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Title page

Body perception disturbance and pain reduction in longstanding Complex Regional Pain Syndrome following a multidisciplinary rehabilitation programme.

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Running title: Complex Regional Pain Syndrome: Rehabilitation outcomes

Abstract

Objective

Clinical guidelines for the treatment of Complex Regional Pain Syndrome recommend multi-disciplinary rehabilitation, yet limited evidence exists to support the effectiveness of this approach. Body perception disturbance, a common and debilitating feature of Complex Regional Pain Syndrome is recommended by guidelines as important to treat. However, no study has yet explored whether disturbances change in response to multidisciplinary rehabilitation. We aimed to determine whether there is a change in body perception disturbance and pain following a two-week multidisciplinary rehabilitation programme for Complex Regional Pain Syndrome.

Methods

Retrospective clinical data from Complex Regional Pain Syndrome patients who completed the programme between September 2014 and December 2016 were extracted and anonymised. Data collected pre- and post-rehabilitation comprising the Bath Body Perception Disturbance scale and a pain intensity numerical rating scale were analysed.

Results

Thirty complete datasets were analysed from a sample of 50 consecutive patient records. Following the programme, there was a significant reduction in body perception disturbance ($p<0.0001$), strength of negative emotional feelings ($p<0.0001$) and pain ($p=0.0038$). There was a significant correlation between a change in disturbance and pain ($r= 0.44$, $p=0.024$). No relationship was found between the duration of symptoms and changes in disturbance ($r=0.04$, $p=0.82$).

Conclusions

This study provides evidence that both body perception disturbance and pain reduce following rehabilitation. Findings suggest that targeting these disturbances may be important

in reducing pain and a potentially useful measure for recovery. Controlled trials are required to confirm the effectiveness of rehabilitation and determine what factors are responsible for these reductions.

Keywords: Complex Regional Pain Syndrome; chronic pain; body perception disturbance; multidisciplinary rehabilitation; clinical outcomes

Introduction

Body perception disturbance (BPD) is recognised as a common feature of Complex Regional Pain Syndrome (CRPS) and adversely influences how patients feel about and engage with their painful limb(1-3) CRPS clinical guidelines highlight the need to treat body perception disturbance (4) however to date, changes in BPD following rehabilitation have not yet been explored. Our study aims to address this important issue.

Up to eighty-four percent of people with CRPS experience perceptions of their painful bodily region which are at odds with reality(2,3,5,6). Strongly negative emotions, such as hate and disgust, are expressed about the limb and individuals describe a loss of self-ownership commonly reporting the limb as alien(2,6,7). Some have a strong desire to amputate the affected part(2,8). Subjectively, the painful body region is perceived as altered in shape, size, temperature and weight in a way that is different from objective assessment (2,9,10). Moreover, with their eyes closed, CRPS patients mentally visualise intensified shape and size distortions of the affected region and some are unable to picture anatomical parts (2). These anomalous perceptions and feelings about the affected limb are believed to impact on the individual's ability to engage with and use their limb in normal daily functioning (1,11)

A positive correlation between BPD and pain has been established demonstrating that those with more severe pain have more extensive BPD (8) We postulate that this correlational relationship with pain is important as, if BPD decreases with treatment, it follows that pain may also reduce.

The exact cause of BPD remains unclear although emerging evidence suggests that body perception disturbances are associated with pathological changes in the brain's representation of the affected limb (12,13). Central body representation is a virtual, dynamic multisensory map of the body within the brain(14). Somatosensory, visual, proprioceptive and vestibular inputs and motor feedback constantly update and modify this representation (14). Brain imaging reveals cortical remapping in the primary somatosensory cortex (S1), a region that contributes to the central representation of the painful CRPS limb (12,15). One study found changes in S1 associated with the healthy limb (16) . These pathological changes are related to pain, as positive correlations have been found between the extent of neuronal remapping in the brain and pain intensity (12,17,18). Notably, this maladaptive S1 representation has also been shown to normalise following rehabilitation(19). Given the association between S1 changes and BPD one would expect that BPD also decreases as a consequence of rehabilitation, yet to date this assumption remains unsubstantiated.

Most cases of CRPS resolve within one year, however, symptoms persist and develop into a long-term condition for up to 27% of patients (20-23). The rate of recovery reduces considerably in those with longstanding CRPS. Seventy percent of these individuals continue with stable or developing symptoms at 5.8 years post condition onset (20)

International clinical guidelines recommend that multidisciplinary team (MDT) rehabilitation is the gold standard treatment for more severe and/or longstanding CRPS (4,24,25). The aim of treatment is functional recovery through improving function and quality of life, reducing pain and promoting self-management(4). A combination of rehabilitation interventions such as mirror visual feedback (MVF), sensory re-education, postural control and strategies to increase engagement with the affected body part are commonly delivered in a programme

format by at least two health care professionals (4). Physiotherapy and occupational therapy play an essential role in the delivery of this rehabilitation (4).

A MDT rehabilitation programme that typifies this model is the two-week CRPS-specific inpatient course at The Royal National Hospital for Rheumatic Diseases, Bath, UK (RNHRD) (26). Patients that are eligible for the programme have met the Budapest clinical diagnostic criteria for CRPS (29) as confirmed by a physical examination from the team's pain specialist and have failed local uni-disciplinary treatment hence require MDT rehabilitation in accordance with the UK CRPS treatment guidelines (4). Delivered by Occupational Therapy, Physiotherapy and Psychology professionals with input from Nursing and Pain Medicine, rehabilitation is guided by the functional goals that the patient identifies as important to them. Treatment approaches are selected based on the individual's needs (26).

Despite international guideline recommendations, only two studies to date have evaluated the effectiveness of an MDT programme in the treatment of CRPS (27,28). Both studies evaluated a four-week outpatient MDT programme, one (27) in longstanding (mean symptom duration= 39 months) CRPS (n=49), the other (28) in upper limb CRPS (n=12, mean symptom duration = 18 months). Both studies showed significant improvements in physical functioning, perceived disability and pain coping strategies. However, there was no significant change in pain and neither study measured BPD as an outcome (27,28).

In summary, despite the prevalence and debilitating nature of BPD which clinical guidance advises to specifically target in treatment, no study has yet evaluated changes in BPD following an MDT programme. Such an evaluation may provide evidence for the effectiveness of MDT rehabilitation, support the importance of addressing BPD when treating

CRPS patients and determine whether BPD is a useful clinical outcome in monitoring progress.

In this single cohort study, we set out to answer this important research question “Does an MDT rehabilitation programme change BPD in CRPS?” Our primary hypothesis was that there will be a significant reduction in BPD following an MDT rehabilitation programme.

Secondary hypotheses were that following the rehabilitation programme;

a) There will be a change in emotional feelings about the CRPS affected region

b) There will be a relationship between changes in BPD and changes in pain

c) There will be a relationship between change in BPD and symptom duration

Methods

Study cohort and design

This is a cohort study to explore whether there is a change in BPD and pain following MDT rehabilitation. Retrospective clinical data were extracted from the medical notes of patients who had completed the RNHRD two-week CRPS MDT rehabilitation programme between September 2014 and December 2016. Data were extracted for individuals who met the following inclusion criteria; a) aged 18 or over, b) met the Budapest clinical diagnostic criteria for CRPS (29) c) two Bath CRPS BPD scales completed, one pre- and one post-programme. Data was anonymised by a suitably qualified clinician (JL) at the point of extraction and each patient data set was allocated a unique identification number. A consecutive sample of 50 datasets that met the inclusion criteria were extracted.

Measures

1) Measurement of body perception disturbance

The Bath CRPS Body Perception Disturbance (Bath BPD) scale was used to measure the nature and extent of changes in body perception of the affected limb (1). The measure comprises seven items covering different aspects related to the affected limb. These are: (a) a sense of ownership; (b) limb position awareness; (c) attention paid to the limb; (d) emotional feelings towards the limb; (e) perceptual disparities in size, temperature, pressure and weight (compared to the unaffected limb); (f) a desire to amputate the limb; and (g) a mental representation of the affected limb.

The sum of the scale is calculated with a possible maximum of 57 (see (1) for scoring guidance). A higher score indicates greater BPD. Psychometric scale testing indicates

adequate internal consistency and interrater reliability (8) We were particularly interested in whether there was a change in emotions about the limb (item d) (secondary hypothesis a).

2) Pain rating

A numerical rating scale (NRS) is a widely used, valid and reliable scale to measure pain intensity and is shown to have high compliance rates in chronic pain populations (30,31). The NRS is an 11-point verbal rating scale ranging from 0 (no pain) to 10 (worst imaginable pain).

Timepoints of measurement completion

Both measures were recorded by Occupational Therapy clinicians on the first day of the inpatient programme prior to rehabilitation and on the last programme day following rehabilitation two weeks later (26).

Data management and statistical methods

Fifty anonymised and numbered data sets were transposed from paper copies into a Microsoft Excel Spreadsheet then exported into SPSS version 22 (IBM SPSS Statistics for Windows, IBM Corp, Armonk, NY) and analysed.

In 20 of these datasets, some individual items within the Bath BPD scale at baseline and post-rehabilitation had not been completed by clinicians therefore a total BPD score could not be calculated or imputed. These datasets were excluded and the remaining 30 datasets were analysed. Mean values and standard deviations were calculated to describe age, symptom duration and pain intensity of the cohort. Gender, reported inciting incident, and affected body part were summed for the group and presented as percentages.

Subscale analysis was performed on item (d) of the BPD scale to determine ratings for emotional feelings about the limb. A Shapiro-Wilk test was performed on mean pre- and

post- programme scores for BPD, pain and emotional ratings to test whether the data were normally distributed. BPD and pain were normally distributed therefore paired sample t-tests were used to identify changes over time. Emotional ratings were not normally distributed therefore a Wilcoxon test was used. To calculate changes in BPD and pain intensity following rehabilitation, the respective post-programme score was subtracted from the pre-programme score to determine change scores. For additional information, standard errors (SEM) have been included in Figure 2. A Spearman's rank order test was performed to calculate a correlation coefficient between pain intensity and symptom duration and BPD change following the rehabilitation programme. Alpha was set at $p<0.05$ for all statistical analyses.

Ethics

This study was approved by the Faculty Research Ethics Committee of University of the West of England (approval number HAS.16.12.075)

Results

Thirty complete data sets (21/70% women, 9/30% men) were included in the analyses. Participants in the cohort had a mean age of 44.7 years (SD ±11.3), mean symptom duration of 41.6 (±42.1) months and mean baseline pain intensity of 7.5 (±1.84). There was no significant difference in baseline pain intensity (p=0.6) between this group and those that were excluded (mean baseline pain intensity= 6.65, SD±1.9). Patient related clinical characteristics are presented in Figure 1 A&B.

Change in body perception disturbance following rehabilitation

The mean Bath BPD total score was significantly lower (p<0.0001) post-rehabilitation (23.83± 11) than pre-rehabilitation (34.3 ±10.8). See Figure 2A. A post hoc analysis of effect size of a MDT programme on BPD was calculated using paired sample testing which resulted in a Cohens d = -0.96 with a confidence interval of -1.31 to -0.6.

Change in emotional feelings about the CRPS affected region

The mean emotional rating was significantly lower (p<0.0001) post-rehabilitation (5.2 ± 2.7) than pre-rehabilitation (7.5 ±2.5). See Figure 2B.

Change in pain

The mean pain intensity rating was significantly lower (p=0.0038) post-rehabilitation (6.2 ± 2.7) than pre-rehabilitation (7.5 ±2.5) See Figure 2C.

Relationship between changes in BPD and pain

A significant correlation (r=0.44, p=0.024) was found between the change in BPD and change in pain following rehabilitation (see Figure 3).

Relationship between changes in BPD and symptom duration

No significant correlation was found between either baseline BPD or change in BPD and symptom duration (r= -0.15, p=0.42, and r=0.04, p=0.82 respectively).

Discussion

These findings support our primary hypothesis that BPD significantly reduces following a MDT rehabilitation programme in patients with CRPS. We reveal for the first time that BPD is responsive to MDT treatment and decreases accordingly. Results confirm our secondary hypotheses that; a) there is a change in emotional feelings following rehabilitation and b) there is a significant correlation between changes in BPD and pain. Contrary to previous findings (8), we found no relationship between change in BPD and symptom duration (hypothesis c).

Previous research has shown that rehabilitation programmes help CRPS patients to improve pain coping strategies (27), yet ours is the first study to show a reduction in pain intensity. Furthermore, we also found a reduction in BPD following MDT treatment. Our findings offer objective evidence in support of clinical guidance to address BPD in treating CRPS (4).

A reduction in strength of negative emotional feelings about the affected limb supports the view that patients become more positive about their limb as a consequence of rehabilitation. This may have some potential for promoting functional improvement (1) .

We are unable to directly compare our BPD change findings with earlier research as no previous studies exist in this specific area. Nonetheless, our findings do provide further support for MDT rehabilitation in the treatment of CRPS(27).

When comparing changes in pain, our results were not consistent with those of McCormick et al. (2015). We found a significant reduction in pain intensity (mean change 1.3) following the programme whereas they found no change in pain despite a patient cohort with a similar symptom duration to ours (27). One possible explanation for this disparity is that the intensity of an MDT programme delivered on an inpatient basis such as at RNHRD, may be more

effective than the outpatient model evaluated by McCormick et al. (2015). Although statistically significant, it should be noted that our pain results do not quite meet the clinical significance threshold of a two-point reduction in NRS (32)

Notably, we found a direct correlation between reductions in pain and BPD following rehabilitation. Evidence of a relationship between BPD and pain corroborates with findings from an earlier study in a Canadian CRPS population where BPD was found to positively correlate with pain demonstrating that those in greater pain had more extensive body perception disturbance (8) Whether pain is the cause or the effect of BPD is yet to be determined. Given that current pharmacological treatments aimed at directly targeting chronic pain have limited effect(33), the interplay between these two factors suggest that treating BPD to *indirectly* reduce pain, may have useful potential in providing pain relief for patients. Further investigation is required to test the merits of this hypothesis.

In contrast to earlier studies (8-10) we found no correlation between BPD and symptom duration. This is of clinical interest as those with a longer symptom duration may still respond positively to rehabilitation aimed at reducing BPD.

Although the size of our cohort precludes making broad generalisations, our preliminary findings add to the emerging evidence base in this field. Future controlled trials with larger CRPS cohorts are now required to confirm our findings.

Given the retrospective nature of this study, it is not known which component(s) of the MDT programme were effective in reducing BPD and pain. The goal-centred nature of the RNHRD programme leads to variability in treatment approaches between patients, therefore it is more difficult to identify specific elements of the programme that might be responsible for the

observed changes. Intervention based randomised controlled trials could identify the active components responsible for the effectiveness of an MDT programme and lead to future studies that could establish the optimal frequency and duration of these effective interventions for best clinical outcome.

Outcome measures in this study were repeated immediately after the programme, therefore it is unknown whether reductions in BPD, pain and negative emotions can be sustained over a longer period. Further research is necessary to establish whether the reductions we found, can be maintained over time.

Our findings are relevant to clinical practice as we provide clinical evidence to support the importance of actively treating BPD within an MDT programme. Findings indicate that treatment interventions aimed at reducing body perception disturbance may reduce pain. Furthermore, measuring changes in BPD before and following rehabilitation is a potentially useful clinical outcome to measure progress in rehabilitation and one possible indicator of recovery.

Conclusion

In conclusion, we have found for the first time that BPD and pain reduce in response to MDT rehabilitation. This confirms clinical guidance about the importance of addressing BPD and adds to the growing evidence base in support of MDT rehabilitation in the treatment of CRPS. Furthermore, the relationship between changes in BPD and pain suggests the potential for indirectly targeting pain by directly treating BPD. We also found a reduction in strength of negative emotional feelings about the affected limb but no relationship between

change in BPD and symptom duration. Further work is required to identify the effective components of an MDT programme and whether these outcomes of rehabilitation can be maintained over time.

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Conflicts of Interest

No conflicts of interest are declared for all the authors. This project was part of a physiotherapy undergraduate research dissertation therefore no additional funds were required to undertake this study.

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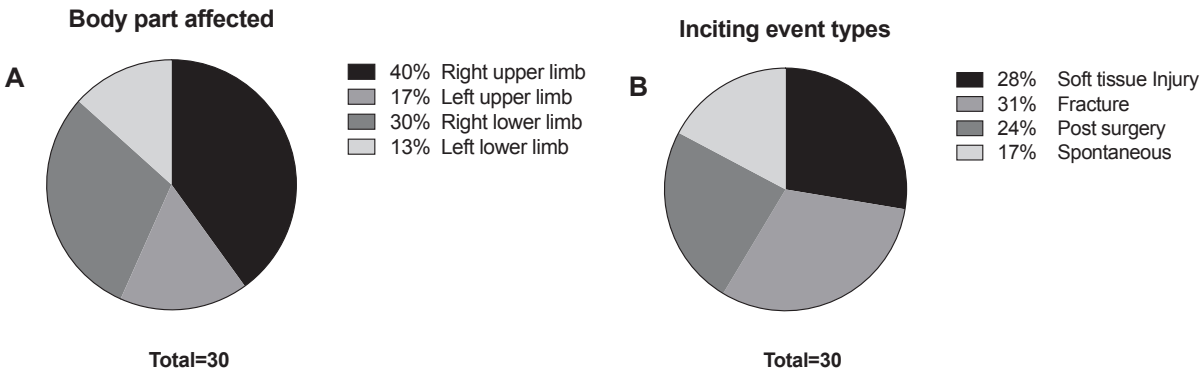
Figure legends

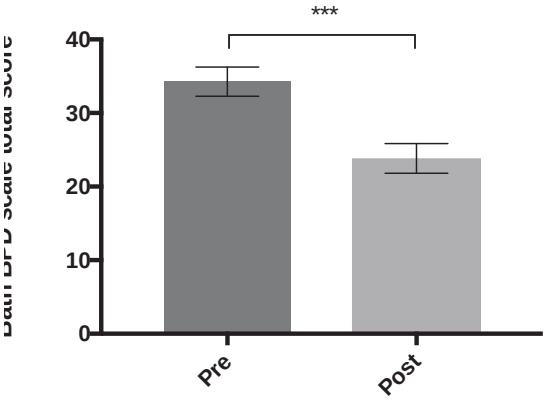
Figure 1 A & B Clinical characteristics of cohort

Figure 2 A,B&C Changes in body perception disturbance, emotional feelings and pain

Figure 3 Correlation between body perception disturbance and pain intensity following rehabilitation

Figure 1 A & B clinical characteristics of cohort





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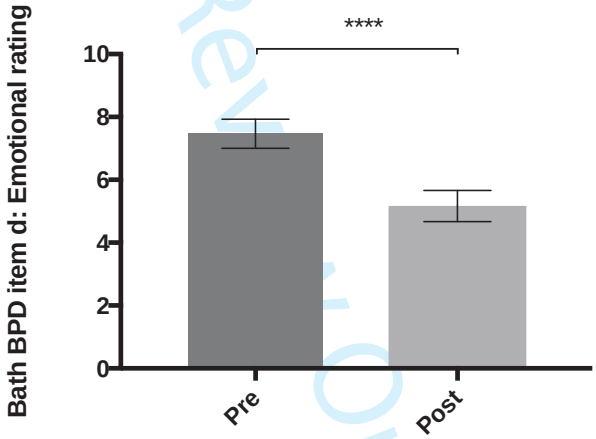

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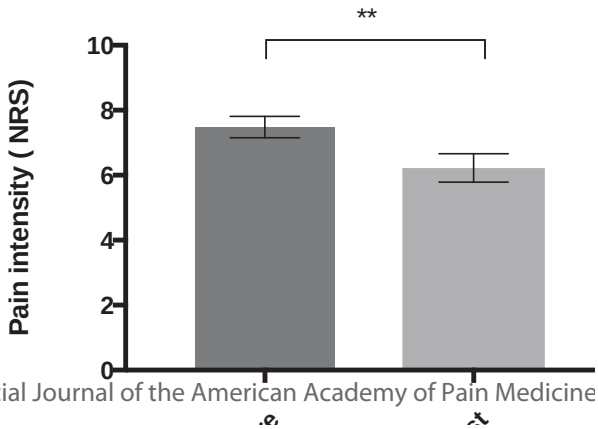

Figure 3. Correlation between body perception disturbance and pain intensity following rehabilitation