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Title

An investigation into enlarging and reducing the size of mirror reflections of the hand on experimentally-induced cold-pressor pain in healthy human participants

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This research has not been presented elsewhere at the time of submission

Running head
Mirror reflections and cold pressor pain

ABSTRACT [500 words]

Background and aims

Mirror visual feedback may be a useful clinical tool for reducing pain. Research suggests that reducing the size of a non-painful reflected hand can alleviate complex regional pain syndrome in the affected hand that is out of view. In contrast, research on healthy humans exposed to experimentally induced pain suggests that reducing the appearance of the size of a reflected body part can increase pain. The aim of this study was to investigate the effect of enlarging and reducing the visual appearance of the size of a hand using mirror visual feedback on pain threshold, intensity and tolerance in healthy human participants exposed to cold-pressor pain.

Methods

Participants were a convenience sample of 20 unpaid, healthy pain free volunteers aged 18 years or above. Each participant took part in one experiment where they completed cold-pressor pain tests whilst observing normal, enlarged and reduced size reflections of a hand congruent to a hand immersed in the ice cold water. A 4×2 factorial repeated measures analysis of variance (ANOVA) was performed on time to pain threshold and pain tolerance, and pain intensity with Condition (four levels: no reflection, reduced reflection, normal reflection, enlarged reflection) being the within-subject factors and Sex (two levels: female, male) between-subject factors.

Results

There were no significant effects for Condition, Sex, or Condition x Sex interaction for pain threshold, intensity or tolerance ($P>0.05$). There were no significant differences between the 3 mirror reflection conditions for agreement with the statements: “It felt like I was looking directly at my hand rather than at a mirror image”; “It felt like the hand I was looking at was my hand”; and “Did it seem like the hand you saw was a right hand or a left hand?”.

Conclusion

Enlarging or reducing the size of a hand using mirror visual feedback did not alter pain perception in healthy human participants exposed to cold-pressor pain. The different sizes of hands generated by mirror visual feedback created an illusion of looking at their own hand but this was not as strong as looking directly at the hand.

Implications

In future, investigators and clinicians using mirror visual feedback may consider including an adaptive phase to ensure the reflection has been perceptually embodied. Reasons for the lack of effects are explored to inspire further research in the field.

HIGHLIGHTS

- Mirror visual feedback produces relief of pain
- We assessed different sized hand reflections on cold-pressor pain
- Changing the size of mirror reflections of the hand did not affect pain variables
- Studies on relationships between embodiment, reflections and pain are needed

KEYWORDS

Pain; mirror visual feedback; cold pressor pain; pain threshold; pain tolerance.

INTRODUCTION

Pain is a complex sensory, emotional and cognitive phenomenon that is influenced by a variety of biopsychosocial factors including fear, anxiety, attention and expectation. Painful conditions including phantom limb pain and complex regional pain syndrome are known to distort the sense of body image [1-3]. In complex regional pain syndrome the affected limb may be perceived as large, swollen, heavy or stuck in one position and this may lead to neglect and/or learned non-use of the limb [4, 5]. Pain perception can be modulated by observing a non-painful limb whilst a painful limb is hidden behind the mirror (i.e. out of view), termed mirror visual feedback (mirror therapy). Mirror visual feedback using normal size reflections of non-painful limbs has been found to reduce clinical and experimentally-induced pain of hands and feet [6-10].

The findings of studies on patients in pain suggest that reducing the visual appearance of the size of the painful body part reduces pain. Moseley et al. [11] used binoculars to change the visual appearance of chronically painful hands and found that enlarging the view of the hand increased pain and swelling evoked by movement and reducing the view of the hand decreased pain and swelling evoked by movement. Ramachandran et al. [12] used mirror visual feedback to reduce the size of a reflected hand and found that this reduced phantom limb pain. In contrast, a study using healthy human participants by Mancini et al. [13] found that enlarging a reflected view of the hand reduced experimentally-induced contact heat pain (i.e. increased pain threshold) and reducing the size of the reflected view of the hand pain increased pain. One possible reason for the difference in findings was that there were no cues of the presence of injury or of an impending noxious threat in the study by Mancini et al. [13] because the Peltier-type contact thermode used to elicit experimental heat pain was visually inert.

Studies using experimentally induced pain afford a greater degree of control over the environment reducing the impact of confounding variables and maximizing the internal validity of the research [14]. Experimentally induced cold-pressor pain involves immersing an extremity into iced water to produce a deep aching pain. Cold-pressor pain has excellent test-retest stability to assess pain threshold and pain tolerance in student populations [15] and generates higher pain intensity ratings than contact thermode-delivered cold stimuli [16]. Most individuals expect exposure to ice to generate pain and therefore cold-pressor pain is likely to be perceived as a more authentic noxious stimulus than that delivered by a contact thermode. The aim of our study was to compare the effect of enlarging and reducing the visual appearance of a hand using mirror visual feedback on pain threshold, intensity and tolerance in healthy human participants exposed to cold-pressor pain.

METHODS

Study design

A repeated measures crossover design was used to compare pain threshold, intensity and tolerance response whilst participants observed a normal size, enlarged size and reduced size reflection of their hand. Ethical approval was received from the Research Ethics Committee of Leeds Beckett University.

Recruitment of participants

A convenience sample of 20 unpaid, healthy pain free volunteers aged 18 years or above were sought based on previous similar study design [13]. The study was advertised to staff and students at our university using a poster and announcements in lectures. The recruitment protocol included initial screening for eligibility when volunteers expressing interest in the study made initial contact with the investigators. At this time volunteers expressing interest received a participant information pack that stated "*During the experiment you will take part in four tests. Each test involves you placing your hand in a container filled with crushed ice and water. Whilst your hand is placed within the iced water you will observe a reflection of your other hand in a mirror that is attached to the side of the container with the iced water. We will be measuring your pain threshold and pain tolerance during each test. We will also be altering the visual appearance of the size of the reflected hand for each test.*" (Supplementary Appendix 1). Then they were given 48 hour to consider participation before a formal invitation to enrol in the study was made. Block randomisation was used to allocate equal numbers of women and men into the study because there is evidence of gender differences in response to cold-pressor pain [17, 18]. There was no restriction on ethnicity although this was recorded.

Each participant attended our pain research laboratory for one experimental visit lasting no longer than two hours. Each experiment was conducted by the principal investigator (MG: 20 year old male, physiotherapist, Indian national) who was fluent in English language and who read instructions verbatim from a crib sheet that ensured that there were no leading statements that could bias outcome. On arrival participants were greeted and briefed about the study, including hazards and control measures. They were then screened for eligibility against a list of self-exclusion criteria. Volunteers were requested not to take part in the study if they did not consider themselves ‘healthy’, had a long-term illness, were currently seeking medical care, were experiencing pain or sensory disturbances, taking any medication, were known to be pregnant, had a dermatological condition or participated in sports that involved regular exposure of hands to cold (e.g. <5^{o}C) conditions. Eligible volunteers were then enrolled by signing a written consent form. Participants were reminded that they could withdraw consent at any time and without reason and that they could stop the experimental pain stimulus at any time during the experiment by removing their hand from the ice-water slurry.

Experimental procedure

Each participant took part in one experiment that measured pain threshold, intensity and tolerance response in a hand immersed in ice-water slurry under four conditions (Figure 1):

- Whilst viewing the painful (immersed) hand (i.e. no reflection control)
- Whilst viewing a normal size reflection of a hand aligned with the painful (immersed) hand (i.e. normal mirror image)
- Whilst viewing an enlarged size reflection of a hand aligned with the painful (immersed) hand (i.e. enlarged size mirror image)
- Whilst viewing a reduced size reflection of a hand aligned with the painful (immersed) hand (i.e. reduced size mirror image)

[Insert Figure 1 here – Experimental set-up. (a) no reflection control, (b) normal size mirror image, (c) enlarged size mirror image, (d) reduced size mirror image]

Block randomization was used to sequence the order of presentation of the four experimental conditions between participants (operationalized using computerised random numbers and sealed enveloped) and a washout period between conditions of 5 minutes was used to minimise contamination of findings from potential carryover effects and a learning effect from repetitive exposure to cold pressor pain.

Cold pressor pain

During each cold pressor pain test the participant sat on a seat with both arms resting on a desk and flexed at the elbows. They then immersed their non-dominant hand (19 left hand, 1 right hand) in warm water maintained at 37°C for 3 minutes to neutralize hand temperature with core body temperature [19, 20]. One minute prior to the removal of their non-dominant hand from the warm water participants aligned their dominant forearm so that they could observe a reflection of the hand in a mirror that was fixed to the side of a container containing a thick slurry of crushed ice and water maintained at 1°C-2°C as measured by a digital thermometer. Participants then transferred their non-dominant hand into the iced-water slurry and aligned it with the reflection of the dominant hand. To achieve congruence between the non-dominant hand in ice and the reflected hand, participants had to position their head so that the dominant hand remained out of view. Participants were instructed to observe the reflection of their dominant hand in a mirror whilst concentrating on any sensations occurring in the non-dominant hand in the iced water. Participants stated 'Pain' when they experienced the first sensation of pain anywhere in the non-dominant hand (Figure 2). The hand remained in the ice-water slurry and a verbal rating of pain intensity was taken 10 seconds after pain threshold prompted by a visual analogue scale (VAS) where 0 cm = no pain and 10 cm = worst pain imaginable. The hand remained in the ice-water slurry until the participant could no longer tolerate pain at which point they removed their hand. It was planned that participants would be asked to remove their hand from the ice-water slurry 5 minutes after 'Pain' if they had not done so themselves, although no participants reached this cut point. Participants dried their hand, completed a Longo questionnaire [6] and silently waited until the beginning of the next experimental cycle by resting both arms on the table. Pain threshold was measured as the time from immersion of the non-dominant hand in ice-water slurry to 'Pain'. Pain tolerance was measured as the time from pain threshold until removal of the hand from the ice-water slurry.

[Insert Figure 2 here]

Longo questionnaire

The Longo questionnaire was used to determine whether the mirror prompted an illusion that the reflected hand was like viewing a real hand directly and consists of 3 items:

- It felt like I was directly looking at my hand rather than a mirror image
- It felt like the hand I was looking at was my hand
- Did it feel like the hand you saw was a right hand or a left hand?

The questionnaire was delivered in an identical manner to a study by Longo et al. in 2009 [6]. Items 1 and 2 were rated according to agreement or disagreement on a 7-point Likert scale (+ 3 = 'strongly agree' to – 3 = 'strongly disagree'). Item 3 was rated using a scale from 0 to 100 (+100 = strong feeling of viewing the right [dominant non-immersed] hand to −100 = strong feeling of viewing the left [non-dominant immersed] hand) with the scale reversed for the one participant whose left hand was dominant.

Normal, enlarged and reduced size mirror image conditions

Standard (normal size), convex (enlarged size) and concave (reduced size) circular mirrors (diameter = 200mm) were attached to the side of the ice-water slurry container to produce mirror images of the dominant (non-immersed) hand. Participants were seated at a table with their dominant forearm aligned parallel with the mirror so that the middle finger was at a distance of 20 cm perpendicular from the mirror. This enabled participants to view the mirror image of their dominant (non-immersed) hand so that, with minor adjustments it gave an illusion that the hand was attached to the partially visible foreman of the non-dominant hand which as out of view and immersed in the ice-slurry. A distance of 20 cm perpendicular from the mirror enabled the reflected image created by the normal mirror to be the same size as the real hand. Reflections for the enlarged and reduced size conditions were by a factor of x2 normal size. A white neutral background was used so that there were no additional images in the background that could distract the participant from viewing the reflected hand.

No reflection control

In this condition participants were seated at a table so that the middle finger of their dominant forearm was aligned parallel and at a distance of 20 cm to the wall of a container containing the thick slurry of crushed ice. The container was transparent which allowed participants to view their non-dominant immersed hand whilst it was immersed in the slurry of crushed ice.

Data Management and Analysis

The mean score for each item of the Longo questionnaire was calculated for each condition. One sample t-tests against zero were used to determine whether the mirror prompted an illusion that the reflected hand was like viewing a real hand directly. A within-subject 4×2 factorial repeated measures analysis of variance (ANOVA) was performed on each pain outcome measure (i.e. pain threshold, pain intensity (VAS) and pain tolerance) and each item of the Longo questionnaire. Within-subject factors were Condition (four levels: no reflection, reduced reflection, normal reflection, enlarged reflection) and between-subject factors was Sex (two levels: female, male). A Greenhouse–Geisser correction was used if Mauchly's test showed that sphericity could not be assumed. Adjustments were made for multiple comparisons using the Bonferroni correction. Statistical significant was set at $p \leq 0.05$.

RESULTS

Twenty healthy volunteers expressed interest in the study and all started and completed the experiment session (mean±SD age = 23.55±4.01 years, maximum = 36 years, minimum = 18 years; mean±SD weight = 71.9±15.57kg; mean±SD height = 168.39±9.53cm; female n=10; right handed n=19).

Summary data is shown in Table 1. It was noteworthy that SDs for pain threshold and pain tolerance were large and inspection of raw data revealed that values from two participants were large and outliers. A sensitivity analysis was conducted by removing these data points and it was found that this brought the SD values into range but did not change the findings of the statistical analysis. Therefore, the statistical analysis that included data from these two participants is presented below.

[Insert Table 1 here]

Mauchley's test showed that sphericity of pain threshold data could not be assumed so Greenhouse-Geisser corrections were used. There were no significant effects for Condition (F (2.06, 37.02) = 0.79, p=0.464), Sex (F (1,18) = 1.15, p=0.298) or Condition x Sex interaction (F (2.06, 37.02) = 1.22, p=0.308). Mauchley's test showed that sphericity of pain intensity data could be assumed. There were no significant effects for Condition (F (3, 54) = 0.58, p=0.62), Sex (F (1,18) = 1.15, p=0.298) or Condition x Sex interaction (F (3, 54) = 1.58, p=0.20). Mauchley's test showed that sphericity of pain tolerance data could not be assumed so Greenhouse–Geisser corrections were used. There were no significant effects for Condition (F (1.93, 34.7) = 1.88, p=0.169), Sex (F(1,18) = 2.19, p=0.157) or Condition x Sex interaction (F (1.93, 34.7) = 2.08, p=0.141).

The no reflection condition produced the strongest illusion of viewing one's own left hand when viewing the right hand when compared with all reflection conditions (Table 1). Mauchley's test showed that sphericity of each item of the Longo questionnaire could not be assumed so Greenhouse-Geisser corrections were used. For item 1 there were significant effects for Condition (F (2.45, 44.11) = 11.715, p<0.001) but no significant effects for Sex (F (1, 18) = 0.028, p=0.868) or Condition x Sex interaction (F (2.45, 44.11) =0.855, p=0.452). Pairwise comparisons revealed that participants agreed more strongly with the statement “It felt like I was looking directly at my hand rather than at a mirror image” for the no reflection condition compared with the 3 mirror reflection conditions. There were no significant differences between the 3 mirror reflection conditions.

For item 2 there were significant effects for Condition (F (2.05, 45.01) = 8.09, p<0.001) but no significant effects for Sex (F (1, 18) = 1.53, p=0.232) or Condition x Sex interaction (F (2.05, 45.01) = 1.76, p=0.176). Pairwise comparisons revealed that participants agreed more strongly with the statement “It felt like the hand I was looking at was my hand.” for the no reflection condition compared with the 3 mirror reflection conditions. There were no significant differences between the 3 mirror reflection conditions.

For item 3 there were significant effects for Condition (F (2.80, 50.24) = 6.75, p=0.001) but no significant effects for Sex (F (1, 18) = 0.013, p=0.912) or Condition x Sex interaction (F (2.80, 50.24) = 0.677, p=0.56). Pairwise comparisons revealed that participants agreed more strongly with the statement “Did it seem like the hand you saw was a right hand or a left hand?” for the no reflection condition compared with the 3 mirror reflection conditions. There were no significant differences between the 3 mirror reflection conditions.

DISCUSSION

Mirror visual feedback was originally used to relieve post amputation phantom limb pain [21] and nowadays it is has been found to be beneficial for the management of chronic pain of hands and feet [22], especially complex regional pain syndrome [23] and phantom limb pain [24]. There is also evidence that mirror visual feedback is beneficial for rehabilitation of limb(s) following, stroke, traumatic injury or surgery [25]. Evidence suggests that there is a relationship between pain reduction during mirror visual feedback and a reversal of dysfunctional cortical reorganization in primary somatosensory cortex and a decrease of activity in the inferior parietal cortex [26]. Mirror visual feedback also increases neural activity in brain regions associated with motor control, attention and cognitions accompanying motor action control [10]. Most practitioners use normal size reflected images of the non-painful limb during mirror visual feedback training.

Our study found that enlarging and reducing the size of a hand using mirror visual feedback did not affect pain threshold, intensity and tolerance in healthy human participants exposed to cold-pressor pain. Mirror visual feedback, graded motor imagery and sensory discrimination retraining are techniques that have been developed to normalise cortical remapping of limbs in some chronic pain sates including phantom limb pain and complex regional pain syndrome. Mirror visual feedback may have less influence on experimentally-induced pain in healthy particpants because of the absence of cortical remapping. Nevertheless, previous studies using healthy human participants have detected changes. Our findings differed from Mancini et al. [13] who found that enlarging the view of a reflected hand reduced pain (increased pain threshold) of a hand exposed to contact heat delivered using a Peltier-type thermode 13 mm in diameter and held on the skin by a mechanical arm. Mancini et al. [13] also found that reducing the size of the reflected hand increased pain (decreased pain threshold). Recently, Romano et al. [27] used a lens to magnify the view of a hand and found that enlarging the appearance of a hand reduced the intensity of experimental pain induced by pressing the blunt end of a needle on the surface of the skin. They suggested that magnifying the appearance of body parts results in cognitive and anticipatory reactions, mediated by expectancies about the intensity of painful stimuli, to prepare the individual for contact with the noxious stimulus [27]. We selected cold pressor pain because individuals are familiar with the association between exposure to ice and a resultant pain sensation [28] and this would be stronger than expectancies about Peltier-type contact thermode attached to the skin [13] which provides no visual threat, at least on first exposure, because the individuals have no prior association with a Peltier-type contact thermode and pain. Our study design did not enable estimation of the influence of expectancy of the intensity of the painful stimulus and outcome. However, Romano et al. [27] did detect differences in experimental pain to different sized reflected limbs to stimuli that would be expected to produce pain (i.e. a blunt end of a needle pressed on the surface of the skin). This suggests that our inability to detect differences was not predominantly due to expectancy.

The fact that we did not detect a difference in cold-pressor pain between reflected and non-reflected conditions is of concern and may be explained in part by the strength of the mirror visual feedback illusion. The no reflection condition which involved participants observing their hand directly, was reported to produce a stronger sense of viewing one's own hand compared with all of the reflection conditions. This may suggest that mirror visual feedback was not strong. Alternatively, it is possible that participants interpreted the questions literally, for example, "I was directly looking at my hand rather than a mirror image" instead of "It felt I was directly looking at my hand rather than a mirror image". This is supported by the fact that the hand was not entirely visible in the no reflection condition as it was submerged in ice and observed through a semi-opaque container wall. Furthermore, the reflected hand did not appear to be sub-merged in ice-water slurry and this might have compromised the feeling that they were looking at a real hand rather than a mirror image. We plan to modify the experimental set up in future studies by generating a mirror reflection that generates an illusion that the reflected hand is sub-merged in ice-water slurry.

The function of mirror visual feedback is to create a sense that the reflected limb belongs to oneself, that is, the reflection is perceptually embodied within the body schema. We did not measure perceptual embodiment in the current study, and it would be interesting to determine whether there were differences in the degree of perceptual embodiment achieved using the different sized mirror reflections. In future investigators using mirror visual feedback may consider measuring perceptual embodiment in their studies using tools that capture subjective experience (e.g. the three item embodiment scale adapted from Mussap and Salton [29]) or physiological correlates (e.g. proprioceptive drift [30] or skin conductance response [31-33]. Moreover, it may also be important to include an adaptive phase to ensure the mirror reflection has been perceptually embodied in the clinical setting.

In contrast to studies using experimental pain the findings of studies using individuals with pre-existing painful conditions suggest that enlarging painful limbs increases pain. Moseley et al. [11] found that magnifying the view of a chronically painful and dysfunctional arm using binoculars increased pain and swelling evoked by movement and Ramachandran et al. [12] reducing the size of a reflected limb using mirror visual feedback reduced phantom limb pain. Preston and Newton [34] used real-time video capture techniques to manipulate a first person view of their hand so that it appeared stretched and shrunk in 20 individuals with painful osteoarthritic hands. They found that 85% of participants reported benefit, but only when the painful part of the hand was manipulated. There was no reported benefit when the appearance of the whole hand, which had painful and non-painful areas, was enlarged or reduced. Interestingly, some participants found that pain was reduced when the painful area was stretched and shrunk whereas others found that pain reduction was greater when the painful area was stretched or when the painful area was shrunk for some participants. The authors suggested that participants may vary in their cortical representations causing variations in matching of cortical representations and reduction of apparent swelling. Inter and intra individual variation in response to visual distortion of the size of painful limbs was large and they speculated that their findings may also represent experimental ‘noise’ and or placebo effects.

Study shortcomings

Our findings appear to add to this contradictory evidence base. The unevenness of sensations associated with cold pressor pain may have contributed to inter and intra variability and discrepancies in findings with previous studies. Mancini et al. [13] used a Peltier-type thermode 13 mm in diameter that delivers a stimulus to a small discrete area of the skin resulting in a localised sharp 'burning' pain whereas immersion of a hand in iced water generates a variety of pain sensations across a larger area of the hand, for example with stinging sensations at the finger tips and dull aches in the palm, that changes in quality over time. It seems unlikely that differences in peripheral mechanisms responding to noxious heat and cold stimuli may have contributed in part to differences in findings because mirror visual feedback modulates pain centrally. We cannot discount the possibility that experimental 'noise' resulted in a type II error (false negative). Inter and intra individual variability in response was large as reflected in SDs that were larger than mean values for pain threshold and pain tolerance, although mean values themselves were similar to those obtained in previous research by ourselves and others [15, 19, 35]. A sensitivity analysis that removed outlier data of two participants markedly reduce SDs bringing them back into the range of our previous research and did not alter our main findings of no effects between the groups. Our research team have used the cold pressor pain technique for over 25 years and all investigators in this study received formal training in experimental techniques and used crib sheets so that identical instructions were given to participants to prevent variations in words and mannerisms used during giving instructions to the participants. This would have reduced the influence of expectations associated with unplanned inferences during delivery of instructions to participants. Thus, we believe that the large inter and intra individual variability in response was not a reflection of shortcomings in the operational delivery of experiments.

Conclusion

In conclusion, enlarging and reducing the visual appearance size of a hand using mirror visual feedback did not alter pain threshold, intensity and tolerance in healthy human participants exposed to cold-pressor pain. The different sizes of hands generated by mirror visual feedback created an illusion of looking at their own hand but this was not as strong as looking directly at the hand. We hope that these findings catalyse further research, including investigations to determine relationships between perceptual embodiment and mirror reflections of different sized body parts. In this regard, investigators and clinicians using mirror visual feedback may consider including an adaptive phase to ensure the reflection has been perceptually embodied.

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DECLARATION OF INTEREST

The authors declare no conflicts of interest. This research received no external funding.

ETHICAL APPROVAL

Ethical approval was received from the Research Ethics Committee of Leeds Beckett University.

REFERENCES

[1] Lotze M, Moseley GL. Role of distorted body image in pain. Current rheumatology reports. 2007;9:488-96.

[2] Foell J, Bekrater-Bodmann R, Flor H, Cole J. Phantom limb pain after lower limb trauma: origins and treatments. Int J Low Extrem Wounds. 2011;10:224-35.

[3] Moseley GL. Distorted body image in complex regional pain syndrome. Neurology. 2005;65:773.

[4] Lewis JS, Kersten P, McCabe CS, McPherson KM, Blake DR. Body perception disturbance: a contribution to pain in complex regional pain syndrome (CRPS). Pain. 2007;133:111-9.

[5] Punt TD, Cooper L, Hey M, Johnson MI. Neglect-like symptoms in complex regional pain syndrome: learned nonuse by another name? Pain. 2013;154:200-3.

[6] Longo MR, Betti V, Aglioti SM, Haggard P. Visually induced analgesia: seeing the body reduces pain. The Journal of neuroscience : The fficial journal of the Society for Neuroscience. 2009;29:12125-30.

[7] McCabe P, Nason F, Demers Turco P, Friedman D, Seddon JM. Evaluating the effectiveness of a vision rehabilitation intervention using an objective and subjective measure of functional performance. Ophthalmic Epidemiol. 2000;7:259-70.

[8] Sumitani M, Miyauchi S, McCabe CS, Shibata M, Maeda L, Saitoh Y, Tashiro T, Mashimo T. Mirror visual feedback alleviates deafferentation pain, depending on qualitative aspects of the pain: a preliminary report. Rheumatology (Oxford). 2008;47:1038-43.

[9] McCabe CS, Haigh RC, Blake DR. Mirror visual feedback for the treatment of complex regional pain syndrome (type 1). Curr Pain Headache Rep. 2008;12:103-7.

[10] Deconinck FJ, Smorenburg AR, Benham A, Ledebt A, Feltham MG, Savelsbergh GJ. Reflections on Mirror Therapy: A Systematic Review of the Effect of Mirror Visual Feedback on the Brain. Neurorehabil Neural Repair. 2014.

[11] Moseley GL, Parsons TJ, Spence C. Visual distortion of a limb modulates the pain and swelling evoked by movement. Curr Biol. 2008;18:R1047-8.

[12] Ramachandran VS, Brang D, McGeoch PD. Size reduction using Mirror Visual Feedback (MVF) reduces phantom pain. Neurocase. 2009;15:357-60.

[13] Mancini F, Longo MR, Kammers MP, Haggard P. Visual distortion of body size modulates pain perception. Psychol Sci. 2011;22:325-30.

[14] Handwerker HO, Kobal G. Psychophysiology of experimentally induced pain. Physiol Rev. 1993;73:639-71.

[15] Koenig J, Jarczok MN, Ellis RJ, Bach C, Thayer JF, Hillecke TK. Two-week test-retest stability of the cold pressor task procedure at two different temperatures as a measure of pain threshold and tolerance. Pain Pract. 2014;14:E126-35.

[16] Ruscheweyh R, Stumpenhorst F, Knecht S, Marziniak M. Comparison of the cold pressor test and contact thermode-delivered cold stimuli for the assessment of cold pain sensitivity. J Pain. 2010;11:728-36.

[17] Neziri AY, Scaramozzino P, Andersen OK, Dickenson AH, Arendt-Nielsen L, Curatolo M. Reference values of mechanical and thermal pain tests in a pain-free population. Eur J Pain. 2011;15:376-83.

[18] Mitchell LA, MacDonald RA, Brodie EE. Temperature and the cold pressor test. J Pain. 2004;5:233-7.

[19] Tashani OA, Alabas OA, Johnson MI. Cold pressor pain responses in healthy Libyans: effect of sex/gender, anxiety, and body size. Gend Med. 2010;7:309-19.

[20] Keogh E, Bond FW, Hanmer R, Tilston J. Comparing acceptance- and control-based coping instructions on the cold-pressor pain experiences of healthy men and women. Eur J Pain. 2005;9:591-8.

[21] Ramachandran VS, Rogers-Ramachandran D. Synaesthesia in phantom limbs induced with mirrors. Proc Biol Sci. 1996;263:377-86.

[22] Bowering KJ, O'Connell NE, Tabor A, Catley MJ, Leake HB, Moseley GL, Stanton TR. The effects of graded motor imagery and its components on chronic pain: a systematic review and meta-analysis. J Pain. 2013;14:3-13.

[23] O'Connell NE, Wand BM, McAuley J, Marston L, Moseley GL. Interventions for treating pain and disability in adults with complex regional pain syndrome. Cochrane Database Syst Rev. 2013;4:CD009416.

[24] Hagenberg A, Carpenter C. Mirror visual feedback for phantom pain: international experience on modalities and adverse effects discussed by an expert panel: a delphi study. PM & R : the journal of injury, function, and rehabilitation. 2014;6:708-15.

[25] Thieme H, Mehrholz J, Pohl M, Behrens J, Dohle C. Mirror therapy for improving motor function after stroke. Cochrane Database Syst Rev. 2012;3:CD008449.

[26] Foell J, Bekrater-Bodmann R, Diers M, Flor H. Mirror therapy for phantom limb pain: brain changes and the role of body representation. Eur J Pain. 2014;18:729-39.

[27] Romano D, Maravita A. The visual size of ones own hand modulates pain anticipation and perception. Neuropsychologia. 2014;57:93-100.

[28] Atlas LY, Wager TD. How expectations shape pain. Neurosci Lett. 2012;520:140-8.

[29] Mussap AJ, Salton N. A 'rubber-hand' illusion reveals a relationship between perceptual body image and unhealthy body change. JHealth Psychol. 2006;11:627-39.

[30] Tsakiris M, Haggard P. The rubber hand illusion revisited: visuotactile integration and self-attribution. J Exp Psychol Hum Percept Perform. 2005;31:80-91.

[31] Armel KC, Ramachandran VS. Projecting sensations to external objects: evidence from skin conductance response. Proc Biol Sci. 2003;270:1499-506.

[32] Braithwaite JJ, Broglia E, Watson DG. Autonomic Emotional Responses to the Induction of the Rubber-Hand Illusion in Those That Report Anomalous Bodily Experiences: Evidence for Specific Psychophysiological Components Associated With Illusory Body Representations. J Exp Psychol Hum Percept Perform. 2014.

[33] Ocklenburg S, Ruther N, Peterburs J, Pinnow M, Gunturkun O. Laterality in the rubber hand illusion. Laterality. 2011;16:174-87.

[34] Preston C, Newport R. Analgesic effects of multisensory illusions in osteoarthritis. Rheumatology (Oxford). 2011;50:2314-5.

[35] Alabas OA, Tashani OA, Johnson MI. Gender role expectations of pain mediate sex differences in cold pain responses in healthy Libyans. Eur J Pain. 2012;16:300-11.

TABLES

Table 1

Summary data (Mean + SD). Pain intensity was recorded on a 10 cm visual analogue scale where 0 cm = no pain and 10 cm = worst pain imaginable.

Condition	**No reflection**	**Reduced size mirror image**	**Normal size mirror image**	**Enlarged size mirror image**	**RM ANOVA for Condition**
Pain Threshold (s)	17.70+30.33	16.095+24.92	13.67+16.01	16.645+23.75	p=0.464
Pain Intensity (cm)	6.40+1.81	6.4750+1.90	6.325+1.52	6.125+1.64	p=0.62
Pain Tolerance (s)	22.435+37.29	13.965+15.34	15.82+16.84	25.87+43.90	p=0.141
Longo Questionnaire					
Item 1 It felt like I was directly looking at my hand rather than a mirror image	2.40+1.09 #p<0.001	-0.30+1.66 #p=0.428	0.55+1.79 #p=0.186	0.30+1.87 #p=0.481	p<0.001
Item 2 It felt like the hand I was looking at was my hand	2.60+0.88 #p<0.001	.60+1.63 #p=0.117	1.10+1.71 #p=.010	0.85+1.69 #p=0.037	p<0.001
Item 3 Did it feel like the hand you saw was a right hand or a left hand?	-60.00+64.07 #p<0.001	-2.50+59.55 #p=0.853	-10.00 +59.82 #p=0.464	-2.5+69.73 #p=0.874	p=0.001

#p = one sample t-test (2 tailed) comparison with zero

FIGURE LEGENDS

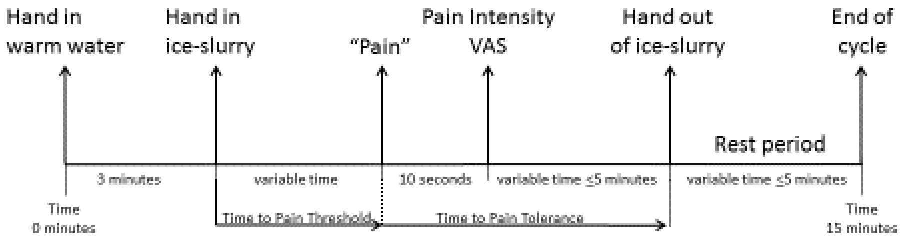
Figure 1

Experimental set up. (a) no reflection control, (b) normal mirror image, (c) enlarged size mirror image, (d) reduced size mirror image

Figure 2

Cold-pressor pain: One measurement cycle


a
Ice slurry
b
c
d


Hand in warm water
Hand in ice-slurry
"Pain"
Pain Intensity VAS
Hand out of ice-slurry
End of cycle
Rest period
3 minutes
variable time
10 seconds
variable time ≤5 minutes
variable time ≤5 minutes
Time 0 minutes
Time to Pain Threshold
Time to Pain Tolerance
Time 15 minutes