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Clinical Note

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Visually evoked pain and its extinction using virtual reality in a patient with complex regional pain syndrome type II

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Abstract

In this case report, we used virtual reality (VR) to explore pain evoked by only the appearance of being touched (rather than actually being touched) in a person with complex regional pain syndrome type II. Furthermore, we explored the degree to which this visually evoked pain could be extinguished by applying exposure principles in VR. In stage 1, we identified 4 specific scenarios where pain was triggered by visually simulated touch (without physical stimulation) and used these scenarios to quantify baseline sensitivity to visuotactile stimulation. In stage 2, the patient undertook a 12-week virtual exposure program, and the visual triggers were reassessed 3 weeks after the commencement and immediately upon completion of the program. At baseline, severe pain and a profound cold sensation were immediately and consistently evoked in concert with visually simulated touch. At 12-week follow-up, only one of the initially provocative visual stimuli triggered pain and only after 60 seconds of repeated stimulation. Unfortunately, the transfer of desensitisation from VR to the real world was limited. This case report describes the phenomena of visually evoked pain. Moreover, it describes the near complete extinguishing of visually evoked pain through virtual graded exposure. How improvements gained in VR might be better transferred to real-word improvements merits further investigation.

Keywords: Multisensory integration, Neuropathic pain, Complex regional pain syndrome, Case report

1. Introduction

Complex regional pain syndrome (CRPS) is characterized by severe pain, including pain in response to tactile and other nonnoxious stimuli.[4] Although not fully understood, contributors to CRPS may include peripheral and central sensitisation, autonomic, immune and psychological factors, and cortical reorganisation.[4]

Some people with CRPS present with dysynchiria, where watching a reflected image of their unaffected limb being touched evokes pain in the affected limb.[1,10] Pain evoked by the appearance of being touched in the absence of corroboratory tactile input from that body part, as occurs in dysynchiria, provides support for centrally based pain mechanisms, perhaps involving bilateral projections to the sensory cortices, the mirror neuron system, or multisensory visuotactile areas.[2,6,12] Here, we use virtual reality (VR) to explore pain triggered by the appearance of touch but in the *absence of any physical stimulation* to either hand. We hypothesized that this effect would be extinguished through graded exposure to visually simulated touch.

2. Methods

2.1. Case description

A 43-year-old man with neuropathic hand pain was identified through a secondary care pain clinic. He had a 3-year history of severe pain localized to his left thumb following a laceration caused by a slip when cutting a cable tie with a pocketknife. The flexor pollicis longus tendon and a palmar digital nerve were severed. Treatment included 4 surgeries to repair the tendon, release scarring, replace the tendon (silicone and autologous), and repair the nerve. He described his hand as feeling like it was “in a freezer.” Aggravating factors included touch, movement, cold air, talking about pain, and watching his wife cut vegetables. Physical therapy, mirror therapy, natural therapies, and medications had been attempted with limited benefit. Ethical approval was obtained (Griffith University #2019/763). The participant gave written consent, including consent to disclose.

2.2. Clinical assessment

The CRPS diagnosis was confirmed using the Budapest Criteria.[7] The participant demonstrated symptoms in 3 of the 4 categories (self-reported allodynia, skin temperature/colour changes, reduced range of movement, and reduced motor function) and signs in 2 of the 4 categories (testing positive for allodynia, skin trophic changes, reduced thumb movement, and motor dysfunction; see **Figure 1**). The area of reduced sensation

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corresponded with a palmar digital nerve injury, supporting a CRPS type II diagnosis.

2.3. Equipment and procedure

An Oculus Quest II head mounted display (Oculus, Facebook Technologies, LCC, Menlo Park, CA) was used. On-board hand tracking technology synchronized real and virtual hands so that hand controllers were not required. Using Vacation Simulator (www.oculus.com/experiences/quest/), a hierarchy of stimuli was established from those the participant estimated would be least to most painful (**Fig. 1**; visually evoked pain assessment items). A wirelessly connected iPad Pro (Apple Inc., Cupertino, CA, 2020) relayed the virtual imagery to the experimenter to enable guiding of the participant experience.

2.4. Outcomes

The visually evoked pain assessment items were assessed sequentially during face-to-face sessions at baseline, after 3 weeks, and after 12 weeks. Time to pain (seconds) and evoked pain intensity (0-10) were collected during each exposure. Expectation of pain, fear of pain, and pain intensity ratings were collected before each exposure using 0 to 10 rating scales. Pain intensity (0-10) and evoked cold sensation (yes/no) were recorded after each exposure. Pain intensity and the global perceived effect (GPE) scale[9] (with the anchors: −3 = very much worse, 0 = no change, +3 = very much improved) were used to assess overall change at 3 and 12 weeks after enrolment. The Body Perception Disturbance Scale,[14] Tampa Scale of Kinesiophobia,[15] and a Patient Specific Functional Scale[8] were used to explore other clinical outcomes that may be relevant in cases of CRPS. Finally, to confirm an experience of ownership and agency over the avatar, we asked the participant to rate their agreement with the following statements using a 0 to 10 scale, where 0 is "completely disagree" and 10 is "completely agree." During the task, when looking at the virtual hand, it felt as (1) I was looking at my own hand, (2) the virtual hand was my hand, (3) the virtual hand was under my control, and (4) the virtual hand moved when I moved. The questions were derived from a validated questionnaire originally designed to quantify embodiment during the rubber hand illusion.[11]

2.5. Repeated exposure intervention

After baseline assessment, the participant undertook in-home self-guided exposure for 12 weeks following agreed principles (**Table 1**).

3. Results

Following initial immersion in VR, the participant reported a good degree of embodiment (mean rating: 7/10). Stronger agreement ratings were given for questions related to a sense of agency over the avatar compared with those related to a sense of body ownership (ie, It felt as 1. I was looking at my own hand: 4/10; 2. The virtual hand was my hand: 4/10; 3. The virtual hand was under my control: 10/10; 4. The virtual hand moved when I moved: 10/10). During the 12-week intervention, an average of 10 min/d of in-home VR exposure was performed, with a frequency of 4 to 5 times/week.

3.1. Sensitivity to visually simulated touch

Visually evoked pain outcomes at each timepoint are summarised in **Table 2**. At baseline, simply putting his hand under a virtual tap simulating running water evoked instant and severe "sharp" pain (**Table 2**, column 4), an immediate withdrawal response, and a "freezing" cold sensation (**Table 2**, column 6). In addition to the pain response concordant with the onset and offset of visuotactile

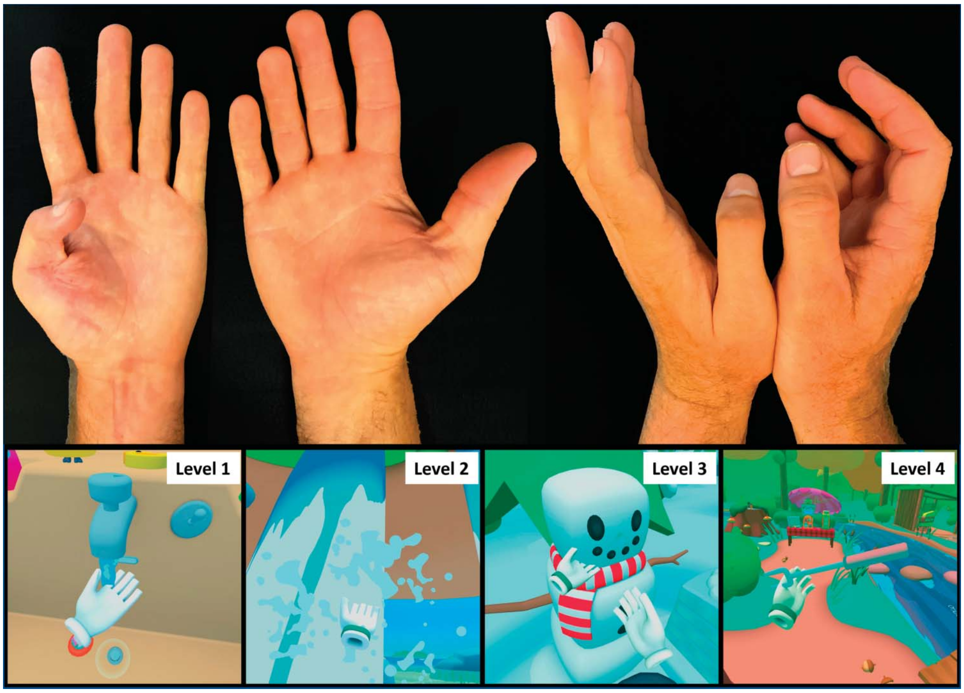

Figure 1. Top panel shows the participant's painful left hand compared against his nonpainful right hand. The bottom panels show the individualised hierarchy of visually provocative scenarios, consisting of putting the virtual hand under a running tap (level 1), putting the virtual hand under a waterfall (level 2), putting the virtual hand into snow (level 3), and inserting a virtual poker through the virtual hand (level 4).

Table 1

Principles of the graded exposure to visually simulated touch program.

Week 1: acclimatisation and free movement (5-10 min, 6-d/week)
Focus on simple hand movements in VR while observing virtual hands
Limit touching, grasping, and manipulating of virtual objects
Week 2-12: graded exposure to simulated touch (5-10 min, 6-d/week)
Explore the vacation simulator (beach, forest, mountain)
Use nonpainful hand to interact, while consciously increasing CRPS hand use
Recognise that some pain is inevitable but limit to activities that are tolerable
If sensitivity to given activities diminishes, move to more provocative activities

CRPS, complex regional pain syndrome; VR, virtual reality.

stimulation, a sustained increase in his general “dull ache” type pain was also reported (**Table 2**, column 5). At the 3-week assessment, a marked reduction in visually evoked pain was apparent, and by week 12, 3 of the 4 assessment items no longer provoked pain. The fourth visually evoked pain assessment item (**Fig. 1**) still provoked pain but only after 60 seconds of repeated visuotactile stimulation, further confirming a marked reduction in sensitivity to visuotactile stimulation. While not recorded in **Table 2**, the “sharp” type pain was always 0/10 prior to visuotactile stimulation and quickly returned to 0/10 after the stimulus was removed. This is in contrast with the “dull” background pain that was ever present and often elevated following stimulation.

3.2. Clinical outcomes

Clinical outcomes are summarised in **Table 2**. The participant rated their overall change in pain and function in VR as “very much

Table 2

The results at baseline, and 3- and 12-week time points for each of the 4 levels of visually provocative stimuli (A.) and for secondary outcomes (B).

A. Visually evoked pain assessment

	Baseline “dull” pain (/10)	Time to evoked “sharp” pain(s)	Evoked “sharp” pain (/10)	Postexposure “dull” pain (/10)	Evoked “freezing” sensation	Expected pain (/10)	Fear rating (/10)
Level 1—Putting virtual hand under a running tap							
Baseline	7	**0**	**8^**	8	Yes	10	4
3 wk	7	**21**	**8^**	7.5	Yes	7	1
12 wk	6.5	**>70**	**Nil**	6.5	No	0	0
Level 2—putting the virtual hand under a waterfall							
Baseline	*Not able to complete task due to pain/fear of pain						
3 wk	6	**10**	**8^**	8	Yes	7	0
12 wk	6.5	**>70**	**Nil**	6.5	No	0	0
Level 3—putting virtual hand into snow							
Baseline	*Not able to complete task due to pain/fear of pain						
3 wk	7.5	**23**	**9^**	8	Yes	8	4
12 wk	6.5	**>70**	**Nil**	6.5	Yes	1	0
Level 4—inserting a virtual poker through the virtual hand							
Baseline	*Not able to complete task due to pain/fear of pain						
3 wk	6.5	**0**	**9.5^**	9.5	Yes	10	10
12 wk	6.5	**60**	**7^**	6.5	Yes	0	0

B. Secondary outcomes

	Average pain last week	Worst pain last week	Global change		Kinesiophobia (TSK-17)	Body perception (BPD) scale	Neglect-like symptoms (NLS)	Patient specific functional scale (PSFS)
			Real world	VR				
Baseline	70/100	95/100	n/a	n/a	37	34	13	13%
12 wk	65/100	90/100	+1	+3	38	35	11	13%

Time to pain(s) and evoked pain intensity, the outcomes of primary interest, are highlighted in bold.

*Baseline and post-exposure “dull” pain = background constant pain, Evoked “sharp” pain = immediate pain ‘like knives/lightening’ and aligned to visuotactile stimulation timing and location and distinct to “dull” pain, Global change = Global Perceived Effect scale (anchors +3 = Very Much Improved, 0 = No change, −3 = Very Much Worse), TSK-17 = Tampa Scale of Kinesiophobia, BPD = Bath Perception Disturbance, ^ = Observable withdrawal response.

improved" (GPE +3) but real-world change as "minimally improved" (GPE +1), reporting a small reduction in "psychologically triggered pain" and no change regarding overall symptoms. Similarly, average and worst pain over the last week did not change meaningfully and function (Patient Specific Functional Scale) remained as at baseline. No clinically meaningful changes were detected in kinesiophobia, body-related perceptual disturbances, or body-related neglect.

4. Discussion

In this case report, we outlined an unreported form of visually evoked pain, occurring in the absence of any tactile input. This phenomenon is distinct from dysynchiria,[1,10] which by definition requires that pain is evoked on the affected side by actual tactile stimulation of the opposite side, reflected in a mirror. Given this, we propose to call this visually evoked pain "*visuodynia*" so as to clearly delineate between phenomena. Repeated exposure to visuotactile stimulation resulted in marked desensitisation; however, no clinically meaningful real-world benefit ensued.

4.1. Potential mechanisms

The mechanisms underpinning the observed phenomenon must account for a number of observations. This includes that the visually simulated touch triggered pain independent of any tactile input and that the transient increases in pain aligned with the location and timing of visuotactile stimulation. The fact that pain was visually evoked implies that bimodal visual-tactile and/or mirror neurones may be involved and solely activated by vision. Moreover, it implies that cortical networks associated with pain may have become hypersensitive to such input. The temporal pairing between pain and visuotactile stimulation points to a mechanism capable of immediate effects. For example, visuodynia could be explained using a Bayesian predictive processing account of pain. That is, where pain is considered the result of available sensory and nonsensory data that together contribute to a probability-based estimate that relevant bodily danger is present.[13] Based on this framework, visuodynia may have emerged, in this case, as a result of the (nonconscious) integration of threatening nociceptive and nonnociceptive (visual) cues that together predict relevant bodily danger. The same approach may be used to explain the extinction of visuodynia. That is, through repeated exposure, the visuotactile cues may have been rendered less threatening, and thereby less pain provoking, by virtue of being proven unreliable predictors of danger.

It may also be relevant to distinguish between possible cognitive–affective contributors (eg, pain expectancy and fear) and the noted sensory integration mechanisms. Unsurprisingly, expected pain and pain-related fear ratings were reasonably aligned with subsequent pain reports (**Table 2**). However, while this may have contributed to both the effect and its extinction, the close temporal pairing between visuotactile stimulus and experienced pain suggests against anticipatory effects as the sole contributor.

Other recent findings might also aid interpretation. For example, a recent study found an increase in light sensitivity that was specific to the CRPS affected side,[5] suggesting that CRPS-related central sensitisation extends beyond the somatosensory system to include other inputs spatially oriented toward the painful hand.

4.2. Limitations

Without corroborating neurophysiological data, it is not possible to draw conclusions regarding the mechanisms underlying the apparent effects on pain, and further work is needed. Moreover, had we assessed whether pain was specifically provoked by "imagining being touched," we might have gained insight on whether visually simulated touch may be viewed as an enhanced form of tactile imagery. This would be analogous to what is understood in the motor imagery domain, where the use of mirror-based visuomotor feedback is considered a progression from imagined movement.[3]

While there was no transfer of the in-VR desensitisation effect to meaningful benefit outside the VR setting, we cannot rule out a potential clinical effect under different VR parameters. For example, the virtual hands and environment used were not photorealistic. Further, while participant ratings of agency over the virtual hands were high (10/10), ratings related to ownership were lower (4/10). As such, it remains possible that greater realisms might facilitate greater virtual embodiment and more real-world generalisation of the observed in-VR effects. While photorealistic VR experiences are available, we were limited to applications that were compatible with Oculus hand tracking technology because the participant was too sensitive to utilise the hand controllers that are typically required. Furthermore, a more realistic scenario may have been initially poorly tolerated, and future studies may consider photorealism as a progression. Clinical benefit would also likely be enhanced by purposeful use of real-world exposure once visuodynia is extinguished in VR settings.

5. Conclusion

This case of visually evoked pain raises important questions regarding the nature of central mechanisms involved in neuropathic hand pain. The observation that visually evoked pain was almost entirely extinguished through repeated exposure to visually simulated touch in VR suggests the potential for therapeutic development. However, despite the profound reduction in sensitivity to visually simulated touch, the exposure intervention resulted in limited real-world improvement. Thus, although not yet a viable treatment in isolation, future work that embeds a transition to real-world exposure is warranted, perhaps utilising augmented reality or mirror therapy, which more closely reflect the real world. Understanding the prevalence of "visuodynia" in CRPS and other persistent pain conditions, its functional distinction from tactile imagery, and its response to other brain-based treatments using visual cues to target cortical reorganisation warrants further investigation.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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