



Expectation of pain replicates the effect of pain in a hand laterality recognition task: Bias in information processing toward the painful side?

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Abstract

Background: People in pain, or expecting pain, sometimes bias their attention towards pain-relevant cues. Perhaps they also bias their attention towards the body part in question.

Aim: To determine if experimentally induced pain, and the expectation of pain, involve an information processing bias towards the hand in question.

Methods: Seventeen asymptomatic subjects performed a hand laterality recognition task during three conditions: control, during hand pain induced by intramuscular injection of hypertonic saline (pain), and during expectation of hand pain, induced by isotonic saline injection (expectation). Mean response time (RT) was determined for three 45 s epochs within each condition and RT was compared between hands, conditions and epochs using a $2 \times 3 \times 3$ repeated measures multivariate analysis of variance.

Results: There was a hand \times condition interaction and a hand \times condition \times epoch interaction ($p < 0.05$ for both). RT to recognise the opposite hand was ~ 600 ms longer during epochs when subjects were in pain or expected pain than during control trials. During those epochs, RT to recognise the opposite hand was ~ 600 ms longer than RT to recognise the injected hand, which was consistent across conditions and across epochs.

Conclusions: Both pain and the expectation of pain increased RT to recognise the opposite hand. The findings are consistent with a bias in information processing toward the painful or impending painful hand.

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Keywords: Response time; Attention; Body schema; Hypertonic saline

1. Introduction

Patients with chronic pain demonstrate bias in information processing towards pain and injury-related cues. It has been proposed that bias can occur in the allocation of attentional resources, so-called 'attentional bias',

in interpretation of ambiguous cues or cues which may have one of two sensible interpretations, 'interpretive bias', and in the recall and recognition of cues, 'memory bias' (Pincus and Morley, 2001). There is a large amount of literature in this area (e.g., Asmundson et al., 1997; Crombez et al., 2000; Eccleston, 1995; Eich et al., 1990; Keogh et al., 2001a; Pearce and Morley, 1989; Roelofs et al., 2003; Snider et al., 2000; Wright and Morley, 1995) and the data are not straight-forward (see, Eccleston and Crombez, 1999 for review). Pincus

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and Morley (2001) proposed the schema enmeshment model with which to investigate and understand the nature of information processing bias associated with chronic pain. Inherent to that model are three schema: pain, illness and the self. A strength of that model is that it accounts for complex interactions between those schema. A limitation of that model is that it does not address information processing biases with regards to the physical self. For example, it would seem sensible to prioritise sensory information regarding a particular body part if that body part was under threat.

We have recently become interested in this issue because of a number of findings from people with complex regional pain syndrome. People with complex regional pain syndrome of one hand take longer to recognise a pictured hand if it corresponds to their affected side (Moseley, 2004b,c; Schwoebel et al., 2001). Extensive work by Parsons (2001) suggests that when we recognise a pictured hand as either a left- or right-hand, we initially make a rapid selection of one of two possible responses and then mentally manoeuvre our own hand to match the position of the pictured hand in order to confirm that initial selection. That is called the confirmation method (Parsons, 1987). The hand laterality recognition task therefore, provides a measure of the integration between information processing, working body schema and premotor processes, which implies that in people with complex regional pain syndrome there is disruption in one or more of those processes. Early work proposed that this effect occurred because pain disrupted the body schema (Schwoebel et al., 2001), yet we have shown that experimentally induced pain does not affect RT to recognise the painful hand. Rather, it increases RT to recognise the opposite hand (Moseley, 2004a). Thus, during experimental hand pain, there seems to be no disruption of working body schema of the painful hand, nor is there disruption of the integration of working body schema with motor processes. In fact, increased RT for the non-painful hand probably reflects an increased likelihood of incorrectly selecting the painful hand and then having to change the selection when the mental manoeuvre of that hand does not confirm the initial choice. This increased likelihood of incorrectly selecting the painful hand may reflect a bias in processing information in the somatic domain that is similar to that discussed for word cues (Pincus and Morley, 2001). If the delay in RT observed during experimental hand pain reflects a bias in information processing, it should be replicated by the expectation of hand pain. Van Damme et al. have demonstrated an effect of impending pain on information processing using a spatial cueing task in which coupling a painful stimulus with a spatial cue disrupted disengagement from that cue (Van Damme et al., 2004).

The current study aimed: (i) to replicate previous findings of a delayed RT to recognise the non-painful

hand during experimentally induced hand pain; (ii) to determine whether the expectation of pain has the same effect. We hypothesised that the mean RT to recognise the laterality of the non-injected hand would be increased during hand pain and during the expectation of hand pain.

2. Methods

2.1. Subjects

Twenty-one right-handed (11 females) healthy subjects (mean \pm standard deviation age = 30.58 ± 10.42) volunteered for the study. Subjects were excluded if they had any orthopaedic or neurological condition of the upper limb, if they were visually impaired, had been diagnosed with dyslexia or had difficulty with a rapid naming task, or if they had any pain on the day of testing. Subjects were screened prior to testing for unhelpful pain-related cognitions (>24 on the pain catastrophising scale, PCS, Sullivan et al., 1995) or signs of somatic hypervigilance (>7 on the modified somatic pain questionnaire, MSPQ, Main, 1983). Written informed consent was obtained from all subjects. The study was approved by the university research ethics committee and conformed to the National Statement on Ethical Conduct in Research Involving Humans by the National Health and Medical Research Council of Australia.

2.2. Protocol of study

2.2.1. Injection of hypertonic saline to elicit experimental hand pain

A 0.4 ml bolus of hypertonic saline (5% NaCl) was injected with a 30 G needle over 5 s, 1.5 cm medial to the base of the first metacarpal at a depth of approximately 1 cm. The sensory profile of this stimulus has been evaluated previously (Moseley, 2004b). The laterality of the injected hand was alternated between participants.

2.2.2. Injection of isotonic saline to elicit the expectation of experimental hand pain

Subjects were advised to return 30 min after the first injection. As long as there were no residual symptoms and consent was not revoked, the second injection was then performed. It has been previously determined that there is no effect on RT of this second (isotonic saline) injection when it is not associated with the expectation of pain (Moseley, 2004a). Subjects were advised that the second saline injection was identical to the first injection but had a slightly different sensory profile. Specifically, subjects were told that the second injection had a latency of between 15 and 45 s for the onset of pain but otherwise pain was of similar intensity and duration

as that caused by the first injection. The first injection procedure was repeated, such that an identical bolus, but this time of isotonic saline, was injected at the same site.

2.2.3. Procedure

The hand recognition task was composed of fourteen photographs of a right-hand in a variety of postures, which were digitally mirrored to produce otherwise identical pictures of a left-hand, to form a total of 28 pictures. Using Matlab 6.5 (release 13, Mathworks, Natic, MA, USA), hand pictures were presented in random order on a monitor in front of the seated subject. It was explained that the task was to be performed as quickly and as accurately as possible. Subjects responded by pressing the left or right mouse button to indicate whether they recognised the pictured hand to be a left-hand or a right-hand. A new picture was displayed 5 s after the previous picture.

After two practice trials for which data were not analysed, subjects performed the hand laterality recognition task during three conditions: control, pain and expectation of pain. The control condition was conducted first in all cases and then subjects were advised about the effects of hypertonic saline and the likely duration of pain. Prior to both the pain and expectation conditions, using a numerical rating scale (NRS), subjects were asked “On a scale of 0–10 with 0 being ‘no pain’ and 10 being ‘worst possible pain’, what are you expecting to experience with this injection?” Following those conditions, subjects were asked, “on a scale of 0–10, with 0 being ‘no pain’ and 10 being ‘worst possible pain’, what was the worst pain you experienced with that injection?”

On completion of the experiment, subjects were debriefed as to the true purpose of the study and the importance of maintaining naivety in order to create a genuine expectation of pain.

2.3. Statistical analysis

To verify previous findings of a delayed RT to recognise the opposite hand during experimentally induced hand pain, mean RT across all trials was used for analysis. To determine if the expectation of hand pain has the same effect as hand pain, mean RT during three consecutive 45 s epochs was used for analysis. This duration was selected because in our manipulation subjects were advised that the onset of pain occurred between 15 and 45 s. Thus, any effect of expected pain should subside when the expected latency (<45 s) of the onset was surpassed.

All statistics were performed using SPSS 11.0.0 (SPSS, Chicago, IL, USA). Kolmogorov–Smirnov and visual inspection of the data verified their normality, which meant that parametric statistics were appropriate. A two (hand) \times three (condition) \times three (epoch) re-

peated measures multivariate analysis of variance (MANOVA) compared the effect of pain and expectation within and between conditions. A *t* test compared recognition of left- and right-hands during control trials. We did not correct for this additional measure because we wanted to maximise the chance of detecting a difference between hands in control conditions.

3. Results

3.1. Subjects

No subjects were excluded on the basis of the MSPQ or PCS data (mean \pm SD for MSPQ = 3.0 ± 0.3 and for PCS = 15.2 ± 7.9). Three subjects revoked consent prior to the second injection because of excessive symptoms and one data set was lost due to an unforeseen technical problem. Thus, full data sets were obtained from 17 (9 female) subjects. Mean \pm standard deviation (SD) NRS for maximum pain was 5.2 ± 2.0 after the first injection and 0.7 ± 0.7 after the second injection. Mean \pm SD NRS for the expected maximum pain was 5.1 ± 2.3 for the first injection and 5.4 ± 2.1 for the second injection, which implies that our manipulation was effective.

3.2. Hand laterality recognition task

During control trials, there was no difference in mean RT between recognition of left-hands and recognition of right-hands ($p > 0.42$). For the repeated measures MANOVA, there were no main effects but a hand \times condition interaction ($F(2, 15) = 5.50$, $t = 0.73$, $p = 0.016$) and a hand \times condition \times epoch interaction ($F(4, 13) = 3.50$, $t = 1.08$, $p = 0.038$). Data for each condition, hand and block are shown in Fig. 1. The following results directly relate to the experimental hypotheses: for recognition of the opposite hand: (i) mean RT during the first 45 s epoch was longer during pain (mean \pm standard deviation, SD = 2.42 ± 0.58 s) and during expectation (2.30 ± 0.59 s) than it was during control (1.74 ± 0.73 s; $t > 3.11$, $p < 0.01$ for both); (ii) mean RT during the second 45 s epoch was longer during pain (2.37 ± 0.72 s) than it was during expectation (1.95 ± 0.54 s) or control (1.78 ± 0.59 s; $t > 1.79$, $p < 0.05$ for both); (iii) mean RT during the first 45 s epoch of expectation was longer (2.30 ± 0.59) than during the second (1.95 ± 0.54 s) or third 45 s epoch of expectation (1.79 ± 0.57 s; $t > 1.85$, $p < 0.05$). Comparison between hands corroborates those results: mean RT was greater for the opposite hand than for the injected hand: (i) during the first and second 45 s epochs of the pain condition ($t > 3.35$, $p < 0.01$ for both); (ii) during the first 45 s epoch of the expectation condition ($t = 4.70$, $p < 0.01$) (Fig. 1).

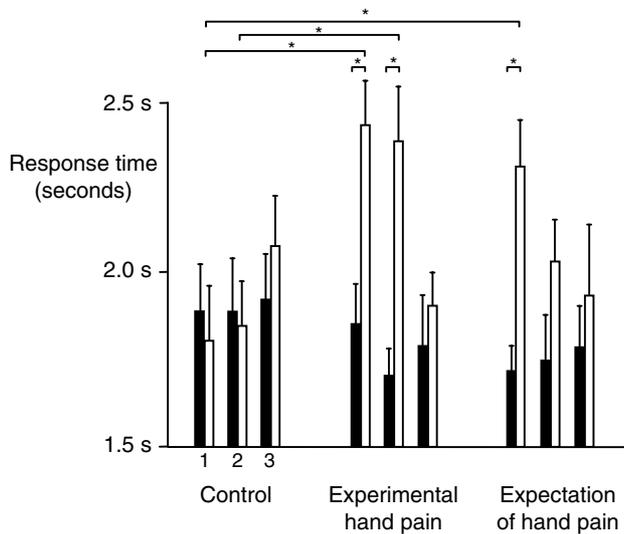


Fig. 1. Mean (columns) and standard error of the mean (error bars) for response time (RT) to recognise the laterality of hands that coincided with the injected (filled columns) and opposite (open columns) hand for the first (1), second (2) and third (3) 45 s epoch. Asterisk denotes significant difference at $p = 0.05$.

4. Discussion

In this study, we aimed to determine whether the effect of pain, and the expectation of pain, was consistent with an information processing bias towards the painful part. We proposed that if the delay in RT observed during experimental hand pain reflects a bias in information processing, it should be replicated by the expectation of hand pain. We therefore hypothesised that mean RT to recognise the laterality of the non-injected hand would be increased during hand pain and during the expectation of hand pain. The results uphold that hypothesis and therefore support the proposal. That position is supported by three results. First, RT for the non-injected hand was greater when subjects were in pain than when they were not and also when they expected pain when they did not. Second, RT for the non-injected hand was greater than that for the injected hand during those same epochs. Third, mean RT for the injected hand remained stable across conditions and epochs.

The results are consistent with previous findings obtained using this laterality recognition task during control trials (Moseley, 2004c) and during experimentally induced pain (Moseley, 2004a). In each case, the delay induced by hand pain was in the order of 400–700 ms and there was no effect on RT to recognise the painful hand. We proposed that such a delay probably reflects an increased likelihood of incorrectly selecting the painful hand and then having to change the selection when the mental manoeuvre of that hand does not confirm the initial choice. That process may reflect an attentional bias, via a disengagement effect whereby the central ner-

vous system has difficulty allocating attentional resources away from the painful hand. Van Damme et al. (2004) demonstrated such a disengagement effect, which was evoked by the expectation of a noxious cutaneous stimulus, on spatial attention. They also showed a facilitatory effect, whereby attention was transiently engaged by the impending stimulus, but that facilitatory effect was also observed with impending non-painful cutaneous stimulus. The authors made two proposals: that the salience of an impending stimulus influences engagement of attention, and that its threat value determines disengagement of attention. Our results are consistent with the latter proposal but inconsistent with the former: we observed an increased RT to the non-injected hand, which is not observed after injection of non-painful isotonic saline (Moseley, 2004a), but we did not observe a decreased RT to the injected hand in either case. Because isotonic saline injection does not change RT either before or after injection (Moseley, 2004a), we contend that the current findings do not reflect a general effect of cognitive appraisal (e.g., “something is going to happen to my hand”).

An alternative explanation of our results is that hand pain evoked an interpretation bias on information processing (Pincus and Morley, 2001). Interpretation bias is thought to occur when there is some ambiguity about the stimulus that is presented and there are two (or more) reasonable interpretations. For example, chronic pain patients asked to spell the spoken word “pane/pain” are more likely to spell out “pain” than “pane”, purportedly because they have an interpretation bias towards pain-related cues (Pincus et al., 1994). The initial decision during recognition of hand laterality involves a choice between two reasonable interpretations and it is not until motor processes confirm that choice that the central nervous system delivers a definitive response. As such, our results may reflect bias in the initial decision such that the working body schema of the painful hand is more accessible than that of the other hand.

A final possibility is that anxiety or fear caused a delay in RT. Rhudy and Meagher (2000) showed decreased pain threshold when an impending pain stimulus was possible and increased pain threshold when it was certain and unavoidable, situations they interpreted to reflect anxiety and fear, respectively. Further, we have shown that the effect of predictability of a painful stimulus was variable between individuals but was dependent on anxiety (Moseley et al., 2003), which would be consistent with the suggestion that different people are affected by potentially painful events in an individually specific manner that is dependent on the cognitive and emotional characteristics of the individual (Keogh et al., 2001a,b). That said, if the effects observed in the current study were mediated by global effects such as fear or anxiety, we would expect a similar impact on recognition of both hands, which we did not observe.

Thus, although those issues may have had subtle effects not detected here, they are unlikely to explain the main findings.

The current results are contrary to those observed in patients with CRPS1, in which several studies have shown a delay to recognise the affected hand (Moseley, 2004b,c, 2005; Schwoebel et al., 2002, 2001). Interpretation of those data according to the current work is problematic because (i) experimentally induced pain is fundamentally different to non-experimental pain, and (ii) CRPS1 involves physiological changes that are not observed in non-CRPS1 musculoskeletal pain (see, Janig and Baron, 2004 for review). However, a bias in information processing opposite to that observed here would be consistent with other findings from patients with CRPS1. For example, patients with CRPS1 demonstrate disruption in sensory processing that extends to the affected quadrant or to a hemispacial distribution in up to 77% of cases (Rommel et al., 1999) and they often report neglect-like symptoms such as “my limb feels foreign to me” (Forderreuther et al., 2004; Galer and Jensen, 1999). Further research is required to evaluate the possibility that such findings are mediated by changes in information processing.

One interesting issue raised by the current results is that if the expectation of pain results in an information processing bias towards the affected body part, it may actually increase the likelihood of pain eventuating. That possibility is broadly consistent with early social schema theories (Anderson and Pennebaker, 1980; Leventhal and Everhart, 1979) in which the expectation of pain is said to activate pain schemas that selectively filter and augment sensory input until perception matches expectation. Several studies have since shown that pain expectancies alone probably do not cause pain in the absence of nociceptive input (see, Crombez et al., 1994 for review and Bayer et al., 1991 for contrary view). However, it is difficult to exclude the possibility that sensory stimuli that approach the pain threshold may evoke pain if information processing is biased toward the body part in question. Such a self-fulfilling prophecy may be advantageous for acute noxious stimuli but disadvantageous in some chronic pain states, when the synaptic efficacy of pain mechanisms is already enhanced. In such states, an attentional bias toward the body part in question may be sufficient to activate the pain neurosignature (Melzack, 1996). Obviously, these possibilities are speculative and remain to be verified.

Interpretation of the current results should consider several aspects of the methodology. First, the sensory profile of experimental pain induced via intramuscular injection of hypertonic saline has been widely studied (e.g. Graven-Nielsen et al., 1997), including injection into the thenar eminence (Moseley, 2004b). It is well recognised that even though this type of experimentally induced pain simulates non-experimental pain, it re-

mains fundamentally different to non-experimental pain because it is known to not be dangerous, it is of a known time-course and a known cause. Generalisation of the current results should consider this limitation. Second, although the location of pain evoked by intramuscular injection of hypertonic saline into the thenar eminence is consistent between hands for an individual subject, it may differ between subjects in its distribution, referral pattern and intensity (Moseley, unpublished data). The current experiment would not have detected any subtle effects of these variations. Finally, the approach does not exclude the possibility that pain in a different body part may have the same effect. That said, if the effect was a general response to anticipating pain, it would not be limited to recognition of one hand, regardless of handedness, and it was previously shown that there is no effect of experimental elbow pain on RT to recognise hand laterality (Moseley, 2004b).

In summary, during the hand laterality recognition task, the expectation of pain had a similar effect to that imparted by pain, which supports the hypothesis. The effect was lost once the proposed latency for the onset of pain was surpassed. The results are consistent with the proposal that both pain and the expectation of pain impart an information processing bias toward the affected body part.

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