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Seeing an embodied virtual hand is analgesic contingent on co-location

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Short running title: Visually-induced analgesia by virtual embodiment

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Highlights

• Seeing your embodied virtual body in virtual reality increases pain threshold.

• To increase pain threshold your virtual and real body should be co-located.

• For the arm, this analgesic effect diminishes when there are 30 cm between virtual and real arm.

Abstract

Seeing one's own body has been reported to have analgesic properties. Analgesia has also been described when seeing an embodied virtual body co-located with the real one. However, there is a controversy regarding whether this effect holds true when seeing an illusory-owned body part, such as during the rubber-hand illusion. A critical difference between these paradigms is the distance between real and surrogate body part. Co-location of real arm and surrogate is possible in an immersive virtual environment, but not during illusory ownership of a rubber arm. The present study aimed at testing whether the distance between real and virtual arm can explain such differences in terms of pain modulation. Employing a paradigm of embodiment of a virtual body allowed us to evaluate heat pain thresholds (HPT) at co-location and at 30-cm distance between real and virtual arm. We observed significantly higher HPT at co-location than at 30-cm distance. The analgesic effects of seeing a virtual co-located arm are eliminated when increasing the distance between real and virtual arm which explains why seeing an illusorily owned rubber arm does not consistently result in analgesia. These findings are relevant for the use of virtual reality in pain management.

Perspective

Looking at a virtual body has analgesic properties similar to looking at one's real body. We identify the importance of co-location between real and surrogate body for this to occur and thereby respond to a scientific controversy. This information is useful for immersive virtual reality in pain management.

Key words

Analgesia, body ownership, pain, rubber hand illusion, virtual environments.

Introduction

Looking at one's own body has been reported to have analgesic effects. When looking at one's own hand, painful stimuli applied to that hand are rated as being less painful[28,29,31] and heat pain thresholds (HTP) increase[32]. Coupled with such behavioral insights, these studies also revealed reduced activity in primary and secondary somatosensory cortices (SI and SII) during the processing of painful stimuli while looking at one's own body: for example, a reduced Blood-Oxygen-Level Dependent (BOLD) signal was reported in SI and the operculoinsular cortex in functional Magnetic Resonance Imaging (fMRI)[29], and reduced power of event-related beta oscillations[31] as well as reduced laser-evoked potentials[28] were reported in SI and SII.

Nonetheless, the representation of one's own body is not stable but can be experimentally manipulated. It is possible to induce an illusion of ownership over a surrogate body part by means of congruent multisensory stimulation. For example, to evoke the rubber hand illusion[3] a rubber hand and one's real hand are stroked simultaneously with (e.g.) a paint brush, while the real hand is hidden from view. Similarly, through multisensory stimulation[55] or sensorimotor correlations[52] it is possible to induce the illusion of ownership of the arm of a virtual body, also referred to as virtual "embodiment".

These bodily illusions have been recently applied to the study of pain perception leading to results that are disputed. Mohan and coworkers[40] showed no changes in pain perception during the rubber hand illusion , so that the analgesic effects of looking at one's own body would not hold true when the body part is fake, even though it is attributed to oneself. In contrast, other studies showed that during the rubber hand illusion the vision of the "owned" rubber hand leads to an increase in HTP[19] and higher resistance to painfully cold stimuli[16,54]. This held true for a virtual arm, since Martini and coworkers[36] found increased HTP when participants looked at an embodied virtual arm compared to two different control conditions (looking at a non-corporeal object in a virtual environment or at a fixation point in the real world).

To understand these different findings we looked into the methodological differences between these studies. Since some studies were using heat and other cold stimuli we focused on three studies with different findings that used all heat stimuli[19,36,40]. However, there are two studies that reported modulation of HTP by body ownership[19,36], whereas in the study by Mohan et al.[40] the position of the rubber hand during synchronous and asynchronous stimulation conditions was kept the same. Hegedüs et al.[19] rotated the rubber hand during the asynchronous stimulation condition in order to reduce the strength of this control condition. A major difference between the studies involving a rubber arm versus a virtual arm illusion is the relative location of the real with respect to the illusory-owned arm. While a virtual arm can be co-located or not with the real arm, a rubber arm can never be co-located with the real arm for obvious reasons. The distance between real and fake limb has been identified as critical factor for body ownership, in the vertical[27] and in the horizontal plane[22]. On the other hand, body ownership over a fake body part seems to affect pain perception[16,19,36,54].

In the present experiment we aimed at testing whether the distance between real and virtual hand can play a major role on pain perception. In four different conditions participants reported their HPT and rated their feeling of ownership over the virtual body. Conditions differed in visuotactile stimulation (VTS) – synchronous or asynchronous – and in distance between real and virtual arm, which could be either 0 cm (co-located) or 30 cm apart. We hypothesized that during co-location there is an analgesic effect and thus higher HPT than when there is distance between the real and the virtual arm.

Methods

Participants

Although the current experiment took into account a within-subjects experimental design, in order to take account of variability among participants, we decided to control for factors that contribute to variation in pain sensitivity such as sex[46] and menstrual cycle[49]. Therefore, only male participants were considered in this study. Initially, 24 right-handed healthy males with normal or corrected-to-normal vision, no history of chronic pain, no neurological or psychological disorders, and no medication for the last 24 hours participated in this experiment. All participants were naïve to the research question and gave written informed consent before starting the experiment. Five participants were removed from further analysis due to either technical problems (two participants), extremely high HPT (one participant who reached the maximum temperature of 51° without indicating a HPT), extremely low HPT (one participant with HPT below 38.9 °C[62]), or because they were identified as outlier (one participant, see also results section), which lead to a final sample size of 19 participants (*Mean* age 24.1, *SD*: ± 5.1; laterality quotient of the Edinburgh Handedness Questionnaire[45]: *Mean*: 65.8, *SD*: ± 25.3, *Range*: 12.5 – 100). Participants received five Euros for their participation. The experiment was approved by the local ethics committee (Comité Ético de Investigación Clínica de la Corporación Sanitaria Hospital Clínic de Barcelona).

Virtual reality system

We used a head-mounted display (Rift Development Kit 2, Oculus, Menlo Park, CA, USA) with a resolution of 960 × 1080 pixels per eye and a nominal horizontal field of view of 100°, displayed at 75 Hz to show the virtual environment, which was programmed in Unity 4.5.3 (Unity Technologies, San Francisco). The virtual male body was taken from the Rocketbox library (Rocketbox Studios GmbH, Hannover). A virtual replica of the thermode used for heat stimulation was attached to the dorsum of the virtual right hand. The virtual environment was the same during all conditions and is shown in Figure 1A and B.

[insert Figure 1 about here]

Thermal stimulation

Heat stimuli were applied with a 25 × 50 mm thermode (Somedic Thermotest, Stockholm, Sweden) that was tied to the dorsum of the right hand. HPT were measured by the method of limits[62]: temperature was increased from a constant baseline temperature of 32 °C at 2 °C/s. When pressing the button the temperature of the thermode rapidly decreased to baseline (6 °C/s). Maximal temperature was set to 51 °C for safety reasons. An NI-6008 card (National Instruments Corporation, Austin, TX, USA) was used for data acquisition via MatLab Simulink (The MathWorks Inc., Natick, MA, USA), which was run on a separate computer.

Tactile stimulation

For tactile stimulation we used two vibrators controlled by Unity through an Arduino MEGA microcontroller board. Vibrations had a duration of 1.0 seconds.

Experimental procedure

Participants were sitting comfortably in a chair with both arms resting on a table in front of them. The thermode was attached to the dorsum of their right hand with Velcro strap. Two vibrators were attached to the dorsal distal phalanges of their right index and middle fingers for the delivery of tactile stimuli. Noise isolation was ensured by administration of pink noise.

Familiarization phase. Participants were first familiarized with the virtual body illusion: they donned the head-mounted display through which they saw a virtual male body located at the same place of their own body. When they looked down they saw this virtual body sitting on a chair with its arms resting on a table in front. Both virtual arms were at the same position as the real arms – the left elbow was positioned under the left shoulder and the right elbow/forearm was lying at the body midline. Like the real body, the virtual body was holding a button in its left hand and a virtual thermode attached to the dorsum of the right hand. Participants were instructed to look around in the virtual room, to describe what they saw and to look down at the virtual body. After this initial exploration of the virtual scenario, participants were asked to concentrate on their right virtual hand. They saw a ball tapping in random order the virtual right index and middle fingers and felt synchronous tactile feedback (vibration) on their real right index and middle fingers (synchronous visuotactile stimulation (VTS)). They were also instructed that they should report out loud when they saw a letter appearing on the virtual thermode. This was to ensure participants kept their attention towards the right hand. The letter appeared at the end of the 30-second-stimulation period for 1 second (jittered in a time window of 5 seconds). The level of attention was defined as sufficient when participants correctly reported the displayed letter. In case the letter was not reported correctly the 30-second visual tactile stimulation period was repeated (including the display of another letter at the end). In the 360 trials that were presented to the 19 subjects included in the analysis, only in four cases (1.1% of the trials) we repeated the stimulation, which we consider can rule out the possibility of this having affected our results. This happened maximum once during one condition, meaning that there were still four other trials—which happened to be equally distributed over the four experimental conditions—taken into account in our statistics. Then the screen went black and they were asked to answer a questionnaire.

Next, participants were familiarized with the HPT measurement and the baseline for their HPT was taken. During this part they did not wear a head-mounted display. Participants were instructed to look during the whole procedure at their right hand. When the thermode heated up they had to press a button in their left hand as soon as the heat stimulation started to become painful. Seven heat stimuli were delivered during this phase, the first two were for the participant to become familiar with the task and the mean of the following five stimuli was later used as baseline. We specifically did not randomize the order of the two familiarization tasks because it has been shown that strength of the rubber hand illusion increases linearly with time[14] and we wanted to account for possible carry-over effects from the familiarization phase of the illusion to the first experimental condition.

Experimental phase. The experiment had a two-by-two factorial within-participants design, with one factor "distance" (co-location vs. 30 cm distance between the real and the virtual arm) and a second factor "VTS" (synchronous vs. asynchronous). Therefore we had four conditions: synchronous VTS at 0 cm distance, synchronous VTS at 30 cm distance, asynchronous VTS at 0 cm distance, and asynchronous VTS at 30 cm distance. The order of conditions was balanced among participants. We decided to use balancing instead of randomization because we wanted to have the same number of participants for each possible order of conditions. The fact that we excluded participants from the analysis did not undermine the balancing since the four participants we removed due to technical problems, who had extremely high, or extremely low heat pain thresholds were already identified during the data acquisition phase and we replaced them with four other participants maintaining the balance. Therefore we had only one participant who we removed from analysis due to being an outlier. The position of the virtual body was the same for all conditions and the same as described for the familiarization period. Depending on the experimental condition, the real right arm was at the body midline, the same position as the virtual arm, (co-location condition) or 30 cm to the right of the body midline (30cm distance condition; see Figure 1). To make sure that participants were able to keep their trunk straight in all conditions, we elevated the arm in the distance conditions by 4 cm. This ensured that participants with shorter arms were able to comfortably keep their forearm at the indicated position. At the beginning of each condition participants donned the head-mounted display and were asked to look around in the virtual room and to look down the virtual body. Participants were then asked to concentrate during the whole condition on their right hand only. Each condition consisted in five trials (one heat stimulus per trial): Each trial started with 30 seconds of VTS during which participants had to report the name of the letter they saw, then there was a pause of 2 to 4 seconds, the thermode heated up and participants press the button in their left hand when the increasing heat reached their individual HPT. The left virtual arm was occluded from sight during the heat stimulation to make sure the right arm was the only focus of participants' attention. At the end of each condition the screen turned black and participants were asked to answer the same questionnaire as mentioned above (a description of the questionnaire can be found in the section "response variables" and in Table 1), which took about 2 – 3 minutes.

Response variables

Heat pain threshold (HPT). It was carefully explained to participants that the HPT is the temperature where the sensation of a raising heat stimulus changes from a hot to painful percept. They were further instructed to look at their real (during the baseline) or the virtual (during the experimental conditions) right hand and press a button located in their left hand as soon as they perceived the stimulus to be painful. The initial two stimulations allowed the experimenters and the participants to confirm whether the task had been well understood. The baseline and all four experimental conditions consisted each of five heat stimulations.

Questionnaire. A questionnaire was administered after the familiarization phase and after each condition of the experimental phase. The items (translated from Spanish) are shown in Table 1. The first 6 items were presented in random order and participants were asked to report their degree of agreement with each statement on a seven point Likert scale (1= absolutely disagree, 7= absolutely agree). Question 7 was asked at the end to get participant's overall rating of the illusion. It is important to note that while question 3 is meant to assess the presence of the body ownership illusion, question 7 assesses the strength of it. Questionnaire items were adapted from[3] and the additional question from[40]. Participants were wearing the head-mounted display with the screen black while the experimenter read the items of the questionnaire out loud and they gave oral response, during which time pink noise was turned off.

[insert Table 1 about here]

Data handling

All statistical tests were performed in Stata 14 (StataCorp LP, College Station, TX, USA). Mean values of the five HPT measured during each experimental condition and five HPT during baseline, were used for subsequent analysis. The variable of interest was $\Delta HPT = HPT_{experimental} - HPT_{baseline}$. Each participant carried out 4 different experimental conditions. This is therefore a mixed-effects design, with fixed-effects "distance" and "VTS", and random effects over the "individual subjects", and is appropriately analyzed by a Multilevel Mixed-Effects Linear Regression (the 'mixed' function in Stata). Questionnaire data were analyzed with a Multilevel Mixed-Effects Ordered Logistic Regression (the 'meologit' function in Stata) with fixed-effects "distance" and "VTS", and random effects "individual subject". Due to the ordinal nature of questionnaire data a mixed-effects Gaussian linear model design as used for the HPT data would not be appropriate, plus non-parametric statistical tests do not allow testing for multiple factors and their interaction effects. We measured the overall strength of ownership illusion in two ways – with the question OwnershipStrength and with a principle component analysis. The latter constructed a single variable (V) as the highest variance linear combination of the 4 original body ownership questions. A mixed effects regression using the Stata 'mixed' function, with fixed effects over the two factors (distance and VTS) and covariate OwnershipStrength or V, and random effects over the individuals, showed that the response variable ΔHPT is linearly associated with OwnershipStrength (or V).

Results

Heat pain threshold analysis

Figure 2 shows the means and standard errors of ΔHPT by distance and VTS. There is an apparent large effect of distance, with the heat pain threshold lower for the 30cm distance. The mixed effects ANOVA shows that this difference is significant, with main effect for distance ($z = -2.24$, $P = 0.025$; see supplementary material I for the analysis of normal distribution of residuals). The analgesic effect of seeing the virtual arm was therefore lower when the virtual hand was located at 30 cm from the real hand than when co-located. Table 2 shows mean and standard error of mean (SE) of the raw HPT. A likelihood ratio test comparing the full model including the interaction term (distance + VTS + distance.VTS) with the model that only includes distance shows no difference at all between these (e.g., $P > 0.9$, $AIC = 232$ for the full model and 236 for the reduced model). Hence there is clearly no effect of VTS. One extreme outlier was removed for all analysis above based on visual inspection of HPT during baseline plotted against HPT during the experimental conditions.

[insert Figure 2 about here]

Analysis of questionnaire responses

Ownership related questions. From Figure 3 and Table 2 regarding the ownership related questions, OwnershipPresence (Q3) and OwnershipStrength (Q7) showed similar response patterns. They were both negatively influenced by distance, meaning that during co-location ratings were significantly higher than during 30-cm distance (OwnershipPresence: $z = -3.98$, $P < 0.001$; OwnershipStrength: $z = -3.96$, $P < 0.001$). Further both were positively influenced by synchrony of VTS, meaning that during synchronous VTS ratings were higher than during asynchronous VTS (OwnershipPresence: $z = 3.03$, $P = 0.002$; OwnershipStrength: $z = 4.10$, $P < 0.001$). Moreover, both showed no significant interaction between distance and synchrony of VTS (OwnershipPresence: $z = -0.06$, n.s); OwnershipStrength: $z = -0.88$, n.s).

Illusion-induction related questions. The two questions related to illusion induction, TappingLocation (Q1) and BallCausesTouch (Q2), showed a similar response pattern. Both were positively influenced by synchrony of VTS – synchronous VTS led to higher ratings than asynchronous VTS (TappingLocation: $z = 5.02$, $P < 0.001$; BallCausesTouch: $z = 5.94$, $P < 0.001$). Distance had no influence on neither of them (TappingLocation: $z = -0.73$, n.s.; BallCausesTouch: $z = -0.78$, n.s.), but in both was a significant interaction between distance and VTS (TappingLocation: $z = -2.09$, $P = 0.037$; BallCausesTouch: $z = -2.04$, $P = 0.041$). During co-location there was a bigger difference between synchronous and asynchronous VTS than during 30-cm distance conditions.

Illusion-perception related questions. MultipleHands (Q4) was positively influenced by distance – during 30-cm distance ratings were significantly higher than during co-location ($z = 2.22$, $P < 0.026$); further MultipleHands was negatively influenced by synchrony of VT-Stimulation, meaning during asynchronous VTS ratings were higher than during synchronous VTS ($z = -2.12$, $P = 0.034$); there was no significant interaction between synchrony of VTS and distance on MultipleHands ($z = 1.19$, n.s).

VibrationBetweenRealAndVirtualHand (Q5) was neither influenced by distance (z = –0.10, n.s.) nor by synchrony of VTS (z = –0.14, n.s.); there was no significant interaction between synchrony of VTS and distance (z = 0.10, n.s).

RealHandTurnsVirtual (Q6) was negatively influenced by distance, meaning that during co-location ratings were significantly higher than during 30-cm distance (z = –3.64, P < 0.001); further RealHandTurnsVirtual was positively influenced by synchrony of VTS, meaning that during synchronous VTS ratings were higher than during asynchronous VTS (z = 3.66, P < 0.001); there was no significant interaction between synchrony of VTS and distance (z = 1.33, n.s).

[insert Figure 3 about here]

[insert Table 2 about here]

The score OwnershipStrength is an overall indication of ownership. A mixed effects regression of ΔHPT on OwnershipStrength reveals a significant positive relationship (z = 2.52, P = 0.012). The coefficient of OwnershipStrength in the linear model has 95% confidence interval 0.03 to .22. In contrast if we take the scores of the same question for the baseline then there is no relationship at all (z = 0.10, P > 0.90).

If we take all of the questions indicating a relationship (TappingLocation, BallCausesTouch, OwnershipPresence, OwnershipStrength) then a principal components factor analysis yields one variable accounting for 72% of the variance giving almost equal weight to all four scores. We refer to this variable as OwnershipPCA. The mixed effects regression of HPT on OwnershipPCA similarly shows a positive association (z = 2.2, P = 0.028). In the baseline condition z = 0.68, P = 0.5. Hence greater levels of ownership are associated with higher ΔHPT. This is independent of

VTS or distance. It could be that since distance as we have seen is also associated with ownership that this relationship reflects the impact of distance rather than ownership. Indeed this is likely to be the case since when these regressions are run for each level of distance separately then the relationship between ownership and ΔHPT is not found. However, this does suggest that ownership modulates the effect of distance on ΔHPT, that it is not 'distance' in itself responsible for the effect but the effect of distance via ownership.

Discussion

In this study we investigated [28,29,31,32] whether the distance between real and virtual arm had an impact on pain perception, thus explaining disputed findings in the literature[15,16,19,36,37,40,54]. Our analysis confirmed that the threshold to perceive a heat pain stimulus as painful is modulated by seeing virtual embodied arm and that the pain threshold is higher when the virtual arm is co-located with the real arm than when the virtual arm is 30 cm away from the real arm. The latter 30-cm distant condition is a similar arrangement to the one in a rubber arm illusion experiment. We further find that participants who report stronger ownership illusion over the virtual arm tend to have higher pain thresholds. Below we discuss possible interpretations of the obtained results.

Introducing a distance eliminates the analgesic effect of co-location

Our data show similar HPT when looking at the co-located virtual body compared to looking at the real hand during the baseline measurement (see Figure 2), which was conducted outside virtual reality. This is consistent with the whole body of literature showing an analgesic effect of looking at one's own hand[28,29,31,32]. Specifically, in an earlier experiment we showed that looking at a virtual hand that is perceived as one's own hand is analgesic compared to looking at a virtual non-corporeal object or compared to not seeing one's limbs[36]. Building on this finding the responses during co-location conditions could be interpreted as analgesic. However when introducing a distance between real and virtual hand, our data show significant differences between the baseline and the distance condition and between the co-location and the distance condition. In other words, our results show that looking at a surrogate hand that is attributed to the self when surrogate and real hand are co-located has similar analgesic effects as looking at one's real hand. This effect diminishes when introducing a distance between real and surrogate hand.

Baseline levels were always taken *before* the conditions in virtual reality, thus the effect of habituation would not affect the baseline values. For the four conditions the potential effect of habituation should have been removed by balancing their order. On the other hand, it is interesting to note that, without the potential effect of habituation, the vision of the real hand brought about the highest average HPT, equalized only by the synchronous co-located VR condition.

A significant body of literature shows an analgesic effect of looking at one's own body[28,29,31] (see for a review[33]). However, in the present study we did not manipulate the vision of the embodied virtual body versus for example a non-corporeal object which would have allowed us to replicate the analgesic effect of looking at one's embodied virtual arm[36]. Therefore we cannot show that this effect is in our data, however we think that we can build on this known effect.

Distance alters multisensory remapping into common reference frame

The analgesic effect of seeing one's own body has been explained by two mechanisms: (1) an increase in intracortical inhibition and (2) reorganization of somatotopic maps in terms of sharpening receptive fields in primary somatosensory areas. Several pieces of evidence support this view: for instance, it has been shown that the vision of one's own hand increases intracortical inhibition compared to seeing an object[6]. Furthermore, several forms of chronic pain are associated with reduced inhibition in sensorimotor cortex[10,26,53] and treatments that foster this inhibition, like GABA-agonistic drugs or TMS, are used as effective treatments for chronic pain[5,25]. These findings can be related to the effect of GABAergic inhibition sharpening the size of tactile perceptive fields in primary somatosensory areas[9]. Studies of chronic pain typically report reduced tactile sensitivity on the painful body part[41,43,48] and disorganization of somatotopic maps[12,24,30,48,57,59]. Studies on chronic pain show further that the relationship between chronic pain and body representation seems to be more complex. Chronic pain is connected to changes in the central nervous system and reorganization processes in the brain are assumed to contribute to its chronification[12,44]. Pain has a multifactorial nature[4] and the conscious perception of pain is even more disconnected from the actual tissure damage in chronic pain than in acute pain[44,61]. Further cognitive, affective, and behavioral factors play an important role in the development and maintenance of chronic pain[60]. Body representation has been shown to be distorted in chronic pain[1,10,11,17,42,43,57,58] but the extend of this distortion seems to vary in different chronic pain syndromes[7]. When surrogate limbs are used to modify such distorted body representations, the ability of the patient to accept the surrogate limb as his/her own limb seems to play an important role. A recent study by Foell and colleagues in chronic phantom limb pain patients showed that perceived co-location of both phantom and surrogate arm plays a crucial role to have analgesic effects in mirror therapy[13]. In this study two groups of chronic phantom limb pain patients were compared – one group had the telescopic phenomenon where the phantom arm is perceived as if it was pulled into the stump while the other group did not have this phenomenon. Importantly, they show that only the group without telescopic phantom gained from the mirror therapy (i.e. showed the analgesic effect) indicating that co-location of phantom arm and surrogate arm is an important factor. In line with these findings our results show that co-location of real and surrogate arm is also important in acute pain.

Reduced embodiment mediated through distance reduces predictability of heat stimulus

The perception of our own body is a flexible multisensory construction[23]. This construction is based on principles of multisensory integration[2], which in the case of conflicting sensory information result in a compromise. Such conflicting information is for example present during asynchronous visuotactile stimulation of real and surrogate body part, or for example when there is a distance between the two. Both, asynchronous stimulation[3,23] and distance[22,27], have been shown to reduce the feeling of body ownership over the surrogate body, a finding that we replicate in the present study (see questionnaire results, Figure 3A and B). Interestingly, although asynchronous stimulation is associated with reduced body ownership, the analgesic effect of looking at one's embodied surrogate arm persists in the asynchronous condition under co-location. This is probably due to the fact that, in virtual reality, the co-location of the virtual arm together with being immersed in the first-person perspective are strong enough input to induce ownership. This induces a large tolerance towards the asynchronous stimuli[56], which can still induce ownership and analgesia albeit to a (non-significant) lesser extent than synchronous stimuli. Indeed, non-significant differences in analgesia between synchronous and asynchronous conditions was already reported in previous studies[35,36].

Non co-location (i.e. distance) as opposed to asynchronous visuotactile stimulation could be potentially perceived as stronger multisensory inconsistency. Such mismatching multisensory information might lead to blurry receptive fields and body boundaries. The predictability of potential harm would be decreased when body boundaries are blurry. In order to cope for this uncertainty, the brain might lower the general HPT to strengthen the body's protective mechanisms. A recent study showed for example that perceiving strong ownership over a transparent body (i.e. a body with blurry body boundaries) results in lower HPT[34]. This would negatively add up to the reduced embodiment effect on pain in the distance conditions.

Ownership and viewpoint of the virtual body affect pain processing

Pain perception is highly subjective and it can be modulated by different bodily representations. This relation between body representations and the processing of painful stimuli was recently investigated by Romano and colleagues[50]. In their study they used changes in skin conductance as indirect physiological measure of pain and found lower physiological responses when the virtual body was co-located with the real body compared to when the virtual body was spatially misaligned. Our results are in line with the physiological results of this study, and we further provide evidence that can be directly linked to pain perception (see Figure 2). Furthermore, we find that people who perceive stronger ownership over the virtual arm have also higher pain thresholds, in other words, the more people perceive the illusion that the virtual hand is theirs the more analgesic is the effect of looking at it. This goes in line with a previous finding that looking at a virtual body reduces the skin conductance response to painful stimuli compared to looking at a virtual object. Similarly to our findings this study found a negative correlation between reported body ownership and skin conductance response.

Synchronity of visuotactile stimulation does not affect heat pain thresholds

Body ownership over a surrogate body can be induced through visuotactile[3,55], visuomotor[8,21,52], or like in the case of co-location through visuoproprioceptive contingencies[38,39]. While the rubber-hand illusion is limited to visuotactile or visuomotor contingencies, all three induction methods can be executed in a virtual environment. Our findings confirm that both visuotactile as well as visuoproprioceptive contingencies induce feelings of body ownership, reflected in high ratings of body ownership related statements in the questionnaire (see Figures 3A and B). Synchronous visuotactile stimulation versus asynchronous did not result in different HPT; however there was an effect of virtual body ownership on HPT. Therefore, the relevant aspect is the ownership developed over the virtual body which does not necessarily require exogenous stimulation but that can be induced by first person perspective together with co-location[38]. A similar finding has been reported by Hänsel and colleagues[18] who studied the perception of pressure pain during an out-of-body experience.

Virtual reality in pain treatment

Virtual reality has been effectively used for pain management (for example[20,51]) for its power to draw attention away from pain, but its usefulness goes beyond mere distraction processes. For example in paradigms making use of virtual body ownership it has been shown that when the virtual body is attributed to oneself, looking at that body has analgesic effects. Further, the color of a virtual body that is attributed to oneself can influence HPT, so that pain stimuli on a red colored virtual arm are perceived as more painful than on a normal or bluish colored arm[35]. It is relatively easy to change the properties of a virtual body, so virtual reality has a big potential to take advantage of these body related top-down modulations on pain perception. The results of the present study support the use of virtual reality for pain treatment but only when real and virtual limb are co-located. The relation between body representation and chronic pain is more complex and needs further investigation. One problem is that in many states of chronic pain the body representation is disrupted[58], including Complex Regional Pain Syndrome[1,42], chronic phantom limb pain[17], and chronic back pain[11,43]. Therefore treatments like mirror therapy lose their analgesic effect in patients with strong distortions of the body representation like the telescopic phenomenon[13]. A very recent study in an immersive virtual environment demonstrated an analgesic effect in out-of-body illusions in chronic pain patients[47].

Conclusion

It is known that the vision of the own body has analgesic effects and that similar analgesic effects are induced by looking at the embodied virtual body, when co-located with the real body. However, increasing the distance between the real and the virtual body eliminates this analgesic effect. This finding not only explains some disputed reports in the literature regarding whether the rubber hand illusion has an analgesic effect or not. It also has relevant implications in the field of pain management with virtual reality tools, pointing out to the importance of co-locating the real and virtual limb in such applications.

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Figure legends

Figure 1. Experimental setup. The participant was using a head-mounted display providing an immersive virtual environment including a virtual own body that was perceived from a first person perspective. The transparent arm outlined with a white dashed line indicates the position of the virtual arm. Position of participant during (A) co-location, where virtual and real arm were co-located, and (B) when there was a distance of 30 cm between real and virtual arm. (C) The virtual body from first person perspective (participant's point of view). The red dot displays the ball that was tapping the fingers during the visuotactile stimulation (VTS) phase at the beginning of each trial. Participants were asked to look at the right virtual arm throughout all experimental trials.

Figure 2. Mean of difference in heat pain threshold (ΔHPT) in the four different experimental conditions with respect to the baseline. VTS = visuotactile stimulation; error bars indicate the confidence interval of the coefficient for the factor distance.

Figure 3. Boxplots of questionnaire ratings after each experimental condition. **A.** OwnershipPresence (It seemed as if the virtual hand was my real hand.), **B.** OwnershipStrength (On a scale from 1-10, how strong did you have the illusion that the virtual hand was your real hand?), **C.** TappingLocation (It seemed as if I were feeling the tapping in the location where my fingers where.), **D.** BallCausesTouch (It seemed as if the vibration I was feeling on my fingers was caused by the ball touching the virtual fingers.)

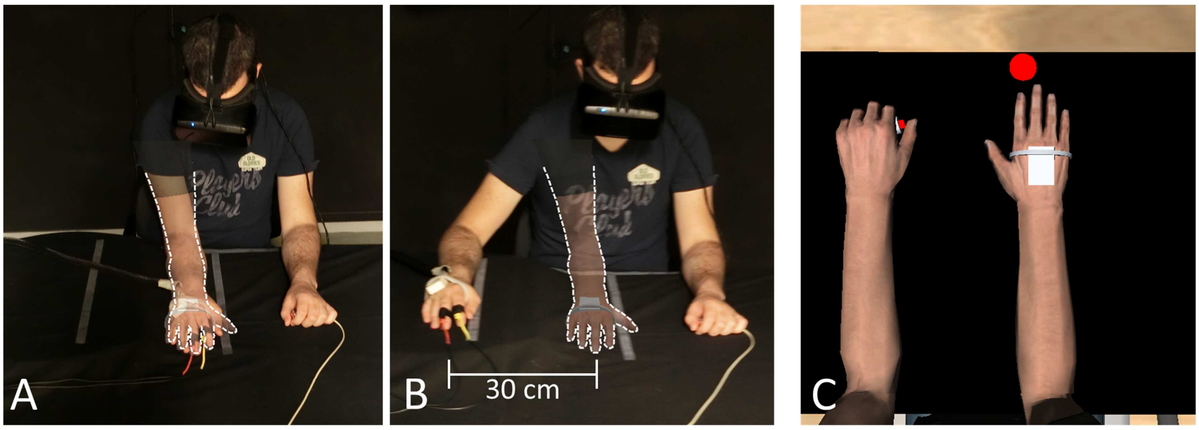
Table legends

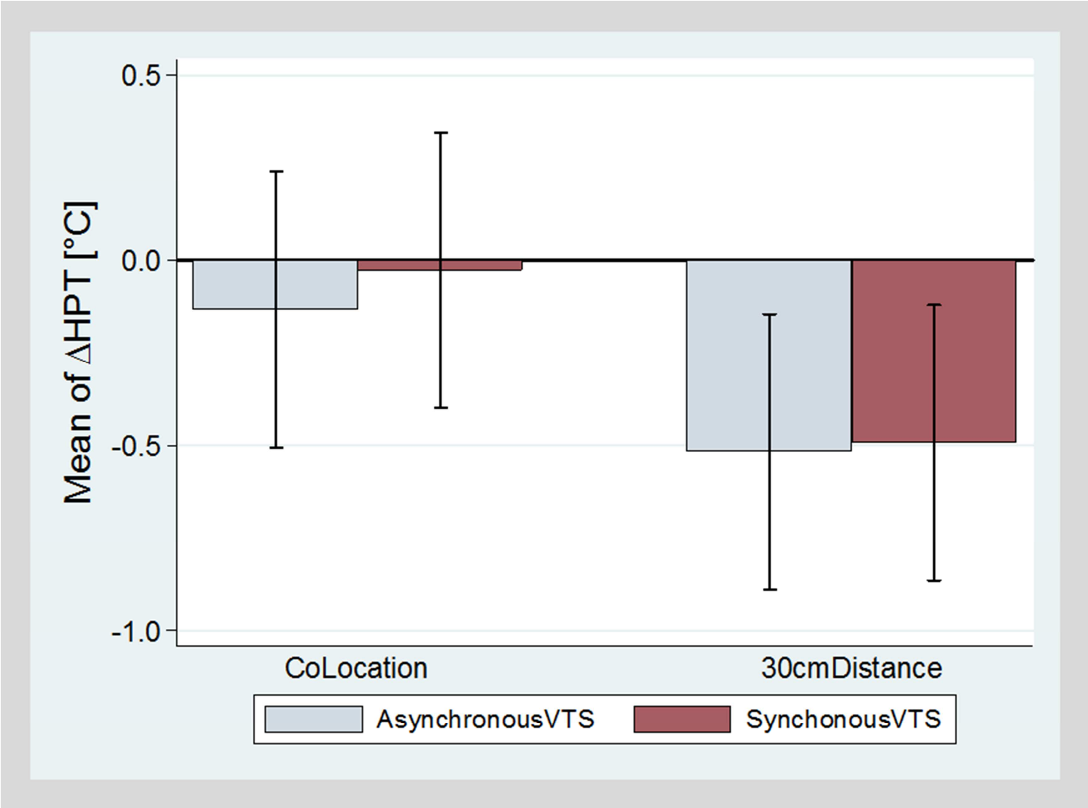
Table 1. Questionnaire given after familiarization phase and after each experimental phase. Note that each question was given a brief name in order to better refer to their content.

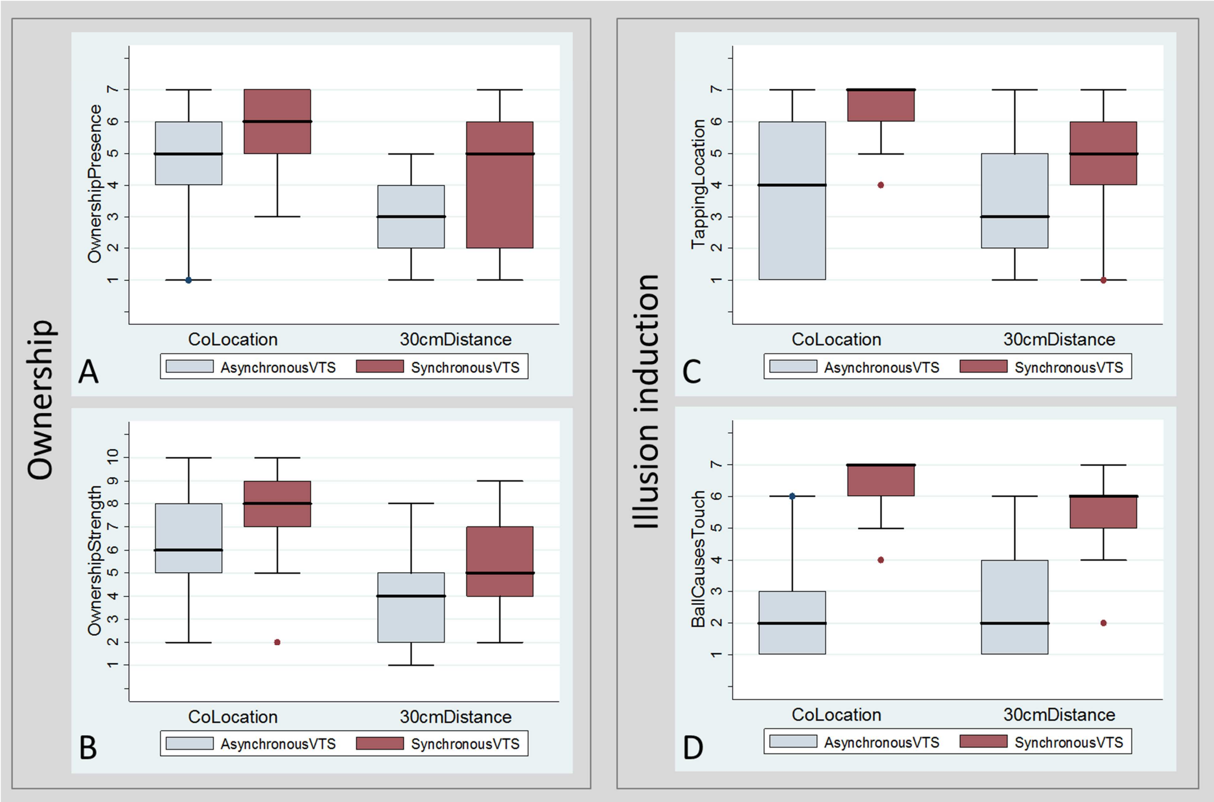
Table 2. Upper part: Mean and standard error of mean (SE) of the raw heat pain threshold (HPT) in the baseline and the four different experimental conditions (in °C). Lower part: Median values and Interquartile Ranges (IQR) of questionnaire ratings. Ratings could range in the first six questions from 1 to 7 and in the last question from 1 to 10. VTS = visuotactile stimulation.

Questionnaire item	Item tag
1. It seemed as if I were feeling the tapping in the location where my fingers where.	TappingLocation
2. It seemed as if the vibration I was feeling on my fingers was caused by the ball touching the virtual fingers.	BallCausesTouch
3. It seemed as if the virtual hand was my real hand.	OwnershipPresence
4. I felt as if I had more than one hand.	MultipleHands
5. It seemed as if the vibration I felt came from a place between my real hand and the virtual hand.	VibrationBetweenHands
6. It seemed as if my real hand were becoming virtual.	RealHandTurnsVirtual
7. On a scale from 1-10, how strong did you have the illusion that the virtual hand was your real hand?	OwnershipStrength

Response variable	Baseline		Synchronous VTS				Asynchronous VTS			
			Co-location		30cm distance		Co-location		30cm distance	
	Mean	*SE*	*Mean*	*SE*	*Mean*	*SE*	*Mean*	*SE*	*Mean*	*SE*
Heat Pain Threshold (HPT)	45.0	0.4	45.2	0.4	44.7	0.4	45.1	0.5	44.7	0.5
			Median	*IQR*	*Median*	*IQR*	*Median*	*IQR*	*Median*	*IQR*
Ownership										
OwnershipPresence (Q3)			6	5 – 7	5	2 – 6	5	4 – 6	3	2 – 4
OwnershipStrength (Q7)			8	7 – 9	5	4 – 7	6	5 – 8	4	2 – 5
Illusion induction										
TappingLocation (Q1)			7	6 – 7	5	4 – 6	4	1 – 6	3	2 – 5
BallCausesTouch (Q2)			7	6 – 7	6	5 – 6	2	1 – 3	2	1 – 4
Illusion perception										
MultipleHands (Q4)			1	1 – 2	3	2 – 4	2	1 – 3	4	2 – 5
VibrationBetweenHands (Q5)			3	2 – 5	4	2 – 5	3	2 – 5	3	2 – 6
RealHandTurningVirtual (Q6)			6	6 – 6	4	3 – 6	5	4 – 6	3	2 – 5


A
B
30 cm
C


0.5
0.0
-0.5
-1.0
Mean of ΔHPT [°C]
CoLocation
30cmDistance
AsynchronousVTS
SynchonousVTS



Ownership
Illusion induction
A
OwnershipPresence
1 2 3 4 5 6 7
CoLocation
30cmDistance
AsynchronousVTS
SynchronousVTS
B
OwnershipStrength
1 2 3 4 5 6 7 8 9 10
CoLocation
30cmDistance
AsynchronousVTS
SynchronousVTS
C
TappingLocation
1 2 3 4 5 6 7
CoLocation
30cmDistance
AsynchronousVTS
SynchronousVTS
D
BallCausesTouch
1 2 3 4 5 6 7
CoLocation
30cmDistance
AsynchronousVTS
SynchronousVTS

Seeing an embodied virtual hand is analgesic contingent on co-location

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Short running title: Visually-induced analgesia by virtual embodiment

Highlights

• Seeing your embodied virtual body in virtual reality increases pain threshold.

• To increase pain threshold your virtual and real body should be co-located.

• For the arm, this analgesic effect diminishes when there are 30 cm between virtual and real arm.

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