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Research Report

Experimental hand pain delays recognition of the contralateral hand—Evidence that acute and chronic pain have opposite effects on information processing?

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Abstract

Recognising the laterality of a pictured hand involves making an initial decision and confirming that choice by mentally moving one's own hand to match the picture. This depends on an intact body schema. Because patients with complex regional pain syndrome type 1 (CRPS1) take longer to recognise a hand's laterality when it corresponds to their affected hand, it has been proposed that nociceptive input disrupts the body schema. However, chronic pain is associated with physiological and psychosocial complexities that may also explain the results. In three studies, we investigated whether the effect is simply due to nociceptive input. Study one evaluated the temporal and perceptual characteristics of acute hand pain elicited by intramuscular injection of hypertonic saline into the thenar eminence. In studies two and three, subjects performed a hand laterality recognition task before, during, and after acute experimental hand pain, and experimental elbow pain, respectively. During hand pain and during elbow pain, when the laterality of the pictured hand corresponded to the painful side, there was no effect on response time (RT). That suggests that nociceptive input alone is not sufficient to disrupt the working body schema. Conversely to patients with CRPS1, when the laterality of the pictured hand corresponded to the non-painful hand, RT increased ~380 ms (95% confidence interval 190 ms–590 ms). The results highlight the differences between acute and chronic pain and may reflect a bias in information processing in acute pain toward the affected part.

Theme: Motor systems and sensorimotor integration
Topic: Control of posture and movement, cognition

Keywords: Body schema; Laterality recognition; Information processing; Complex regional pain syndrome

1. Introduction

Recognition of the laterality of a pictured hand involves making an initial decision and mentally moving one's own hand to adopt the posture of the hand shown in the picture in order to confirm the accuracy of that decision [4]. The time required to make the laterality judgement is proportional to the angular rotation and the duration of the movement required to adopt the posture and the time it would take to imagine adopting it [23]. Imagined movements, executed movements, and recognition of hand laterality depend on an intact body schema, which is the real-time and dynamic representation of one's body in space, constructed from sensory input and integrated with motor processes [12].

People with unilateral upper limb chronic regional pain syndrome type 1 (CRPS1) take longer to recognise the laterality of a pictured hand if the pictured hand corresponds

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to their affected side [21,29,30]. It has been proposed that the cause of this increased RT is a disrupted body schema caused by nociceptive input. We have found a moderate relationship between duration of CRPS1 and the extent of the delay in RT to recognise the affected hand [21]. That finding indirectly offers some support for the proposal because in other groups the duration of symptoms relates to the extent of cortical reorganisation in primary sensory cortex, which in turn is argued to provide a neural correlate of body schema [11]. However, we also found a strong relationship between the RT for each picture and the predicted level of pain that would occur if the patient adopted the posture shown in the picture, which raises the possibility that a guarding-type mechanism contributes to the delay.

Other factors may contribute to the delay in patients with chronic CRPS1. For example, chronic CRPS1 is associated with profound changes in the organisation of the primary sensory cortex, in which the representation of the affected limb is smaller than that for the opposite limb [14,17]; up to 50% of CRPS1 patients demonstrate hemisensory deficits [28] which is consistent with findings of neglect-like symptoms [7] and impaired self-perception of the affected area [6] in these patients. Finally, chronic pain is characterised by complex issues from across cognitive, behavioural, and emotional domains, all of which may feasibly impact on the self [16].

Thus, nociceptive input is one of many factors that may affect RT to recognise hand laterality in people with CRPS1. If delayed RT in patients simply reflects the disruptive effect of nociceptive input on body schema, then acute pain elicited experimentally should impart a similar effect. To investigate this issue, we conducted three experiments. The first study aimed to determine the temporal and perceptual characteristics of hand pain elicited by injection of hypertonic saline into the thenar eminence. The second study evaluated the effect of experimental hand pain on recognition of hand laterality. The third study evaluated the effect of experimental elbow pain on recognition of hand laterality. Acute pain in a distinct but immediately proximal segment should impart a similar effect because the body schema for distal segments depends upon a frame of reference of a more proximal segment [3,18]. Thus, we hypothesised that recognition of hand laterality is delayed during experimentally induced hand pain and during experimentally induced elbow pain when the laterality of the pictured hand corresponds to the injected side.

2. Materials and methods

2.1. Subjects

Eleven (5 females) subjects participated in study one, eighteen (11 females) subjects participated in study two, and a further seventeen (8 females) participated in study three. All subjects were asymptomatic and healthy at the time of testing. Subjects were excluded if they had any orthopaedic or neurological disorder of the upper limb, were visually impaired or had any pain prior to testing. Written informed consent was obtained from all subjects and the studies were approved by the institutional research ethics committee and conformed to the Declaration of Helsinki.

2.2. Protocol study 1. Experimental hand pain—bench study

Bench studies were conducted to evaluate the time course and perceptual characteristics of hand pain elicited by intramuscular injection of hypertonic saline (5% NaCl). A 0.4-ml bolus was injected with a 30G needle over 5 s, 1 cm medial to the base of the first metacarpal at a depth of ~1 cm. Participants were asked “How intense is your pain?” to which they responded using an 11-point numerical rating scale (NRS) anchored with ‘no pain’ (0) and ‘worst possible pain’ (10). The NRS was completed 10, 20, and 30 s after injection and then every 15 s until pain returned to zero. Subjects completed a McGill Pain Questionnaire [20] relating to the pain as it was at its strongest. The protocol was repeated for the opposite hand on a separate day.

2.3. Protocol study 2. Hand laterality recognition during experimental hand pain

Using an established protocol [21], fourteen photographs of a right hand in a variety of postures were digitally mirrored to construct otherwise identical pictures of a left hand, to form a bank of 28 pictures.

An in-house software program was developed so that hand pictures were presented in random order, at 4-s intervals, on a monitor in front of the sitting participant. Each picture was displayed twice. Participants responded by pressing a button as quickly as possible according to whether they recognised the pictured hand to be a left hand or a right hand. Emphasis was placed on the speed and accuracy of performance.

After habituation to the task (two trials), an initial control trial was conducted followed by an experimental trial during experimentally induced hand pain, elicited using the protocol described for the bench study. The hand recognition task was commenced 30 s after withdrawal of the needle. This was based on the results of the bench studies that indicated that 90% of subjects had reached maximum pain intensity by this time. For control and experimental trials, the non-injected hand pressed the button.

The hand to be injected was determined by a random numbers table. Thirty minutes after the experimental trial and when subjects were pain free on all movements, another control trial was conducted. The procedure was repeated for the opposite hand on a separate day.

Trials were rejected if the proportion of incorrect responses (i.e., the laterality of pictured hand was judged incorrectly) was >10%. The response time (RT) to recognise the laterality of the pictured hand, and the difference in RT

between experimental and initial control trials, were used for analysis.

2.4. Statistical analysis

All statistics were performed using SPSS 11.0.0 (SPSS, Chicago, IL, USA). Differences between injected hands (order and dominance), and between males and females, were tested with *t* tests. Because the data did not demonstrate homogenous variance, a Friedman's two-way analysis of variance was used to compare RT between conditions and between pictures of the injected and non-injected hand. Scheffé tests were selected for post hoc analyses because it was the most conservative test for which the data satisfied all assumptions. Two linear regressions evaluated the relationship between McGill Pain Questionnaire sub-scores (independent variables) and the difference in RT between control and experimental trials (dependent variable) for recognition of the injected and non-injected hand. Significance was set at $\alpha = 0.05$.

2.5. Protocol study 3. Hand laterality recognition during experimental arm pain

Experimental arm pain was elicited by intramuscular injection of hypertonic saline (5% NaCl) into the common extensor origin ~1.5 cm distal to the lateral epicondyle of the dominant arm. The lateral epicondyle is a readily identifiable bony landmark. The needle was inserted slowly until bony contact was made and was then withdrawn 3 mm [31]. A 0.5-ml bolus was delivered via a 26G needle over 5 s. When pain had returned to zero, participants completed a McGill Pain Questionnaire [20] relating to the pain when it was at its strongest. The temporal and perceptual characteristics of arm pain induced using the current protocol have been presented elsewhere [31].

The hand laterality recognition task was performed according to the protocol described for study two such that a control trial was followed by an experimental trial during experimentally induced arm pain, and then a follow-up trial 30 min after injection.

2.6. Statistical analysis

All statistics were performed using SPSS 11.0.0 (SPSS, Chicago, IL, USA) and were analogous to those used in study one.

3. Results

3.1. Study 1. Time course and sensory characteristics of experimental hand pain

The time course of experimentally induced hand pain was consistent between subjects. Pain level peaked by 30 s at ~6/10 and returned to zero in ~7 min (range = 5–8 min) (Fig. 1). McGill Pain Questionnaire data were dominated by items from the sensory domain, "boring" and "cramping" were checked in >80% of cases and "dull" was checked in 60% of cases. Items from the evaluative section were checked in ~40% of cases and items from the affective section were checked in <10% of cases. The location of pain varied between subjects but was consistent between hands for individual subjects (Fig. 2). Most subjects described pain at the injection site and the first metacarpophalangeal joint. Pain commonly extended into the lateral thumb. Several subjects described pain on the medial aspect of the second digit and extending from the hand into the lateral forearm.

3.2. Study 2. Hand laterality recognition during experimental hand pain

Two subjects did not return for the second injection, which meant data were collected for 32 (17 left) hands. Accuracy of responses was greater than 90% throughout, which meant no data sets were rejected, and there was no difference in accuracy between conditions (mean ~95%, $P > 0.62$ for all). The mean ± SD maximum intensity of pain was 5.8 ± 0.9 and reported pain at completion of the hand laterality recognition task (duration ~4 min) was greater than four in all subjects. There were no differences in pain intensity or McGill Pain Questionnaire scores between hands or between males and females ($P > 0.47$ for all). RT to recognise the injected hand was not affected by experimentally induced pain (Scheffé's $P > 0.11$ for both). RT to recognise the non-injected hand was longer during pain than during either control condition [Friedman's $(5,27) = 53.3$, $P < 0.01$, Scheffé's $P < 0.01$ for both] (Fig. 3). During pain, RT to recognise the non-injected was longer than RT to recognise the injected hand (mean difference = 382 ms, 95% confidence interval = 590 ms–190 ms).

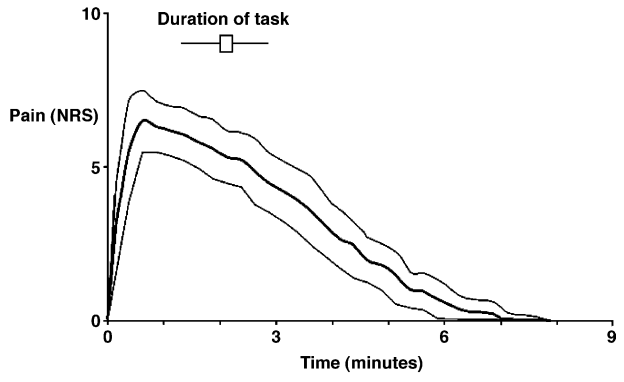

Fig. 1. Time course of pain. The mean ± standard deviation of the intensity of pain elicited by intramuscular injection of 5% hypertonic saline into the thenar eminence in eleven asymptomatic subjects (22 hands). Subjects completed an 11-point numerical rating scale (NRS) every 15 s until pain returned to zero.

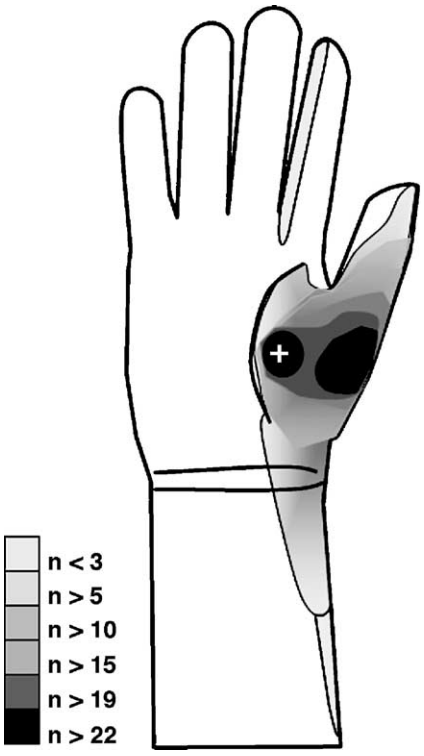

Fig. 2. Location of pain. The reported location of pain elicited by intramuscular injection of hypertonic saline into the thenar eminence (white cross). The degree of shading reflects the proportion of subjects reporting pain in that area. Note the common referral pattern to the first metacarpophalangeal joint.

3.3. Study 3. Hand laterality recognition during experimental arm pain

Data were collected from 17 subjects. The mean ± SD pain on the NRS was 6.3 ± 1.8, which was not different to experimental hand pain ($P = 0.32$) and the mean duration of pain was 10 ± 1.1 min, which was longer than experimental hand pain ($P = 0.04$). The reported pain on completion of the hand laterality recognition task was greater than 4 in all subjects. Taken together, the data suggest that there was no difference in the intensity or characteristics of the pain caused by injection at the hand and injection at the elbow. There was no effect of experimental condition on RT and there was no difference in RT between hands ($P > 0.32$ for all) (Fig. 4).

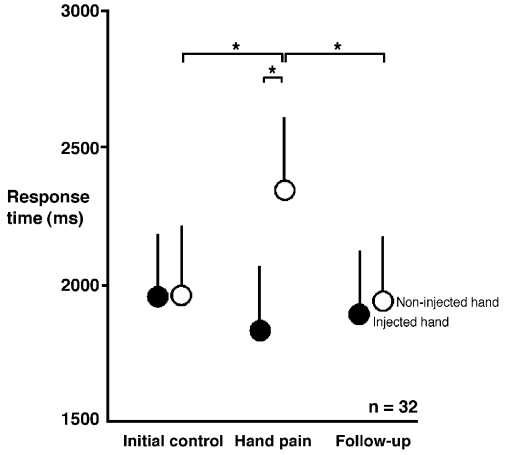

Fig. 3. Response time data during experimental hand pain. Mean (circles) and standard error of the mean (error line) response time to recognise the laterality of a pictured hand when the laterality of the pictured hand corresponded to the injected hand (filled circles) and to the non-injected hand (open circles), during initial control, experimentally induced hand pain, and follow-up control conditions. Asterisk denotes $P < 0.01$.

4. Discussion

These results show that nociception alone is not sufficient to delay the RT to recognise hand laterality. We hypothesised that both acute experimental hand pain and acute experimental elbow pain would delay the RT to recognise hand laterality when the laterality of the pictured hand was the same as the painful hand and the data clearly refute that hypothesis. The main finding was that acute hand pain had no effect on recognition of the painful hand, but it delayed recognition of the non-injected hand such that, during hand pain, the RT to recognise the non-painful hand was ~380 ms more than the RT to recognise the painful hand. This effect was not replicated by experimental arm pain of similar intensity and characteristics. These findings are both intriguing and important, for several reasons. First, the results suggest that nociceptive input and acute experimental pain do not disrupt the working body schema, because that would have increased RT to recognise the painful hand. Second, they suggest that acute experimental pain does not evoke guarding-type responses on premotor processes because that too would have increased RT to recognise the painful hand. Third, they raise the possibility that acute experimentally induced pain may evoke an information processing bias towards the painful hand. Finally, and importantly, the results highlight the fundamental differences in cognitive processes involved in the construction of pain and of the body schema.

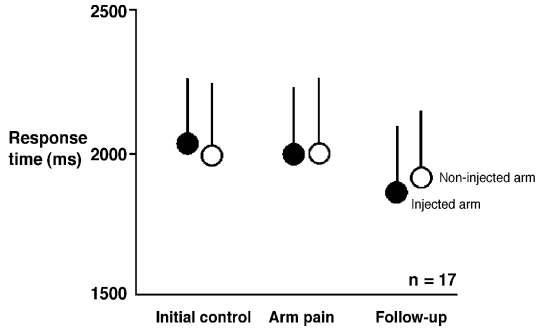

Fig. 4. Response time data during experimental arm pain. Mean (circles) and standard error of the mean (error line) response time to recognise the laterality of a pictured hand when the laterality of the pictured hand corresponded to the injected arm (filled circles) and to the non-injected arm (open circles), during initial control, experimentally induced arm pain, and follow-up control conditions.

The time course and perceptual characteristics of acute hand pain elicited by injection of hypertonic saline into the thenar eminence are consistent with a body of work using intramuscular injection at other anatomical sites [2,9,13,34]. The protocol achieved moderate to strong pain of sufficient duration to perform the hand laterality task (~2 min) and which subsided completely within ~7 min. Importantly, the intensity of the pain was comparable to that reported by CRPS1 patients.

However, the current work highlights two fundamental differences between the pain elicited here and chronic non-experimental pain. First, the quality of the pain appeared to be different. The McGill Pain Questionnaire data were dominated by sensory characteristics and affective characteristics were reported in <10% of instances, whereas in CRPS1 patients, affective and evaluative characteristics are usually reported [8]. Second, the current study used experimentally induced pain. This distinction between experimental and non-experimental pain presents a paradox to pain research because it is not possible to accurately impart the threat value of non-experimental pain, including its unknown time course, unknown underlying cause, and unknown possible consequences. This issue does not threaten the main finding of the current work but it should be remembered when extrapolating these results to patients.

The main finding of the current work was that acute hand pain delayed RT to recognise the laterality of the non-painful hand, although there was no decrease in the accuracy of responses. The mechanism by which this occurs is not clear but extensive work by Parsons (see Parsons [24] for review) offers a likely explanation. The hand laterality recognition task is thought to involve an initial pre-conscious perceptual analysis of hand shape and provisional decision, which is followed by mental manoeuvring of that hand to match the stimulus and thus confirm the choice. In the uncommon event that the mental manoeuvre reveals that the initial pre-conscious decision was incorrect, the opposite hand is manoeuvred to confirm the new choice. This situation would cause a delay in RT. According to that model, our data suggest that when the hand is painful, there may be a bias in information processing towards the painful hand.

Different types of information processing bias may be involved. An increase in RT for the opposite hand rather than a decrease in RT for the painful hand, would suggest disrupted disengagement, rather than facilitated engagement, of attentional resources from the painful hand [32]. Alternatively, perhaps the results reflect an interpretation bias [25]. Interpretation bias is thought to occur when there is some ambiguity about the stimulus that is presented and there is more than one reasonable interpretation. For example, patients with chronic pain who are asked to spell the spoken word “pane” are more likely to spell out “pain” than “pane” [26]. The hand laterality recognition task may evoke interpretation bias as it relates to the constructed internal body schema, perhaps because the body schema for the painful hand becomes more accessible for executive action. One finding that is relevant to that possibility concerns the production of somatic sensations in response to visual information alone [22], which is thought to be mediated via bimodal visual–somatosensory cells [10]. There is some evidence that these cells are primed during acute pain [15], which may underlie the findings reported here. These possibilities are speculative and cannot be evaluated on the basis of the current data alone, but they appear worthy of further interest.

The results of the experimental elbow pain study are intriguing. They too refute the hypothesis that the effect of hand pain on laterality recognition simply reflects nociceptive disruption of the body schema. That is because we would expect to see a delay in RT to recognise the hand that corresponds with the painful arm, by virtue of the distal body schema being dependent on a more proximal frame of reference provided by the proximal part [3,18]. However, if altered RT during acute hand pain reflects a bias in information processing towards the painful hand, then a lack of effect during experimental arm pain suggests that this bias is specific to the body part involved. If bimodal visual–somatosensory cells are involved, as appears feasible, we may have observed an effect of experimental elbow pain if the pictures included the elbow or the task involved recognition of arm laterality. Alternatively, perhaps the current study was underpowered to detect an effect of experimental elbow pain. Certainly, the cortical representation of the elbow is small compared to the hand, which may feasibly reduce an effect such as that observed here. Although it is not clear that the area of cortical representation is important and we did not see any obvious trend in the elbow data, this possibility cannot be excluded.

The main finding of this work contrasts with what is observed in patients with CRPS1—an increased RT to recognise the painful hand. One interpretation of this contrast is that CRPS1 involves an opposite bias in information processing—*away* from the painful hand. That would be consistent with findings of hemisensory deficit [28] and neglect-like symptoms [7] in CRPS1 patients. Perhaps the hand laterality recognition task reflects a quantified account of such clinical findings. Notably, patients with diagnosed neglect perform badly at this task [5], which lends some support to that possibility. Another finding that is relevant to this issue is that physical treatments, for example, mirror movements that appear to be effective for CRPS1, (i) involve graded and sustained attention to the affected part, and (ii) are also effective in improving motor and functional recovery after stroke (see [22] for review). Thus, the opposing nature of the current results and previous data from CRPS1 patients may also reflect the particular characteristics, in addition to pain, of CRPS1.

The pain-relieving effect of mirror movements in people with CRPS1 [19] and phantom limb pain [27] is intriguing and may be relevant to our results. It has been suggested that

the effect of mirror movements in CRPS1 and phantom limb pain is due to reconciliation of motor output and sensory feedback [19]. That suggestion builds on the hypothesis that ongoing pain in the absence of tissue damage is caused by incongruence between the intent to move and sensory feedback about the outcome of the movement [11], which is analogous to the so-called reafference principle [33]. The hypothesis states that because the cortical representation of the body is inaccurate in chronic pain, then feedback about any movement will be similarly inaccurate and thus continue to cause pain until it is corrected. Perhaps a delay in recognising the painful hand in CRPS1 reflects an unconscious compensatory mechanism whereby the body schema is made less accessible in order to avoid provocation. On the other hand, perhaps performance of the hand laterality recognition task involves access to alternate body schema held elsewhere in the cortex. This possibility has been raised by the finding in amputees with phantom limb pain that caloric stimulation transiently evokes an accurate and pain-free phantom [1]. These possibilities are speculative but worthy of further investigation.

In summary, acute hand pain does not delay recognition of the laterality of a pictured hand when the laterality of the pictured hand corresponds to that of the painful hand. In contrast, when the laterality of the pictured hand corresponds to the non-painful hand, RT is increased. These findings suggest that the delay in RT to recognise the painful hand, observed in CRPS1 patients, does not simply reflect nociception disrupting the working body schema. Rather, there may be several processes involved. Importantly, the pain evoked here was different to that evoked in non-experimental situations and to chronic pain, which is associated with myriad psychosocial factors that are likely to impact on the cognitive production of body schema. Notwithstanding, the current results offer new hypotheses with regard to the findings in CRPS1. Those hypotheses relate to information processing mechanisms and the accessibility or otherwise of the working body schema for the affected part.

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