of pain justifies seeking an appropriate therapeutic strategy. Immersive virtual reality (VR) has emerged as a first-line non-pharmacological option for pain management. However, the growing literature has not been accompanied by substantial progress in understanding how VR could reduce the pain experience, with some user experience factors being associated with the hypoalgesic effects of immersive VR. The aim of this review is (i) to summarize the state of the art on the effects of VR on adults and children suffering from pain conditions; (ii) to identify and summarize how mechanisms across immersive VR user experience influence hypoalgesic effects in patients with acute and chronic pain among adults and children. A critical narrative review based on PICOT criteria (P = Patient or Population and Problem; I = Intervention or Indicator; C = O = Outcome; T = Type) was conducted that includes experimental studies or systematic reviews involving studies in experimentally induced pain, acute pain, or chronic pain in adults and children. The results suggest an association between immersive VR-induced hypoalgesia and user experience such as distraction, presence, interactivity, gamification, and virtual embodiment. These findings suggest that hierarchical relationships might exist between user experience-related factors and greater hypoalgesic effects following an immersive VR intervention. This relationship needs to be considered in the design and development of VR-based strategies for pain management.

Keywords: immersive virtual reality; pain; user experience

1. Introduction

Pain perception is defined as an unpleasant sensory and emotional experience associated with or resembling actual or potential tissue damage according to the Association for the Study of Pain (IASP) [1,2]. The perception of pain involves a complex, dynamic, and emergent process in which multiple factors contribute to the outcome and in which relatively small triggers can evoke powerful responses [3]. Indeed, pain has been identified as one of the main clinical conditions needing health care routines associated with a higher total utilization of publicly funded physician visits (58.8%), diagnostic imaging visits (57.6%), and hospital admissions (54.2%) [4], implying a significant economic impact.



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Copyright: © 2024 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). Specifically, it is estimated that musculoskeletal pain (excluding cancer pain) affects more than 30% of the world's population with growth every year [5]. A large percentage of these people will suffer from a process of chronicity, which is defined as pain that persists or recurs for more than 3 months [6]. Overall annual direct health care costs for chronic pain were estimated up to EUR 32 billion in Europe [7], and up to USD 300 billion in the United States [8]. Innovation is required in pain management [9], both in acute pain due to the increasing demand and overuse of opioids, and in the multidisciplinary management of chronic pain where the effect size of standard interventions is often modest [10].

Within non-pharmacological innovative strategies for pain management, extended reality (XR) has emerged as a tool with promising potential for pain relief [11]. XR is an umbrella term that encompasses all virtual technologies, including current technologies such as augmented reality (AR), mixed reality (MR), or virtual reality (VR) [12]. XR refers to a wide range of hardware and software platforms, from partial sensory inputs to fully embodied avatars, through which the users can experience the sense of being in another reality, owning another body, and interacting with virtual characters that do not exist in the real world [13]. In detail, VR refers to simulated experiences through which it is possible to manipulate different sensory inputs intentionally presented to the individual, and integrated by multisensory integration processes [11]. One of the main factors related to user experience in VR environments that differentiates some types of VR from others is the level of immersion [12,14]. The level of immersion in VR has been defined as "an objective property of a system, and greater or lesser immersion as the degree to which a VR system can withstand natural sensorimotor contingencies for perception" [15]. Hence, VR environments can be immersive or non-immersive. According to this, depending on the intensity and quality of the experience generated by the virtual environment, as well as the type of device used according to the degree of immersion and stimulation of the sensory systems, the different modalities within the continuum of extended reality can be differentiated. However, within the different types of VR, it has been shown that immersive virtual reality might provide the greatest potential on pain management [16].

Immersive Virtual Reality in the Approach to Pain

Although a large amount of the available evidence on VR in pain management has been reported through studies of experimentally induced pain in healthy subjects, hypoalgesic effects of VR that have been studied in clinical populations were obtained from clinical studies in acute and chronic pain in adult and pediatric populations [17–19]. The available evidence reports that VR appears to be effective in reducing pain intensity in acute pain and chronic pain populations [20–22] that it has been studied in multiple clinical pictures of musculoskeletal pain [23]. Indeed, VR has been noted to bring several advantages over more conventional treatments in pain management [24], such as increased patient enjoyment and adherence, the safety of the simulated environment, and greater possibilities for customization [25]. However, some barriers to its implementation have also been reported, such as adverse effects, lack of knowledge about the technology, limitation in exposure times, or the hygiene of the device [25,26].

The use of the term "umbrella" of VR has been a real barrier in the comparability of the results obtained in the research on the hypoalgesic effects of VR, where the heterogeneity in the type of VR used, the characteristics present in the immersive VR scenario applied, the dosimetry in the treatment, the outcome measures collected, and factors related to user experience have shown the need to carry out studies with higher methodological quality [16,27]. Therefore, better reported studies on these parameters are required to provide greater strength to the available evidence on the use of immersive VR in people suffering from pain conditions [11,28].

The decrease in pain reported by most patients suffering from pain after being exposed to a VR environment is what we refer to as "immersive virtual reality-induced hypoalgesia". It has been suggested that VR-induced hypoalgesia might result from changes in the activity of the body's pain modulation system through an emotional and cognitive evaluation of nociceptive stimuli [29,30]. However, recent models suggest that the hypoalgesic effects of immersive VR may include changes in sensory and motor processing of the pain experience [11,31]. Hence, the hypoalgesic mechanisms of VR could include the different dimensions of pain experience: sensory–discriminative, affective–motivational, evaluative–cognitive, and motor behavior. This is in accordance with the complex nature of the multidimensional experience of pain, in which there are (i) the somatosensory perception of the characteristics of the threatening event; (ii) the encoding, within emotional and motivational circuits, of the significance or valence of the nociceptive stimuli, where they are categorized as positive (positive valence), neutral (neutral valence), or threatening (negative valence); (iii) an evaluation and modulation of the experience of pain by both cognitive and executive circuits; and (iv) the protective response to this potential threat to our homeostasis [32,33].

Likewise, hypoalgesic effects of immersive VR have been associated with two general categories that are related to the type of experience modality: short-term distraction and long-term neuroplasticity [17]. The most investigated experience modality in VR is distraction (78.6%) followed by virtual embodiment (17.1%). However, although distraction is the mechanism used in 97.8% of acute or experimental pain studies, virtual embodiment was more commonly used in chronic pain conditions (54.5%) [23]. Indeed, it has been shown that the short-term hypoalgesic effects of distraction from pain had a lower impact on pain relief in chronic pain conditions [9]. However, its long-term efficacy, particularly in chronic pain management, is still an important area for further research [34]. In this regard, some evidence had shown that the modalities and features in which the immersive VR experience is induced might have an influence on the magnitude of the outcomes obtained for a pain decrease, as well as on the responsiveness to the intervention between different clinical profiles suffering from chronic pain [28]. Indeed, some factors related to user experience such as presence, interactivity, gamification, and virtual embodiment have also been highlighted as being significant in the immersive VR experience in people suffering from pain conditions [35,36] (Table 1).

Table 1. Factors related to user experience in Immersive Virtual Reality for pain management.

Feature	Definition
Distraction	It refers to the redirection of an individual's attentional resources away from pain, towards other stimuli (visual, auditory, tactile, and cognitive), resulting from a competition for the limited attentional resources shared between the sensory inputs proposed by VR and the incoming nociceptive signals [37].
Presence	It defines the subjective experience of being in one place or environment, even when physically in another place, allowing the user to easily "forget" that it is a computer-generated simulation [38].
Interactivity	It refers to the level of participation allowed by the user in the virtual reality environment [39].
Gamification	It refers to the application of game elements in non-game contexts [40].
Virtual Embodiment	It refers to the replacement of a person's real body with a virtual body representation, allowing the subject to feel embodied in a virtual body [36].

In the past few years, there has been significant advancement in effectiveness and hypoalgesic outcomes of VR technology in both acute and chronic pain [41,42]. However, the growing body of the literature in VR has not been accompanied by substantial advances in the understanding of how factors related to the user experience in VR impact on the hypoalgesic and clinical effects of immersive VR (Figure 1). For this purpose, this article aims to address the state of the art on the relationship between the experience-related factors embedded in immersive VR scenario and the magnitude of the hypoalgesic effect following the intervention.



Figure 1. Factors related to user experience in immersive virtual reality for adults and children in pain.

Trost et al., 2021, have proposed a heuristic model that distinguishes between VR shaping technical factors, user experiential factors, and pain targets that contribute to hypoalgesic effects, to facilitate a common taxonomy of the key elements driving VR's hypoalgesic effects on pain experience [11]. Different studies have shown the quality of the experience delivered with VR, where the level of immersion, presence, and interactivity directly correlates with the magnitude of the hypoalgesic effect compared to non-immersive VR [43-46]. Nevertheless, studies conducted to explore the hypoalgesic effects of immersive VR have given little attention to experience-related factors and have been largely underreported [11]. Similarly, few studies have explored the relationship between the magnitude of hypoalgesia effects, the clinical profile, and user experience factors. As noted, research to understand the mechanisms behind immersive VR has mostly been conducted with adults who have been experimentally pain-induced [11]. The transferability of these findings to clinical scenarios or to people suffering from chronic pain has been required. For instance, several of these factors have been included under the umbrella term of VR, representing a real challenge to understand the specific characteristics of the interventions such as the magnitude of the effect of each of them [27]. Hence, the relationship between user experience factors and hypoalgesic effects of immersive VR in people suffering from pain conditions is still unclear [41]. Translating these scenarios to children with acute or chronic pain can become even more complex. All these components vary significantly more when the patient is a child. The hardware is often designed for adults, the recreated scenarios may be overly detailed for young children or insufficiently detailed for adolescents, and even the generated avatars may not match their appearance, which can sometimes hinder interaction with the system [47]. The intended hypoalgesic effect may even increase adverse effects. Considering the potential impact of certain features of the user experience on pain reduction, the central question arises: which is the impact of user experience factors on hypoalgesic effects in patients with acute and chronic pain when using immersive VR?

2. Materials and Methods

This is a critical narrative review, which aims to address and understand the above specified question.

For the search strategy, we searched for experimental studies, both randomized control trial and non-randomized control trial design, using PubMed, PEDro, Web of Science,

Cochrane CENTRAL, and CINAHL from inception up to March 2024. We also searched the reference lists of the included articles related to the scope of our study. Only studies written in English were included. We developed a search strategy using Medical Subject Heading (MeSH) terms and keywords: "chronic pain", "acute pain", "pain" AND "immersive virtual reality" AND "Distraction", "Presence", "Immersion", "Interactivity", "Gamification", "embodiment" OR "full body virtual avatar", OR "Virtual Embodiment".

With respect to the eligibility criteria, the selection criteria used in this review were based on PICOT criteria for "population: adults and children, adolescents pain patients", "intervention: immersive virtual reality", and "study design: experimental studies in experimental induced pain, acute pain or chronic pain in humans". Exclusion criteria were studies that do not report information about user experience-related factors, non-immersive virtual reality, studies using animal pain models, case studies, qualitative studies, book chapters, non-English language, articles published over 15 years ago, and abstracts with no full published text.

Two independent reviewers (J.G. and G.C.B.) have conducted the literature search, composed both by clinical experts on pain and VR. After identifying studies meeting inclusion criteria, we screened potential articles by title and abstract, after removing duplicates manually, and performed the trial selection.

3. Results

A comprehensive summary of the evidence on the user experience-related factors and immersive virtual reality-induced hypoalgesia is presented below. Results were extracted in Table 2 where the articles are characterized with information on country; year; type of study; type of patient; type of VR user-related factor; main objective; and main results. Finally, we examined the proposed hierarchical relationship between immersive VR-induced hypoalgesia and the user experience factor, by evaluating the body of evidence suggesting that the inclusion of certain user experience factors in immersive VR may enhance the magnitude of the hypoalgesic effect of the intervention.

Author and Year	Country	Study Details Design Number (n) Target Population	Type of VR User-Related Factor	Main Objective	Main Results
Araujo-Duran et al. (2024) [48]	United States	Randomized control trial design 106 adults with acute postoperative pain after hip arthroplasty	Immersive VR passive distraction	Examine if virtual reality program decreases acute postoperative pain and opioid requirements in patients recovering from hip arthroplasty	A virtual reality program did not provide significant reductions in average pain (NRS virtual reality group mean = 3.4; NRS reference group mean = 3.5 ; $p = 0.391$) scores or opioid consumption compared with 2-dimensional sham video presentations.
Mohammad et al. (2019) [49]	Jordan	Randomized control trial design 80 female patients with chronic pain related to breast cancer	Immersive VR passive distraction	Assess the effectiveness of immersive VR distraction in reducing pain and anxiety among female patients with breast cancer	Findings showed that one session of the immersive VR plus morphine made a significant reduction in pain (pre–post intervention means = 7.32–0.33 and $p < 0.001$, pre–post comparation means = 7.33–4.84 and $p < 0.001$) and anxiety (pre–post intervention means = 64.98–37.68 and $p < 0.001$, pre–post comparation means = 63.30–50.13 and $p < 0.001$) self-reported scores, compared with morphine alone, in breast cancer patients.
Tesarz et al. (2023) [45]	Germany	A within-subject randomized control trial design 28 individuals with chronic pain and 31 pain-free controls received painful stimuli	Immersive VR distraction and presence	Investigate the direct effects of an immersive VR environment on the perception of experimental pain in individuals with chronic pain and pain-free controls	VR effectively modulates pain perception in both patients and controls; specifically, the presence in a VR has an increasing effect on pain thresholds (F = 22.946, $p < 0.001$) and reduces pain inhibition (t = 2.777, $p = 0.018$) in a conditioned pain modulation paradigm.
McSherry et al. (2017) [50]	United States	A within-subject randomized control trial design 18 adults during painful wound care procedures	Immersive VR distraction and interactivity	Evaluate the effect of immersive VR distraction therapy during painful wound care procedures in adults on the amount of opioid medications required to manage pain	Pain and anxiety scores were similar for the wound procedures with and without immersive VR ($p > 0.05$). Immersive VR significantly reduced the amount of opioid medication administered during painful wound care procedures when IVR was used compared with no IVR (t = -2.7 ; df = 14; p = 0.02).
Patterson et al. (2023) [51]	United States	A within-subject non-randomized trial design 44 adults during painful wound care procedures	Immersive VR distraction, presence, and interactivity	Explore the feasibility of immersive VR during burn debridement, and whether interactive VR would reduce pain more effectively than nature stimuli viewed in the same VR goggles	No significant differences in pain unpleasantness or "presence in VR" between the two conditions were found ($p > 0.05$). Participants reported significantly less worst pain when distracted with adjunctive computer-generated VR than during standard wound care without distraction ($p < 0.05$, SD = 17.38).

Table 2. Summary of results of studies assessing the hypoalgesic mechanisms associated with factors related to user experience in people in pain.

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Author and Year	Country	Study Details Design Number (n) Target Population	Type of VR User-Related Factor	Main Objective	Main Results
Colloca et al. (2020) [46]	United States	Within-subject non-randomized trial design 59 healthy adults received heat thermal painful stimuli	Immersive VR passive distraction, presence, and interactivity	Explore how immersive VR can increase individual heat-pain tolerance limits	It found a significant main effect of the five conditions (1. immersive VR Ocean, 2. immersive VR Opera, 3. control (non-immersive) Ocean, 4. control (non-immersive) Opera, 5. 2-Back Memory Task) on heat-pain tolerance limit increases (F4,176 = 7.47, Greenhouse–Geisser-corrected $p < 0.001$). Bonferroni-corrected post hoc comparisons indicated that immersion in the VR Ocean condition led to significantly greater increase in heat-pain tolerance limits (mean increase: 1.025 ± 0.517 °C, baseline temperature: 46.19 ± 2.93 °C; during VR Ocean: 47.09 ± 2.05 °C; scale from 32 to 52 °C) than the VR Opera condition ($p = 0.001$), control Ocean ($p = 0.001$), and control Opera ($p < 0.001$). The VR Ocean condition led to significantly greater increase in the duration ($10.04 \pm 3.27\%$) of heat-pain tolerance limits than the VR Opera condition ($4.47 \pm 2.67\%$; $p = 0.001$), control Ocean ($3 \pm 2.56\%$; $p = 0.001$), and control Opera ($1.53 \pm 1.95\%$; $p < 0.001$). The results provided evidence that the immersive VR Ocean intervention induced a larger activation of the parasympathetic nervous system compared to the other four conditions. Immersive VR Ocean condition yielded significantly higher SDNN compared to immersive VR Opera ($p = 0.017$), non-immersive control Ocean ($p = 0.022$), non-immersive control Opera ($p = 0.023$), and 2-Back Memory Task ($p = 0.013$). The immersive VR Ocean condition was characterized by a higher level of SDNN, which was associated with greater gain in the painful intensities that were tolerated ($\mathbf{r} = 0.529$, $p < 0.001$).
Guiterrez-Maldonado et al. (2011) [44]	Spain	Randomized control trial design 68 healthy adults received cold thermal painful stimuli	Immersive VR passive distraction, presence, and interactivity	Evaluate effects of interactive versus passive VR distraction on the sense of presence and pain intensity	Most of the participants (73.5%) who experienced the interactive VR distraction reported less pain intensity relative to the no-VR trial ($\chi 2 = 7.5$, $p < 0.01$). In the passive VR condition, only 5.9% of participants showed a decreased level of pain intensity and the change did not reach statistical significance ($\chi 2 = 0.47$, $p = 0.49$). Participants reported a greater sense of presence during interactive VR distraction (M = 3.5, SD = 1.0), compared with the passive VR condition (M = 2.7, SD = 1.2, t (66) = 3.0, $p < 0.005$). The relationship between presence and pain intensity in VR conditions was assessed using Pearson product–moment correlation coefficients. The amount of VR presence reported correlated significantly and negatively with pain intensity (r (68) = -0.29 , $p < 0.05$).

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Author and Year	Country	Study Details Design Number (n) Target Population	Type of VR User-Related Factor	Main Objective	Main Results
Wender et al. (2009) [52]	United States	Randomized control trial design 21 healthy adults received heat thermal painful stimuli	Immersive VR passive distraction, presence, and interactivity	Explores the effect of interactivity on the hypoalgesic effectiveness of virtual reality	Compared to the non-interactive VR group, participants in the interactive VR group showed 75% more reduction in pain unpleasantness ($p < 0.005$) and 74% more reduction in worst pain ($p < 0.005$) and in fun ($p = 0.10$), but not in time spent thinking about pain ($p = 0.10$).
Hoffman (2021) [43]	United States	A within-subject randomized crossover design study 24 adults received heat thermal painful stimuli	Immersive VR passive distraction, presence, interactivity, and virtual embodiment	Evaluate if presence, interactivity, and virtual embodiment would increase VR hypoalgesia	Compared to the passive VR condition, during the interactive avatar VR, participants reported statistically significant reductions in worst pain ($\chi 2 = 31.74$, $p = 0.000$), pain unpleasantness ($\chi 2 = 34.87$, $p = 0.000$), and time thinking about pain ($\chi 2 = 31.17$, $p = 0.000$) and increased fun ($\chi 2 = 30.61$, $p = 0.000$) during the pain stimulus.
Lier et al. (2020) [53]	United States	Within-subject randomized crossover design study 30 adults received painful electrical stimuli	Immersive VR passive distraction, presence, and interactivity	Investigated the effect of two VR conditions on reported pain	Active VR significantly decreased pain scores ($p = 0.005$) (NRS = 3.17 ± 1.54) but passive VR (NRS = 4.93 ± 1.53) and no VR had no analgesic effect (NRS = 5.59 ± 1.35).
MacIntyre et al. (2023) [54]	Norway	Multiple-baseline single-case experimental design (SCED) 10 adults with chronic low back pain (CLBP)	Immersive VR presence, gamification, and interactivity	Evaluate the effects of a gamified VR graded activity intervention in people with CLBP	The VR graded activity intervention resulted in a significant reduction in pain intensity ($p = 0.016$) Average pain (NRS) decreases (1.0 \pm 0.27).
Ozlu et al. (2024) [55]	Turkey	Randomized crossover design study 73 patients with knee osteoarthritis (OA)	Immersive VR presence, gamification, and interactivity	Assess the disease-specific gamification through immersive VR on pain, disability, functionality, and balance in knee osteoarthritis (OA)	Gamification through immersive VR added to the conservative treatment has a positive effect on pain ($p = 0.000$), functionality pain ($p = 0.000$), and balance pain ($p = 0.013$) Pain (VAS) from 5.57–0.88 to 4.05–0.72.
Hofman et al. (2023) [56]	United States	Randomized crossover design study 48 healthy adults received heat thermal painful stimuli	Immersive VR passive distraction, presence, interactivity, and virtual embodiment	Evaluate if adding tactile feedback increases virtual embodiment and hypoalgesic effects	Tactile feedback significantly decreased pain intensity (VR analgesia, $p < 0.01$), compared to VR with no tactile feedback, and compared to no VR (baseline); $r = 0.4$, medium effect size. Tactile feedback also significantly increased avatar embodiment. Worst pain (NRS) from 4.71 ± 1.25 to 3.08 ± 1.65 .

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Author and Year	Country	Study Details Design Number (n) Target Population	Type of VR User-Related Factor	Main Objective	Main Results
Eccleston et al. (2022) [57]	Finland	Three-arm, prospective, double-blind, pilot, randomized, controlled trial 42 adults with chronic low back pain	Immersive VR passive distraction, presence, interactivity, and virtual embodiment	Compare active VR intervention (Digital Therapeutics for Pain, DTxP) with a sham placebo comparator and a standard care group	Immersive VR was superior to both a sham placebo comparator and standard care control in reducing fear of movement and reinjury ($p < 0.04$ and $p < 0.01$) but no differences between groups at any time point for average pain intensity ($p > 0.05$). Average pain (NRS) from 6.0 (1.4) to 4.1 (1.7) in DTxP intervention group.
Matamala-Gomez et al. (2020) [58]	Spain	Within-subject non-randomized trial design 27 healthy adults received painful stimuli	Immersive VR presence and virtual embodiment	Investigate whether distorting an embodied virtual arm in virtual reality modulated pain perception	In the distorted virtual arm conditions, the higher the level of ownership of the distorted (rs = 0.226, $p < 0.01$) and reddened–distorted (rs = 0.225, $p < 0.01$) virtual arm, the higher the pain/discomfort perception (VAS).
Matamala-Gomez et al. (2019) [59]	Spain	Within-subject non-randomized trial design 19 adults with chronic neuropathic pain	Immersive VR presence and virtual embodiment	Explore whether varying properties of an embodied virtual arm modulated pain ratings in patients with chronic pain due to complex regional pain syndrome (CRPS) type I or peripheral nerve injury (PNI)	Increasing transparency decreased pain in CRPS but did the opposite in PNI, whereas increasing size slightly increased pain ratings only in CRPS. No correlation was statistically significant ($p > 0.05$).
Harvie et al. (2024) [60]	Australia	Non-blinded pilot randomized controlled trial 30 adults with chronic low back pain	Immersive VR presence, interactivity, and virtual embodiment	Evaluate whether embodying superhero-like avatars can change self-perceptions in people with chronic low back pain	In the VR-Play condition, body image scores were improved during (F (3, 83) = 18.83, $p < 0.001$) but not immediately after or at one-week follow-up. No differences in pain intensity, force production, and fear of movement.
Álvarez de la Campa Crespo et al. (2023) [61]	Spain	A single-arm pre–post non-randomized trial design 21 adults with acute and chronic shoulder pain	Immersive VR presence and virtual embodiment	Ascertain whether the experience of movement of an embodied virtual arm, in the absence of actual physical movement, could enhance the range of pain-free motion for patients suffering from shoulder pain related to movement	After completing 15 min VR embodiment intervention, a significant difference in active abduction range of the affected shoulder was found. The mean improvement was 12.3° (95%CI 4.94–19.57; Student's <i>t</i> -test, <i>p</i> = 0.002, Cohen's d = 0.76). Also, there was a significant difference in active hand behind-the-back range of motion (95%CI 0.473–0.916; Wilcoxon signed-rank test, <i>p</i> = 0.004; rank biserial correlation, 0.778). Positive correlations between virtual body ownership and levels of improvement in both hand-behind-back movements (Spearman's ρ = 0.635, <i>p</i> = 0.004) and flexion movements (Spearman's ρ = 0.603) were found.

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Author and Year	Country	Study Details Design Number (n) Target Population	Type of VR User-Related Factor	Main Objective	Main Results
Hua et al. (2015) [62]	China	A prospective randomized study. Sixty-five children (4 to 16 years) with chronic pain in lower limbs	Immersive VR distraction, interactivity, and virtual embodiment	To investigate the effect of virtual reality distraction on alleviating pain during dressing changes in children with chronic pain	Virtual reality distraction significantly relieved pain before ($p = 0.016$), during ($p = 0.001$), and after ($p = 0.034$) the dressing change. Anxiety scores during dressing were reduced by 43% as compared to the control group ($p < 0.001$). VR distraction group had lower pulse rates during dressing change as compared to the control group (106.2 ± 11.45 vs. 98.88 ± 11.57 , $p < 0.05$). Time length of dressing change was significantly reduced in the VR distraction groups as compared to the control group (27.9 ± 6.83 vs. 22.3 ± 7.85 min, $p < 0.01$).
Ryu et al. (2018) [63]	Korea	Prospective randomized control trial. Seventy children scheduled for elective surgery under general anesthesia were randomly divided into either the control or gamification group	Immersive VR presence, gamification, and virtual embodiment	To evaluate whether gamification of the preoperative process—via VR gaming that provides a vivid, immersive, and realistic experience—could reduce preoperative anxiety in children	Preoperative anxiety (mean = 28.3 [23.3–36.7] vs. mean = 46.7 [31.7–51.7]; $p < 0.001$) and intraoperative compliance ($p = 0.038$) were lower in the gamification group than in the control group.
Dumoulin, et al. (2019) [64]	Canada	Three-arm randomized controlled trial. Fifty-nine children (8–17 years old) from an emergency department were randomized to the three groups	Immersive VR distraction, interactivity, gamification	To document the efficacy of VR as a mode of distraction during a medical procedure (needle-related procedures) compared with two comparison conditions: watching television (TV, minimal control condition) and distraction provided by the Child Life (gold standard control condition) program	A significant reduction in fear of pain and pain intensity was reported in all three conditions ($p < 0.05$). A larger and statistically significant reduction in fear of pain was observed among children who used VR ($p < 0.0001$) distraction compared with the CL and TV conditions ($p = 0.002$). The children's satisfaction with the VR procedure was significantly higher than for TV and comparable to CL ($p < 0.05$).
Griffin, et al. (2020) [65]	United States	Clinical trial Seventeen children with chronic pain enrolled from a pediatric pain rehabilitation program	Immersive VR interactivity, gamification, presence, body embodiment	Initial implementation of a VR program in pain rehabilitation intervention to enhance function in youth with chronic pain	Overall reports of presence were high (mean of 28.98; max of 40; SD of 4.02), suggestive of a high level of immersion. Among those with multisession data (n = 8), reports of pain ($p < 0.001$), fear ($p = 0.003$), avoidance ($p = 0.004$), and functional limitations ($p = 0.01$) significantly decreased. Qualitative analysis revealed (1) a positive experience with VR (e.g., enjoyed VR, would like to utilize the VR program again, felt VR was a helpful tool); (2) feeling distracted from pain while engaged in VR; (3) greater perceived mobility; and (4) fewer clinician-observed pain behaviors during VR.

Table ? Cont

NRS: Numeral pain score; VAS: Visual Analogic Scale.

3.1. Distraction

Distraction involves redirecting an individual's attentional resources to pain by diverting attention from pain to other sensory stimuli or cognitive tasks, activities, or thoughts, and although it is commonly used and widely acknowledged as a strategy to modulate the experience of pain control, its effectiveness varies according to different factors [66]. This implies that the nervous system's processing of sensory signals requires attention and, due to the individuals' limited cognitive capacity for attention at any given time, the ability to manage nociceptive stimuli will be reduced and thus the painful experience will emerge [67]. Distraction in children will be highly dependent on various factors, from developmental age and the ability to maintain concentration to the behavioral responses of parents and clinicians during the treatment [18,19,47]. It will also depend on familiarity with digital systems and previous negative experiences [21,68–71].

Hence, the factor of distraction has been the most commonly studied and used VR modality in pain management in adults and children, with positive results on the decrease in experimental and acute clinical pain conditions [37]. However, the effects beyond the short term of passive distraction are less conclusive in patients suffering from chronic pain [9]; some studies suggested that the hypoalgesic effects of VR may not be fully attributable to distraction [72]. It should be noted that the mechanisms underlying acute and chronic pain are different [33], and therefore this would be an explanation about the different results of the distraction factor when using immersive VR on pain perception [64–66].

In children, interventions with VR have shown significant effects primarily on pain intensity and anxiety when used as a distraction-from-pain strategy [18,19,73,74]. It is difficult to determine whether the distraction is acting mainly on pain intensity or anxiety, but it seems that the effect on both factors is contributing to the hypoalgesic effects in these patients. A safe and comfortable environment is a favorable factor for these effects as it directly impacts affective–emotional processing, generating short-term hypoalgesic effects [21,71]. On the other hand, the absence of parents near the child during the process, an excessive duration of the treatment, or a device not adapted to the child's physical needs may cause the effect to be non-hypoalgesic or even increase pain and distress [47].

3.2. Presence

The essence of immersive VR hypoalgesia is based on the patient's perceptual illusion of being present in a different place, the subjective experience of "feeling present" in the computer-generated world [75]. The perceptual experiences induced by immersive VR are enabled by a dynamic integration of sensory signals from different modalities (visual, tactile, vestibular, and proprioceptive) that is constantly updated to encode the representation and configuration of the body in space and its relationship to the environment in a process known as "multisensory integration" [76]. Immersive VR (IVR) aims to eliminate the sensory flow of information from the real world and replace it with multisensory perceptual information to induce the illusion that the virtual world is the real world [77]. Technical specifications of IVR hardware, including the head-mounted display, the controllers or haptic devices, and the elements of the software used, can influence the quality of the experience delivered to the person. It has been observed that the higher the sense of presence within the virtual environment, the higher the feeling of being immersed into the immersive VR scenario [43,45]. Hence, higher levels of presence and higher levels of multisensory experience delivered within an immersive VR environment are related to greater hypoalgesic effects compared to non-immersive VR environments [46,78,79]. Indeed, the characteristics of presence in children can differ from those in adults due to developmental and cognitive factors [21,47,71]. Children may experience a heightened sense of presence in virtual environments due to their typically more vivid imaginations and greater capacity for immersive play [47]. Their natural propensity for imaginative engagement can enhance their subjective experience of "being there" in the virtual world [47]. Additionally, the simplicity of the virtual environment and the presence of familiar elements can significantly influence the effectiveness of VR interventions in children. It is crucial to design VR

experiences that are age-appropriate, visually appealing, and engaging to maximize the hypoalgesic effects [47,71]. Ensuring that the VR content is easy to understand and interact with can also enhance the sense of presence and contribute to the overall effectiveness of the intervention. Additionally, the immersive nature of VR can be particularly beneficial for children as it may more effectively divert their attention away from pain compared to traditional methods [68–70].

Nevertheless, it has been highlighted that immersive VR environments may be susceptible to sensorimotor uncertainty due to conflicts or discrepancies with sensory, bodily, or spatial representations; multisensory processing; and/or multisensory integration, and might have various consequences for the efficacy of the immersive VR intervention [80]. These technical and user experience aspects must be considered when designing and developing VR-induced experiences for patients suffering from pain conditions. According to this, new haptic devices potentially allow for combining visual, sound, tactile, and olfactory stimuli that could further enhance the sense of presence [81]. In children, these potential conflicts or discrepancies with sensory and spatial representations may be more pronounced due to their developing sensory and cognitive systems [47]. Factors such as age-appropriate content, user-friendly interfaces, and adequate support from caregivers or health care providers become even more crucial in ensuring a positive and effective immersive VR experience for pediatric pain management [47]. Additionally, the introduction of new haptic devices holds promise in addressing these challenges. These devices potentially allow for the combination of visual, sound, tactile, and olfactory stimuli, which could further enhance the sense of presence in virtual environments [82]. By providing a more immersive and multisensory experience, these advancements in haptic technology have the potential to improve the effectiveness of VR interventions for pain relief, especially in pediatric patients where engagement and distraction are key components of successful pain management strategies [21,71].

3.3. Interactivity

Immersive virtual reality offers more than attention control; it is a technology that is designed to achieve a controlled dissociation, aimed at reframing and shaping the painful experience, where one of the strengths comes from the idea that the subject is no longer a mere external spectator but an actor in a condition of complete sensory immersion [83]. Motion tracking systems such as controllers or hand tracking systems allow the movements of a virtual body (i.e., an avatar) to be controlled by the movements of the user's real body, resulting in an interactive experience [84]. A factor related to active participation/interaction is the amount of body movement while navigating the game. Indeed, the amount of movement allowed during VR exposure has been found to be associated with decreased pain [52,85]. Likewise, it has been observed that greater interactivity has been associated with a greater hypoalgesic effect in comparison to passive modalities [52,84,86]. The interactive mode of VR can be easily adapted, and a higher level of engagement can produce a greater hypoalgesic effect [87], which has been correlated with neuroimaging changes in motor and cognitive cortical areas [88]. It has recently been observed that the interactivity enabled by a hand tracking system within an immersive VR environment using only natural hand gestures synchronized to the observed virtual hand movement through the head-mounted display may improve motivation, is well tolerated by motor rehabilitation patients, and is effective in promoting motor performance [89]. Immersive VR with motion tracking systems, such as controllers or hand tracking systems, allows children to control the movements of a virtual character (for example, a pediatric avatar) synchronized with their own body movements. This ability to interact and move in the virtual world not only provides an immersive gaming experience but can also enhance the child's emotional connection to the virtual environment, thus enhancing therapeutic effects [47]. The quantity of movement permitted during exposure to VR can also be crucial for children. It is important that software allows for modifications in this aspect, being able to adapt to the clinical demands of each child in the treatment phase while also controlling for possible compensations, always considering that the child's active participation in treatment can enhance its benefits [47,90]. The adaptability of the interactive mode of VR is another important advantage in the pediatric context. Virtual games and activities can be specifically designed to address the needs and preferences of the children, increasing their motivation and engagement with the treatment [91]. This increased participation can be translated into better therapeutic outcomes and an overall more positive experience for children facing acute or chronic pain [47].

3.4. Gamification

The concept of gamification is based on the application of "game design elements in a non-game context" to motivate participation, adherence to system utilization, and overall sustainability of health behaviors [92]. The growing interest in applying gamification in this context is due to the lack of adherence to conventional treatments, resulting in an impact on reported clinical outcomes [93]. It has been noted that the gamification of virtual reality promotes greater satisfaction with the experience, greater adherence to treatment, higher attentional resource requirements, and reduced perception of fatigue during physical activity [94] through the integration of game elements or attributes such as interactivity, game fiction, challenge, assessment, or cognitive tasks in the design and development of the software [95,96]. This technology might include gamification features such as music, cues, rewards, and performance metrics that can provide motivation and enjoyment during immersive VR exposure.

Gamification strategies in rehabilitation have been studied mainly in the areas of neurorehabilitation and pediatrics [97], where it has been shown that game-based rehabilitation achieves similar results to conventional rehabilitation with the added effect of increased adherence and enjoyment during the treatment program [98]. Despite the broad application of game elements in a variety of areas of pain management, the mechanisms underlying these effects are not well established. However, within the management of musculoskeletal pain, it has been observed that the inclusion of gamification elements results in improved function, both in increasing range of motion and strength, and decreased pain perception [35,55,99]. Even if hypoalgesic effects have been observed in gamified interventions in patients suffering from pain conditions, the added value of this user experience factor in immersive VR environments has not been extensively investigated. Few investigations suggested that the combined effect of gamification and other VR experience-related factors such as immersion and presence may contribute to the hypoalgesic and anxiety-reducing effects observed in pediatric patients [100]. Likewise, immersive VR gamification added to conservative treatment has been reported to have a positive effect on pain, function, and balance in patients with knee osteoarthritis (OA) [55]. Positive effects of gamification in chronic musculoskeletal pain have also been reported in pain-related fear and anxiety [100], which have been highlighted as relevant psychological factors in the transition from acute to chronic pain [101].

3.5. Virtual Embodiment

People suffering from pain conditions can experience modulations at a neural level in the sensorimotor area, affecting different sensorimotor functions such as motor function, sensory feedback, cognitive representations of the body and its surrounding space, multisensory processing, and sensorimotor performance [102,103]. Moreover, it is known that in patients suffering from chronic pain conditions, the experience of pain is accompanied by a variety of body perception disturbances that have been previously highlighted [104]. Indeed, people suffering from pain conditions often exhibit distortions in their perception of the positions and sizes of the affected body parts [105]. Several studies have shown that there is a bi-directional link between body perception and pain experience [105]. According to this, some studies have shown that using multisensory interventions for pain relief may be effective in refining the distorted body image in people suffering from pain conditions [104–107].

When a proper multisensory integration manipulation is provided, a perceptual experience is induced, where both interoceptive (e.g., proprioception) and exteroceptive (e.g., vision) senses are stimulated by the technology, enabling a modulation in the bodyenvironment link of the person in pain [31]. In detail, it has been shown that by providing synchronous visuo-tactile or visuo-motor correlations between the real and the virtual body, it is possible to generate the sense of embodiment toward a virtual body [108]. As a result of this process, the sense of being embodied in a virtual body replaces the contents of bodily self-awareness towards the virtual body through the activation of somatosensory and premotor circuits related to the embodied body parts [109]. In this perspective, experiencing the sense of embodiment towards a virtual body refers to feeling inside a virtual body, a body that moves in relation to our intentions, and a body capable of interacting with the surrounding environment. "Virtual embodiment" is considered to arise from a complex interaction between bottom-up and top-down signals from our central nervous system [36]. Thus, virtual embodiment can facilitate a greater integration of the bodily experience by allowing children to explore and manipulate virtual representations of their own body within a safe environment [18,47,68,90]. In addition, it has been shown that training fine motor skills and hand-eye coordination by interacting with virtual tools and objects can improve daily life activities, which are normally impacted by pain conditions [47]. It has been highlighted that children with chronic pain may be more sensitive to these internal or interoceptive signals [110], and might experience a greater connection between their mind and body when interacting with the virtual environment. Thus, VR can amplify interoceptive signals by providing a sensorially rich and immersive experience and stimulates the body's interoceptive responses, such as heart rate, breathing, and body temperature [68,69].

To maximize the sense of embodiment, immersive VR systems need to induce the four sub-components of embodiment in order to modulate the users' internal representation and impact on the individual's experience [111,112]:

- (i) Co-localization: being co-located in the same place, time, and space of the real body.
- (ii) Agency: having perceived control of the intentions, movements, and actions of the virtual body.
- (ii) Ownership: having the feeling or perception of owning a certain part of the virtual body.
- (iv) Perspective: observing the virtual body from an egocentric or allocentric point of view.

It has been proposed that congruent multisensory integration, together with synchronous visuo-motor feedback between the movements of the virtual avatar and one's own body, induces a sense of embodiment within a full-body avatar [113]. In fact, it has been shown that the sense of agency toward the virtual body movements can enhance the sense of embodiment [114]. Recently, the relationship between the impact of different levels of self-representation and body tracking on the feeling of presence and embodiment in immersive VR has been investigated [107]. In detail, it has been shown that in healthy subjects, adding hip tracking overhead, hand, and feet tracking (when using a full-body avatar) allows for a more realistic response to stimuli (agency) and a higher overall feeling of embodiment (ownership) toward the virtual body [115].

A recent study has shown that inducing virtual body ownership illusions through the use of virtual avatars may enhance the hypoalgesic effect of immersive VR, compared to immersive VR exposure without the use of virtual avatars, and may increase the sense of presence in the generated VR environment [59]. In this regard, several studies have shown that by manipulating the morphological characteristics of the embodied virtual body, it is possible to modulate the internal representation of the body, which can have an impact on the decrease in pain perception in people under pain conditions [59]. Hence, using immersive VR systems, it is possible to induce the sense of embodiment toward virtual bodies, showing different morphological characteristics of the painful part of the body, modulating pain perception in both healthy subjects and in clinical populations with painful conditions [106]. In a recent study using full-body virtual-embodied avatars in patients with low back pain, the patients reported not only hypoalgesic effects, but also increased self-efficacy, improved mood, increased motivation and confidence, and feeling more able to exercise when being embodied in the virtual body [60,116]. These results show that the use of virtual avatars can have an impact not only on sensory processing, but also on the affective-motivational dimension of patients with musculoskeletal pain [116].

3.6. Hierarchical Relationship of Hypoalgesic Effects and Factors Related to User Experience in Immersive Virtual Reality

In relation to the influence of the user experience (UX) factors when using immersive VR systems to induce a hypoalgesic effect, the reviewed evidence in this study suggests that there may be a link between the magnitude of hypoalgesic effects obtained with immersive VR exposure and the integration of different user experience-related factors. As previously noted, even though the main UX factor investigated when using immersive VR systems for pain relief is the distraction, other factors can enhance or have an overlapping effect, inducing the hypoalgesia effect, in a clinical population suffering from chronic pain [42]. Indeed, some authors highlighted the need for further research on the mechanisms of VR hypoalgesia in the different groups of patients suffering from pain conditions when using immersive VR systems [28,117]. Hence, passive distraction is one of the main mechanisms of VR-induced hypoalgesia [29]. However, as discussed in this review, there are other potential mechanisms related to the UX factors, underlying pain relief when using immersive VR. According to this, some authors suggested that there might be a hierarchical relationship of hypoalgesic effects and factors related to UX in immersive VR (Figure 2).

Although the hypoalgesic effect of distraction has been widely reported both in VR intervention and in other modalities, several aspects have been outlined that might modify this hypoalgesic effect. For example, Bascour-Sandoval et al., 2019 [66], indicate that the hypoalgesic effect of distraction by visual, auditory, tactile, and mixed distractors shows positive effects in acute pain; however, it is not effective in healthy children and in adults with chronic pain. Similarly, other authors suggested that the decrease in pain cannot be explained by the distraction effect alone, especially when using psychophysical measures of pain assessment such as conditioned pain modulation [72,118]. However, studies that have compared the hypoalgesic effect between non-immersive VR and immersive VR have reported positive results in the reduction in pain in favor of the immersive VR modality [42]. Some authors have suggested that these differences may be due to the sense of presence in the generated VR environment [79]. Moreover, it has been shown that within the immersive VR modality, when comparing a passive environment versus an interactionenabled environment, the interactive VR modality induced a greater hypoalgesic effect [44]. The difference in the magnitude of pain relief from passive to active modalities has also been reported in non-immersive VR environments [84].

The role of gamification in pain relief has been outlined in non-immersive VR and other strategies [119], as well as in some immersive VR studies [55,92]. In this sense, gamification may have an impact on the affective motivational dimension of pain, and in the pediatric population [98], as in chronic pain [100], it could represent a significant user experience-related factor in the magnitude of response to VR intervention. At last, the contribution of virtual embodiment to the hypoalgesic effects of immersive VR has been studied by several authors [43,59,120]. The bi-directional relationship between pain and altered body image paves the way to new possibilities to optimize both sensory and sensorimotor aspects of the pain experience [104], especially in chronic pain conditions [121]. However, according to the existing evidence, few studies have combined all the factors related to user experience for pain relief. In this regard, the study by MacIntyre et al., 2023 [54], can be highlighted, as it includes different UX factors such as the sense of presence, interactivity, gamification, and virtual embodiment. In this study, the authors found a significant reduction in pain intensity in 40% of the participants, achieving $\geq 30\%$ pain reduction (minimum important change).



Immersive VR-induced hypoalgesia

Figure 2. The hierarchical relationship of hypoalgesic effects and factors related to user experience in immersive virtual reality. Passive distraction has been used mostly in studies evaluating immersive VR-induced hypoalgesia. Whether the magnitude of the hypoalgesic effects obtained with the immersive virtual reality intervention is greater (+) or lesser (-) depends on the inclusion of the different factors related to the user experience. A funnel-type figure has been proposed; considering that the magnitude of the effects is summative, the addition of each user experience factor might enhance the hypoalgesic effect of the intervention, where the use of virtual embodiment, especially through full-body virtual avatars with motion tracking elements and haptic devices that boost multisensory integration, maximizes the immersive VR-induced experience.

Based on the available literature, one may postulate that an overlapping or summative mechanism of UX factors added in the immersive VR applications can have an impact on the magnitude of hypoalgesic effect response in people suffering from pain conditions. Further investigations are needed to compare and investigate the different UX factors when using immersive VR for pain relief.

4. Discussion

The growing interest in the use of immersive VR applications in the treatment of patients suffering from pain conditions, in both research and clinical settings, calls for a deeper understanding of the UX factors underlying the effect of immersive VR for pain relief. The results show that in addition to the distraction effect, interactivity, sense of presence, and gamification in immersive VR-induced hypoalgesia, but in particular sense of embodiment, are crucial UX factors to induce when using immersive VR systems for pain relief. Although the generic term VR has generally been used in both clinical and research settings, we can consider immersive VR UX factors as active components of a complex intervention, having a significant impact on the efficacy of pain relief therapy. Thus, the understanding and embedding of these active components may improve the optimal patient–treatment relationship, providing a personalized treatment approach [122]. This review contributes with enough evidence to understand the impact of the different UX factors, when using immersive VR systems, on immersive VR-induced hypoalgesia.

Immersive VR applications can enhance the effectiveness of pain interventions by inducing pain relief through the immersive virtual environments or by providing virtual

body ownership illusions through the use of embodied virtual avatars to modulate the representation of the painful part of the body [122]. Previous evidence has shown that the inclusion of some UX factors such as full-body virtual avatars, gamification, interactivity, and the sense of presence has a relevant impact on pain relief, increasing the patients' self-efficacy, and inducing positive effects on body image [60,116]. However, the potential impact of UX factors on the hypoalgesic effects of immersive VR has not been widely reported in many of the clinical studies in acute and chronic pain populations, as well as the precise parameters for the best dose recommended in each clinical profile [122]. As described in the reviewed studies for this review, there is a significant variability in the clinical profiles of the patients suffering from pain conditions included in the studies, as well as in the UX factors included in the immersive VR interventions. These findings are in accordance with the reported conclusions of other authors. In the study from Lier et al., 2023 [28], the authors observed modest to no effects for different factors related to the type of immersive VR intervention applied, including the type of software and interactivity. However, the authors suggested that the results can be affected by the variety of conditions in the immersive VR intervention, the small number of studies investigating chronic pain conditions, and the fact that a large number of studies used video content displayed through the head-mounted device (HMD) [28]. The studies examined during this review that provide information on the type of factor related to user experience presented a high degree of variability in the type of pain present, as well as in the clinical profile studied, which included healthy subjects with pain induced experimentally (n = 7), acute pain after pain intervention (n = 3), or individuals with chronic pain of various types (n = 7). Due to the small sample of the studies, it is difficult to develop generalized conclusions.

Additionally, a large number of studies have been conducted to evaluate hypoalgesic effects in childhood populations, where positive effects have also been reported [18,68–70,90]. Differences in response to immersive VR treatment between adults and children have also not been studied, nor have possible differences in UX factors. It has been suggested that interactivity and gamification may have a significant impact on pain reduction in children [98]. While immersive VR holds the potential for a hypoalgesic effect, there are adaptations necessary specifically for adults. The adaptation of software to clinical, visual, and motor needs is essential when it comes to applications targeted at children [90]. Each child has a unique combination of skills and challenges, so the development of software specific to this population is crucial to ensure the effectiveness of treatment. This involves not only considering differences in children's motor and cognitive abilities but also considering potential neurodevelopmental conditions, such as autism, attention deficit hyperactivity disorder, or cerebral palsy, among others. The presence of these conditions can significantly influence how children interact with the software and their ability to participate in interventions [47]. For example, a child with autism may have specific sensory needs that must be addressed in the software design, while a child with cerebral palsy may require adaptations to access the content effectively [90]. Additionally, the visual characteristics of the software, such as interface design and color palette, must be carefully selected to ensure accessibility for all users, regardless of their visual abilities.

On the other hand, addressing the development of hardware used in pediatric interventions is crucial. Frequently, systems of hardware originally designed for adults are employed in pediatric settings, a practice that raises a series of significant concerns [47]. This approach can entail risks of adverse effects for children, as the size, ergonomics, and functionality of these devices may not properly cater to their unique physical and cognitive needs. Furthermore, the use of inadequate hardware can increase the likelihood of equipment damage, which, in turn, may disrupt the course of interventions and incur additional costs for repair or replacement [91]. In addition to practical considerations, the use of hardware designed for adults can have a negative impact on the motivation of both children and clinicians. Devices that are not tailored to the age and capabilities of children may be intimidating or discouraging, potentially reducing children's active participation in interventions [47]. Similarly, health care professionals may experience frustration when

attempting to adapt the equipment for use with pediatric patients, which could affect their commitment and enthusiasm for implementing effective interventions [47]. Therefore, it is essential to allocate resources and efforts to the development of hardware specifically designed for use in pediatrics. These devices should be properly sized, ergonomic, and safe for use in children, which entails considerations not only about their physical design but also about their functionality and adaptability to the clinical and therapeutic needs of this unique population.

However, no significant adverse effects have been reported, demonstrating that VR is a safe intervention. Adverse effects from prolonged and continuous exposure to VR could cause a disorder called "cybersickness", characterized by dizziness, headache, nausea, postural pain, or disorientation [123], and have been highlighted as a major barrier to the clinical implementation of immersive VR. However, the rate of side effects in VR is still very variable, with a reported average prevalence of 15.6% [124], due to the influence of factors related to both the type of device of VR and the characteristics of the software used [125,126]. Since etiopathogenic mechanisms of these side effects are not yet known, it is hypothesized that virtual reality might cause a conflict in the multisensory integration [125]. It has been identified that certain user experience factors might be related to the onset of cybersickness, such as the type of content or virtual environment [126], where it has been reported that a higher presence of cybersickness correlates inversely with the likelihood of this adverse effect on users [125].

The ongoing progress in VR technology, along with decreasing equipment costs, has resulted in the emergence of more user-friendly, useful, and accessible VR systems that can uniquely address a wide scope of physical, psychological, and cognitive rehabilitation problems as well as research challenges [127]. Birckhead et al. encourage the development of VR solutions to consider starting with direct input from end-users, both providers and patients, to optimize human-centered design [128]. Thus, more interdisciplinary collaboration between technology specialists such as virtual reality experts, game developers, and engineers, in the design and development of VR software and applications with a health care purpose, and the clinicians who make use of this technology is needed to optimize the acceptability, safety, and clinical outcomes of VR in pain management. Recommendations for the design and application of virtual reality in rehabilitation have been proposed for patients requiring neurorehabilitation [129]. However, these recommendations have not yet been proposed for the management of pain patients. These recommendations include enduser involvement, participatory factors, researcher involvement, rehabilitation principles, and technological design and development [129,130]. This might be due to the fact that more advancement and evidence are available on the application of immersive VR in the neurorehabilitation field compared to pain management. Some of these recommendations also include aspects related to user experience factors that have been highlighted in this review such as enriched environments and multisensory information or gamification [130]. Recently, a multimodal and personalized virtual reality-integrated physiotherapy intervention for patients with complex chronic low back pain has been developed using the Medical Research Council (MRC) framework in collaboration with end-users, including patients, physiotherapists, and researchers [131]. The development of VR as an application for health and pain management requires a broad intersection of theoretical and technical lenses that refer to interdisciplinary collaboration [95]. It is therefore necessary to establish collaborative and consensus-based frameworks to define standardized processes to support the multidisciplinary team in the design and development of immersive VR-based interventions for people with pain. Co-design is a consumer-driven approach that involves consumers in the process of developing meaningful solutions to complex problems and is increasingly seen as necessary to improve clinical translation [132]. A non-hierarchical participatory methodology has been proposed for identifying innovative, consumer-preferred solutions with the potential to overcome the existing gaps between research and practice [132].

Certain limitations should be noted when interpreting results in immersive VR studies in pain management, due to high heterogeneity, especially in terms of study design, clinical pain profiles, factors related to the user experience, and dosimetry of immersive VR intervention [28]. More detailed reporting of scientific studies on pain, including the experience-related factors used, is needed to more adequately explore the hypoalgesic effects of immersive VR [117]. Hence, it is recommended to carry out studies that better compare the hypoalgesic effects of immersive VR between different user experience-related factors with measures that allow us to know the possible differences in the hypoalgesic mechanisms present in each modality and their response in the different clinical profiles. Comparative studies including subgroups of patients with both acute and chronic pain are recommended to determine the magnitude of the hypoalgesic effects obtained after the inclusion of the different factors related to user experience mentioned in this review. Likewise, there is a need for research studies in the chronic pain population, both adult and pediatric, to understand the long-term effects and sustainability of pain relief after VR intervention. Studies by Maddox et al. [133] in patients with low back pain can serve as a reference on the medium- and long-term effectiveness of an intervention with VRI.

5. Conclusions

Immersive virtual reality offers an innovative non-pharmacological strategy in pain management, with demonstrated positive effects on pain relief. The present review shows the contribution of UX factors to the magnitude of the hypoalgesic effect following immersive VR intervention. Moreover, available evidence suggests that hierarchical relationships might exist between user experience-related factors and greater hypoalgesic effects following immersive VR intervention in adults and children. Therefore, it is necessary to consider these factors in both the design and co-creation of VR-based strategies, as outlined in the findings of scientific studies in the field of pain, with the main aim to enhance pain relief, providing new knowledge in immersive VR mechanism-based scenarios, which will pave the way to a personalized treatment approach in patients suffering from pain conditions.

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References

- Raja, S.N.; Carr, D.B.; Cohen, M.; Finnerup, N.B.; Flor, H.; Gibson, S.; Keefe, F.J.; Mogil, J.S.; Ringkamp, M.; Sluka, K.A.; et al. The revised International Association for the Study of Pain definition of pain: Concepts, challenges, and compromises. *Pain* 2020, 161, 1976–1982. [CrossRef] [PubMed]
- 2. Williams, A.C.d.C.; Craig, K.D. Updating the definition of pain. *Pain* **2016**, *157*, 2420–2423. [CrossRef] [PubMed]
- 3. Chapman, C.R.; Tuckett, R.P.; Song, C.W. Pain and stress in a systems perspective: Reciprocal neural, endocrine, and immune interactions. *J. Pain* **2008**, *9*, 122–145. [CrossRef] [PubMed]
- Foley, H.E.; Knight, J.C.; Ploughman, M.; Asghari, S.; Audas, R. Association of chronic pain with comorbidities and health care utilization: A retrospective cohort study using health administrative data. *Pain* 2021, 162, 2737–2749. [CrossRef] [PubMed]
- 5. Blyth, F.M.; Briggs, A.M.; Schneider, C.H.; Hoy, D.G.; March, L.M. The global burden of musculoskeletal pain—Where to from here? *Am. J. Public Health* **2019**, 109, 35–40. [CrossRef] [PubMed]
- Cohen, S.P.; Vase, L.; Hooten, W.M. Chronic pain: An update on burden, best practices, and new advances. *Lancet* 2021, 397, 2082–2097. [CrossRef] [PubMed]
- Gustavsson, A.; Bjorkman, J.; Ljungcrantz, C.; Rhodin, A.; Rivano-Fischer, M.; Sjolund, K.F.; Mannheimer, C. Socio-economic burden of patients with a diagnosis related to chronic pain–Register data of 840,000 S wedish patients. *Eur. J. Pain* 2012, *16*, 289–299. [CrossRef] [PubMed]
- 8. Gaskin, D.J.; Richard, P. The economic costs of pain in the United States. J. Pain 2012, 13, 715–724. [CrossRef] [PubMed]
- 9. Harvie, D.S.; Smith, R.T.; Martin, D.; Hirsh, A.T.; Trost, Z. Novel applications of virtual and mixed reality in pain research and treatment. *Front. Virtual Real.* 2022, *3*, 1018804. [CrossRef]

- 10. Volkow, N.D.; Blanco, C. The changing opioid crisis: Development, challenges and opportunities. *Mol. Psychiatry* **2021**, *26*, 218–233. [CrossRef]
- 11. Trost, Z.; France, C.; Anam, M.; Shum, C. Virtual reality approaches to pain: Toward a state of the science. *Pain* **2021**, *162*, 325–331. [CrossRef] [PubMed]
- 12. Skarbez, R.; Smith, M.; Whitton, M.C. Revisiting Milgram and Kishino's reality-virtuality continuum. *Front. Virtual Real.* **2021**, *2*, 647997. [CrossRef]
- 13. Zhao, J.; Riecke, B.E.; Kelly, J.W.; Stefanucci, J.; Klippel, A. Human spatial perception, cognition, and behaviour in extended reality. *Front. Virtual Real.* **2023**, *4*, 1257230. [CrossRef]
- 14. Kardong-Edgren, S.S.; Farra, S.L.; Alinier, G.; Young, H.M. A call to unify definitions of virtual reality. *Clin. Simul. Nurs.* 2019, *31*, 28–34. [CrossRef]
- 15. Nilsson, N.C.; Nordahl, R.; Serafin, S. Immersion revisited: A review of existing definitions of immersion and their relation to different theories of presence. *Hum. Technol.* **2016**, *12*, 108–134. [CrossRef]
- 16. Brady, N.; McVeigh, J.G.; McCreesh, K.; Rio, E.; Dekkers, T.; Lewis, J.S. Exploring the effectiveness of immersive Virtual Reality interventions in the management of musculoskeletal pain: A state-of-the-art review. *Phys. Ther. Rev.* 2021, 26, 262–275. [CrossRef]
- 17. Mallari, B.; Spaeth, E.K.; Goh, H.; Boyd, B.S. Virtual reality as an analgesic for acute and chronic pain in adults: A systematic review and meta-analysis. *J. Pain Res.* **2019**, *12*, 2053–2085. [CrossRef] [PubMed]
- 18. Tas, F.Q.; van Eijk, C.A.M.; Staals, L.M.; Legerstee, J.S.; Dierckx, B. Virtual reality in pediatrics, effects on pain and anxiety: A systematic review and meta-analysis update. *Pediatric Anesthesia* **2022**, *32*, 1292–1304. [CrossRef] [PubMed]
- Eijlers, R.; Utens, E.M.W.J.; Staals, L.M.; de Nijs, P.F.A.; Berghmans, J.M.; Wijnen, R.M.H.; Hillegers, M.H.J.; Dierckx, B.; Legerstee, J.S. Systematic review and meta-analysis of virtual reality in pediatrics: Effects on pain and anxiety. *Anesthesia Analg.* 2019, 129, 1344–1353. [CrossRef]
- Hadjiat, Y.; Marchand, S. Virtual reality and the mediation of acute and chronic pain in adult and pediatric populations: Research developments. Front. Pain Res. 2022, 3, 840921. [CrossRef]
- 21. Viderman, D.; Tapinova, K.; Dossov, M.; Seitenov, S.; Abdildin, Y.G. Virtual reality for pain management: An umbrella review. *Front. Med.* **2023**, *10*, 1203670. [CrossRef] [PubMed]
- 22. Zhang, T.; Li, X.; Zhou, X.; Zhan, L.; Wu, F.; Huang, Z.; Sun, Y.; Feng, Y.; Du, Q. Virtual Reality Therapy for the Management of Chronic Spinal Pain: Systematic Review and Meta-Analysis. *JMIR Serious Games* **2024**, *12*, e50089. [CrossRef] [PubMed]
- Baker, N.A.; Polhemus, A.H.; Ospina, E.H.; Feller, H.; Zenni, M.; Deacon, M.; DeGrado, G.; Basnet, S.; Driscoll, M. The state of science in the use of virtual reality in the treatment of acute and chronic pain: A systematic scoping review. *Clin. J. Pain* 2022, *38*, 424–441. [CrossRef] [PubMed]
- 24. Garrett, B.; Taverner, T.; Gromala, D.; Tao, G.; Cordingley, E.; Sun, C. Virtual reality clinical research: Promises and challenges. *JMIR Serious Games* **2018**, *6*, e10839. [CrossRef]
- Glegg, S.M.N.; Levac, D.E. Barriers, facilitators and interventions to support virtual reality implementation in rehabilitation: A scoping review. PM&R 2018, 10, 1237–1251.
- Brepohl, P.C.A.; Leite, H. Virtual reality applied to physiotherapy: A review of current knowledge. *Virtual Real.* 2023, 27, 71–95. [CrossRef]
- 27. Donegan, T.; Ryan, B.E.; Swidrak, J.; Sanchez-Vives, M.V. Immersive virtual reality for clinical pain: Considerations for effective therapy. *Front. Virtual Real.* 2020, 1, 9. [CrossRef]
- 28. Lier, E.J.; De Vries, M.; Steggink, E.M.; Broek, R.P.G.T.; Van Goor, H. Effect modifiers of virtual reality in pain management: A systematic review and meta-regression analysis. *Pain* **2023**, *164*, 1658–1665. [CrossRef] [PubMed]
- Mahrer, N.E.; Gold, J.I. The use of virtual reality for pain control: A review. *Curr. Pain Headache Rep.* 2009, 13, 100–109. [CrossRef] [PubMed]
- Gold, J.I.; Belmont, K.A.; Thomas, D.A. The neurobiology of virtual reality pain attenuation. *CyberPsychology Behav.* 2007, 10, 536–544. [CrossRef]
- 31. Guerra-Armas, J.; Flores-Cortes, M.; Pineda-Galan, C.; Luque-Suarez, A.; La Touche, R. Role of Immersive Virtual Reality in Motor Behaviour Decision-Making in Chronic Pain Patients. *Brain Sci.* **2023**, *13*, 617. [CrossRef]
- 32. Lindsay, N.M.; Chen, C.; Gilam, G.; Mackey, S.; Scherrer, G. Brain circuits for pain and its treatment. *Sci. Transl. Med.* 2021, 13, eabj7360. [CrossRef] [PubMed]
- 33. De Ridder, D.; Adhia, D.; Vanneste, S. The anatomy of pain and suffering in the brain and its clinical implications. *Neurosci. Biobehav. Rev.* **2021**, *130*, 125–146. [CrossRef] [PubMed]
- 34. Moreau, S.; Thérond, A.; Cerda, I.H.; Studer, K.; Pan, A.; Tharpe, J.; Crowther, J.E.; Abd-Elsayed, A.; Gilligan, C.; Tolba, R.; et al. Virtual reality in acute and chronic pain medicine: An updated review. *Curr. Pain Headache Rep.* **2024**, 1–36. [CrossRef] [PubMed]
- Stamm, O.; Dahms, R.; Müller-Werdan, U. Virtual reality in pain therapy: A requirements analysis for older adults with chronic back pain. J. Neuroeng. Rehabil. 2020, 17, 129. [CrossRef] [PubMed]
- 36. Matamala-Gomez, M.; Donegan, T.; Bottiroli, S.; Sandrini, G.; Sanchez-Vives, M.V.; Tassorelli, C. Immersive virtual reality and virtual embodiment for pain relief. *Front. Hum. Neurosci.* **2019**, *13*, 279. [CrossRef] [PubMed]
- Indovina, P.; Barone, D.; Gallo, L.; Chirico, A.; De Pietro, G.; Giordano, A. Virtual reality as a distraction intervention to relieve pain and distress during medical procedures: A comprehensive literature review. *Clin. J. Pain* 2018, 34, 858–877. [CrossRef] [PubMed]

- 38. Slater, M.; Lotto, B.; Arnold, M.M.; Sanchez-Vives, M.V. How we experience immersive virtual environments: The concept of presence and its measurement. *Anu. Psicol.* **2009**, *40*, 193–210.
- 39. Burdea, G.C.; Coiffet, P. Virtual Reality Technology; John Wiley & Sons: Hoboken, NJ, USA, 2003.
- 40. King, D.; Greaves, F.; Exeter, C.; Darzi, A. 'Gamification': Influencing health behaviours with games. J. R. Soc. Med. 2013, 106, 76–78. [CrossRef] [PubMed]
- Dreesmann, N.J.; Su, H.; Thompson, H.J. A systematic review of virtual reality therapeutics for acute pain management. *Pain Manag. Nurs.* 2022, 23, 672–681. [CrossRef] [PubMed]
- 42. Goudman, L.; Jansen, J.; Billot, M.; Vets, N.; De Smedt, A.; Roulaud, M.; Rigoard, P.; Moens, M. Virtual reality applications in chronic pain management: Systematic review and meta-analysis. *JMIR Serious Games* **2022**, *10*, e34402. [CrossRef]
- Hoffman, H.G. Interacting with virtual objects via embodied avatar hands reduces pain intensity and diverts attention. *Sci. Rep.* 2021, 11, 10672. [CrossRef] [PubMed]
- 44. Gutierrez-Maldonado, J.; Gutierrez-Martinez, O.; Cabas-Hoyos, K. Interactive and passive virtual reality distraction: Effects on presence and pain intensity. *Annu. Rev. Cybertherapy Telemed.* **2011**, 2011, 69–73.
- Tesarz, J.; Herpel, C.; Meischner, M.; Drusko, A.; Friederich, H.-C.; Flor, H.; Reichert, J. Effects of virtual reality on psychophysical measures of pain: Superiority to imagination and nonimmersive conditions. *Pain* 2024, *165*, 796–810. [CrossRef] [PubMed]
- 46. Colloca, L.; Raghuraman, N.; Wang, Y.; Akintola, T.; Brawn-Cinani, B.; Colloca, G.; Kier, C.; Varshney, A.; Murthi, S. Virtual reality: Physiological and behavioral mechanisms to increase individual pain tolerance limits. *Pain* 2020, 161, 2010–2021. [CrossRef] [PubMed]
- 47. Won, A.S.; Bailey, J.; Bailenson, J.; Tataru, C.; Yoon, I.A.; Golianu, B. Immersive virtual reality for pediatric pain. *Children* **2017**, *4*, 52. [CrossRef] [PubMed]
- Araujo-Duran, J.; Kopac, O.; Campana, M.M.; Bakal, O.; Sessler, D.I.; Hofstra, R.L.; Shah, K.; Turan, A.; Ayad, S. Virtual Reality Distraction for Reducing Acute Postoperative Pain After Hip Arthroplasty: A Randomized Trial. *Anesth. Analg.* 2024, 138, 751–759. [CrossRef] [PubMed]
- 49. Mohammad, E.B.; Ahmad, M. Virtual reality as a distraction technique for pain and anxiety among patients with breast cancer: A randomized control trial. *Palliat. Support. Care* **2019**, *17*, 29–34. [CrossRef] [PubMed]
- McSherry, T.; Atterbury, M.; Gartner, S.; Helmold, E.; Searles, D.M.; Schulman, C. Randomized, crossover study of immersive virtual reality to decrease opioid use during painful wound care procedures in adults. *J. Burn. Care Res.* 2018, 39, 278–285. [CrossRef] [PubMed]
- Patterson, D.R.; Drever, S.; Soltani, M.; Sharar, S.R.; Wiechman, S.; Meyer, W.J.; Hoffman, H.G. A comparison of interactive immersive virtual reality and still nature pictures as distraction-based analgesia in burn wound care. *Burns* 2023, 49, 182–192. [CrossRef]
- 52. Wender, R.; Hoffman, H.G.; Hunner, H.H.; Seibel, E.J.; Patterson, D.R.; Sharar, S.R. Interactivity influences the magnitude of virtual reality analgesia. *J. Cyber Ther. Rehabil.* 2009, 2, 27.
- 53. Lier, E.J.; Oosterman, J.M.; Assmann, R.; de Vries, M.; Van Goor, H. The effect of Virtual Reality on evoked potentials following painful electrical stimuli and subjective pain. *Sci. Rep.* **2020**, *10*, 9067. [CrossRef] [PubMed]
- 54. MacIntyre, E.; Sigerseth, M.; Larsen, T.F.; Fersum, K.V.; Meulders, M.; Meulders, A.; Michiels, B.; Braithwaite, F.A.; Stanton, T.R. Get your head in the game: A replicated single-case experimental design evaluating the effect of a novel virtual reality intervention in people with chronic low back pain. *J. Pain* 2023, 24, 1449–1464. [CrossRef] [PubMed]
- Özlü, A.; Ünver, G.; Tuna, H.İ.; Menekşeoğlu, A.K. The effect of a virtual reality-mediated gamified rehabilitation program on pain, disability, function, and balance in knee osteoarthritis: A prospective randomized controlled study. *Games Health J.* 2023, 12, 118–124. [CrossRef] [PubMed]
- Hoffman, H.G.; Fontenot, M.R.; Garcia-Palacios, A.; Greenleaf, W.J.; Alhalabi, W.; Curatolo, M.; Flor, H. Adding tactile feedback increases avatar ownership and makes virtual reality more effective at reducing pain in a randomized crossover study. *Sci. Rep.* 2023, 13, 7915. [CrossRef] [PubMed]
- 57. Eccleston, C.; Fisher, E.; Liikkanen, S.; Sarapohja, T.; Stenfors, C.; Jääskeläinen, S.K.; Rice, A.S.; Mattila, L.; Blom, T.; Bratty, J.R. A prospective, double-blind, pilot, randomized, controlled trial of an 'embodied' virtual reality intervention for adults with low back pain. *Pain* 2022, *163*, 1700–1715. [CrossRef] [PubMed]
- 58. Matamala-Gomez, M.; Nierula, B.; Donegan, T.; Slater, M.; Sanchez-Vives, M.V. Manipulating the perceived shape and color of a virtual limb can modulate pain responses. *J. Clin. Med.* **2020**, *9*, 291. [CrossRef] [PubMed]
- 59. Matamala-Gomez, M.; Gonzalez, A.M.D.; Slater, M.; Sanchez-Vives, M.V. Decreasing pain ratings in chronic arm pain through changing a virtual body: Different strategies for different pain types. *J. Pain* **2019**, *20*, 685–697. [CrossRef] [PubMed]
- Harvie, D.S.; Kelly, J.; Kluver, J.; Deen, M.; Spitzer, E.; Coppieters, M.W. A randomized controlled pilot study examining immediate effects of embodying a virtual reality superhero in people with chronic low back pain. *Disabil. Rehabil. Assist. Technol.* 2024, 19, 851–858. [CrossRef] [PubMed]
- de la Campa Crespo, M.Á.; Donegan, T.; Amestoy-Alonso, B.; Just, A.; Combalía, A.; Sanchez-Vives, M.V. Virtual embodiment for improving range of motion in patients with movement-related shoulder pain: An experimental study. *J. Orthop. Surg. Res.* 2023, 18, 729. [CrossRef]
- 62. Hua, Y.; Qiu, R.; Yao, W.; Zhang, Q.; Chen, X. The effect of virtual reality distraction on pain relief during dressing changes in children with chronic wounds on lower limbs. *Pain Manag. Nurs.* **2015**, *16*, 685–691. [CrossRef]

- 63. Ryu, J.H.; Park, J.W.; Nahm, F.S.; Jeon, Y.T.; Oh, A.Y.; Lee, H.J.; Kim, J.H.; Han, S.H. The effect of gamification through a virtual reality on preoperative anxiety in pediatric pa-tients undergoing general anesthesia: A prospective, randomized, and controlled trial. *J. Clin. Med.* **2018**, *7*, 284. [CrossRef]
- 64. Dumoulin, S.; Bouchard, S.; Ellis, J.; Lavoie, K.L.; Vézina, M.-P.; Charbonneau, P.; Tardif, J.; Hajjar, A. A randomized controlled trial on the use of virtual reality for needle-related procedures in children and adolescents in the emergency department. *Games Health J.* **2019**, *8*, 285–293. [CrossRef] [PubMed]
- Griffin, A.; Wilson, L.; Feinstein, A.B.; Bortz, A.; Heirich, M.S.; Gilkerson, R.; Wagner, J.F.; Menendez, M.; Caruso, T.J.; Rodriguez, S.; et al. Virtual reality in pain rehabilitation for youth with chronic pain: Pilot feasibility study. *JMIR Rehabil. Assist. Technol.* 2020, 7, e22620. [CrossRef]
- 66. Bascour-Sandoval, C.; Salgado-Salgado, S.; Gómez-Milán, E.; Fernández-Gómez, J.; Michael, G.A.; Gálvez-García, G. Pain and distraction according to sensory modalities: Current findings and future directions. *Pain Pract.* **2019**, *19*, 686–702. [CrossRef]
- 67. Johnson, M.H. How does distraction work in the management of pain? *Curr. Pain Headache Rep.* 2005, 9, 90–95. [CrossRef] [PubMed]
- 68. Gao, Y.; Xu, Y.; Liu, N.; Fan, L. Effectiveness of virtual reality intervention on reducing the pain, anxiety and fear of needle-related procedures in paediatric patients: A systematic review and meta-analysis. *J. Adv. Nurs.* **2023**, *79*, 15–30. [CrossRef]
- Simonetti, V.; Tomietto, M.; Comparcini, D.; Vankova, N.; Marcelli, S.; Cicolini, G. Effectiveness of virtual reality in the management of paediatric anxiety during the peri-operative period: A systematic review and meta-analysis. *Int. J. Nurs. Stud.* 2022, 125, 104115. [CrossRef] [PubMed]
- Lluesma-Vidal, M.; González, R.C.; García-Garcés, L.; Sánchez-López, M.I.; Peyro, L.; Ruiz-Zaldibar, C. Effect of virtual reality on pediatric pain and fear during procedures involving needles: Systematic review and meta-analysis. *JMIR Serious Games* 2022, 10, e35008. [CrossRef]
- 71. Addab, S.; Hamdy, R.; Thorstad, K.; Le May, S.; Tsimicalis, A. Use of virtual reality in managing paediatric procedural pain and anxiety: An integrative literature review. *J. Clin. Nurs.* **2022**, *31*, 3032–3059. [CrossRef]
- Do, A.L.; Enax-Krumova, E.K.; Özgül, Ö.; Eitner, L.B.; Heba, S.; Tegenthoff, M.; Maier, C.; Höffken, O. Distraction by a cognitive task has a higher impact on electrophysiological measures compared with conditioned pain modulation. *BMC Neurosci.* 2020, 21, 53. [CrossRef]
- 73. Smith, K.L.; Wang, Y.; Colloca, L. Impact of virtual reality technology on pain and anxiety in pediatric burn patients: A systematic review and meta-analysis. *Front. Virtual Real.* 2022, 2, 751735. [CrossRef] [PubMed]
- 74. López-Valverde, N.; Muriel Fernandez, J.; López-Valverde, A.; Valero Juan, L.F.; Ramírez, J.M.; Flores Fraile, J.; Herrero Payo, J.; Blanco Antona, L.A.; Macedo de Sousa, B.; Bravo, M. Use of virtual reality for the management of anxiety and pain in dental treatments: Systematic review and meta-analysis. *J. Clin. Med.* **2020**, *9*, 1025. [CrossRef]
- 75. Slater, M.; Wilbur, S. A framework for immersive virtual environments (FIVE): Speculations on the role of presence in virtual environments. *Presence Teleoperators Virtual Environ*. **1997**, *6*, 603–616. [CrossRef]
- 76. Tseng, P.; Juan, C.-H. Virtual reality in the neuroscience of multisensory integration and consciousness of bodily self. *J. Neurosci. Neuroeng.* **2013**, *2*, 387–392. [CrossRef]
- 77. Bohil, C.J.; Alicea, B.; Biocca, F.A. Virtual reality in neuroscience research and therapy. *Nat. Rev. Neurosci.* **2011**, *12*, 752–762. [CrossRef]
- 78. Brown, P.; Powell, W.; Dansey, N.; Al-Abbadey, M.; Stevens, B.; Powell, V. Virtual reality as a pain distraction modality for experimentally induced pain in a chronic pain population: An exploratory study. *Cyberpsychol. Behav. Soc. Netw.* 2022, 25, 66–71. [CrossRef] [PubMed]
- 79. Hoffman, H.G.; Sharar, S.R.; Coda, B.; Everett, J.J.; Ciol, M.; Richards, T.; Patterson, D.R. Manipulating presence influences the magnitude of virtual reality analgesia. *Pain* **2004**, *111*, 162–168. [CrossRef]
- 80. Flores-Cortes, M.; Guerra-Armas, J.; Pineda-Galan, C.; La Touche, R.; Luque-Suarez, A. Sensorimotor Uncertainty of Immersive Virtual Reality Environments for People in Pain: Scoping Review. *Brain Sci.* **2023**, *13*, 1461. [CrossRef]
- 81. McAnally, K.; Wallis, G. Visual–haptic integration, action and embodiment in virtual reality. *Psychol. Res.* **2022**, *86*, 1847–1857. [CrossRef]
- 82. Choudhury, S.; Charman, T.; Bird, V.; Blakemore, S.-J. Adolescent development of motor imagery in a visually guided pointing task. *Conscious. Cogn.* 2007, *16*, 886–896. [CrossRef]
- 83. Gupta, A.; Scott, K.; Dukewich, M. Innovative technology using virtual reality in the treatment of pain: Does it reduce pain via distraction, or is there more to it? *Pain Med.* **2018**, *19*, 151–159. [CrossRef] [PubMed]
- 84. Wittkopf, P.G.; Lloyd, D.M.; Coe, O.; Yacoobali, S.; Billington, J. The effect of interactive virtual reality on pain perception: A systematic review of clinical studies. *Disabil. Rehabil.* **2020**, *42*, 3722–3733. [CrossRef] [PubMed]
- Czub, M.; Piskorz, J. Body movement reduces pain intensity in virtual reality-based analgesia. Int. J. Hum. Comput. Interact. 2018, 34, 1045–1051. [CrossRef]
- Wiederhold, M.D.; Wiederhold, B.K. Virtual reality and interactive simulation for pain distraction. *Pain Med.* 2007, 8 (Suppl. S3), S182–S188. [CrossRef]
- 87. Lier, E.J.; Harder, J.; Oosterman, J.M.; de Vries, M.; van Goor, H. Modulation of tactile perception by Virtual Reality distraction: The role of individual and VR-related factors. *PLoS ONE* **2018**, *13*, e0208405. [CrossRef] [PubMed]

- 88. Deng, X.; Jian, C.; Yang, Q.; Jiang, N.; Huang, Z.; Zhao, S. The analgesic effect of different interactive modes of virtual reality: A prospective functional near-infrared spectroscopy (fNIRS) study. *Front. Neurosci.* **2022**, *16*, 1033155. [CrossRef] [PubMed]
- 89. Juan, M.-C.; Elexpuru, J.; Dias, P.; Santos, B.S.; Amorim, P. Immersive virtual reality for upper limb rehabilitation: Comparing hand and controller interaction. *Virtual Real.* 2023, 27, 1157–1171. [CrossRef] [PubMed]
- 90. Fandim, J.V.; Saragiotto, B.T.; Porfírio, G.J.M.; Santana, R.F. Effectiveness of virtual reality in children and young adults with cerebral palsy: A systematic review of randomized controlled trial. *Braz. J. Phys. Ther.* **2021**, *25*, 369–386. [CrossRef]
- 91. Evans, C.; Moonesinghe, R. Virtual reality in pediatric anesthesia: A toy or a tool. Pediatr. Anesthesia 2020, 30, 386–387. [CrossRef]
- 92. Alfieri, F.M.; da Silva Dias, C.; de Oliveira, N.C.; Battistella, L.R. Gamification in musculoskeletal rehabilitation. *Curr. Rev. Musculoskelet. Med.* 2022, 15, 629–636. [CrossRef]
- Primack, B.A.; Carroll, M.V.; McNamara, M.; Klem, M.L.; King, B.; Rich, M.; Chan, C.W.; Nayak, S. Role of video games in improving health-related outcomes: A systematic review. *Am. J. Prev. Med.* 2012, 42, 630–638. [CrossRef] [PubMed]
- 94. Mouatt, B.; Smith, A.E.; Mellow, M.L.; Parfitt, G.; Smith, R.T.; Stanton, T.R. The use of virtual reality to influence motivation, affect, enjoyment, and engagement during exercise: A scoping review. *Front. Virtual Real.* **2020**, *1*, 564664. [CrossRef]
- 95. Tao, G.; Garrett, B.; Taverner, T.; Cordingley, E.; Sun, C. Immersive virtual reality health games: A narrative review of game design. *J. Neuroeng. Rehabil.* **2021**, *18*, 31. [CrossRef] [PubMed]
- 96. Miller, A.S.; Cafazzo, J.A.; Seto, E. A game plan: Gamification design principles in mHealth applications for chronic disease management. *Health Inform. J.* 2016, 22, 184–193. [CrossRef]
- 97. Janssen, J.; Verschuren, O.; Renger, W.J.; Ermers, J.; Ketelaar, M.; Van Ee, R. Gamification in physical therapy: More than using games. *Pediatr. Phys. Ther.* 2017, 29, 95–99. [CrossRef] [PubMed]
- Suleiman-Martos, N.; García-Lara, R.A.; Membrive-Jiménez, M.J.; Pradas-Hernández, L.; Romero-Béjar, J.L.; Dominguez-Vías, G.; Gómez-Urquiza, J.L. Effect of a game-based intervention on preoperative pain and anxiety in children: A systematic review and meta-analysis. J. Clin. Nurs. 2022, 31, 3350–3367. [CrossRef] [PubMed]
- 99. Naqvi, W.; Quershi, M.I. Impact of Gamification on Pain, Range of Motion, Muscle Strength, and Functional Independence Post Distal Radius Fracture. *Arch. Phys. Med. Rehabil.* **2024**, *105*, e163. [CrossRef]
- Gava, V.; Fialho, H.R.F.; Calixtre, L.B.; Barbosa, G.M.; Kamonseki, D.H. Effects of gaming on pain-related fear, pain catastrophizing, anxiety, and depression in patients with chronic musculoskeletal pain: A systematic review and meta-analysis. *Games Health J.* 2022, 11, 369–384. [CrossRef] [PubMed]
- 101. Meulders, A. From fear of movement-related pain and avoidance to chronic pain disability: A state-of-the-art review. *Curr. Opin. Behav. Sci.* **2019**, *26*, 130–136. [CrossRef]
- 102. Vittersø, A.D.; Halicka, M.; Buckingham, G.; Proulx, M.J.; Bultitude, J.H. The sensorimotor theory of pathological pain revisited. *Neurosci. Biobehav. Rev.* **2022**, *139*, 104735. [CrossRef]
- 103. Kantak, S.S.; Johnson, T.; Zarzycki, R. Linking pain and motor control: Conceptualization of movement deficits in patients with painful conditions. *Phys. Ther.* **2022**, *102*, pzab289. [CrossRef] [PubMed]
- Senkowski, D.; Heinz, A. Chronic pain and distorted body image: Implications for multisensory feedback interventions. *Neurosci. Biobehav. Rev.* 2016, 69, 252–259. [CrossRef]
- 105. Lotze, M.; Moseley, G.L. Role of distorted body image in pain. Curr. Rheumatol. Rep. 2007, 9, 488–496. [CrossRef]
- 106. Martini, M. Real, rubber or virtual: The vision of 'one's own' body as a means for pain modulation. A narrative review. *Conscious. Cogn.* 2016, 43, 143–151. [CrossRef] [PubMed]
- 107. Boesch, E.; Bellan, V.; Moseley, G.L.; Stanton, T.R. The effect of bodily illusions on clinical pain: A systematic review and meta-analysis. *Pain* **2016**, 157. [CrossRef]
- 108. Kokkinara, E.; Slater, M. Measuring the effects through time of the influence of visuomotor and visuotactile synchronous stimulation on a virtual body ownership illusion. *Perception* **2014**, *43*, 43–58. [CrossRef] [PubMed]
- Buetler, K.A.; Penalver-Andres, J.; Özen, Ö.; Ferriroli, L.; Müri, R.M.; Cazzoli, D.; Marchal-Crespo, L. 'Tricking the Brain' Using Immersive Virtual Reality: Modifying the Self-Perception Over Embodied Avatar Influences Motor Cortical Excitability and Action Initiation. Front. Hum. Neurosci. 2022, 15, 787487. [CrossRef] [PubMed]
- 110. Hechler, T. Altered interoception and its role for the co-occurrence of chronic primary pain and mental health problems in children. *Pain* **2021**, *162*, *665–671*. [CrossRef]
- 111. Arzy, S.; Thut, G.; Mohr, C.; Michel, C.M.; Blanke, O. Neural Basis of Embodiment: Distinct Contributions of Temporoparietal Junction and Extrastriate Body Area. *J. Neurosci.* 2006, *26*, 8074. [CrossRef]
- 112. Matamala-Gomez, M.; Maselli, A.; Malighetti, C.; Realdon, O.; Mantovani, F.; Riva, G. Virtual Body Ownership Illusions for Mental Health: A Narrative Review. *J. Clin. Med.* **2021**, *10*, 139. [CrossRef]
- 113. Joy, T.; Ugur, E.; Ayhan, I. Trick the body trick the mind: Avatar representation affects the perception of available action possibilities in virtual reality. *Virtual Real.* **2022**, *26*, 615–629. [CrossRef]
- 114. Tsakiris, M.; Prabhu, G.; Haggard, P. Having a body versus moving your body: How agency structures body-ownership. *Conscious. Cogn.* **2006**, *15*, 423–432. [CrossRef]
- Gonçalves, G.; Melo, M.; Barbosa, L.; Vasconcelos-Raposo, J.; Bessa, M. Evaluation of the impact of different levels of self-representation and body tracking on the sense of presence and embodiment in immersive VR. *Virtual Real.* 2022, 26, 1–14. [CrossRef]

- 116. Kelly, J.M.; Coppieters, M.W.; Kluver, J.; Deen, M.; Rio, E.; Harvie, D.S. 'It made you feel like you've still got it': Experiences of people with chronic low back pain undertaking a single session of body image training in virtual reality. *Physiother. Theory Pract.* 2023, *39*, 2651–2661. [CrossRef]
- 117. Austin, P.D. The Analgesic Effects of Virtual Reality for People with Chronic Pain: A Scoping Review. *Pain Med.* **2022**, 23, 105–121. [CrossRef] [PubMed]
- 118. Moont, R.; Pud, D.; Sprecher, E.; Sharvit, G.; Yarnitsky, D. 'Pain inhibits pain' mechanisms: Is pain modulation simply due to distraction? *Pain* 2010, *150*, 113–120. [CrossRef]
- 119. Parker, M.; Delahunty, B.; Heberlein, N.; Devenish, N.; Wood, F.M.; Jackson, T.; Carter, T.; Edgar, D.W. Interactive gaming consoles reduced pain during acute minor burn rehabilitation: A randomized, pilot trial. *Burns* **2016**, *42*, 91–96. [CrossRef] [PubMed]
- 120. Ho, J.T.; Krummenacher, P.; Lesur, M.R.; Saetta, G.; Lenggenhager, B. Real Bodies Not Required? Placebo Analgesia and Pain Perception in Immersive Virtual and Augmented Reality. J. Pain 2022, 23, 625–640. [CrossRef] [PubMed]
- 121. McNaughton, D.; Beath, A.; Hush, J.; Jones, M. Perceptual sensory attenuation in chronic pain subjects and healthy controls. *Sci. Rep.* **2022**, *12*, 8958. [CrossRef]
- Flor, H.; Noguchi, K.; Treede, R.-D.; Turk, D.C. The role of evolving concepts and new technologies and approaches in advancing pain research, management, and education since the establishment of the International Association for the Study of Pain. *Pain* 2023, 164, S16–S21. [CrossRef]
- 123. Simón-Vicente, L.; Rodríguez-Cano, S.; Delgado-Benito, V.; Ausín-Villaverde, V.; Delgado, E.C. Cybersickness. A systematic literature review of adverse effects related to virtual reality. *Neurología* 2022. [CrossRef]
- 124. Caserman, P.; Garcia-Agundez, A.; Zerban, A.G.; Göbel, S. Cybersickness in current-generation virtual reality head-mounted displays: Systematic review and outlook. *Virtual Real.* **2021**, 25, 1153–1170. [CrossRef]
- 125. Weech, S.; Kenny, S.; Barnett-Cowan, M. Presence and cybersickness in virtual reality are negatively related: A review. *Front. Psychol.* **2019**, *10*, 158. [CrossRef] [PubMed]
- 126. Saredakis, D.; Szpak, A.; Birckhead, B.; Keage, H.A.D.; Rizzo, A.; Loetscher, T. Factors associated with virtual reality sickness in head-mounted displays: A systematic review and meta-analysis. *Front. Hum. Neurosci.* **2020**, *14*, 96. [CrossRef] [PubMed]
- 127. Fan, T.; Wang, X.; Song, X.; Zhao, G.; Zhang, Z. Research status and emerging trends in virtual reality rehabilitation: Bibliometric and knowledge graph study. *JMIR Serious Games* **2023**, *11*, e41091. [CrossRef]
- 128. Birckhead, B.; Khalil, C.; Liu, X.; Conovitz, S.; Rizzo, A.; Danovitch, I.; Bullock, K.; Spiegel, B. Recommendations for Methodology of Virtual Reality Clinical Trials in Health Care by an International Working Group: Iterative Study. *JMIR Ment. Health* 2019, *6*, e11973. [CrossRef] [PubMed]
- 129. Brassel, S.; Power, E.; Campbell, A.; Brunner, M.; Togher, L. Recommendations for the Design and Implementation of Virtual Reality for Acquired Brain Injury Rehabilitation: Systematic Review. *J. Med. Internet Res.* **2021**, 23, e26344. [CrossRef] [PubMed]
- 130. Badia, S.B.I.; Fluet, G.G.; Llorens, R.; Deutsch, J.E. Virtual Reality for Sensorimotor Rehabilitation Post Stroke: Design Principles and Evidence. In *Neurorehabilitation Technology*; Springer International Publishing: New York, NY, USA, 2016; pp. 573–603.
- Slatman, S.; Groenveld, T.; Ostelo, R.; van Goor, H.; Staal, J.B.; Knoop, J. Development of a Multimodal, Personalized Intervention of Virtual Reality Integrated within Physiotherapy for Patients with Complex Chronic Low-Back Pain. J. Med. Ext. Real. 2024, 1, 30–43. [CrossRef] [PubMed]
- 132. Braithwaite, F.; Arnold, J.; Davis, A.; Gwilt, I.; MacIntyre, E.; Morris, S.; James, K.; Lee, K.; Marshall, H.; Ninnes, P.; et al. Osteoarthritis consumers as co-researchers: Identifying consumer insights to improve osteoarthritis management by co-designing translational research solutions. *Osteoarthr. Cartil.* **2023**, *31*, 944–953. [CrossRef]
- 133. Maddox, T.; Garcia, H.; Ffrench, K.; Maddox, R.; Garcia, L.; Krishnamurthy, P.; Okhotin, D.; Sparks, C.; Oldstone, L.; Birckhead, B.; et al. In-home virtual reality program for chronic low back pain: Durability of a randomized, placebo-controlled clinical trial to 18 months post-treatment. *Reg. Anesthesia Pain Med.* **2024**, *49*, 373–375. [CrossRef]

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