Pain Management

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| Journal: | *Pain Management* |
| Manuscript ID | PMT-2019-0019.R2 |
| Manuscript Type: | Research Article |
| Keywords: | virtual arm, body ownership, pain modulation |
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# Visuo-tactile stimulation, but not type of movement, modulates pain during the vision of a moving virtual limb.

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**First draft submitted: 14 April 2019; Accepted for publication: 24 June 2019; Published online: TBC**

## *Abstract*

**Aims**: Evidence has revealed a relationship between pain and the observation of limb movement, but it is unknown whether different types of movements have diverse modulating effects. In this immersive virtual reality study we explored the effect of the vision of different virtual arm movements (arm vs. wrist) on pain threshold from heat applied to the wrist. **Patients & Methods**: Forty healthy participants underwent four conditions in virtual reality while heat pain thresholds were measured. Visuo-tactile stimulation was used to attempt to modulate the feeling of virtual limb ownership. **Results**: Effects on pain threshold were present for type of stimulation but not type of movement. **Conclusions**: The type of observed movement does not appear to influence pain modulation, at least not during acute pain states.

**Keywords:** virtual arm, virtual reality, body ownership, pain threshold, pain modulation, multisensory integration, illusory kinesthesia.

## *Introduction*

Pain and motor activity can have a reciprocal influence. Not only can the presence of pain affect motor performance but also motor activity can shape the way pain is felt. At a neural level, this bidirectional influence is explained by a considerable connectivity between motor and pain-related neural circuits [1,2]. For example, in therapeutic trials, non-invasive brain stimulation activating the motor cortex has been found to inhibit pain [3,4]. It has also been suggested that motor cortex excitability may indirectly affect cortical structures that process pain, such as the thalamus [5,6]. Interestingly, even the observation of limb movement has demonstrated efficacy as a therapeutic intervention for chronic pain management [7]. Indeed, there is a robust relationship between limb/extremities movement observation and increases in activity in the motor cortex [8–11], which suggests that movement observation may induce neuronal activity that can facilitate analgesia. Furthermore, long lasting pain can be associated with maladaptive neural plasticity in the sensorimotor cortices, in a time-dependent fashion [12–15]. Subsequently, techniques that employ movement representation often aim to reverse this cortical reorganization, normalizing the functionality in the affected cortices and reducing pain [16]. Evidence from behavioral studies supports the use of movement observation to relieve chronic limb pain in some types of patients [7]. Studies that investigate neuropathic pain disorders such as Phantom Limb Pain (PLP) or Complex Regional Pain Syndrome (CRPS) have found movement representation techniques to be useful in reducing painful exacerbations [17–24]. The movement representation technique is often based on the provision of an illusory experience, namely that the afflicted limb is moving. Mirror box therapy, which utilizes a mirror placed between a healthy and an amputated limb, to create the illusion of movement of the latter, has been found to provide analgesic effects from upper limb PLP [17–19,25], CRPS [19], and lower limb PLP [20]. Similarly, studies using 2-dimensional or immersive Virtual Reality (VR) systems to present digital moving limbs have found reductions in neuropathic pain from upper limb paralysis or amputation [21–24,26,27], lower-limb amputation [21,24] or incomplete spinal cord injury [28]. In addition, movement observation has been found to be useful for reducing chronic pain when supplement to physical training, in patients with total knee replacements [29].

The analgesic effects of movement observation have also been explored in healthy participants exposed to acute pain. However, evidence in favor of a modulation of pain by movement observation in healthy participants is much less clear. In one recent study, Volz and colleagues showed that the observation of a moving left hand can increase pressure pain threshold in the left hand of male participants [30]. By contrast, in an immersive virtual reality (VR) study, Zanini et al. recently explored the effects of observing an avatar's arm movement, while being exposed to ramps of increasing heat stimuli, in healthy participants [31]. Despite finding significantly higher heat-pain thresholds (HPT) when viewing a virtual arm versus a virtual object, no significant difference in HPT was found between conditions where the virtual arm was moving, versus when it remained still.

So, whether limb movement observation can effectively modulate pain felt in the corresponding limb of healthy participants remains to be clarified. One reason why Zanini and colleagues did not find an effect of movement observation on pain could reside on the type of movement being presented. Indeed, in such study, the painfully stimulated area was restricted and localized to a small area of the palmar side of the wrist, but the movement shown utilized the avatar's whole forearm and hand, mostly engaging muscles of the upper arm. So, no muscles in the area affected by the pain were actually involved in any movement. It has previously been reported that observing actions performed with different body parts, by another individual, leads to the activation of different sectors of the pre-motor cortex [11]. Therefore, it remains to be clarified as to whether a congruency between the body district interested by the movement and the site of pain application, is needed to obtain analgesic effects. Moreover, it should be noted that movement observation distracts attention away from painful stimuli, so the results of Volz and colleagues [30] could have been different if attention had been controlled for.

Based on such premises, in the present study we investigated whether the observation of two different types of limb movement modulated the participants' pain threshold according to the type of movement observed. Specifically, we wanted to see whether the observation of a hand movement (flexion and extension of the hand at the wrist), involving muscles and tendons affected by the pain, had a stronger pain analgesic effect compared to the observation of a whole lower arm movement (flexion and extension of the lower arm at the elbow), which did not directly recruit the pain-affected area. Therefore, in our study, healthy participants observed either an avatar's moving wrist or a moving forearm, whilst being exposed to increasing heat stimuli. Drawing on Zanini's study, we considered the same forearm movement used in their study to be compared, in the present experiment, with the wrist movement. Any significant differences between the two types of movements could reveal whether spatial congruence between the body district interested by the movement and the body area when pain originates, plays a role in pain perception. Furthermore, to be consistent with Zanini's study, and in an attempt to mimic, at least partially, the immobilization suffered by some types chronic pain patients [32,33], we also asked our participants to keep their arms still during each condition.

Finally, we aimed at examining the possible interaction effect of the type of movement with the one derived by the vision of 'one's own body' on the participants' pain. In fact, the vision of the *own* body can influence both the neural coding of noxious stimuli and the consequent experience of pain, in a mechanism referred to as 'visual analgesia' [34]. Thus, seeing a moving limb could bring about a stronger analgesic effect if the seen limb is felt as part of the own body. In experimental set-ups making use of fake limbs, synchronous visuo-tactile stimulations have been shown to increase the participant's body ownership sensation over the external body part, even in presence of visuo-motor mismatch [35]. After all, although the finding is a bit controversial [36], a sensation of body ownership fostered by synchronous multisensory stimulations has been shown to have a pain modulatory effect in experiments displaying fake limbs [37,38].

## *Material and methods*

### *Participants*

Forty-one participants were recruited for the study. One participant was removed from analysis due to multiple HPT scores <39.5°c, that is below the cut-off set in accordance with data on normative ranges [39] and in line with a previous study [31]. The final sample consisted of forty healthy participants (26 females and 14 males), with ages ranging from 18 to 44 years (mean = 24.5 years, SD = 5.1). All participants had: normal or corrected-to-normal vision, no current condition that could interfere with pain sensitivity, no current usage of psychoactive drugs or painkillers, and no history of neurological or psychiatric disorders. All participants were right-handed, as assessed before the study began with the Edinburgh Handedness Inventory [40]. Participants were recruited through advertisements within the University of East London (UEL), and were provided with a consent form to read through upon arrival to the lab. The study was approved by the UEL Ethics Committee.

### *Virtual reality system*

The stereoscopic head-mounted display (HMD) was an Oculus Rift DK2 (Oculus VR, Irvine, CA) with a resolution of 960x1080 per eye and a field of view of 100º, displayed at 60Hz. The virtual environment was programmed using the Unity platform (Unity Technologies, San

Francisco, CA). Noise isolation was ensured by the administration of pink noise via headphones, with a constant volume set at 70 dB SPL.

### *Thermal stimulation*

Thermal heat stimuli were delivered by means of a TSA-II Neuro Sensory Analyzer (Medoc Ltd., Ramat Yishai, Israel), with a 30x30mm thermode tied with a Velcro strap on the palmar side of the right wrist. The probe temperature was increased from normal skin temperature (constant baseline temperature = 32 °C) at 2 °C/s. Participants were asked to press a button with their left hand as soon as they perceived the stimulation as being painful. Immediately after pushing the kill-switch button, the probe temperature rapidly decreased to the baseline temperature. Maximal temperature was set at 51 °C.

### *Procedure*

The thermode was attached to the participant’s forearm, close to the wrist on the palmar side of the arm, and was secured to ensure it was flush against the skin. Participants were given two/three unrecorded trials to familiarize themselves with the heat stimulus. Once the participant put the HMD on, the experimenter made sure the placement of the participants’ arms were closely matched to the avatar’s, to ensure the highest chances of body ownership. The HMD presented them with a first-person perspective of an avatar in a virtual room sat in front of a table, with both arms laid on the table-top. The right arm was visible on the table surface, and the left arm was hidden behind a barrier, to ensure their focus was solely on the right limb. The virtual arms were customized by skin color (black, white, & tan) and sex (male & female), to match the participant’s physical features. The experimenter laid the participant’s elbow on a small box, suspending their right forearm in mid-air, to limit tactile stimulation to the right arm from the table.

During the experimental conditions a vibrating sensor, controlled by Unity through an Arduino MEGA microcontroller board (Arduino LLC, Ivrea, Italy), was attached to the right arm. This sensor vibrated either synchronously or asynchronously with an animated white ball, seen in the VR, which bounced vertically up and down on the virtual arm. The ball touched the avatar's wrist every 2 seconds and the vibrator had a frequency of 8Hz. In synchronous conditions the sensor buzzed when the virtual ball touched the arm, imitating contact, and in asynchronous conditions the sensor buzzed when the ball was at the furthest point from the arm. These visuo-tactile vibrations commenced at the same time as the virtual arm movements began, and continued throughout each experimental trial, until the HMD was removed.

All participants experienced five conditions during which they: i) looked at moving arm and received a synchronous vibration; ii) looked at a moving arm and received an asynchronous vibration; iii) looked at a moving wrist and received a synchronous vibration; iv) looked at a moving wrist and received an asynchronous vibration; v) looked at a fixation cross and received no vibration. In the latter, baseline condition, the HMD was not used and the participant instead fixated on a cross on the table in front of them. In this condition a barrier was used to obstruct their view of their right arm, and the pink noise was played over a pair of headphones. In all virtual conditions, participants were presented with a virtual arm undergoing horizontal movement. In the arm conditions the right forearm moved, parallel with the table, 45° in both directions, pivoting at the elbow. In the wrist conditions, the virtual lower arm was rotated 90° along the transverse plane to allow the hand movement to be similar to the arm movement (both horizontal). The avatar’s hand assumed a relaxed fist position, before undergoing movement 45° in both directions, pivoting at the wrist (see Fig.1). In all conditions virtual movements occurred at a constant angular speed ($\omega$) of 5.0, which was a speed close to the slower movements recommended for maximizing a body ownership illusion (BOI) in previous findings [35]. Before the start of each condition the experimenter made sure that the participants' real arm/hand mimicked the virtual counterpart (Fig.1) and that they kept their limb completely still during each condition. The ordering of each condition was counterbalanced across all participants to reach a perfectly even distribution of the condition/order. After each virtual condition a subjective experience questionnaire was administered. In each of the five conditions, four instances of heat stimuli were delivered, producing a total of 20 HPT readings across the whole experiment.

### *Subjective measures*

A questionnaire was administered after each virtual condition in order to measure the subjective experiences of the participant throughout the VR. A number of items were adapted from previous studies that measured strength of BOI [41,42]. The questions were read out by the experimenter in a random order, and participants responded verbally with a number on a 7-point Likert scale (1 = 'totally disagree', 7 = 'totally agree').

Items:

- Q1. During the last condition there were moments in which I felt as if the virtual arm was my own arm
- Q2. During the last condition there were moments in which it seemed that my real arm was moving
- Q3. During the last condition there were moments in which I felt as if my real arm was becoming virtual
- Q4. During the last condition there were moments in which the virtual arm started to look like my own arm in some aspects

- Q5. During the last condition there were moments in which I had the sensation of having more than one right arm
- Q6. During the last condition there were moments in which I had the sensation that the heat was coming from the virtual arm
- Q7. I had a strong feeling of being in the lab (1), in the virtual room (7)
- Q8. During the last condition there were moments in which I felt as if I was controlling the movements of the virtual arm
- Q9. During the last condition there were moments in which I felt as if the virtual arm was controlling my movements
- Q10. During the last condition there were moments in which I felt as if the virtual arm had a will of its own
- Q11. My attention was totally focused on other things, for example on what I was watching, (1) or totally on the thermal stimulus (7)

**-----------Fig. 1 about here------------**

*Data handling*

Single pain threshold values, in Celsius degrees, were firstly cleaned of any value below 40°C [43] and then averaged per each condition and participant. Excluded values represented only the 2% of the total. Values were then normalized according to the formula: x = VR condition – Baseline. Resulting data from all conditions were normally distributed according to the Kolmogorov-Smirnov tests (all $p_s$>0.05). To check for differences in pain thresholds among VR scenarios a 2x2 repeated measures ANOVA was conducted [two factors, namely

Type of Movement with 2 levels (‘Arm’ and ‘Hand’) and Type of Stimulation with 2 levels (‘Synchronous’ and ‘Asynchronous’ tactile stimulation)].

Questionnaire scores collected right after each VR condition were averaged across subjects per each item and condition. The resulting mean scores were subjected to Friedman ANOVAs (per each item separately), with “Condition” as the only factor with 4 levels. Post-hoc analysis was carried out with Conover’s test.

All statistical analysis were conducted with JASP (JASP Team (2018). JASP (Version 0.9)[Computer software]).

## Results

*Pain threshold*

The 2x2 repeated-measures ANOVA on the four VR conditions revealed no effect of the factor “Type of Movement” ($F_{1,39}$=2.408, $p$=0.129, $\eta^2_p$=0.058). Since null-hypothesis testing does not provide a coherent approach to determining whether non-significant results support a null hypothesis over a theory [44,45], we additionally ran a Bayesian Repeated Measures Anova to calculate the Bayes Factor (BF). Although not strikingly, the estimated Bayes factor (alternative/null) was in favor of the null hypothesis ($BF_{10}$=0.426), with the data being approximately half as likely to occur under a model which does not include an effect of type of movement rather than a model with it. On the other hand, the factor “Type of Stimulation” did have a main effect on pain ($F_{1,39}$=4.677, $p$=0.037, $\eta^2_p$=0.107; $BF_{10}$=5.19; see Fig.2). No interaction effect was found between the two factors (“Type of Movement” x “Type of Stimulation”: $F_{1,39}$=0.331, $p$=0.568, $\eta^2_p$=0.008).

**-----------Fig. 2 about here------------**

*Subjective scores*

Mean scores relative to the subjective reports are shown in table 1 (see also fig.3).

The Friedman ANOVA computed on Q1 scores, linked to the sensation of virtual arm ownership did not show an effect of the factor “Condition” ($\chi^2_3$=3.10, *p*=0.37). No significant differences were found for Q2 either, ($\chi^2_3$=5.90, *p*=0.11) relative to the sensation that the real arm was moving, or for Q3 ($\chi^2_3$=4.10, *p*=0.25), referred to the sensation that the real arm was becoming virtual. The Friedman ANOVA computed on Q4 scores, associated to the feeling of seeing the virtual arm physically similar to the own real arm, did not evidence any differences across conditions ($\chi^2_3$=4.81, *p*=0.18), while the Friedman ANOVA on Q5, an item previously linked to ownership [41,46] and specifically related to the sensation of having more than one right arm, showed a strong trend towards significance ($\chi^2_3$=7.45, *p*=0.058), with the ‘Arm Sync’ condition reporting the higher score. The sensations that the heat was coming from the virtual arm (Q6), of being present in the virtual room (Q7), of being in control of the virtual arm movements (Q8), that the virtual arm was controlling the real arm movements (Q9) and that the virtual hand had a will of its own (Q10), did not show statistically different scores across conditions (respectively: $\chi^2_3$=1.18, *p*=0.75; $\chi^2_3$=1.98, *p*=0.57; $\chi^2_3$=3.14, *p*=0.37; $\chi^2_3$=1.34, *p*=0.71; $\chi^2_3$=4.07, *p*=0.25). Also the attentional levels did not differ among conditions although a trend towards significance was found ($\chi^2_3$=6.45, *p*=0.09), with the asynchronous conditions reporting a slightly more accentuated focus of attention toward the heat stimulus rather than toward the visual cue.

**-----------Table 1 and Fig. 3 about here------------**

### *Discussion*

The aim of this study was to investigate whether the observation of two different types of limb movement, represented in immersive VR, had different modulatory effects on pain perception, and if the type of movement interacted with the feeling of body ownership over the moving virtual limb. We hypothesized that a greater HPT would be found during the observation of a moving fist at the wrist, versus a moving forearm at the elbow, since the first type of movement involved the muscles and tendons in the area of the painful stimulation. This hypothesis was also based on a previous study [31] which showed that the vision of the forearm movement did not bring about higher pain thresholds compared to the vision of a still arm. Contrary to what was expected, our results did not show different pain thresholds following the vision of a wrist movement compared to the vision of a forearm movement. This suggests that the observation of a specific type of limb movement may not be any more effective than others, at least not during acute pain states. Unexpectedly, we also found a decrease of the pain threshold during asynchronous visuo-tactile conditions, which we will discuss later on this section.

The act of observing movement of a relevant limb per se has demonstrated efficacy in both acute and chronic pain literature [7,47]. Our finding complement this notion by showing that the type of movement per se, does not play a role in pain modulation.

On the other hand, the type of the visuo-tactile stimulation provided was found to have a significant effect on analgesia, with HPT scores shown to be higher in conditions where the vibrations were synchronized with the animation in the VR scenario. Synchronous visuo-tactile stimulations in body ownership paradigms have been shown to increase the chances of feeling the dummy body part as belonging to one’s own body [48]. This feeling of body ownership seems to be crucial to produce an analgesic effect during the vision of external limbs [37]. Our finding that synchronous multisensory stimulation, meant to facilitate BOI, yields a significant increase in pain threshold compared to asynchronous conditions, may be in line with similar pain studies that have exposed participants to the vision of dummy limbs [38,49,50]. However, with the present findings we could not confirm a role of the vision of the 'own' body on pain perception. Also, the pain thresholds measured during the synchronous conditions are very similar to those gauged during the baseline, where the participants were looking at a fixation cross. So, the present results may be more in line with those studies which have questioned the robustness of visual analgesia [51,52], or failed to find an analgesic effect during synchronous multisensory stimulation in BOI paradigms [36,53]. Nevertheless, variability in findings could be explained by the fact that the effect size is usually quite small in this type of experiments, especially when compared to other factors which may modulate pain like, for instance, VR-based distraction [54]. Also, key divergences in the experimental design of these studies could account for such contradicting outcomes [55–57]. For instance, a systematic review has shown that aerobic exercise has a remarkable effect on pressure pain threshold (Cohen's $d = 0.58$), but not so much on heat pain threshold (Cohen's $d = 0.04$) [58].

Unexpectedly, our results show a decrease in pain thresholds during the asynchronous visuo-tactile conditions. The thresholds are not only lower in respect to those recorded during the synchronous conditions, but they are also lower than the baseline. Such unpredicted finding could be explained taking into account the insights deriving from multisensory research. For example, by relying on a classical rubber hand illusion paradigm, Perez-Marcos and colleagues [59] have recently noted an interesting phenomenon, according to which their healthy participants reported a distortion of body image following asynchronous visuo-tactile stimulation. During the asynchronous stimulation of their lower arm, participants perceived it as elongated, thus showing a transitory distortion of the representation of their body. Such phenomenon did not occur during synchronous visuo-tactile stimulations or other control conditions. An alteration of body image has been linked to the presence of various forms of chronic pain, like for instance osteoarthritis [60], CRPS [61] and phantom limb pain [62]. The mechanism responsible for the presence of pain following altered body representations would consist of multisensory incongruences, for instance between motor intention, proprioception and vision, that would promote plastic changes of cortical sensory maps [63]. A disorganized or inappropriate cortical representation of the body may, in its turn, falsely signal sensory incongruence which would result in pathological pain [63]. In agreement with this hypothesis an altered cortical representation of the body has been reported in different types of chronic pain [64] and multisensory incongruence, for instance visuo-motor incongruence, has been found to induce altered body image and pain in healthy subjects [65]. Therefore, we speculate that, in our experiment, the vision of the avatar's moving arm/hand may have yielded a transitory alteration in the representation of our participants' limb, due to the visuo-motor mismatch present in all VR conditions. Such distortion may have been particularly pronounced during the asynchronous visuo-tactile conditions, and could have led to the abovementioned decrease of the pain thresholds, even lower than those recorded at the baseline.

We should also acknowledge that in our study the synchronous stimulation did not clearly lead to a strong BOI. Indeed, although higher body ownership scores were consistently reported during synchronous conditions than during asynchronous conditions, no clear differences were found between any conditions on any of the items of the questionnaire which would indicate the presence of body ownership (i.e. items Q1, Q3, Q4 and Q5), and mean scores were generally quite low. If no BOI is induced over the external arm, then the seen movement can be attributed to someone else's body. As it has been previously suggested, this could have completely different effects at cortical level [66,67], and it could be the focus of future investigations.

One explanation for the weak feeling in subjective ownership is the incongruence between the participant's still arm, and their observation of a moving virtual arm, present in our study. The literature suggests that a spatial match between felt and observed limb is not essential for a BOI, however, congruence between seen and felt movements is of crucial importance [68]. Conversely, a recent investigation into the optimal conditions to induce a BOI suggests that ownership over an avatar's arm is still possible during visuo-motor mismatch, provided that concomitant synchronous visuotactile stimulation is present [35]. However, it is important to note that the ownership mean scores in such study were lower compared to BOIs in studies without visuo-motor mismatch and that these were compared with ownership scores toward a non-corporeal object [35]. Also, the slightly different VR scenario compared to Caola's study and the presence of painful stimuli might have contributed, in the present experiment, to hinder the BOI.

The mismatch between real and observed virtual arm in this study is, therefore, a likely contributor towards the low feelings of ownership reported in the subjective measures. Nonetheless, having the participants still during the vision of the arm movement can have the advantage of possibly extending the study's methodology to the chronic pain population, where immobilization or reduced mobility can be a natural part of the clinical condition (for ex. in CRPS). But on the same line, it is also important to note that the findings in this study only have relevance for a healthy population experiencing acute pain exacerbations. Previous research has shown that the same experimental manipulation can have contrasting effects on the experience of pain, depending on whether the sample is exposed to acute pain [69], or is suffering from a chronic limb pain condition [70]. To gain a more comprehensive understanding of the analgesic effects produced in virtually represented movement paired with a concomitant visuo-tactile stimulus, a similar design to the one employed in this study could be applied to a sample experiencing a chronic pain condition. Differences in methodology and design could be at the basis of key differences in the results, even if the same type of participants is considered. This critical point has already been raised in previous commentaries [55,56] and could explain the contrasting findings between our study and the ones reported by Volz and colleagues [30]. For instance, while these authors measure mechanical pain, in our study we refer to heat pain. Different pain types are not necessarily correlated and can react differently to different modulators [71,72]. In addition, electrical, thermal, and mechanical stimuli belong to three separate clusters of pain measures, and these stimuli seem to be processed differently in the brain [73]. Thus, the choice of the type of pain to measure, together with other methodological components, can really make a huge difference in these types of experiments, driving the final outcome toward one end rather than the other.

## Conclusion

To conclude, our findings show that the synchronicity of a visuo-tactile stimulus can modulate HPT when a participant is observing the movement of a virtual limb in an immersive VR environment, with a greater pain threshold found in conditions where there is synchronicity between the seen and the felt vibro-tactile stimulation, compared to when this stimulation is asynchronous. However, such modulation seems to be more likely driven by an hyperalgesic effect occurring during the asynchronous conditions rather than by an analgesic effect of the synchronous ones. Also, the type of movement observed does not appear to make a difference to the experience of pain. In other words, a strict congruency between the body area interested by the movement and the site of pain does not seem to play a role in the modulation of acute pain during limb movement observation. So, whether limb movement observation can effectively modulate pain felt in the corresponding limb of healthy participants remains to be clarified.

## Summary Points

- Past research on pain has revealed a link between pain perception and the observation of limb movement, with many studies finding movement observation to have analgesic effects.
- It is currently unknown whether the observation of different types of limb movement within the same body district has modulating effects for pain.
- This study recruited 40 healthy participants to undergo 4 conditions in virtual reality while heat pain was applied to their wrist.
- Virtual wrist movements, which were spatially closer to site of pain, where compared to virtual arm movements, which did not directly interest the wrist area.
- Visuo-tactile stimulation was also applied to modulate the feeling of virtual limb ownership.
- Results found no effect for type of movement on heat pain threshold.
- However, an effect was found for type of visuo-tactile stimulation, with lower pain thresholds reported during asynchronous visuo-tactile stimulation.
- These findings indicate that the type of observed movement does not appear to influence pain modulation, and spatial congruency between site of pain and site of movement may not be clinically relevant.
- On the other hand, incongruent multisensory stimulation may promote hyperalgesia.

## Financial & competing interests disclosure

This research was supported by UEL Research Capital Fund. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

### *Acknowledgments*

The authors are thankful to Chloe Lattimore, for their help with data collection.

## Ethical conduct of research

The study was approved by the University of East London Ethics Committee. The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, the authors state that they have obtained verbal/written informed consent from the patients for the inclusion of their medical and treatment history within this research article.

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*** In this systematic review the authors synthesize the evidence for the efficacy of movement representation techniques (ie, motor imagery, mirror therapy, or action observation) for treatment of limb pain.**

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*** In this narrative review the author summarizes the evidence in favor of the so-called 'visual analgesia' and provides some useful insights which could be relevant to future clinical studies.**

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## Figure Captions

**Figure 1.** A vision of the different experimental conditions from the participant's point of view (first person perspective). In four different conditions the avatar could either move its forearm (left image) or its hand (right image) and the virtual ball could either bounce on the avatar's arm synchronously or asynchronously with the vibratory stimulation administered to the participant's arm.

**Figure 2.** 'Pirate plots' of the normalized pain thresholds, per each VR condition. Single points depicts raw data, the bar lines the means, the so-called 'beans' (or smoothed density curves) show the data full distribution, and the 'bands' (boxes) the confidence intervals. The statistically significant comparison between the synchronous and the asynchronous conditions is marked wit an asterisk ($p<0.05$). Values were normalized according to the formula: x = VR condition – Baseline.

**Figure 3.** Box-and-whisker plots of the subjective ratings per each question ("Q") and VR condition. Boxes represent upper and lower quartiles, bold lines are medians, vertical lines are upper and lower extremes, while individual points depict outliers.

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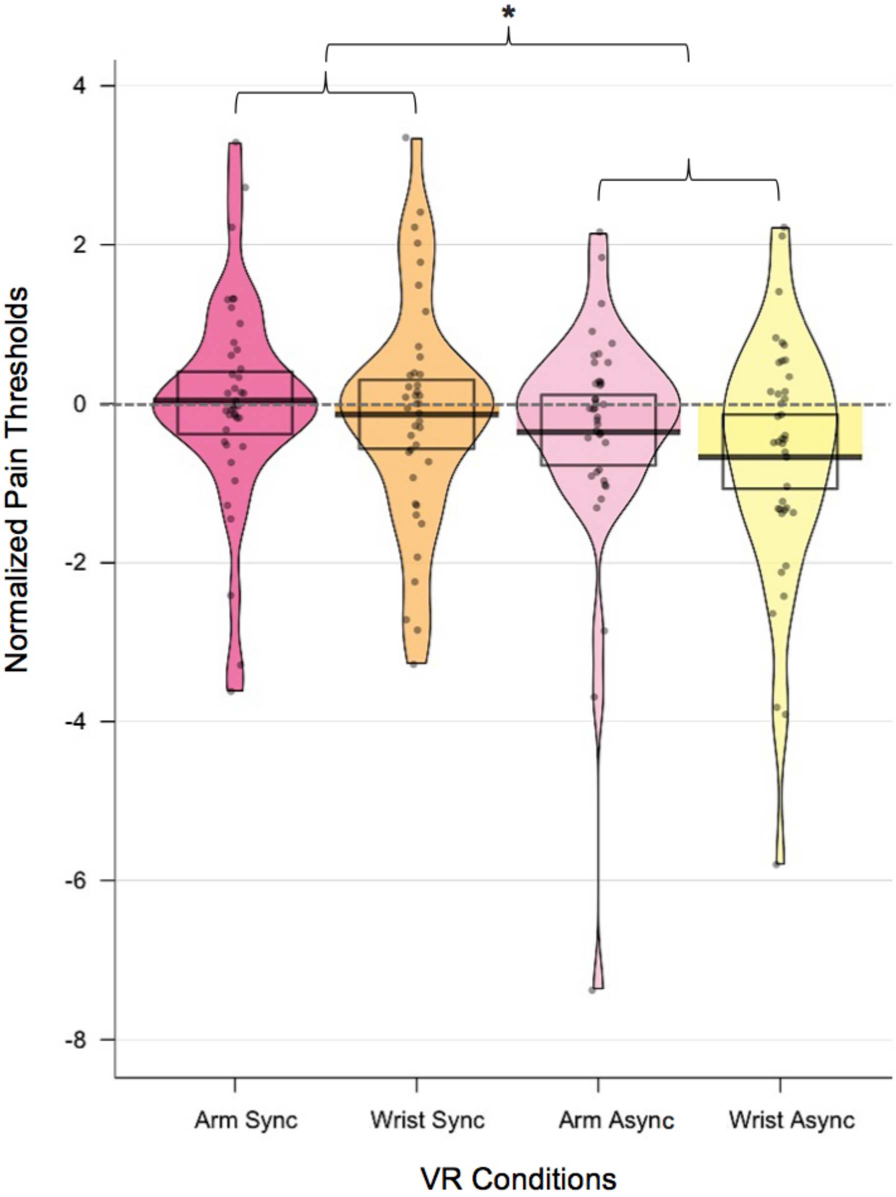
316x227mm (96 x 96 DPI)



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254x335mm (72 x 72 DPI)

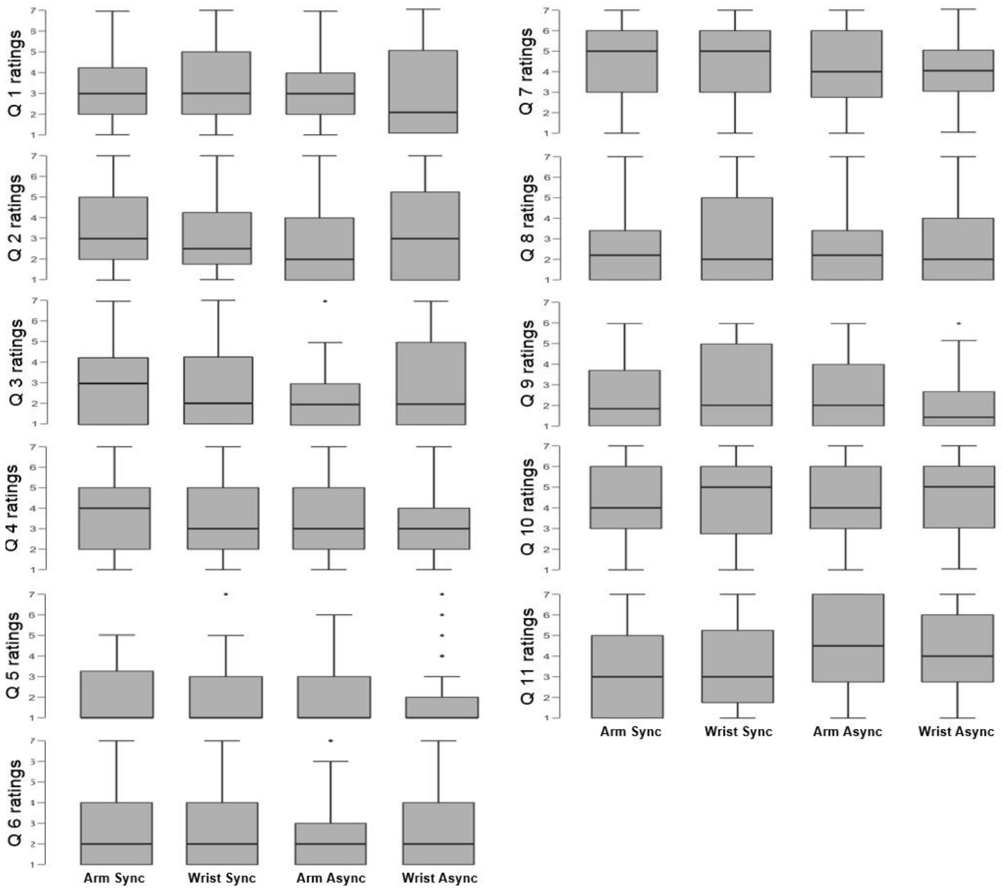

Figure 3. Box-and-whisker plots of the subjective ratings per each question ("Q") and VR condition. Boxes represent upper and lower quartiles, bold lines are medians, vertical lines are upper and lower extremes, while individual points depict outliers.

269x237mm (96 x 96 DPI)

**Table 1.** Mean scores (and SD) relative to the subjective feelings per each VR condition and question.

| | Arm Sync | Arm Async | Wrist Sync | Wrist Async |
|---|---|---|---|---|
| **Q1** | 3.75 (1.86) | 3.02 (1.75) | 3.25 (1.81) | 2.97 (1.99) |
| **Q2** | 3.2 (1.76) | 2.78 (1.91) | 3 (1.78) | 3.4 (2.2) |
| **Q3** | 2.98 (1.95) | 2.33 (1.53) | 2.65 (1.83) | 2.80 (1.96) |
| **Q4** | 3.6 (1.77) | 3.35 (1.87) | 3.38 (1.76) | 2.98 (1.66) |
| **Q5** | 2.35 (1.9) | 2.18 (1.68) | 2.05 (1.55) | 1.83 (1.52) |
| **Q6** | 2.48 (1.77) | 2.38 (1.78) | 2.7 (2.03) | 2.79 (1.99) |
| **Q7** | 4.4 (2) | 4.05 (2.02) | 4.45 (1.99) | 4.13 (1.91) |
| **Q8** | 2.38 (1.53) | 2.35 (1.39) | 2.75 (1.86) | 2.58 (1.87) |
| **Q9** | 2.6 (1.92) | 2.45 (1.68) | 2.7 (1.94) | 2.35 (1.81) |
| **Q10** | 4.18 (1.95) | 4.4 (1.91) | 4.53 (2.09) | 4.58 (1.89) |
| **Q11** | 3.33 (2.1) | 4.25 (2.25) | 3.4 (2) | 4 (2.01) |