

Sensorimotor dysfunction after fracture - an exploratory study

Title - Sensorimotor dysfunction after limb fracture - an exploratory study

Short Title - Sensorimotor dysfunction after fracture - an exploratory study

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What's already known about this topic?

- Limb fracture can be associated with chronic pain.
- Recovery post-fracture is highly variable.
- The incidence of CRPS post-fracture is wide-ranging.

What does this study add?

In the immediate post-fracture period:

- Body Perception Disturbance is reported in the fractured limb.
- Imagined Movements of the fractured limb are less vivid and associated with pain

This study contributes to the incidence literature on CRPS.

Abstract

Background

Chronic pain is often associated with sensorimotor dysfunction but little is known about the early impact of limb fracture on sensory and motor performance. This study sought to assess these changes in patients with recent wrist and ankle fractures. A secondary aim was to determine the incidence of Complex Regional Pain Syndrome (CRPS) and its clinical features.

Methods

53 patients at a UK fracture centre underwent quantitative sensory testing (QST), motor imagery (MI) and body perception disturbance (BPD) assessments ≤ 5 weeks post-fracture (Time 1). Subjective evaluation of recovery and clinical examination for CRPS was conducted 5 weeks later (Time 2). Patient reported outcomes of pain, psychological distress and limb function were collected at Times 1 and 2, and six months after T1 (Time 3).

Results

QST at Time 1 demonstrated cold and pressure-pain hyperalgesia in the fractured limb compared to non-fractured side ($p < 0.05$). Imagined movements were reported as significantly more difficult to perform on the fractured side ($p < 0.001$). There was evidence of BPD in the fractured limb, similar to those found in CRPS. The incidence of CRPS was 9.4%; however individual signs and symptoms of the condition were commonly present (70% reported \geq one symptom). Only 33% of patients reported to being “back to normal” 6 months after fracture with 34% reporting on-going pain.

Conclusions

Limb fracture is associated with changes in pain perceptions, motor planning, and disruption to body perception. Signs and symptoms of CRPS, ongoing pain and delayed recovery post-fracture are common.

Introduction

Limb fracture is a relatively common injury with approximately 55,000 wrist and 60,000 ankle fractures per annum in the UK (Court-Brown *et al.*, 1998; O'Neill *et al.*, 2001; Van Staa *et al.*, 2001). Yet, it is a traumatic event often associated with pain and systemic disability beyond the local effect of the injury. For example, long-term disability and chronic pain have been reported in over 60% of limb fracture patients (Mkandawire *et al.*, 2002) and wrist fracture increases the odds of clinically important functional decline (Edwards *et al.*, 2010).

Limb fracture is also a known trigger for Complex Regional Pain Syndrome (CRPS) (Sandroni *et al.*, 2003; De Mos *et al.*, 2007). CRPS is a persistent pain condition, of unknown aetiology, with pain disproportionate to the inciting event, usually confined to the injured limb. It is characterised by extreme pain and sensory, motor and autonomic disturbances (Harden *et al.*, 2010). Altered sensory perceptions, including allodynia, paresthesias, dysesthesias, disrupted body perception and neglect or disownership of the affected body part, as well as psychological distress are also experienced (Frettlöh *et al.*, 2006; Lewis *et al.*, 2007; McCabe *et al.*, 2009; Lohnberg & Altmaier, 2013; Birklein & Schlereth, 2015). Motor impairment is characteristic of CRPS, reflecting dysfunction in motor planning processes (Maihöfner *et al.*, 2007; Schilder *et al.*, 2012; Bank *et al.*, 2013). This is considered, in part, to be mediated by distortion of mental image of the affected limb (Moseley, 2005; Lewis *et al.*, 2010), which has been reported to occur early in onset (Lewis *et al.*, 2007).

At an early stage after healing of a fracture, between 1% and 37% of patients demonstrate signs and symptoms of CRPS (Atkins *et al.*, 1990; Dijkstra *et al.*, 2003; Beerthuizen *et al.*, 2012; Moseley *et al.*, 2014) and many retain some degree of symptomatology a year or more after fracture (Field *et al.*, 1992; Beerthuizen *et al.*, 2012; Borchers & Gershwin, 2014). Treating a fracture often involves limb immobilisation, which in itself can generate sensory and motor problems that closely mimic those seen in CRPS, such as swelling, changes in skin temperature and pain sensitisation (Guo *et al.*, 2004; Terkelsen *et al.*, 2008).

Despite the literature, the full range of disturbances to sensorimotor function after fracture has yet to be described. For example, it is not known if imagined movements (a pre-cursor of actual movements within the motor pathway (Jeannerod & Frak, 1999) become disrupted, or if body perception is altered, and the potential impact of these changes, if present, on the patient's recovery trajectory. Furthermore, we do not know the prognostic implications of the presence or absence of CRPS-like symptoms post-fracture.

The purpose of this study was to explore the impact of limb fracture on sensory and motor systems in order to identify the frequency of observed changes in these systems in an early post-fracture cohort, and to examine their relationship with patient-perceived recovery. The secondary aim was to determine the incidence of Complex Regional Pain Syndrome (CRPS) and its clinical features.

Patients and Methods

A convenience sample was recruited from adult patients attending the outpatient fracture clinics at a large UK NHS University teaching hospital. Potential participants, with a confirmed diagnosis of unilateral ankle fracture or fracture of the distal radio-

ulnar complex, were recruited by the research nurse. Treatment was by cast immobilisation with or without fracture manipulation or by open reduction and internal fixation as indicated. Exclusion criteria included conditions in which comparison of the fractured to non-fractured limb was not possible (e.g., amputation or medical confirmation of unilateral sensory deficit), lack of understanding of written and verbal English, and inability to give full informed consent. The study received ethical approval by the Institutional Research Ethics Committee. Patients were informed that the purpose of the study was to identify the range of post-fracture experiences in order to inform future therapeutic approaches to recovery.

Over an 18-month period patients were recruited at 1-5 weeks post-wrist or ankle fracture. Following consent, Time 1 (T1) assessments were conducted within five weeks of fracture including collection of demographic data by the researcher. Time 2 (T2) assessments were completed 5-6 weeks after T1. The rationale for this was to allow for immobilisation and fracture healing to be complete and activities of daily living to be resumed. T1 and T2 assessments coincided, where possible, with routine clinic appointments. Time 3 (T3) assessments took place using postal questionnaires approximately 6 months after first assessment.

Measures

Demographic data collected included age, gender, educational attainment, employment status and co-morbidities. Additional data on fracture classification and management were recorded from patient notes.

Measures at T1 included the Brief Pain Inventory (BPI) (Cleeland & Ryan, 1994), the Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983), and, depending on the limb fracture, the Disability of Shoulder, Arm and Hand Questionnaire (DASH) (Hudak *et al.*, 1996) or the Lower Extremity Functional Scale (LEFS) (Binkley *et al.*, 1999).

Also conducted at T1 were quantitative sensory tests (QST); tests of motor imagery (MI) and administration of the Bath CRPS Body Perception Disturbance scale (BPD). For pragmatic reasons, and in order to minimize patient burden, these were not repeated at T2 and T3. Further details of the QST, MI and BPD protocols are given below.

Quantitative Sensory Testing (QST)

Employing a standardized protocol (Kemler *et al.*, 2000), mechanical and thermal stimuli were used to assess pressure pain and hot and cold pain in the fractured and non-fractured hand or foot. Prior to assessment a short practice session for each sensation was carried out to familiarise patients with procedure. Hot and cold pain thresholds (HP and CP) were measured using a MSA Thermotest (Somedic Sales AB, Sweden). For the hand, this assessment involved placing a thermode (2.5 x 5cm) in contact with the skin of the palmar aspect of the index finger. For the foot, the dorsal aspect of the great toe was used. The thermode had a resting temperature of 32°C, which was raised or lowered at a precise 0.5°C/s (Palmer *et al.*, 2000). The patient pressed a response button as soon as each sensation was perceived and the temperature at which they responded was recorded to the nearest 0.1°C. The thermode immediately returned to its resting temperature. The process was repeated 4 times for each sensation, with the mean of the final 3 thresholds used for all data analysis.

Finally, patients' mechanical pain threshold (MPT) was assessed in the same sites using the Algometer II (Somedic Production AB, Sweden) (Palmer *et al.*, 2009). A 1cm² probe was placed at right angles to the skin surface. The manual pressure applied to the skin was increased slowly at a rate of 10 kPa/second using the built-in slope indicator. The pressure was released as soon as the patient reported the 'very first sensation of pain'. This procedure was repeated again three times and the mean of these three measures taken as the MPT. The contralateral hand or foot provided control data for all QST assessments in order that differences between fractured and non-fractured side could be analysed for each of the sensations tested.

Motor Imagery - Assessment of limb laterality

A *Recognise CD Rom*© was used to show images of hands and feet in a variety of postures. Patients were asked to identify 28 randomly selected images of either hands or feet and to respond pressing a button as quickly as possible according to whether the pictured hand/foot was identified as right or left (Moseley, 2004). Emphasis was placed on speed and accuracy. The *Recognise CD Rom*© automatically recorded each patient's recognition time (RT) and accuracy for each image. Patients were asked to repeat the test 3 times and the mean accuracy and RT for images corresponding to a patient's fractured and non-fractured limb were recorded.

Motor Imagery - Assessment of perceived ability to perform and impact of imagined movement (IM) tasks

Patients were asked to close their eyes and to conduct imagined flexion/extension movements of each wrist/ankle in turn, starting with the non-fractured limb. A 1-7 Numeric Rating Scale (1=not at all, 7=very easy) was used to assess patients' perceived ability to perform these IMs (Moore & Leonardi-Bee, 2008; Gregg *et al.*, 2010). Care was taken with instructions not to bias patients towards any one preferred form of imagery. Patients were asked to rate any pain associated with the IM, using an 11-point Verbal Rating Scale (0=no pain, 10=worst pain imaginable) (Jennings *et al.*, 2009).

The Bath CRPS Body Perception Disturbance Scale

This scale provided a means of assessing the presence/absence, nature and extent to which body perception disturbances (BPD) were experienced in the fractured limb (Lewis & McCabe, 2010). The scale was developed for clinical use in CRPS and a maximum score of 57 represents severe BPD in CRPS. In a novel approach, we employed this measure to determine whether body perception disturbance might also be present after limb fracture.

At T2 the BPI, HADS, and DASH or LEFS were repeated. Data were also collected on subjective evaluations of recovery, using the 2-item satisfaction scale by Harris *et al.*, (2009). All patients were assessed for CRPS at T2 using the Budapest diagnostic criteria (Harden *et al.*, 2010), as this time point was considered appropriate for the early detection of CRPS features and is consistent with similar studies (Harden *et al.*, 2001; Pepper *et al.*, 2013). The assessment was by clinical examination and was performed by an experienced senior clinician.

The following data were collected at T3: BPI, HADS, LEFS/DASH, and subjective recovery ratings. A summary of the data collection timeline is given in FigureS1.

[INSERT FIGURE S1 HERE]

Statistical analysis and data management

We examined the data for changes in mood, pain and function over time. As the data set was small and non-normally distributed, change in BPI, HADS, LEFS and DASH scores were examined for statistical significance by applying Friedman's test. The nature and prevalence of altered sensory perception and motor function in the fractured limb in patients with recent wrist/ankle fracture were addressed by examining the differences between fractured and non-fractured limbs. Following inspection of the data, Wilcoxon tests were used to examine the QST data to determine the significance of any differences in pain thresholds between limbs. The relationship between self-reported recovery and limb function was assessed through correlational analyses. From the various statistical analyses, mean and/or median scores are reported, depending on the normality of the distribution of each respective variable. Between-groups comparisons for those with, and without CRPS were not calculated, due to the small sample size of the former group. Results from the drawing component of the Bath CRPS BPD scale were considered in terms of frequency of each distortion, and individual drawings were selected as illustrative examples. However, a substantial proportion of patients expressed difficulty in responding to the rating scale domain questions within this measure (detachment; proprioception; attention; emotional feelings; desire to amputate). These data were therefore considered potentially unreliable and were excluded from our analyses.

Results

Patient demographics and clinical characteristics (see Table 1)

Fifty-three patients were recruited with a mean age of 54 years (S.D. = 18 years); 36 (68%) were female; 36/17 (68/32%) had fractured a wrist/ankle with 13/40 fracturing their dominant side (24.5/75.5%); and the mean time since fracture at T1 was 31 days (S.D. = 12 days). Most had received conservative (57%), treatment with 43% having open reduction and internal fixation. All attended T1, and 50 attended at T2 (94%). Reasons for withdrawal from the study at T2 related to unwillingness or inability to attend a second appointment. Thirty-nine patients responded to the T3 postal questionnaire (74%).

[INSERT TABLE 1 HERE]

QST

Median thresholds of pressure, cold, and heat pain were calculated and compared for fractured and non-fractured limbs at T1. Median pressure pain thresholds were significantly lower in the fractured limb (median = 188.00 kPa, IQR = 142.00) than in the non-fractured limb (median = 208.00 kPa, IQR = 144.00) ($Z = -2.69$, $p < 0.01$), indicating localised pressure hyperalgesia in the fractured limb (Figure 1).

Although median cold pain thresholds were the same in both fractured and non-fractured limbs (5.00°C), results showed a significant difference between the limbs due to a wider interquartile range for the fractured limb (fractured limb IQR = 5.40, non-fractured limb IQR = 0.90; $Z = -2.34$, $p < 0.05$), indicating hyperalgesia to cold in the fractured limb. No differences in heat pain threshold were noted between limbs (fractured limb: median = 46.10°C, IQR = 5.28; non-fractured limb: median = 46.00, IQR = 5.15; $Z = -0.744$, $p > 0.05$).

[INSERT FIG. 1 HERE]

Motor Imagery

Accuracy and reaction times to limb laterality testing were similar between fractured and non-fractured limbs. Although the data (collected at T1) indicated that patients identified images of the fractured limb more quickly than for the non-fractured limb (fractured limb median = 1.99 seconds, IQR = 0.99; non-fractured limb median = 2.09 seconds, IQR = 1.13), this difference was not statistically significant. Similarly, while the data suggested patients identified the fractured limb more accurately than they did the non-fractured limb (fractured limb median = 78.84, IQR = 17.92; non-fractured limb mean = 74.67, IQR = 22.24), no significant difference was detected.

IMs of the fractured limb were significantly more difficult to perform than on the non-fractured side (fractured limb median = 4.00 “not easy/not hard”, IQR = 3.50; non-fractured limb median = 7.00 “very easy”, IQR = 2.00; $Z = -4.19$, $p < 0.001$). Although scores were low, patients reported significantly more pain when imagining movement on the fractured side than non-fractured (fractured side median = 0.50, IQR = 3.25; non-fractured side median = 0.00, IQR = 0.00, $Z = -4.30$, $p < 0.001$).

Body Perception Disturbance

For this study we focused on the drawing component of the BPD scale as a key indicator of BPD at T1. As illustrated in Figure 2, 66% of patients demonstrated some degree of BPD of the fractured limb with 8% reporting multiple differences between the fractured and non-fractured limbs and/or the loss of perception of a segment of the fractured limb. Examples of drawings in each of the possible categories are shown in Figure 3, together with the accompanying narratives of perceptual differences made by the patients in each example.

[INSERT FIGURE 2 HERE]

BPI & HADS

Table 2 shows median scores from the BPI and HADS at each of the study time points. Levels of pain intensity and interference were modest, even at their highest point, however 34% still reported ongoing pain at T3. Pain severity was found to lessen over time ($\chi^2(2, N=35) = 7.67$, $p < 0.05$) as did pain interference ($\chi^2(2, N=35) = 33.37$, $p < 0.001$). Of those patients reporting pain, responses indicated a decreasing trend for the relief provided by pain medications over time

Patients reported little psychological distress and, that which was reported, reduced over time ($\chi^2(2, N=37) = 12.77$, $p < 0.01$). Examination of HADS median scores suggested this change occurred after some delay, as it appeared to be associated with the reduction in distress scores between T2 and T3. Within the subscales, anxiety was low throughout, with no significant overall change over time. Levels of reported depression were also low. Even so, these decreased significantly over time ($\chi^2(2, N=37) = 29.02$, $p < 0.001$).

[INSERT TABLE 2 HERE]

Functional status of the fractured limb

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Self-reported function improved significantly over time, for both wrist and ankle fracture patients (DASH $\chi^2(2, N=23) = 35.83, p < 0.001$; LEFS $\chi^2(2, N=9) = 14.89, p < 0.001$, see Table 2).

Recovery

Patients' satisfaction with the progress of their recovery showed increasing satisfaction over time. The change in median rating from "somewhat satisfied" at T2 to "very satisfied" at T3 was significant ($Z = -1.99, p < 0.05$). Over the same time points, the proportion of patients who reported they were "very satisfied" increased from 42% to 64%. At T2 only 6% of patients perceived they were "back to normal", this increased to 33% by T3. Similarly 32% reported having "significant problems" at T2 and this figure reduced to 15% by T3.

Correlation analyses indicated moderate to strong significant associations between recovery ratings at T3 and the functional scores of both wrist and ankle fracture patients at each time point (T1 wrist fracture $r = .617, p < 0.01$, ankle fracture $r = -.767, p < 0.01$; T2 wrist fracture $r = .647, p < 0.01$, ankle fracture $r = -.650, p < 0.05$; T3 wrist fracture $r = .687, p < 0.01$, ankle fracture $r = -.812, p < 0.01$). High scores on the DASH and low scores on the LEFS indicate greater disability.

CRPS diagnostic criteria

Assessed at T2, five patients (9.43%) met the International Association for the Study of Pain (IASP) diagnostic criteria for CRPS (Harden *et al.*, 2010). The mean age of this cohort was 62 years (range 46-75 years), four were female, and all had suffered a wrist fracture. Two had received conservative treatment, with the remainder undergoing surgery. On the 0-10 visual analogue scale of the BPI, these patients reported considerably higher pain severity and interference for at least 3 months after fracture than indicated by the median scores of the whole sample (CRPS patients median pain severity T1 = 3.75, T2 = 4.25, interference T1 = 6.43, T2 = 3.71; whole sample median pain severity T1 = 1.75, T2 = 1.25; interference T1 = 3.00, T2 = 1.14). CRPS patients also reported higher median levels of psychological distress (T1 = 17.00, T2 = 19.00) than were indicated by the whole sample (T1 = 10.00, T2 = 10.00).

Although the recovery measures data showed improvement with satisfaction over time, patients with CRPS (T2 $n=5$, T3 $n=4$) reported lower satisfaction than indicated by the whole sample (CRPS T2 median rating = "somewhat dissatisfied", T3 = "somewhat satisfied"; whole sample T2 = "somewhat satisfied", T3 = "very satisfied"). Moreover half the CRPS patients reported significant problems at T3 (compared to 15% for the sample as a whole) and only one person with CRPS reported being "back to normal".

While only 5 patients were diagnosed with CRPS, examination of the whole sample data revealed that substantial proportions of patients exhibited one or more individual sign/symptom from within the CRPS diagnostic criteria (see Table 3). In particular, oedema in the fractured limb was reported as a symptom by 70% of patients, and assessed as a sign in 57% of patients. Skin colour asymmetry between the fractured and non-fractured limbs was a symptom in 34% of patients and a sign in 28%. Hair changes were reported by 23% of patients and observed in 25%. Of the total sample 13% exhibited hyperalgesia in the fractured limb.

[INSERT TABLE 3 HERE]

Discussion

The primary aim of this exploratory study was to describe the impact of wrist and ankle fracture on sensory and motor systems using QST, motor planning tests, patient-reported outcomes and their relationship with perceived recovery.

Our results showed significant reduction in pressure pain and cold thresholds in fractured limbs, shortly after fracture and at a site distal to the fracture. Hyperalgesia is caused by peripheral sensitisation of nociceptors and by central sensitisation of the central nervous system. Both mechanical and thermal hyperalgesia have been noted in previous studies of surgically fixated wrist fractures (Birklein *et al.*, 2001), limb immobilization post-hand surgery, and immobilisation per se (Terkelsen *et al.*, 2008; Pepper *et al.*, 2013). This evidence suggests that the combination of bony trauma, surgery and immobilisation affects somatosensory function. However consistent with other research (Wylde *et al.*, 2012) the result of cold hyperalgesia in our study should be treated with caution as some participants did not perceive cold pain before the safety cut-off temperature of 5° .

Limb laterality tasks provided a measure of the integration between patients' information processes, working body schema and premotor processes soon after injury. Recognising the laterality of a pictured limb involves confirming an initial decision by mentally moving one's own limb to match the picture and, arguably, this relies on an intact body schema. We found limb recognition times and accuracy to be independent of fractured or non-fractured side, suggesting that performance was unaffected by fracture. However patients with CRPS have been found to take longer to recognize hands corresponding to their affected side (Schwoebel *et al.*, 2001; Moseley, 2004; Johnson *et al.*, 2012). Moseley *et al.* (2005) postulated information processing between acute and chronic pain may differ, and this may be helpful in interpreting the findings of the present study.

As part of the spectrum of motor imagery techniques, IMs reflect the representation of an inhibited movement plan and constitute an essential component in motor planning (Jeannerod & Frak, 1999). Our patients reported IMs were significantly more difficult to perform on the fractured limb, indicating a disruption to motor planning. This corroborates prior studies where amputation, lower limb immobilization, and stroke were associated with lower imagery vividness, or longer movement times during imagery, on the affected side (Malouin *et al.*, 2004; Malouin *et al.*, 2009). Also consistent with studies of neuropathic pain (Gustin *et al.*, 2008) and chronic arm pain (Moseley *et al.*, 2008), we found evidence to suggest that conduct of IM was associated with pain in the fractured limb. It is plausible that pain reported by our sample was similarly associated with a sensitised nociceptive system, as a result of their limb trauma.

These observations of IM impairment, but not laterality task impairment, in an acute pain cohort, provide an interesting comparator to those with chronic pain where a linear relationship between limb laterality and IM has been proposed (Moseley, 2004).

Results from the drawing component of the BPD scale indicated widespread mild perceptual disturbances early after fracture. Furthermore, a small proportion of the sample ($n=8$) had multiple perceptual differences between fractured and non-fractured limbs, indicating a severe impact of the injury on body perception. The nature of limb fracture and its treatment will affect somatosensory and proprioceptive input, and consequently motor output, and it is therefore unsurprising that BPDs were detected. However, to our knowledge BPD in the immediate post-fracture period has not been previously reported.

Body Perception Disturbance is frequently seen in CRPS (Galer & Jensen, 1999; Förderreuther *et al.*, 2004) and its presence early in onset (Lewis *et al.*, 2007) provokes speculation of its utility as a risk factor for CRPS post-fracture. Nevertheless, our results would not support this, as not all patients who described BPD developed CRPS. Further research is required to confirm our findings and evaluate their significance, especially as BPD is considered to relate to pathological cortical reorganisation in the primary somatosensory cortex (SI) (Juottonen *et al.*, 2002; Maihöfner *et al.*, 2003; 2004; Pleger *et al.*, 2006) and immobilisation per se has been shown to shrink SI representation of the immobilised limb (Lissek *et al.*, 2009).

Whilst, in the present study, levels of pain severity and interference were modest, and reduced over time, our findings suggested that a significant minority of patients (34%) reported ongoing pain as long as six months after injury. Moreover, the effectiveness of analgesic medication was found to diminish over time. These findings are consistent with other post-fracture studies where pain has persisted (MacDermid *et al.*, 2003; Moore & Leonardi-Bee, 2008). As might reasonably be expected, limb function was found to improve over time and patients' satisfaction with recovery increased concurrently. However, even as long as seven months after fracture, only a third of patients considered themselves back to 'normal' and a considerable minority (15%) reported ongoing significant problems.

Levels of psychological distress found in our cohort were reflective of the general UK adult population, as referenced against normative data (Crawford *et al.*, 2001). Results from the HADS subscales showed that anxiety levels were consistent with a general adult population at each time point and, although depression was slightly higher in our sample in the period immediately post-fracture, it was nevertheless within normal range (Snaith, 2003). Levels thereafter corresponded closely with the median scores of the general non-clinical population. These data indicate that fracture was not associated with long-term poor psychological health in our cohort.

The incidence of CRPS after fracture in this study was 9% and confined to patients with wrist fracture, a known risk factor (Pons *et al.*, 2015). The incidence of CRPS is reported in the literature as 5.46-26.2 per 100,000 person years (Sandroni *et al.*, 2003; De Mos *et al.*, 2007) and, for wrist fracture, varies from 1-32% (Field *et al.*, 1994; Dijkstra *et al.*, 2003; Jellad *et al.*, 2014; Moseley *et al.*, 2014; Roh *et al.*, 2014) depending on study design. Within the present study, it was notable that, whilst not meeting the full diagnostic criteria for CRPS, a substantial proportion of our cohort exhibited at least one of the diagnostic signs or symptoms. Consistent with other studies, this suggests clinical similarities after limb trauma between people with and without CRPS (Birklein *et al.*, 2001; Pepper *et al.*, 2013).

Offering an approach to prediction, Moseley et al. (2014) proposed that people with a pain severity rating of $\geq 5/10$ in the first week after fracture should be considered at risk of CRPS. Conversely, at T1 the median pain score of those of our cohort who subsequently met the CRPS criteria was less than 4/10. However, it would be inappropriate to impute meaning from these apparently contradictory results, as the methodologies of the measures and research criteria were not directly comparable.

Our aim was not purely to examine inferential statistics within data but to explore the nature and prevalence of sensory and motor changes and their relationship to self-report function in a consecutive cohort of patients with recent wrist and ankle fracture. The sample size was informed by pragmatic constraints; from hospital activity it was calculated that a 3-month data collection period would enable recruitment of 50 patients. However response rates to recruitment resulted in only 15% of eligible patients giving consent. Therefore any interpretation of our results must consider the potential effects of this response bias. It is plausible that our method of recruitment, governed by ethical constraints, may have affected our response rate, as may patients' negative perceptions of the extended T1 assessment appointment. Future studies would benefit from consideration of the burden of assessment in relation to the specific cohort and the feasibility of reducing this by combining research into existing clinical pathways. In addition, no a priori hypotheses were made on effects of dominance, fracture side or treatment (conservative versus surgical) on outcomes, however accounting for these covariates in any future fully powered investigations would be informative.

In conclusion, this study found considerable delay in self-assessed recovery after limb trauma and fracture healing. Ongoing persistent pain was not unusual post wrist or ankle fracture, with analgesia providing diminishing relief. However, the psychological health of our cohort was not deleteriously affected by the experience of fracture. Fracture was associated with pressure- and cold-pain hyperalgesia in the affected limb but was not found to affect limb recognition abilities when measured early after trauma. However IMs were significantly more difficult to perform on the fractured limb, indicating a disruption to motor planning processes for the affected body part, and were also associated with pain. Furthermore we detected mild, but prevalent, disturbances to body perception relating to the affected limb post-fracture, confirming a similarity in disruption to body schema whether brought about by trauma or by CRPS. Consistent with previous studies, we observed an incidence of CRPS in our cohort of 9% and some interesting results apparently characteristic of those with CRPS. However, we also detected widespread prevalence of individual CRPS signs and symptoms in our wider fracture cohort.

Our data may be used to inform future research to further investigate the extent and impact of sensorimotor changes and persistent pain in post-fracture populations and to determine whether early detection of problems and appropriate intervention can improve outcomes.

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Author Contributions

Dr. J. Hall and Profs S Palmer, R,A. Atkins and C.CS. McCabe - take responsibility for the integrity of the work as a whole, from inception to published article.

Dr. A Llewellyn -substantial contribution to analysis and interpretation of data, drafting the article and approval of final version.

J. Rowett-Harris- substantial contribution to acquisition of data, results discussion, revising the article critically and approval of final version.

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Table 1 Demographic, clinical and assessment characteristics of patients recruited into the study

	Wrist (<i>n</i> = 36)	Ankle (<i>n</i> = 17)	Total (<i>n</i> = 53)	% of total
Mean Age in years (SD)	56.8 (16.8)	48.5 (18.6)	54.0 (17.7)	
Gender: M/F	10 / 26	7 / 10	17 / 36	32 / 68
Fracture side: R/L	11 / 25	5 / 12	16 / 37	30 / 70
Fracture side: D/ND	8 / 28	5 / 12	13 / 40	24.5 / 75.5
Treatment: conservative/surgical	24 / 12	6 / 11	30 / 23	57 / 43
				% of respondents
Highest qualification	No qualification			22.4
	O level / GCSE			10.2
	AS / A level			42.9
	University degree			4.1
	NVQ / Vocational			6.1
	Other			14.3
Employment status	Employed full time			40.8
	Employed part-time			16.3
	Unemployed			4.1
	Housewife/husband			6.1
	Retired			28.6
	Self-employed			4.1
Duration between fracture and assessment (days)	Mean	S.D	Range	
Time 1 (T1)	31	12	8-52	
Time 2 (T2)	70	12	44-95	
Time 3 (T3)	220	40	170-306	

D=dominant hand, ND=non-dominant hand

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Table 2 Median scores from the BPI, HADS, DASH & LEFS

	Time 1	Time 2	Time 3	Friedman test	
Median (IQR), unless otherwise stated	<i>N</i> = 53	<i>N</i> = 50	<i>N</i> = 39	χ^2	<i>p</i>
BPI					
Pain severity	1.75 (2.38)	1.25 (1.82) ²	0.38 (1.75) ³	7.67	0.022 *
Pain interference	3.00 (3.86)	1.14 (2.28) ²	0.00 (0.90) ³	33.37	0.001 ***
Pain today? Yes (% of sample)	29 (55%) ¹	29 (58%)	13 (34%) ³	-	-
If yes: % relief from medications (S.D), <i>n</i> of "yes" to pain today?	65.2% (32.3%) <i>n</i> = 23	60.7% (25.3%) <i>n</i> = 14	53.3% (19.7%) <i>n</i> = 6	-	-
HADS					
Psychological distress	10.00 (10.00)	10.00 (9.00)	7.00 (8.00)	12.77	0.002 **
Anxiety	5.00 (6.00)	6.00 (5.00)	5.00 (5.00)	1.91	0.385
Depression	5.00 (5.00)	4.00 (6.00)	3.00 (3.00)	29.02	0.001 ***
DASH (wrist fractures only)	52.50 (22.50) <i>n</i> = 35	26.68 (27.03) <i>n</i> = 32	8.33 (17.35) <i>n</i> = 26	35.83	0.001 ***
LEFS (ankle fractures only)	31.00 (23.00) <i>n</i> = 17	36.50 (25.00) <i>n</i> = 16	74.00 (11.00) <i>n</i> = 9	14.89	0.001 ***

¹ *N* = 52, ² *N* = 49, ³ *N* = 38; *=*p*<.05, **=*p*<.01, ***=*p*<.001

Scoring procedures for DASH and LEFS are such that high scores on the DASH and low scores on the LEFS indicate greater disability

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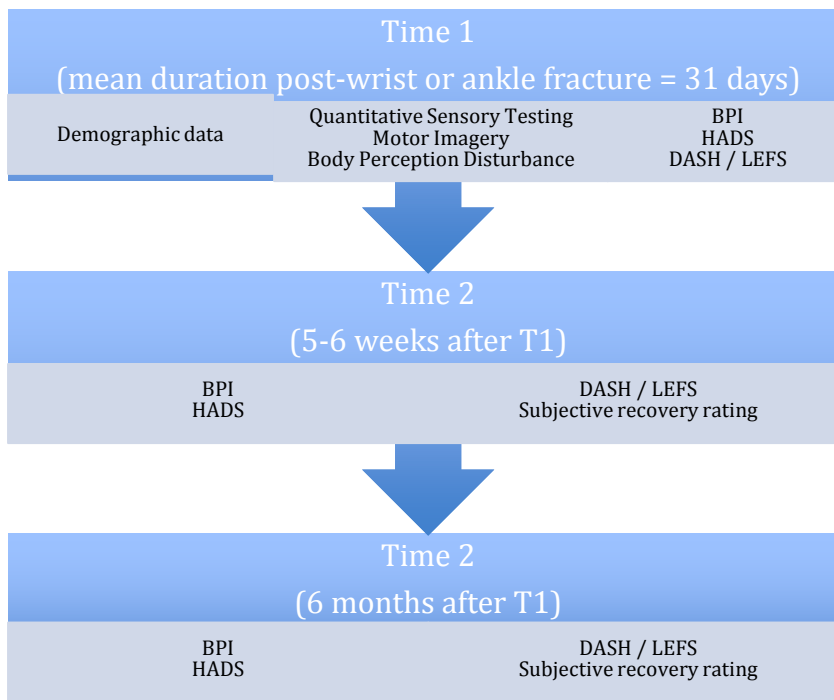
Table 3 Applying the Budapest criteria at T2 (n=50): patients with symptoms “now” and signs “present”.

		N = patients reporting symptom (%)	N = patients exhibiting sign (%)
Sensory	Hyperesthesia and/or allodynia	5 (9.4)	N/A
	Allodynia	N/A	2 (3.8)
	Hyperalgesia	N/A	7 (13.2)
Vasomotor	Temperature asymmetry	17 (32.1)	11 (20.8)
	Skin colour change	14 (26.4)	11 (20.8)
	Skin colour asymmetry	18 (34.0)	15 (28.3)
Sudomotor	Oedema	37 (69.8)	30 (56.6)
	Sweating change	6 (11.3)	8 (15.1)
	Sweating asymmetry	6 (11.3)	10 (18.9)
Motor/Trophic	Decreased range	11 (20.8)	8 (15.1)
	Weakness	8 (15.1)	7 (13.2)
	Tremor	3 (5.7)	3 (5.7)
	Dystonia	2 (3.8)	0 (0.0)
	Hair change	12 (22.6)	13 (24.5)
	Changes in nails	9 (17.0)	2 (3.8)
	Changes in skin	4 (7.5)	3 (5.7)

Assessment of signs was preceded by patient report of distinguishing symptoms and followed the order of the Budapest criteria. Clinical examination, including observation and palpation, comparing affected to unaffected limb, were utilised for vasomotor and trophic signs. Hyperalgesia to gentle pinprick pressure on either wrist/ankle was recorded as present if the patient reported greater pain on the affected side. Allodynia to light touch (gentle stroking on either wrist/ankle with a cotton wool ball) was recorded as present if pain was reported to the stimulation. Motor symptoms were assessed through active range of movement and muscle strength testing of wrist/hand and ankle/toe motions and recorded as present when a reduction compared to the non-affected side was present. Observation during these tests revealed the presence/absence of tremor and dystonia

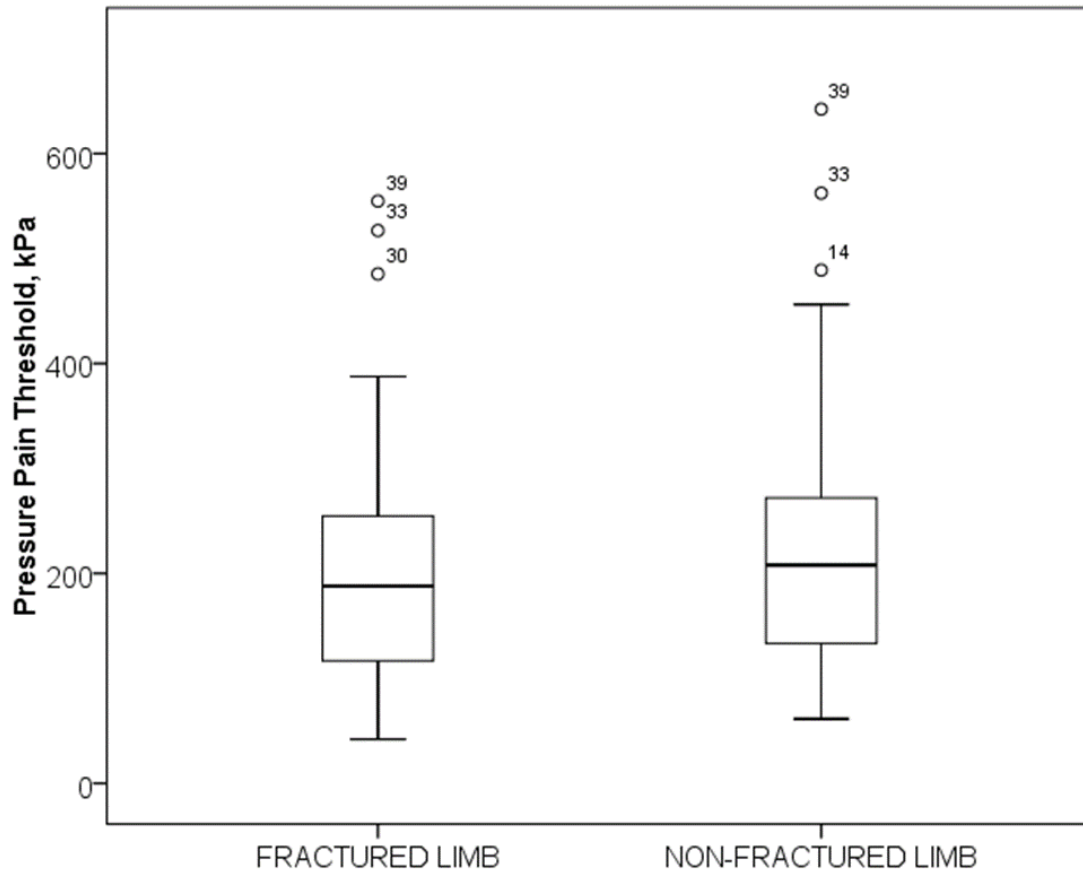
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Figure S1 Data collection



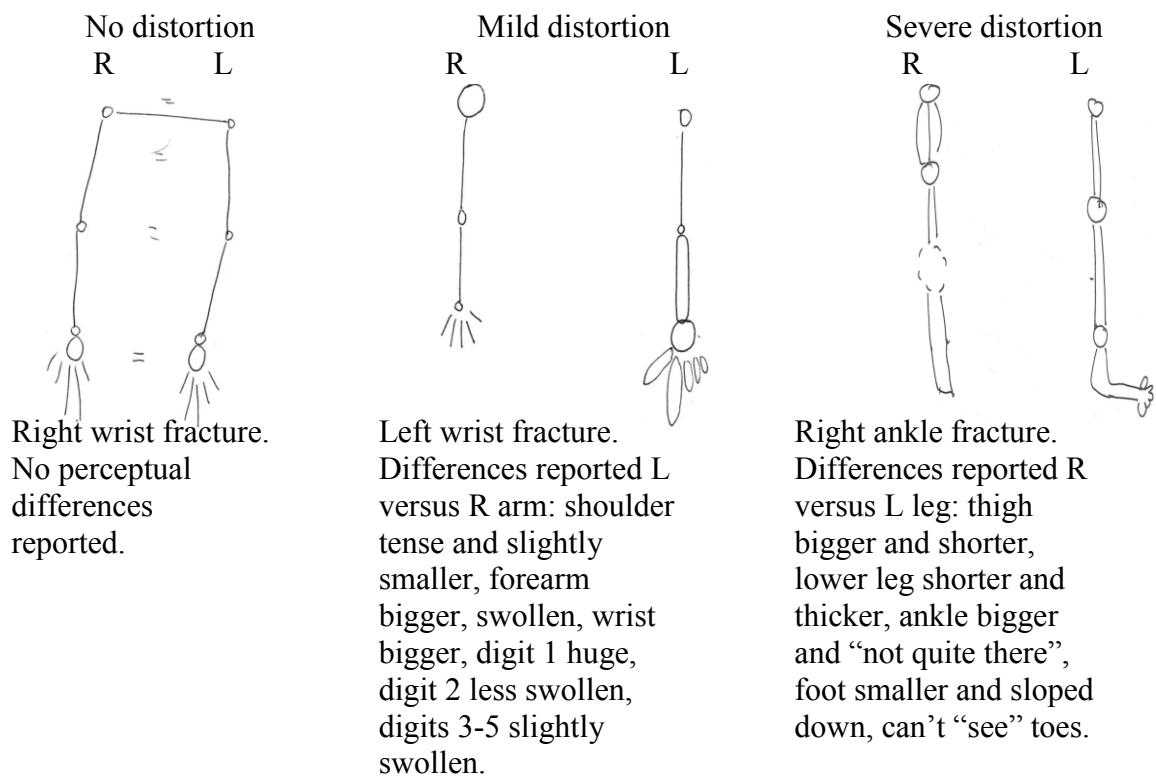
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Figure 1 –Median pressure pain thresholds were significantly lower in the affected/fractured than in the unaffected/non-fractured limb ($Z = -2.69$, $p < 0.01$).



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Figure 2 Mental representations of the fractured limb (N = 50) and exemplar drawings with associated patient narratives.



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