Management of Complex Regional Pain Syndrome following Upper Extremity Trauma

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Course Objectives
1. Describe the epidemiology and prognostic indicators of CRPS in patients presenting with upper extremity trauma;
2. Discuss the diagnostic classifications for CRPS 1 and 2;
3. Describe and critique the evidence on the objective and self-reported outcome measures commonly used in CRPS and link these measures to the ICF constructs;
4. Provide an overview of the literature describing different rehabilitation interventions in patients with CRPS.

Disclosures
The speakers have nothing to disclose.

Historical Overview

Symptom cluster – burning pain, hyperalgesia, vasomotor disturbances, dystrophic changes – first described after Civil War

Prior to 1993:
- Causalgia – symptom cluster present in patients with peripheral nerve injuries
- Algodystrophy – symptom cluster present in patients with minor regional traumatic injury
- Sudeck's dystrophy – symptom cluster present in patients with soft tissue injury where atrophy of bone is main finding
- Shoulder-Hand Syndrome – symptom cluster present, along with, frozen shoulder, in patients with CVA and cervical radiculopathy
- Reflex sympathetic dystrophy – symptom cluster that predominantly improves with sympathetic denervation

After 1993:

Complex Regional Pain Syndrome (CRPS)

What's in the Name?
- Complex – diverse clinical symptoms such as pain, sensorimotor impairment, autonomic dysfunction that do not cluster into a specific pathology
- Regional – distribution is regional, reflective of stocking and glove pattern, versus a dermatome/peripheral nerve distribution
- Pain – though the symptoms are diverse, pain is the most troublesome and prominent symptom

Two types:
- CRPS Type 1: A noxious event or immobilization precedes the onset of symptoms
- CRPS Type 2: Injury to a major peripheral nerve precedes the onset of symptoms
Epidemiology

- Population-based study CRPS Type 1 and 2 (de Mos, 2007)
  - Incidence rate of 26.2 per 100,000 person years
  - Females:Males 3.4:1
  - Type 2 made up < 3.0% of the individuals
- Population-based study CRPS Type I (Sandroni, 2003)
  - Incidence rate 5.46 per 100,000 person years
  - Prevalence rate 20.57 per 100,000
  - Females:Males 4.0:1

Inciting Events

- Fractures 44-46% (Sandroni, 2003 and de Mos, 2007)
- Sprain/strain
- Crush injuries
- Surgery
- Falls
- Immobilization
- Contusion
- "Other"

Spontaneous onset

- 6-10% cases
- De Rooij, 2010
  - Multicenter study
  - N=537
  - NSD on any individual characteristics except:
    - Spontaneous onset were younger (P=0.001)
    - Spontaneous had longer duration of symptoms (P<0.0005)
  - NSD on any sign or symptom

Pathophysiology

- Variability in the average age of onset
  - Average ~40 to 60 years
- Variability in the duration of symptoms (1-168 months)
- Variability in UE versus LE involvement
- Distal preponderance (Fukushima, 2014)
- Less than 1% reporting facial involvement (Allen, 1999)
- Patients with multiple extremities involved (7%) (Allen, 1999)
- No side predominance (Sandroni, 2003)
- 4 to 5 physicians prior to pain clinic evaluation (Allen and Choi)

"Other" Inciting Events

- Venipuncture
- Pacemaker placement
- Vaccinations (HPV, D+T)
- Snakebite
- Herpes Zoster infection
- Mastectomy
- Cardiac cath
- Burn
- Neuroma
- Dermatology surgeries
- Lightning/Electrical
- Spontaneous

• De Rooij, 2010
  - Multicenter study
  - N=537
  - NSD on any individual characteristics except:
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Pathogenesis
Wasner, 2010

- Dysfunction in the sympathetic nervous system
  - Mismatch in sympathetic regulation

INHIBITION of sympathetic vasoconstrictor activity
→ CUTANEOUS DILATION

INCREASE in sudomotor output
→ EXCESSIVE SWEATING

Pathogenesis

- Unclear as to WHY but there are likely multiple and possibly interacting factors
- Several hypotheses exist
  1. Autoimmune processes
  2. Abnormal inflammatory response
  3. Neurogenic inflammation promotes changes in the CNS
  4. Peripheral and central sensitization

Autoimmunity

Human Leukocyte Antigen System

- Many pathologies linked with various HLA types
- Schlereth, 2014
  - HLA alleles are overrepresented in patients with CRPS and their presence has been associated disturbed regulation of inflammation
- Kemler, 1999-HLA-DQ1 associated with RSD
- De Rooij, 2012-HLA-DQ8 and HLA-B62 present in those with dystonia

Autoimmunity


- Patients with CRPS
  - Pre-existing auto-antibodies become pathogenic
  - Identified autoantibodies belong to the IgG class
  - Autoantibodies against sympathetic nervous system receptors
  - Unsure of clinical relevance
  - Studies on success of immunoglobulin treatment for CRPS

Abnormal inflammatory response

ALTERATION in inflammatory cytokines

[Hauser et al, 2013]

- Inflammation that arises from neuropeptide release from the afferent fibers that causes vasodilation and protein extravasation
  1. Calcitonin gene-related peptide (CGRP)
    - Vasodilation
    - Increase sweat gland activity (Leis, 2003)
  2. Substance P (SP)
    - Protein extravasation (Leis, 2003)
    - Migration of inflammatory cells
    - Increase release of histamine and TNFs through activation of the mast cells (Birklein, 2008)
    - Important role in the CNS

Neurogenic inflammation

[Hauser et al, 2013]

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  1. Calcitonin gene-related peptide (CGRP)
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    - Important role in the CNS
Skin biopsies on patients with CRPS (Calder, 1998)

1. (+) Calcitonin gene-related peptide (CGRP)
2. (+) Substance P (SP)
3. Langerhans cells

Langerhans cells: Produce IL-1, TNFα, and nerve growth factor
- Hyperalgesia with no visible signs of inflammation
- Increases CNS cell excitability
- Signals the cell bodies proximally to increase CGRP/SP

Signs and Symptoms

Birklein, 2000

- Variable presentation
- Pain is biggest complaint
  - 77% reported pain at rest and 94% reported pain under certain circumstances
  - 36% stocking-glove and 34% glabrous skin on hands and feet
  - No specific dermatomal pattern
  - Pain is not correlated to the amount of autonomic dysfunction

Signs and Symptoms (Fukushima, 2014)

- Bizarre complaints (spreading)
- Bizarre signs (ulcerations)
- Neuropathic and nociceptive

Signs and Symptoms (Fukushima, 2014)

- Neglect-like symptoms
  - Narrative review (Punt et al, 2013)
  - Neglect shares similarities with neglect post-stroke but differences exist however there is a lack of a more appropriate term
  - CRPS neglect more associated with movement difficulty rather than visual field loss
  - Motor loss in CRPS is greater than what is warranted for the pathology
  - Stroke-limb in dangerous positions versus posturing in CRPS is protective

Clinical picture

<table>
<thead>
<tr>
<th></th>
<th>Sandroni, 2003</th>
<th>Birklein, 2000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom</td>
<td>Sign</td>
<td>Sign</td>
</tr>
<tr>
<td>Sensory</td>
<td>Sensory abnl 45.9%</td>
<td>18.9%</td>
</tr>
<tr>
<td></td>
<td>Allodynia 54%</td>
<td>59.5%</td>
</tr>
<tr>
<td>Vasomotor</td>
<td>Skin color 77%</td>
<td>73%</td>
</tr>
<tr>
<td></td>
<td>Skin temperature 62.2%</td>
<td>59.5%</td>
</tr>
<tr>
<td>Sudomotor</td>
<td>Swelling 97.3%</td>
<td>91.9%</td>
</tr>
<tr>
<td></td>
<td>Sweat abnl 28.4%</td>
<td>24.3%</td>
</tr>
<tr>
<td>Motor/trophic</td>
<td>Motor abnl 56.7%</td>
<td>45.9%</td>
</tr>
<tr>
<td></td>
<td>Trophic changes 0</td>
<td>32.4%</td>
</tr>
</tbody>
</table>
Variability in presentation with prolonged duration

- Cross-sectional study of 145 people with Types 1/2

Vasomotor variation:
- Warmer skin temperature: more acute and cold more chronic
- Color red being more acute and cyanotic more chronic

Sudomotor dysfunction:
- Edema: Higher in acute
- Sweating: Not dependent on duration

Wasner, 2001
- Examined sympathetic activity in the affected limbs in CRPS-1
- Compared with injured-non CRPS and controls

Warm CRPS: correlated with shorter duration
Cold CRPS: correlated with longer duration

What is the difference is pathophysiology in warm versus cold CRPS?

- Koban, 2003
  - Hypoxia on affected limb compared to uninvolved limb
  - No asymmetry in the control group

- Endothelial dysfunction (Groeneweg, 2006, 2008)
  - Over time, the vasoconstrictor response (once inhibited) returns
  - Increase in vasoconstriction and decrease in vasodilation
  - Tissue hypoxia and acidosis
  - Increase in free radicals (human and animal models unsure if cause or consequence)
  - Further endothelial damage → Cycle of impaired perfusion

Wasner, 2010
- CNS Involvement
  - Impaired sympathetic vasoconstrictor activity
  - Vasodilation
  - Pro-inflammatory cytokines ↑
  - Activity of the C-nociceptors ↑
  - Neurogenic inflammation ↑
  - Increased sympathetic vasoconstrictor activity returns

Endothelial dysfunction
  - Tissue hypoxia
  - Acidosis
  - Free radicals
Diagnostic Criteria

Issues with the IASP Criteria

Criteria were developed by experts in the field in a conference setting—did not involve all the stakeholders, most importantly patients suffering from CRPS cluster

No empirical validation of the established criteria

Poor specificity, leading to misclassification of patients with other peripheral neuropathies as having CRPS

A high number of patients with incorrect diagnosis of CRPS, leading to inappropriate interventions

One major concern was clustering vasomotor, sudomotor, and edema as one criteria where any one of these is considered acceptable

Diagnostic Criteria Presented by the International Association for the Study of Pain (IASP) in 1995

CRPS-I (Reflex Sympathetic Dystrophy)

1. Initial noxious event, or a cause of immobilization.
2. Continuing pain, allodynia, or hyperalgesia where the pain is disproportionate to any inciting event.
3. At times presence of edema, changes in skin blood flow, or abnormal sudomotor activity in the region of the pain.
4. Diagnosis is excluded by the existence of conditions that would otherwise account for the degree of pain and dysfunction.

Note: criteria 1-4 must be satisfied.

Stanton-Hicks et al., 1995

CRPS-II (Causalgia)

1. The presence of continuing pain, allodynia, or hyperalgesia after a nerve injury, not necessarily limited to the distribution of the injured nerve.
2. At times presence of edema, changes in skin blood flow, or abnormal sudomotor activity in the region of the pain.
3. Diagnosis is excluded by the existence of conditions that would otherwise account for the degree of pain and dysfunction.

Note: All three criteria must be satisfied.

Budapest Consensus Building Exercise 2003—Definition

"...an array of painful conditions that are characterized by a continuing (spontaneous and/or evoked) regional pain that is seemingly disproportionate in time or degree to the usual course of any known trauma or other lesion. The pain is regional (not in a specific nerve territory or dermatome) and usually has a distal predominance of abnormal sensitivity, motor, sudomotor, vasomotor and/or trophic findings. The syndrome shows variable progression over time."

[Harden et al., 2007, p330]

Budapest Consensus Building Exercise 2003—Diagnostic Criteria

Following three criteria must be met for clinical diagnosis

Disproportionate pain intensity

1. Continuing pain, which is disproportionate to any inciting event

(Harden et al., 2007, p330)

Budapest Consensus Building Exercise 2003—Diagnostic Criteria

Symptom Cluster

2. Must report one symptom in three of the four categories below:

Sensory: Report of hyperesthesia and/or allodynia

Vasomotor: Report of temperature asymmetry and/or skin color changes and/or skin color asymmetry

Sudomotor/Edema: Report of edema and/or sweating changes and/or sweating asymmetry

Motor/Trophic: Report of decreased ROM, and/or motor dysfunction (weakness, tremor, dystonia), and/or trophic changes (hair, nail, skin)

(Harden et al., 2007, p330)
Budapest Consensus Building Exercise 2003 – Diagnostic Criteria

Sign Cluster

3. Must display at least one sign at the time of evaluation in two or more of the four categories below:

- Sensory: Hypersensitivity (to pinprick) and/or allodynia (to light touch, and/or temperature sensation and/or deep somatic pressure and/or joint movement)
- Vasomotor: Evidence of temperature asymmetry (>1°) and/or skin color changes and/or skin color asymmetry
- Sudomotor/Edema: Evidence of edema and/or sweating changes and/or sweating asymmetry
- Motor/Trophic: Evidence of decreased ROM, and/or motor dysfunction (weakness, tremor, dystonia), and/or trophic changes (hair, nail, skin)

(Harden et al, 2007, p330)

What was the accuracy of the modified diagnostic criteria???

<table>
<thead>
<tr>
<th>Decision rule for the Budapest criteria</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>2+ signs and 2+ symptoms</td>
<td>0.94</td>
<td>0.36</td>
</tr>
<tr>
<td>3+ signs and 3+ symptoms</td>
<td>0.70</td>
<td>0.83</td>
</tr>
<tr>
<td>2+ signs and 4 symptoms</td>
<td>0.70</td>
<td>0.94</td>
</tr>
</tbody>
</table>

(Harden et al, 2007, p330)

Prognosis

Literature Search: Prognosis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRPS</td>
<td>Progn*</td>
</tr>
<tr>
<td>Complex regional pain syndrome</td>
<td></td>
</tr>
<tr>
<td>Reflex sympathetic dystrophy</td>
<td></td>
</tr>
<tr>
<td>Sudeck's dystrophy</td>
<td></td>
</tr>
<tr>
<td>Causalgia OR Algodystrophy</td>
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</tbody>
</table>

Independent citations – 418
Removed after title and abstract review – 393
45 remaining for abstract review

What are we predicting?

- Are we predicting the development of CRPS after a condition that affects upper extremity? 
  OR
- Are we predicting the long-term outcomes of CRPS following rehabilitation?

Risk for the Development of CRPS after a Condition that Affects Upper Extremity
**In Patients with Stroke**

**Davies et al. 2002**

**Objective:** To examine the clinical prognostic factors of CRPS I in patients 3 months after stroke

**Results:** History of initial coma, sensorimotor deficits, and spasticity

**Caution:** No information regarding the accuracy, i.e., sensitivity and specificity, in successfully predicting the onset of CRPS I after the stroke

**In Patients with Stroke**

**Vasta et al. 2002**

**Objective:** To assess the predictive ability of the hand edema measurements for developing reflex sympathetic dystrophy (RSD)

**Results:** Presence of hand edema at 4 weeks post-stroke was significantly associated with the development of RSD, with a very high chance of RSD in patients with the RCFM of above 1.0 at 4 weeks poststroke

**Caution:** No information regarding the accuracy, i.e., sensitivity and specificity, smaller sample (N = 34), 8 developed RSD

**In Patients with Wrist Fracture – using Budapest Criteria**

**Bor et al. 2004**

**Objective:** Factors associated with the development of CRPS I after surgically repaired DRF

**Patients:** 477 patients after surgically repaired DRF were followed for 6 months after DRF

**Incidence:** Was 8.8% (42 patients) at 6 months after DRF

**Prediction:** High energy fractures, female sex, and severe fractures (i.e., comminution)

**Caution:** After adjusting for possible covariates, the odds ratios for the above predictors for being associated with CRPS I was in the range of 2-4, which is considered only moderately useful and not definitive

**In Patients with Wrist Fracture – using Budapest Criteria**

**Beerthuiizen et al. 2012**

**Objective:** Investigate the incidence of CRPS I using 3 sets of diagnostic criteria and to evaluate the association between demographic/medical factors and the development of CRPS I diagnosed with the Budapest criteria

**Patients:** 596 patients with single fracture of the wrist or scaphoid were assessed at 3 months and again at 12 months

**Incidence:** Was 7.0% at 3 months and per Budapest criteria, 48.5% as per IASP criteria and 21.3% as per Veldman criteria

**Prediction:** People with low back pain, rheumatoid or osteoarthritis, intrarticular fracture, or fracture with dislocation had greater

**Caution:** No quantitative parameter about relative risk (odds ratio) for developing CRPS I with one or more factors being present

**In Patients with Wrist Fracture – using IASP Criteria**

**Morley et al. 2004**

**Objective:** 1) characterize the incidence of CRPS I after wrist fracture; 2) develop clinical prediction rule for predicting the development of CRPS I at 4 months using the data obtained at 1 week after wrist fracture

**Patients:** 1,549 patients presenting with wrist fracture, assessed in 1 week after fracture and again at 4 months

**Incidence:** At 4 months after wrist fracture was 3.8% as per IASP criteria

**Prediction:** Simply assessing pain intensity at 1 week after wrist fracture was deemed to be highly predictive of CRPS I at 4 months and the pain score of ≥5/10 reported at this assessment should be considered a red flag

**Caution:** The diagnosis of CRPS I was made using the IASP criteria, which are known to have poor specificity which leads showing higher incidence of CRPS I

**In Patients with Wrist Fracture – using IASP Criteria**

**Cissik et al. 2012**

**Objective:** to explore the role of psychological factors in the development of CRPS I after DRF

**Patients:** 58 patients with DRF, treated with plaster cast, were followed up for 2 months after the cast removal

**Incidence:** At 2 months after wrist fracture was 26% as per IASP criteria

**Prediction:** Patients with high anxiety (assessed using State-Trait anxiety score) had significantly higher risk of developing CRPS I

**Caution:** The diagnosis of CRPS I was made using the IASP criteria, which are known to have poor specificity which leads showing higher incidence of CRPS I
In Patients with Wrist Fracture – Systematic Review

Pons et al 2015

Objective: to explore the demographic, health, and injury variables that are associated with the development of CRPS I

Patients: Systematic review of 10 prospective and 6 retrospective studies

Predictions: Being female, particularly postmenopausal female, immobilization, and a report of higher than usual levels of pain in the early phases of trauma are associated with development of CRPS I.

Caution: The studies included in this review used different criteria for characterizing CRPS, so overall message does not give idea about predicting CRPS I using one criteria versus another.

So, what do we interpret from all the data

Consistent messages across the studies

- Higher reporting of pain within 1-2 weeks of wrist fracture has been found to be a concern. 35-10 pain within 1-2 weeks of wrist fracture should serve as red flag.

- Being female is an independent predictor of CRPS I; however, there are 1-2 isolated studies that refute this claim and suggest that this is due to higher incidence of wrist fracture in females.

- Longer periods of immobilisation and high-velocity wrist fractures are also associated with greater odds for developing CRPS I.

Caution: The main concern is that the prognostic literature has not been consistent in using Budapest criteria and therefore there is significant heterogeneity across the literature in what classifies as CRPS I.

Predicting the Outcomes of CRPS following Rehabilitation

Kesler 2001

Objective: identify predictors for the success of PT with regard to treatment effect and patient satisfaction

Patients: 54 patients (37 women and 17 men) with chronic RSD (at least 6 months), age range 21 to 65 years

Predictions: Duration of disease/diagnosis and higher self-reported disability resulted in poor outcomes at 6 months after PT started.

Caution: smaller sample, non-specific PT interventions (improve ROM, reduce pain).

Outcome Measures Used for Assessing Impairment in CRPS

Measurement Issues

- Poorly understood disease
- Heterogeneity in signs/symptoms experienced by the patients making it difficult to assess the spectrum of impairments
- Often pain and functions transition from those related to primary injuries to the ones attributed to the CRPS; making it difficult to isolate impairments related to primary injury versus CRPS I.

This has resulted in a broad range of concepts included in the existing assessments (e.g., pain, swelling, ROM, strength, skin temperature, mobility, participation and independence), assessed both by patients as well as clinicians, but no comprehensive condition-specific tool.
Impairment Score - CRPS I

Oerlemans et al 1998

Composite Score of ROM, Edema, Pain, and Temperature Difference

AROM
- Flex/ext and ER of shoulder
- Flex/ext of elbow
- Pronation/supination
- Flex/ext of wrist
- Flex/ext of MCP and PIP of all fingers and thumb
% of normal mobility was scored with ≥95% scoring 1 point to 5 point for ≥25% mobility for each joint. This was scored for each joint, therefore total score for all 5 joints ranged from 0-25

(Oerlemans et al 1998)

Composite Score of ROM, Edema, Pain, and Temperature Difference

Edema
Volumeter kept on table
Patient sits at the side of the table and immerses hand in volumeter vertically.
The volume of displaced water is assessed first for the unaffected and then for the affected hand
Difference of up to 3.5% (score of 0) is considered normal and the difference of >15% (score of 10) is considered severe, the 0-10 score is given between these two boundaries in equal increment

(Oerlemans et al 1998)

Composite Score of ROM, Edema, Pain, and Temperature Difference

Pain
Numeric pain scale, where pain arising after some effort was recorded
Converted to 0-10 scale

(Oerlemans et al 1998)

Composite Score of ROM, Edema, Pain, and Temperature Difference

Temperature
Patient first remains in room for 15 minutes prior to measuring
Temperature is measured at the middle of the hand at the level of 3rd MC
The temperature at both dorsal and ventral aspect is noted
Temperature difference of 0-0.3 centigrade is given 1 point and thereafter every 0.2 degree increase is given 1 point increase, thereby resulting in 0-10 score

(Oerlemans et al 1998)

Composite Score of ROM, Edema, Pain, and Temperature Difference

McGill Pain Questionnaire
In addition patients also choose up to 20 verbal descriptors for pain from McGill Pain Questionnaire
Each pair of words worth 1 point and therefore a total score between 0 (no descriptor chosen) to 10 (all 20 chosen) – is converted to 0-10 scale

(Oerlemans et al 1998)
What is the Evidence for the Psychometric Properties

Intra-observer reliability assessed using Cronbach’s alpha revealed poor reliability with alpha of 0.42. Construct validity was good when assessed with medical practitioners’ grading of RSD severity ranging from mild, moderate, severe – correlations were high 0.74. Responsiveness was high overall with effect sizes >0.8 across baseline and follow-up sessions.

(Oerlemans et al 1998)

Radboud Skills Questionnaire (RSQ)

Oerlemans et al 2000

Only Assessment for CRPS Based on ICF Categories of Activity Limitations/Participation Restrictions

Hand impairment is assessed across 11 categories. The categories include personal care, domestic activities and other activities such as recreational and social activities. Total 45 questions. A score of 1-5 (with 5 = greater problem) is given and an additional score of 9 is given for patients who have not performed that activity.

(Oerlemans et al 2000)

What is the Evidence for the Psychometric Properties of RSQ

Good reliability
Fair construct validity
The main limitation is that the RSQ is only available in Dutch and German languages.

(Oerlemans et al 2000)

Grip Strength

Geertzen et al 1998

Measured under three conditions measured:
- Full grip
- Three point
- Pinch grip

(Geertzen et al 1998)
What is the Evidence for the Psychometric Properties of Grip Strength

The reliability was poor, mainly because the examiners were not trained adequately to standardize the instructions given to the patients.

(Geertzen et al 1998)

Other Measures Used in CRPS I but Have No Psychometric Evidence

Disabilities of Arm, Shoulder, and Hand
Michigan Hand Questionnaire
Upper limb activity monitor
Short Form 26 and Short Form 12
Radboud Scale of Sensitivity – only available in Dutch, no English version

Summary

No established measure for assessing disease-related impairments
Some efforts have been made by researchers in the Netherlands to develop disease-specific measures, but they are in Dutch and their English version does not exist.
The composite scales/measures that have been used in CRPS have very little evidence for use in CRPS I

RECENT ADVANCES IN TREATING CRPS BY TRAINING THE BRAIN

SUSAN W STRALKA PT,DPT,MS

SIGNIFICANT PROGRESS IN UNDERSTANDING CRPS

Subset of patients CRPS becomes centralized
Mechanical hyperalgesia and allodynia
Non dermatomal sensory deficits
Spread of symptoms - 3 types
Continuity of mirror image, independent, total body
Body perception disturbances-loss of R/L
Movement disorders

CENTRAL SENSITIZATION PAIN CHARACTERISTICS

Symptoms of pain are generalized not localized
Often away from primary site of injury
Spreads throughout body in abnormal pattern
Allodynia and Hyperalgesia present
Increased response to multiple stimuli - Mechanical, thermal or chemical
Basic intolerance to both physical and emotional stressors

Nijs, J, It Hurts when you touch me, March 2012
WHAT HAPPENS IN CENTRAL SENSITIZATION

Exhibit lower pain threshold due to altered Central Processing
Produces pain hypersensitivity by changing the sensory response elicited by normal input
Net effect of Central Sensitization – recruiting sub-threshold synaptic inputs to NOCICEPTIVE NEURON GENERATORS.
Pain memories which fire erratically so maladaptive pain

PERSISTENT PAIN AND THE BRAIN

CRPS - peripheral and central sensitization
Increased excitation or decreased inhibition of nociceptors
Primary and secondary hyperalgesia-increase in pain sensitivity
Alloodynia-painful response to non-nociceptive stimuli


EVIDENCE WITH fMRI RESULTS

SENSORIMOTOR RETURNING IN COMPLEX REGION PAIN SYNDROME PARALLELS PAIN REDUCTION.
PLEGER ET AL., ANNUAL OF NEUROLOGY, 2005

CRPS with impaired two point discrimination threshold on fMRI showed shrinkage of cortical maps in primary S1 and S2
Graded sensorimotor training during a 6 month period showed decrease in pain intensity, restoration of the impaired tactile sensation, and regaining size of the cortical map.
Reversal of tactile impairment and cortical reorganization in CRPS is associated with a decrease of pain.

CENTRAL NERVOUS SYSTEM INVOLVEMENT IN CRPS

BODY PERCEPTION DISTURBANCES

Dislike
Distorted
Lack of ownership
Two point discrimination dysfunction
Denial of limbs
Desire to Amputate
PERCEPTION OF THE PAINFUL BODY

Understanding the relationship between body perception disturbance, pain and tactile acuity might provide insight into alternative avenues for treatment. This study tested the hypotheses that:
1. Body perception disturbance is positively related to pain and
2. Decreased tactile acuity is related to increased body perception disturbance.

Lewis, J., Schwindt, P. 2012 Eur Jour of Pain

EVIDENCE

Cohen, 2012
- Clinical evidence of parietal cortex dysfunction and correlation with extent of allodynia in CRPS type
- Swart, S. H., Beek, O. 2009
- Cortical changes in complex regional pain syndrome (CRPS)
- Hall, I., McCabe, C. 2012
- Sensorimotor dysfunction after limb fracture: an exploratory study.
- Mannix, B., 2011
- Using mirror therapy to reduce pain and improve movement

INTERVENTIONS FOR TREATING PAIN AND DISABILITY IN ADULTS WITH CRPS: OVERVIEW OF SYSTEMATIC REVIEWS

O’Connell, R., Ward, B., McAuley, J., Marston, L., Moseley, G. 2013 Issue 1 (LOE 1) Graded motor imagery (GMI) shows positive results
- Moseley, L. 2003, 2006: Comparison and Conclusions
- Good to very good quality level 1 evidence for the GMI and medical management
- Order-laterality, imagery, mirror therapy
- GMI reduces pain intensity and this reduction is maintained for up to 6 months

FOUNDATION FOR TREATMENT

Identify all peripheral and central pathophysiology
Normalize or calm down hyper-excitability central neural activity
Evidence from fMRI reveals reorganization in S1 and M1
Reorganization - altered central processing of tactile sensation and altered cerebral organization of movement
Clinical changes result in body perception disturbances, mislocation tactile input, distortion and pain amplification, abnormal-refrained sensations and abnormal motor control
Good neuroplasticity


RESEARCH ON TREATMENT

Keep the amygdala under control to reduce threat and fear
- Graded motor imagery and mirror therapy
- Tactile discrimination
- Bio-psycho-social support

Rosen, 2010; McCabe 2010; Issue 2014; Schmidt, 2014
ACTIVATION OF NEUROTAGS

Brains cells that make up the neurotag have to fire together.
Other brain cells must be inhibited so they don’t fire.
So with pain neurotags keep them below activation level.
If pain persists neurotags become sensitized and disinhibited and fire whenever they want.

Example: thinking about movement causes pain.

THE BRAIN-LET’S TRAIN

Voluntary information is controlled by a network of different areas in the brain.
Sensory information is controlled by primary somatosensory cortex.
Clinical outcome of nerve injury treatment depends on brain plasticity.
Brain plasticity can be guided therapeutically to improve clinical outcomes.

RESEARCH SUPPORTED STRATEGIES

Immediate re-education
Sensory and motor imagery
Visual-tactile stimulation with mirrors

Lundborg and Rosen 2003; Bjorkman 2005; Moseley 2012

MECHANISMS FOR REMAPPING

Uncover silent synapses
Form new axon connection by guided neuroplasticity
Immobilization, inflammation, pain, fear of moving cause brain changes
Decreased movement need new cortical mapping since with sensory loss and motor patterns changing.

CRPS TREATMENT - GUIDED PLASTICITY IN REHABILITATION

Start immediately after injury or before surgery
Sensory imagery and touch imagery exercises
Watching other hands moving normally (activates mirror neurons)
Laterality or right-left identification
Imaging from non-threatening and progressing
Mirror therapy
Dedicated and committed patient

Lundborg and Rosen 1993; Walbruch and Kalliammen 2015; McCabe 2014

GRADED MOTOR IMAGERY SENSORIMOTOR RE-EDUCATION

Goal is to improve cortical mapping
Progress exercises as sensation improves
Purposeful movement activities are key with patient specific activities that are important to them
Progress to Bimanual tasks
Functional activities

Lundborg and Rosen 1993; Walbruch and Kalliammen 2015; McCabe 2014
CRPS/CAUSALGIA IS NEUROPATHIC

Treat the rapid reorganisation in somatic sensory
After injury the brain and hand don’t speak the same language
Patient education to understand training of the brain is important
Phase 1 starts immediately after surgery before regenerating axons have reached the hand
Phase 11 starts when the new axons have re‐innervated the skin

CORTICAL EFFECTS OF NERVE INJURY AND REPAIR

Early effect: a "silent” cortical area, deprived of sensory input (phase 1)

Late effect: functional reorganisation of the cortical hand map due to axonal misdirection (phase 2)
Merenich, Jenkins 1995, J Hand Ther;6:89-104

REHABILITATION: NORMALIZE HYPEREXCITABLE CENTRAL NEURAL ACTIVITY AND TREAT THE PERIPHERAL SYMPTOMS

Bio-psycho-social approach
Treat bottom up and top-down
Tactile discrimination/desensitization
Cognitive behavioral training
Mirror therapy graded exposure
Graded motor imagery graded exposure

GRADED MOTOR IMAGERY

Sequential phases - participants who followed the GMI stages had better outcomes with reduced pain rating and increased functional task ability than participants who did not follow the order
Sequential phases - laterality, explicit/implicit imagery and mirror therapy
Moseley L, 2006

MIRROR THERAPY

Movement of the affected limb not performed in synchrony
Produces conflicting sensory feedback
And motor output will be exaggerated
CRPS PAIN CAN BE INCREASED

Mirror therapy performed with both limbs moving in bilateral synchronous manner
Person can feel the movement at the same time as observing the reflection of the normal limb moving
REDUCTION OF PAIN
McCabe 2011

GRADED MOTOR IMAGERY - CORTICAL REORGANISATION

NOT FULLY UNDERSTOOD BUT CAUSED BY MANY PATHOPHYSIOLOGICAL CHANGES
GRADED MOTOR IMAGERY

GMI is a rehabilitation brain based treatment used to treat pain and movement dysfunction. The dysfunction is related to an altered nervous system. By exercising the brain in measured and monitored steps as well as progressing to functional activities helps reorganize cortical networks.

MODIFIED GRADED MOTOR IMAGERY FOR CRPS

Outcome measurements: McGill Pain Questionnaire, grip force, Self-reported function assessed by DASH

Participants: CRPS in L/U, n = 7, patients 18 or older who had symptoms < 6 month

Results: pain decreased especially last 7 days (VAS p=0.046) improvement grip force P=0.042 and global impression of change P=0.013 but DASH not clinically or statistically significant.

Results indicate that modified GMI is a promising modality to reduce pain

Lagueux et al


Moseley’s sequential phases- (2 weeks /14 days) Phase one-laterality followed by phase 2-imagery then phase 3-mirror therapy
Modified fMRI - changes made; 1-3 weeks integration of mirror box into phase 2 which is to imagine the movement(motor imagery) and mirror therapy has been divided into 2 phases

BIO-PSYCHO-SOCIAL APPROACH

Self management of the pain- EDUCATION
Mindful awareness
Cognitive behavioral
Mirror therapy
Graded motor imagery
Exercise regime normal movement without symptoms
Pacing

TREATMENT SUCCESS

Evidence based practice for Top-Down
Multi-disciplinary approach
Good neuroplasticity
Treat the changes in cortical processing and organization - Body perception disturbance - Sensory incongruities - Motor dysfunction

RIGHT AND LEFT IDENTIFICATION

HANDS, FEET, KNEES - R or L
SHOULDER AND BACK - WHICH WAY ARE THEY TURNING