2018

Visually-induced analgesia in a deep tissue experimental pain model: A randomised cross-over experiment

Megan Van Selm
The University of Notre Dame Australia, megan.van.selm@nd.edu.au

William Gibson
The University of Notre Dame Australia, william.gibson@nd.edu.au

Mervyn Travers
The University of Notre Dame Australia, mervyn.travers@nd.edu.au

Lorimer Moseley

Dana A. Hince
The University of Notre Dame Australia, dana.hince1@nd.edu.au

See next page for additional authors

This article was originally published as:
Van Selm, M., Gibson, W., Travers, M., Moseley, L., Hince, D. A., & Wand, B. (2018). Visually-induced analgesia in a deep tissue experimental pain model: A randomised cross-over experiment. *European Journal of Pain, Online First*.
http://doi.org/10.1002/ejp.1234

This is the author's post-print copy of the article published as:

Van Selm, M., Gibson, W., Travers M., Moseley, L., Hince, D., and Wand, B. (2018). Visually-induced analgesia in a deep tissue experimental pain model: A randomised cross-over experiment. *European Journal of Pain*. doi: 10.1002/ejp.1234

This article has been published in final form
at https://www.sciencedirect.com/science/article/pii/S1526590004010132

Original Article

Title: Visually-induced analgesia in a deep tissue experimental pain model: a randomised cross-over experiment.

M.J. van Selm[1], W.I. Gibson[1], M.J. Travers[1,2], G.L. Moseley[3,4], D. Hince[5], B.M. Wand[1]

[1]School of Physiotherapy, The University of Notre Dame Australia, Fremantle, Australia

[2]School of Physiotherapy and Exercise Science, Curtin University, Bentley, Australia

[3]Neuroscience Research Australia (NeuRA), Sydney, Australia

[4]School of Health Sciences, *University of South Australia, Adelaide, Australia*

[5]Institute of Health Research, The University of Notre Dame Australia, Fremantle, Australia

Corresponding author:

Megan van Selm

Email: megan.van.selm@nd.edu.au

Address: School of Physiotherapy, The University of Notre Dame Australia, 19 Mouat Street (PO Box 1225), Fremantle, Western Australia 6959; Telephone +61 8 9433 2009; Facsimile +61 8 9433 0556

Running Head - Visually-induced analgesia in DOMS

Statement of Contribution

All authors provided significant contribution across the categories: 1) substantial contributions to conception and design (MVS, WG, GLM, BMW), or acquisition of data (MVS, WG, GLM, BMW), or analysis and interpretation of data (MVS, WG, GLM, BMW, DH, MT); 2) drafting the article (MVS, WG, GLM, BMW, DH, MT) or revising it critically for important intellectual content (MVS, WG, GLM, BMW, DH, MT); 3) final approval of the version to be published (MVS, WG, GLM, BMW, DH, MT).

Statement of Funding – This project had no external funding

Conflicts of interest – GLM has received support from Pfizer, Australian Institute of Sport, Grunenthal, Kaiser Permanente California, Return to Work SA, Agile Physiotherapy, Results Physiotherapy, the International Olympic Committee, Port Adelaide Football Club, Arsenal Football Club; Research grants from National Health and Medical Research Council of Australia; Speaker fees for lectures on pain and rehabilitation; Royalties for books on pain and rehabilitation. The other authors have no conflicts of interest to declare.

Significance

We present delayed onset muscle soreness as a model for exploring visually induced analgesia. Our findings suggest that this phenomenon is expressed differently in exogenous and endogenous experimental pain models. Further exploration may offer a potential pathway for the integration of visual analgesia into the management of clinical pain.

Abstract

Background: Visualizing one's own painful body part appears to have an effect on reported pain intensity. Furthermore, it seems that manipulating the size of the viewed image can determine the direction and extent of this phenomenon. When visual distortion has been applied to clinical populations the analgesic effects have been in opposition to those observed in some experimental pain models. To help resolve this problem we explored the effect of visualisation and magnification of the visual image on reported pain using a delayed onset muscle soreness (DOMS) pain model.

Methods: We induced DOMS in the quadriceps of 20 healthy volunteers. Forty-eight hours later participants performed a series of painful contractions of the DOMS affected muscle under four randomised conditions: 1. Viewing the injured thigh; 2. Viewing the contralateral thigh; 3. Viewing a neutral object; 4. Viewing the injured thigh through magnifying glasses. For each condition, participants rated their pain intensity during a series of painful contractions.

Results: We observed that direct visualisation of the injured thigh had no effect on pain intensity when compared to viewing the contralateral thigh or neutral object. However, magnification of the DOMS-affected leg during the performance of painful contractions caused participants to report more pain than when viewing the injured thigh normally.

Conclusions: These results further demonstrate that the effect of visualisation varies between different pain conditions. These results may have implications for the integration of visual feedback into clinical practice.

Introduction

Congenitally blind individuals are hypersensitive to painful stimuli applied to the skin (Slimani et al., 2014), suggesting vision may play a role in pain processing. This idea has been explored in experimental studies and it appears that looking at a body part may reduce the pain intensity experienced with superficial noxious stimulation, a phenomenon referred to as visually-induced analgesia. This has been observed during painful infrared laser stimulation (Longo et al., 2009; Longo et al., 2012) or noxious thermal stimulation (Mancini et al., 2011) applied to the viewed hand, though some later studies have failed to fully replicate this phenomenon (Torta et al., 2015; Valentini et al., 2015). Furthermore, when noxious electrical stimulation or pressure were applied to the back, viewing the back evoked less pain than when viewing another body part, in both chronic back pain patients and healthy controls (Diers et al., 2013). It also appears visual distortion of the size of the body part alters this visually-induced analgesia. It has been demonstrated that magnification of the hand's perceived size increases analgesia whilst minification compromises the analgesic effect (Mancini et al., 2011) though there are inconsistencies in the literature (Wittkopf et al., 2018). Thus, it appears viewing the painful body part may influence the pain experience and distorting size perception can determine the direction of this phenomenon in experimental pain models.

Expanding this phenomenon to clinical pain, low back pain patients viewing their own back reported an immediate reduction in their habitual pain while lying down (Diers et al., 2015), during massage (Löffler et al., 2017) and during movement (Wand et al., 2012). These observations suggest visualisation may positively influence the clinical pain state. However, when visual distortion has been applied to clinical populations, the analgesic effects have

been in opposition to those observed in experimental pain models. For example, in people with complex regional pain syndrome (CRPS), magnification of the affected hand increased pain evoked by movement, whereas minification decreased it (Moseley et al., 2008). There are also reports of reduced phantom limb pain using minification (Ramachandran et al., 2009). There are a number of potential explanations for this difference, one issue particularly pertinent to visually-induced analgesia is the use of cutaneous noxious stimulation in experimental studies. Under these circumstances direct visualisation of the stimulated structure is possible. Clinical pain states are often described as deep (Bove et al., 2005) and it is less likely visualisation offers the individual the same information about the state of any noxiously active tissue. To date, no studies have explored visually-induced analgesia using an experimental deep-tissue pain model. Delayed onset muscle soreness (DOMS) represents an ideal form of deep-tissue experimental pain with which to expand our understanding of this topic and help determine if the differences apparent in the literature represent a difference between experimental and clinical pain or between superficial and deep pain. The primary aim of this study was to determine if direct visualisation of a painful body part modulates activity-related pain in people with DOMS. We hypothesised that direct visualisation of the leg in which DOMS was induced would result in reduced pain in comparison to viewing a neutral object or viewing the non-injured leg. The secondary aim was to explore the effect of manipulation of the visual image on reported pain. We hypothesised that pain would be modified by magnification of the DOMS-induced leg in comparison to normal visualisation, though given the variability of previous findings, we had no directional hypothesis.

Methods

Subjects

Twenty healthy adult volunteers participated. Inclusion criteria included proficient written and spoken English and the ability to provide written, informed consent. Participants were excluded if they reported any form of persistent pain, had lower limb pain that required a visit to a health care professional within the previous 12-months, had sustained a traumatic injury (e.g. fracture or dislocation) of the lower limb within the previous five-years, had any ongoing medical or neurological conditions, consumed regular anticoagulant medication or medications known to influence pain sensitivity (e.g. painkillers, anti-inflammatories, anti-depressants) or if they had recently trained the quadriceps with eccentric strength exercises (within the previous six-months). Finally, any participant who required glasses to obtain normal vision was excluded as the experiment involved a magnified condition using a pair of magnifying glasses. Wearing contact lenses at the time of testing was acceptable as long as the subject had normal vision with the lenses in situ. Participants were informed that the study sought to investigate the effect of vision on pain perception, but were blind to the study hypotheses.

Study Overview:

A standardised protocol was used to induce DOMS in the quadriceps of participants' non dominant leg. Forty-eight hours later participants entered into a four phase randomised cross-over experiment. The study was registered with the Australian and New Zealand Clinical Trial Registry (Trial ID: ACTRN12614000563662), a flow chart of the study is presented in Fig. 1. During session one, demographic data were collected and each participant completed two

pain related questionnaires. The Pain Anxiety Symptom Scale (PASS-20), a short form of the original PASS-40 (McCracken et al., 1992), was used to assess pain-related anxiety and the Pain Sensitivity Questionnaire (PSQ) (Ruscheweyh et al., 2009) was used to assess trait pain sensitivity. Maximal isometric knee extension strength was then assessed and the position for the pain provocation test to be undertaken in session two was established. Finally, the subjects underwent an exercise protocol aimed at inducing DOMS in the non-dominant quadriceps muscle. A key feature of this project was the requirement to be able to observe the sore body part with minimal observable body segment movement during pain provoking activities; the quadriceps was considered ideal in this regard.

At session two, subjects completed a previously validated Likert scale of DOMS (Andersen et al., 2008) indicating their perceived level of muscle soreness. A score ≥ 3 on this scale was required for eligibility for participation in the study proper. Eligible participants undertook three repetitions of a pain provocation test at 15-minute intervals under four randomised visual conditions and provided a pain intensity rating for each condition. A counterbalanced randomisation sequence was computer generated and allocation was concealed. The study received institutional ethical approval, all procedures adhered to the declaration of Helsinki and all participants provided signed informed consent before participating.

Session One: Measuring maximal isometric strength

To enable standardisation of the load used in the pain provocation test, maximal isometric strength of the non-dominant quadriceps muscle was established for each participant prior to the induction of DOMS. Testing was performed in a seated position with knees and hips

flexed to 90^{o} and feet flat on the floor. The participant extended the non-dominant knee until 10^{o} short of full knee extension. The assessor then positioned a hand-held dynamometer (Lafayette Manual Muscle Tester - 01165) against the anterior aspect of the distal tibia, just proximal to the talo-crural joint line. The participants performed a maximal isometric contraction and the dynamometer registered the force generated during the contraction. This was repeated three times and the mean of the three scores was used to establish the weight required for resistance in session two. The load used was standardised by calculating 40% of the average force recorded during the maximal isometric contractions.

Session One: Establishing test position and magnification

Next, the appropriate test position and strength of lenses for magnification to be used during session two were established. Participants were seated on an examination table with their thighs fully supported and the hips and knees at 90^{o}. Participants donned the strongest magnifying glasses (+3.5) and looked at their non-dominant thigh to see if the thigh was in clear focus. If the thigh was not in focus the hip was slowly flexed with instruction to stop at the point where the thigh came into focus. If the participant was unable to focus clearly on the thigh at any point through their comfortable range of hip flexion, the same process was repeated using glasses with 0.5 less magnification strength. The same procedure was repeated until the subject was able to find an appropriate pair of glasses and a comfortable position of their thigh to achieve clarity. The lens strength and hip position was documented for use during the magnification condition undertaken in session two. The angle of hip flexion used ranged between 90^{o} and 140^{o} and the strength of the magnifying glasses ranged from +1.5 to +3.5.

Session One: Induction of DOMS

To conclude session one, participants performed an exercise protocol aimed at inducing DOMS in the non-dominant quadriceps muscle group (See Fig. 2). Participants were positioned in half kneeling on the non-dominant knee. The participant was instructed to slowly lean backwards allowing the knee to flex as far as they were comfortable, thus eccentrically loading the quadriceps on the kneeling leg. The researcher stood behind the participant, acting as a physical barrier to falling backwards. At the end of each repetition the researcher helped the participant back to the upright position such that their return was as passive as possible, this was done to minimise fatigue from concentric contractions. Each participant performed 150 repetitions in total, divided into five blocks of three sets of 10 repetitions. A 30 second rest period separated each set of 10 repetitions with a two minute rest between each of the five blocks.

Session Two: Pain provocation testing procedure:

The pain provocation test was designed to provoke pain by loading the DOMS affected muscle in a consistent fashion. Participants were seated on an examination table and an individualised weight was attached to the distal tibia of the DOMS affected leg using a Velcro strap. The researcher passively extended the knee joint to 10° short of full extension and from this position the participant performed a controlled lowering of the foot towards the floor (knee flexion) over a period of three seconds. They immediately rated the pain evoked by each standardised eccentric contraction on an 11-point numerical rating scale (NRS) anchored

at left with “0 - no perceived pain” and at right with “10 - worst possible pain”. This procedure was repeated three times at five second intervals for each condition. The mean of the three pain scores was used for further analysis. To ensure consistency of body position across the four conditions the hip flexion angle established in session one was used for all four conditions.

Session Two: Visual conditions

All eligible participants performed the pain provocation task under four different visual conditions (See Fig. 3) in a randomised order. For each condition, the weights were attached to the ankle and a five minute visual fixation period was utilised prior to the performance of the provocative manoeuvres. Between each condition, the weight was removed and the participant undertook a ten minute washout period.

To determine if visualisation of the affected body part influenced pain associated with noxious input from deep tissue, participants were instructed to observe the injured thigh during the five minute fixation period and during the performance of the provocative tests. The control condition involved observation of a neutral object in the same position as the injured thigh while performing the provocative task. A box was placed over the affected thigh to hide the thigh from view and the participant was instructed to look at the box during the five minute fixation period and during the performance of the provocative tests. To control for the possible confounding of observation of any body part an additional control condition was used in which participants were instructed to look at the unaffected thigh during the five minute fixation period and during the performance of the provocative tests. The unaffected

leg was at rest during this condition. During this condition the affected thigh was hidden from view by placing a box over the thigh.

To determine if magnification of the affected body part influenced pain, participants viewed the affected thigh using magnification glasses during the five minute fixation period and during the performance of the provocative tests. On completion of this condition, a methodological check was undertaken to ensure visual manipulation of leg size had been successful. Participants were presented with a nine point scale ranging from -4 (extremely shrunken), through 0 (normal size) to +4 (extremely enlarged) and asked to rate the perceived size of the thigh while wearing the glasses.

Data analysis

DOMS has been widely used as an experimental model for deep pain (Bishop et al., 2011; Fernandez-Carnero et al., 2010; Gibson et al., 2006; Slater et al., 2003; 2005), but there is a dearth of information regarding the stability of activity-evoked pain in the presence of DOMS. Thus, an ethics approved pilot study on ten healthy volunteers was undertaken to establish the temporal reliability of the pain responses to loading during DOMS and to inform the sample-size calculation for the present study. After consent was obtained, DOMS was induced using the same protocol as described above. Participants returned 48-hours later and undertook the pain provocation procedure outlined above four times at 15-minute intervals under identical conditions. From that pilot data, the within-subject difference in means in pain intensity ratings (NRS) was estimated to be 0.3. This was used as the threshold for determining the minimal detectable change for the power calculation. Using a minimal detectable difference of 0.3 achieved 90% power when a minimum of 17 subjects were

recruited, the standard deviation of the mean differences was 0.34 and the significance level was set at 0.05. We oversampled by three to give a total sample size of 20 subjects. Furthermore, based on the helpful suggestion of the manuscript reviewers the effect size estimate (Cohen's d) for the mean difference will be reported.

The association between pain intensity and visualisation task was assessed using a linear mixed model, with a random factor for participant to account for the repeated measures. Age, gender, test order, PASS-20 and PSQ were also considered for association with pain intensity. Following a significant main effect for visualisation task, *a priori* defined pair-wise comparisons were made between the normal visualisation of the injured thigh condition and each of the other three visualisation tasks. The assumption of normally distributed residuals was verified visually for the final model. All analyses were conducted using IBM SPSS statistics v24, and $p<0.05$ was considered significant.

Results

Twenty-two participants were screened. One participant failed to meet inclusion criteria (taking regular analgesia for cervical spine-related pain), and another was excluded as insufficient pain was produced by the DOMS protocol. The remaining 20 participants completed all components of the study and there were no missing data. Of the 20 participants included in the analysis, seven (35%) were male and the mean (SD) age was 26.5 (7.0) years (range = 20 - 47). As shown in Table 1, the study sample displayed low mean pain-related anxiety, low mean trait sensitivity and moderate exercise induced pain during the 24-hours

prior to testing. Furthermore, all participants perceived the thigh as being larger under the magnification task.

Mean pain intensity scores for each visualisation condition are shown in Fig. 4. Age, gender, test order, PASS-20 and PSQ were not significantly associated with pain intensity, and were therefore not considered as potential confounding factors in the model. Visualisation condition was significantly associated with pain intensity ($F(3, 217) = 5.35$, $p = 0.001$). *A priori* pair-wise comparisons revealed that the magnification condition resulted in higher pain intensity scores (Mean = 3.05; SD = 1.62) than the affected thigh visualisation condition (Mean = 2.60; SD = 1.66) and this difference was statistically significant (mean difference = 0.45, 95% CI 0.21 to 0.69, $p < 0.001$); with an effect size estimate (Cohen's d) for the mean difference was 0.54. Pain intensity scores were not significantly different for the affected thigh visualisation condition when compared with the neutral object (mean difference = 0.08, 95% CI -0.61 to 0.31, $p = 0.537$) or the contralateral thigh condition (mean difference = 0.125, 95% CI -0.11 to 0.36, $p = 0.304$).

Discussion

The primary aim of this study was to examine whether visualisation of the painful body part has an effect on experimental deep tissue pain. We induced DOMS in the quadriceps of a group of 20 healthy volunteers and 48-hours later undertook a randomised cross-over experiment in which participants performed a series of painful contractions of the DOMS affected muscle while they viewed the affected leg, viewed a neutral object or viewed the opposite, unaffected leg. We hypothesised that viewing the affected leg would have an

analgesic effect in comparison to viewing a neutral object or viewing the non-injured leg. Contrary to our hypothesis we found that direct visualisation of the painful body part had no effect on pain intensity. Average pain ratings while visualising the sore body part were the same as when viewing a neutral object in the same position as the injured leg and with viewing the opposite non-injured leg.

The secondary aim was to explore the effect of manipulation of the visual image on reported pain intensity. Participants undertook a fourth condition in which the image of the injured thigh was magnified by the use of magnifying glasses. Given the varied results seen in the literature we hypothesised that visual magnification would produce an effect on the intensity of perceived pain in comparison to normal vision without being able to predict the direction of the effect. Consistent with our hypothesis, magnification of the DOMS-affected leg during the performance of painful contractions appeared to influence pain intensity. Participants reported more pain during the magnified condition than when viewing the thigh normally. When we explored for potential confounding variables, the covariates of age, trait pain sensitivity and pain related anxiety did not demonstrate any significant interactions with the visual conditions and neither did gender and order effect when explored as between-subject factors.

There are no similar data against which our results can be directly compared as no previous studies have investigated the effects of vision on experimental, deep tissue pain. However, the results may be considered in the context of superficial experimental pain studies. Our findings are contrary to those of (Longo et al., 2009; Longo et al., 2012; Mancini et al., 2011) who demonstrated an analgesic effect of visualisation on superficially-induced experimental pain in a healthy population. It is possible that when the tissues being noxiously stimulated

are directly observable the threat value of the noxious input is reduced by providing the individual with information that 'all is well' with the tissues. This is in contrast to deep tissue stimulation where the tissue affected cannot be visualised directly so adding visual input may not have significant informative value in terms of perception of safety of the stimulated structure.

While we think this is a plausible explanation for the difference in results, recent data suggests an alternate perspective. The present experiment used direct visualisation of the affected body part whereas earlier studies utilised a reflected image (Longo et al., 2009; Longo et al., 2012; Mancini et al., 2011). Furthermore, body position was kept constant across all conditions in the present study whereas in the Longo et al., (2009) study body position varied between conditions. More recently, Valentini et al., (2015) only found evidence for visually-induced analgesia with superficial stimulation of the hand when the arms were crossed. Direct visualisation of the hand in the uncrossed position was not analgesic. Torta et al., (2015) also noted no visually induced analgesia with noxious cutaneous stimulation using direct visualisation or with mirror visualisation when body position was standardised across all conditions. The analgesic effect reported in earlier studies may be an artefact of the use of a reflected image or be confounded by variation in hand position between conditions used in some earlier studies (Torta et al., 2015). Clearly further research is required.

When we compare our study to those that investigate the effects of vision in clinical populations, our results also differ from earlier research. Diers et al., (2015); Löffler et al., (2017); Wand et al., (2012) observed analgesic effects with vision of the back in people with chronic back pain. Wand et al., (2012) used a mirror to allow subjects to view their backs, while Diers et al., (2015) and Löffler et al., (2017) used real-time video feedback. Torta et al.,

(2015) suggest that the use of an illusory image could create a conflict between the somatosensory, visual and proprioceptive representations, requiring higher cognitive processing levels such that the illusion rather than visualisation is what produces the analgesic effect and this may explain the differences in the results seen. An alternative and plausible explanation for the positive findings in response to visualisation in these clinical groups may be due to the particular part of the body involved. The back was the painful area in all three studies and is a region of the body not normally subject to visual appraisal. Viewing the back therefore provided participants with novel and potentially reassuring information about the state of the back. In our study, the affected body part is usually visible to the individual so the visual condition might not have offered any novel information or reassurance to the participant.

Our second hypothesis was that visual magnification of a painful body part would have an effect on perceived pain intensity. Our results differ from Mancini et al., (2011) upon which the hypothesis was formulated. Our study found that the visual magnification condition increased pain perception whereas Mancini et al., (2011) noted an analgesic effect. Furthermore, our results differ from those of (Wittkopf et al., 2018) who observed no changes in pain perception associated with cutaneous thermal stimuli when viewing a magnified reflection of the hand in a mirror. While further research is needed to fully understand the relationship between visual size distortion and analgesia, this discrepancy in results is consistent with the discussion presented above. When noxious stimulation is delivered to the skin, an augmented image of the stimulated area showing no injury or threat is likely to offer a stronger safety message than normal visualisation. In contrast an enlarged view of the sore thigh might suggest a swollen, more severely affected leg in which an enhanced protective

response to loading is indicated. Research in clinical populations offers some support for this view. Moseley (2008) also noted an increase in pain with activity when people with CRPS viewed their affected hand through magnifying goggles, while other explanations are offered (Moseley 2008) it might be that making the injured hand look more severely affected (swollen) increased the individuals' protective responses.

In apparent confirmation of this, two recent studies demonstrate that inducing an implicit perception of threat during multi-sensory embodiment illusions reduces pain threshold, pain tolerance and increases pain intensity to psychophysical tests (Giummarra et al., 2015; Osumi et al., 2014). Employing rubber hands with an obvious 'injury' during the rubber hand illusion may create the same sense of threat/need for protection as that proposed in our findings and might account for the increased pain intensity reported here in response to provocation testing under magnified (apparently increased swelling) conditions (Giummarra et al., 2015; Osumi et al., 2014).

Limitations

The results seen here need to be interpreted in light of the potential study limitations. Firstly, while we attributed the alterations in pain perception in the magnification condition to the enlarged appearance, we cannot rule out this is a non-specific effect of simply applying visual distortion. It is possible similar effects would have been observed with other forms of distortion such as minification and colour change. For the neutral object condition in our protocol, we could have placed the neutral object away from the sore leg. However, to do so may have introduced an additional confounder to interpretation as all other conditions

required visually attending to the location of the leg. The perceived pain scores during movement with DOMS may be viewed as being relatively low and, although they approximate those reported in other studies of visual analgesia (Löffler et al., 2017; Torta et al., 2015), it is possible that different results to those presented here might be apparent in tasks with greater pain intensity. While we are confident in suggesting this result does represent an effect of visual distortion on pain perception, it is important to bear in mind this is an experimental pain induction methodology. As such, extrapolating these findings to clinical populations is premature. Further work is required to explore this area.

Conclusion

In the present study we employed an experimental model of deep tissue pain to explore visually induced analgesia during activity evoked pain. Our findings of no analgesic effect from direct visualisation of the painful body part conflicts with some experimental superficial pain models. This may be due to methodological differences in the form of visualisation and standardisation of body position. However, it may also be explained by the different roles that vision might play in offering information of safety in superficial versus deep pain conditions. This explanation is consistent with the results seen in the magnification condition. While enhanced vision of the skin is likely to decrease threat with cutaneous noxious stimulation, enlargement of the sore muscle likely suggests greater damage and an increased need for protective responses. These results suggest that caution be applied to extending the results from exogenous pain studies to endogenous pain states. Future research on visually-induced analgesia should explore visual conditions that increase the perception of safety for the

individual and this line of research may offer a potential pathway for the integration of visual analgesia into the management of clinical pain.

References

Andersen H, Arendt-Nielsen L, Svensson P, Danneskiold-Samsoe B, Graven-Nielsen T. Spatial and temporal aspects of muscle hyperalgesia induced by nerve growth factor in humans. Exp Brain Res 2008;191: 371-382.

Bishop MD, Horn ME, George SZ, Robinson ME. Self-reported pain and disability outcomes from an endogenous model of muscular back pain. BMC musculoskeletal disorders 2011;12: 35.

Bove GM, Zaheen A, Bajwa ZH. Subjective nature of lower limb radicular pain. Journal of manipulative and physiological therapeutics 2005;28: 12-14.

Diers M, Loffler A, Zieglgansberger W, Trojan J. Watching your pain site reduces pain intensity in chronic back pain patients. Eur J Pain 2015;18: 765.

Diers M, Zieglgansberger W, Trojan J, Drevensek AM, Erhardt-Raum G, Flor H. Site-specific visual feedback reduces pain perception. Pain 2013;154: 890-896.

Fernandez-Carnero J, Binderup AT, Ge HY, Fernandez-de-las-Penas C, Arendt-Nielsen L, Madeleine P. Pressure pain sensitivity mapping in experimentally induced lateral epicondylalgia. Med Sci Sports Exerc 2010;42: 922-927.

Gibson W, Arendt-Nielsen L, Graven-Nielsen T. Delayed onset muscle soreness at tendon-bone junction and muscle tissue is associated with facilitated referred pain. Exp Brain Res 2006;174: 351-360.

Giummarra MJ, Georgiou-Karistianis N, Verdejo-Garcia A, Gibson SJ. Feeling the burn: When it looks like it hurts, and belongs to me, it really does hurt more. Conscious Cogn 2015;36: 314-326.

Löffler A, Trojan J, Zieglgänsberger W, Diers M. Visually induced analgesia during massage treatment in chronic back pain patients. European Journal of Pain 2017;21: 1623-1631.

Longo MR, Betti V, Aglioti SM, Haggard P. Visually induced analgesia: seeing the body reduces pain. The Journal Of Neuroscience: The Official Journal Of The Society For Neuroscience 2009;29: 12125-12130.

Longo MR, Iannetti GD, Mancini F, Driver J, Haggard P. Linking pain and the body: neural correlates of visually induced analgesia. The Journal Of Neuroscience: The Official Journal Of The Society For Neuroscience 2012;32: 2601-2607.

Mancini F, Longo MR, Kammers MP, Haggard P. Visual distortion of body size modulates pain perception. Psychological science 2011;22: 325-330.

McCracken LM, Zayfert C, Gross RT. The Pain Anxiety Symptoms Scale: development and validation of a scale to measure fear of pain. Pain 1992;50: 67.

Moseley GL. I can't find it! Distorted body image and tactile dysfunction in patients with chronic back pain. Pain (03043959) 2008;140: 239-243.

Moseley GL, Parsons TJ, Spence C. Visual distortion of a limb modulates the pain and swelling evoked by movement. Current biology : CB 2008;18: R1047-1048.

Osumi M, Imai R, Ueta K, Nobusako S, Morioka S. Negative body image associated with changes in the visual body appearance increases pain perception. PLoS One 2014;9: e107376.

Ramachandran VS, Brang D, McGeoch PD. Size reduction using Mirror Visual Feedback (MVF) reduces phantom pain. Neurocase 2009;15: 357-360.

Ruscheweyh R, Marziniak M, Stumpenhorst F, Reinholz J, Knecht S. Pain sensitivity can be assessed by self-rating: Development and validation of the Pain Sensitivity Questionnaire. Pain 2009;146: 65-74.

Slater H, Arendt-Nielsen L, Wright A, Graven-Nielsen T. Experimental deep tissue pain in wrist extensors--a model of lateral epicondylalgia. European journal of pain (London, England) 2003;7: 277-288.

Slater H, Arendt-Nielsen L, Wright A, Graven-Nielsen T. Sensory and motor effects of experimental muscle pain in patients with lateral epicondylalgia and controls with delayed onset muscle soreness. Pain 2005;114: 118-130.

Slimani H, Danti S, Ptito M, Kupers R. Pain perception is increased in congenital but not late onset blindness. PloS one 2014;9: e107281.

Torta DM, Legrain V, Mouraux A. Looking at the hand modulates the brain responses to nociceptive and non-nociceptive somatosensory stimuli but does not necessarily modulate their perception. Psychophysiology 2015;52: 1010-1018.

Valentini E, Koch K, Aglioti SM. Seeing One's Own Painful Hand Positioned in the Contralateral Space Reduces Subjective Reports of Pain and Modulates Laser Evoked Potentials. Journal of Pain 2015;16: 499-507.

Wand BM, Tulloch VM, George PJ, Smith AJ, Goucke R, O'Connell NE, Moseley GL. Seeing it helps: Movement-related back pain is reduced by visualization of the back during movement. The Clinical Journal of Pain 2012;28: 602-608.

Wittkopf PG, Lloyd DM, Johnson MI. Changing the size of a mirror-reflected hand does not affect pain perception: A repeated measures study on healthy human participants. European Journal of Pain 2018;22: 527-537.

	Mean ± SD	Range
Gender: Male = 7, Female = 13		
Age (years)	26.4 ± 7.1	20 - 47
Pain Anxiety Symptoms Scale-20 (0 - 100)	17.0 ± 15.5	0 - 60
Pain Sensitivity Questionnaire (0 - 10)	2.6 ± 0.8	1.1 - 3.7
Pain intensity 24hr prior to testing	3.9 ± 0.5	3 - 5
Effect of magnification (-4 - +4)	1.8 ±0.7	1 - 3

Table 1 Demographic and questionnaire data

SD: Standard Deviation

Session One

n = 22 - One participant excluded for taking analgesia for cervical pain

1. Complete PASS-20 and PSQ
2. Assess maximal isometric quadriceps strength
3. Determine weight required for session two
4. Establish testing position for session two and strength of magnification
5. DOMS inducing exercise protocol

48 hours

Session Two Eligibility Screening: n = 21

Score ≥ 3 on DOMS Likert Scale = proceed to session two (n = 20)

Score < 3 on DOMS Likert Scale = do not proceed to session two (n =1)

Session Two

n = 20

Randomised sequence of conditions

- Injured thigh
- Neutral object
- Contralateral thigh
- Magnified injured thigh

Start of exposure to visual condition

Weight attached to distal tibia

↓

Five minute fixation period to visual condition

↓

Three submaximal eccentric repetitions performed

↓

Subject rate pain intensity during each contraction

↓

Estimation of perceived magnification of thigh (Mag only)

↓

Weight removed for five minute washout period

↓

Repeat for next condition

Fig. 1 Study flow chart

PASS-20: Pain Anxiety Symptoms Scale-20

PSQ: Pain Sensitivity Questionnaire

DOMS: Delayed onset muscle soreness

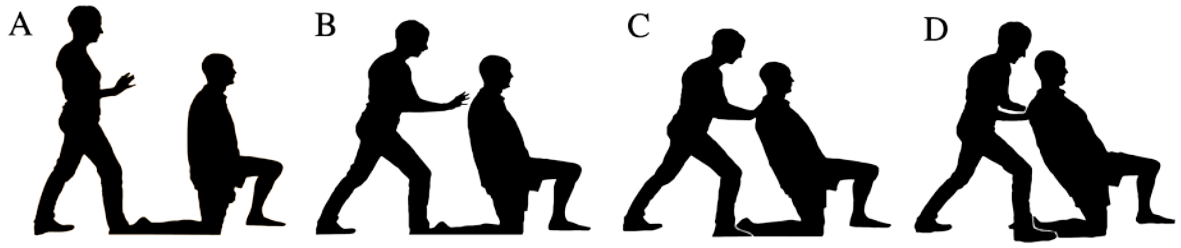

Fig. 2 The DOMS inducing exercise Starting position in half kneeling on non-dominant knee (A); The participant was instructed to lean backwards as far as they were comfortable (B); The researcher stood behind them and acted as a physical barrier to falling backwards (C); The researcher pushed the participant back to the starting position such that their return was as passive as possible (D). 150 repetitions were divided into five blocks of 3 sets of 10 repetitions. A 30 second rest period separated each set of 10 repetitions with and a two minute rest between each of the five blocks.

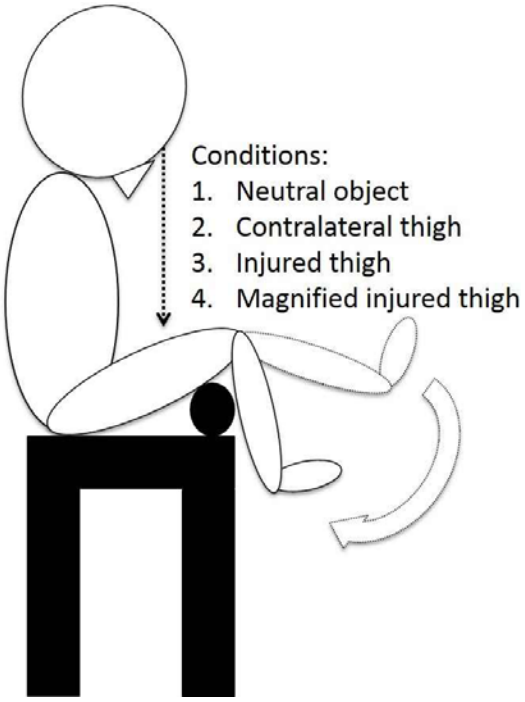

Fig. 3 Visualisation Tasks The four randomised visual conditions were: 1. Neutral object - participants viewed a box placed over the injured thigh. 2. Contralateral thigh – participants viewed the mid-thigh of the non-injured leg. 3. Injured thigh – participants viewed the mid-thigh of the injured leg. 4. Magnified injured thigh – participants viewed the injured thigh through magnifying glasses.

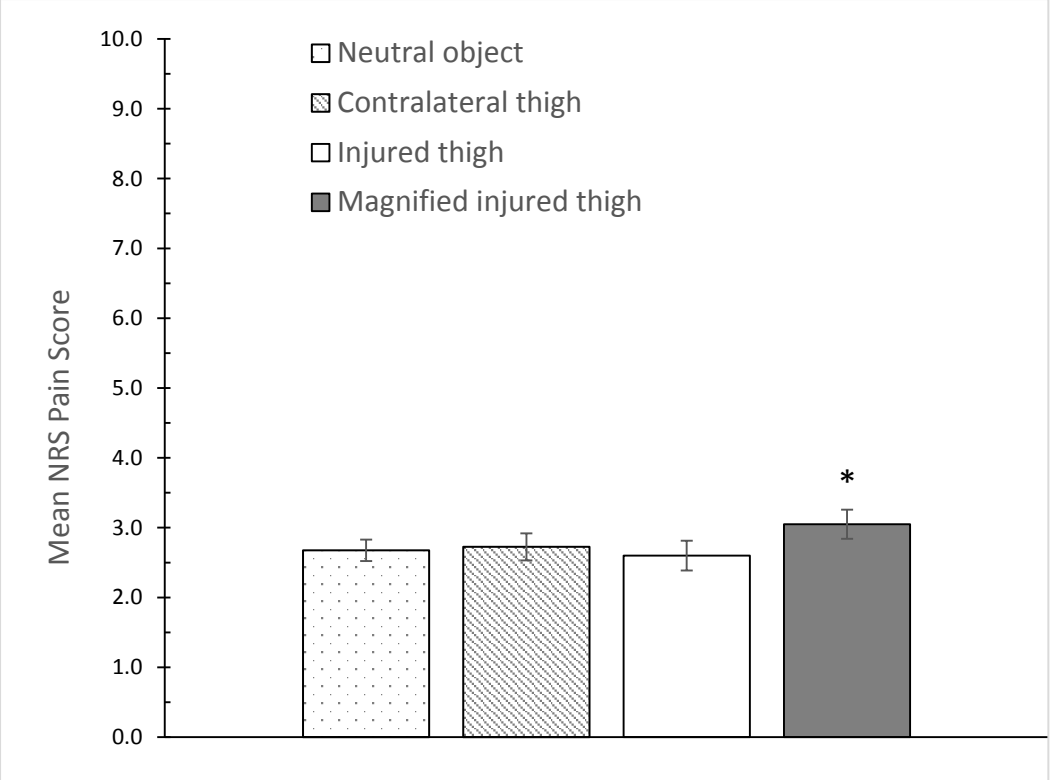

Fig. 4 Mean pain intensity scores for each visualisation task. Error bars represent the standard error of the mean. *Injured thigh v Magnified injured thigh, $p<0.001$.