

Clinical Rehabilitation

<http://cre.sagepub.com>

Pain exposure physical therapy may be a safe and effective treatment for longstanding complex regional pain syndrome type 1: a case series

Jan-Willem Ek, Jan C van Gijn, Han Samwel, Jan van Egmond, Frank PAJ Klomp and Robert TM van Dongen

Clin Rehabil 2009; 23; 1059 originally published online Nov 11, 2009;
DOI: 10.1177/0269215509339875

The online version of this article can be found at:
<http://cre.sagepub.com/cgi/content/abstract/23/12/1059>

Published by:



<http://www.sagepublications.com>

Additional services and information for *Clinical Rehabilitation* can be found at:

Email Alerts: <http://cre.sagepub.com/cgi/alerts>

Subscriptions: <http://cre.sagepub.com/subscriptions>

Reprints: <http://www.sagepub.com/journalsReprints.nav>

Permissions: <http://www.sagepub.co.uk/journalsPermissions.nav>

Citations <http://cre.sagepub.com/cgi/content/refs/23/12/1059>

Pain exposure physical therapy may be a safe and effective treatment for longstanding complex regional pain syndrome type 1: a case series

Jan-Willem Ek, Jan C van Gijn Department of Rehabilitation Medicine, Bethesda Hospital, Hoogeveen, **Han Samwel** Institute for Anesthesiology, Pain Centre and Department of Clinical Psychology, **Jan van Egmond** Institute for Anesthesiology, Pain Centre, **Frank PAJ Klomp** Department of Physical Therapy and **Robert TM van Dongen** Institute for Anesthesiology, Pain Centre, Radboud University Medical Centre, Nijmegen, The Netherlands

Received 5th February 2009; returned for revisions 15th April 2009; revised manuscript accepted 17th May 2009.

Objective: To determine if treatment of longstanding complex regional pain syndrome type 1, focusing on functional improvement only while neglecting pain, results in clinical improvement of this syndrome.

Design: Prospective description of a case series of 106 patients.

Setting: Outpatient clinic for rehabilitation.

Interventions: Physical therapy of the affected limb directed at a functional improvement only while neglecting the pain, was performed following an extensive explanation. Normal use of the limb between the treatments was encouraged despite pain. A maximum of five of these sessions were performed in three months.

Measures: Radboud Skills Test was used to monitor functional improvement of the arms. Speed and walking distance was used as the measure of outcome for the legs.

Results: The function of the affected arm or leg improved in 95 patients. Full functional recovery was experienced in 49 (46%) of them. A reduction in pain presented in 75 patients. In 23 patients functional recovery was reached despite an increase in pain. Four patients stopped early due to pain increase.

Conclusions: Our results suggest that 'pain exposure physical therapy' is effective and safe for patients who are unresponsive to accepted standard therapies. Avoiding the use of a limb due to pain will result in loss of function. Forced usage of limbs restores the function, reverses these adaptive processes and leads to regain of control by practice with a reduction of pain in most cases.

Introduction

Complex regional pain syndrome type 1 (CRPS-1) presents with pain, sensory and motor disturbances and autonomic deregulation.^{1,2} The reported incidence of CRPS-1, depending on the study population and diagnostic criteria used, varies between 5.46 and 26.2 per 100 000 person-years.^{3,4}

Address for correspondence: R van Dongen, Radboud University Nijmegen Medical Centre, 630 Department of Anesthesiology, Pain Centre Nijmegen, The Netherlands.
e-mail: R.vandongen@anes.umcn.nl

© The Author(s), 2009.

Reprints and permissions: <http://www.sagepub.co.uk/journalsPermissions.nav>

10.1177/0269215509339875

Despite a spontaneous restoration in the majority of the cases about 22% show long-lasting symptoms and signs.⁵ These may vary from joint stiffness and pain to a complete paralysis and loss of function of the affected limb in extreme cases. The prognosis of these patients with chronic complaints appears to be poor since they can show severe functional impairments in combination with ongoing pain complaints.⁵ Due to these pain complaints any functional improvement is severely restricted.

Recent research has shown that in CRPS-1 patients, extensive neuroplastic changes have taken place in the brain which by themselves can interfere with the normal use of an extremity.^{6,7} These 'central changes' might explain the inefficacy of an approach that is directed only at a reduction of the pain complaints at this stage. In the past, physical therapy in CRPS mainly focused on a 'pain-contingent' treatment. By respecting pain as a sign of ongoing injury, only non-painful exercises were allowed and tolerated.⁸

Recently, however, an approach called 'graded exposure' has proven to be effective in these patients.⁹ It has been suggested that limiting the use of the extremity due to severe pain could be counterproductive and lead to a further deterioration. In line with these findings an early, more functionally directed approach may result in a better outcome. Although a comparable, more 'aggressive' approach based on these considerations has been published in the past, this has not received widespread attention since then.¹⁰

By coincidence we were confronted by a number of treatment-resistant CRPS-1 patients of our own hospital who, at their own initiative, underwent an 'experimental', unpublished, treatment abroad. This approach was primarily aimed at functional improvement and appeared to have a remarkable positive effect on both function and pain. We therefore decided to treat a sequential group of chronic CRPS-1 treatment-resistant patients who presented to our hospital in a similar way, to determine whether this treatment could result in a similar positive effect.

We chose to call this treatment 'pain exposure physical therapy' or 'PEPT', since our approach, despite pain provocation, was mainly directed at a functional change. With this case series we primarily aim to describe the efficacy and the safety of

this approach. Also, we wanted to interpret the results in a theoretical framework considering the recent information on neuroplastic changes as seen in CRPS-1.

Patients and methods

Study population

All patients studied were diagnosed as having CRPS-1 according the International Association for the Study of Pain (IASP) criteria,¹¹ and were excluded if this diagnosis could not be confirmed at the start of the study. Also, serious depression or psychopathology as determined on clinical grounds and a suspicion of automutilation or severe affective disorders were reasons for exclusion. To determine if the patients were all in a chronic phase the following inclusion criteria were used: longstanding (more than nine months) pain and functional impairment in one extremity despite various treatments (e.g. analgesics, transcutaneous electric nerve stimulation, physical therapy in various ways, nerve blocks and rehabilitation treatment). Since none of these therapies had resulted in further improvement, the patients agreed to this new treatment after information and explanation of the protocol. A possible pain increase was also discussed.

Due to the 'end-stage situation' of CRPS-1 in these patients and failure of previous treatment, further consent by an ethical committee was considered not to be necessary. All patients, however, gave written informed consent. Patients were motivated to perform the exercises at home despite concomitant pain increase and they also agreed that their partner would be present during the treatment. At the moment of inclusion all other treatments were truncated and all drugs aimed at CRPS-1 were tapered and stopped. Since most of the analgesics were ineffective, patients were advised to stop taking them.

Description of the intervention

Patients, in the presence of their partner or relative, were first seen by a rehabilitation physician to exclude any other underlying serious pathology and confirming the diagnosis of CRPS-1.¹¹

After a standardized examination of the affected extremity by a physiotherapist to determine the passive and active range of motion of the joints, a comparison was made with the corresponding healthy side.

Following this examination the rehabilitation physician and physiotherapist talked together with the patient and their partner. Here, it was explained that the persistent pain complaints should be considered to be 'a false warning sign' of the nervous system, instead of a symptom of ongoing tissue injury demanding that the limb be immobilized to prevent further damage. It was also emphasized that CRPS-1 should be considered to be a reversible deregulation of the nervous system. Functional deterioration, vegetative and sensory abnormalities and pain were all explained in this context.

Before the actual treatment started it was discussed extensively that the therapists, although understanding the pain, would not respond to it. An essential part of this approach was, therefore, that both verbal and non-verbal expressions of pain during examination and therapy would be ignored. Also, the contrast with physical therapy as experienced by the patient previously, was underlined at this phase.

The treatment was initiated by using traction and translation of the restrained joints. Also, an assisted or active movement of the joint was combined with passive stretching of hyper- and dystonic muscles. If necessary, this was followed by an intensive manual friction of tender points. The goal of this approach was to increase the active and passive range of motion. The patient was motivated to ignore the pain (even when it increased), allowing the affected limb to be touched and moved. Also direct use of the affected extremity in a functional way immediately thereafter was encouraged (e.g. like holding and opening a bottle with their hand or active walking). When it was necessary to decrease sensitization, it was shown that touching the skin was harmless and could be performed at home as well.

To further attain a rapid and functional use of the affected extremity as quickly as possible in a time-contingent way, patients were instructed to perform the prescribed exercises at home. Functional improvement was the aim of these exercises. Patients, for example, were not allowed

to use their wheelchair or had to aim to walk without crutches a certain distance the following week. Patients were encouraged to practise at least the same exercises that were performed at the end of the previous treatment session. Also, they were given the role of an active coping person instead of a pain-avoiding, passive patient. The partner or relative was also given an active participating role as an instructor and a mental guide.

Two physiotherapists performed all treatments together once weekly at the start, with a greater interval when possible, for a maximum of three months. This was done to show a positive, reinforcing attitude towards the patient. Being together, both therapists could express great confidence with the therapy. No other disciplines were involved during these sessions. The treatment sessions lasted 45 minutes and were limited to a maximum of five. Evaluation of the treatment was performed three months after the last intervention.

Outcome measures

Primary outcome measure: functional improvement

The primary outcome measure of pain exposure therapy is functional improvement of the affected extremity as measured by various objective parameters. To register this the following tests were used before treatment (T_1) and 3–4 months (mean 3.6 months) after the last treatment session (T_2).

- For evaluation of the hand/arm function the Radboud Skills Test was used.¹² This test was specifically developed for CRPS-1 of the arm and consists of 10 two-handed tasks. Each task has two scores. A limitation score determined by an occupational therapist and an effort score determined by the patient. The therapist scored 10 items from 0 (normal) to 4 (impossible) resulting in a maximum limitation score of 40. The patient scored each item from 0 (no effort) to 2 (much effort) providing a maximum effort score of 20. A normal function and thus full recovery of the hand/arm function was defined as a Radboud Skills Test limitation score <3. A partial recovery was defined as an improvement of the Radboud Skills Test limitation score.

- For evaluation of the leg/foot function we determined:
 - (a) Maximum duration/distance of walking in minutes or meters, as reported by the patient (15 minutes walking was taken as 1 km)
 - (b) Time needed to walk 7 m, measured in seconds.
 - (c) Time (in seconds) needed to climb a standard stair consisting of three steps: going three steps up, turning, and going down again.

A normal function and full recovery for the leg was defined as being able to walk either more than 4 km or more than 1 hour, without crutches. Partial recovery was defined as an improvement of the walking-distance, however, less than 4 km.

Secondary outcome measure

Pain scores (visual analogue scale, VAS) were noted as secondary outcome measures before treatment and at three months after treatment.

Statistical analysis

Data were assembled in an Excel database that was imported in SAS (SAS Institute inc, Cary, NC, USA) for statistical analysis. Data are reported as mean (SEM, min-max, *N*). Comparisons of variables at two different occasions (before treatment and three months after the last treatment session) were performed with Student's *t*-test for paired observations, for which *P*-values are reported. *P* < 0.05 was considered significant.

Results

A total of 186 patients were referred and seen by us, of whom 80 could not be included in the study. The majority of these patients either did not meet the International Association for the Study of Pain criteria¹¹ any more or presented with another cause for their pain complaints (e.g. carpal tunnel syndrome, peripheral nerve lesions, arthritis, post-thrombotic syndromes, disuse). A few patients

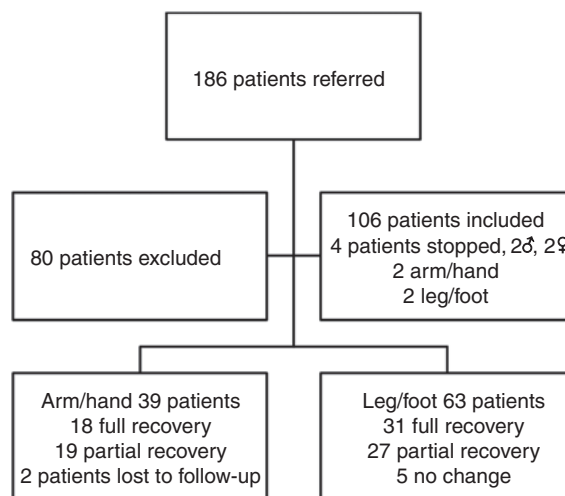


Figure 1 Flowchart of the patients referred and entering the study.

showed a variety of psychosocial complaints (anxiety, depression, etc.) or chose not to participate. As shown in Figure 1, 106 patients entered the study and consented to the treatment protocol.

During treatment, four patients dropped out since they considered the interventions too strenuous and too painful for them. Therefore, 102 patients completed the study with a mean age of 45.0 years (1.37; 12–76; 102). The mean duration of the CRPS-1 symptoms was 55.0 months (4.3; 9–204; 102).

Functional changes

Arm/hand group

The majority of patients improved functionally (Table 1, Figure 1). In 18 patients, full functional recovery, with a limitation score below 3 at three months after treatment, was reached, while partial recovery was noted in another 19 patients.

Leg/foot group

Full functional recovery was reached in 31 patients being able to walk more than 4 km. In 27 patients the walking distance improved, however, they could not reach the 4 km point. Five patients did not show an improvement. In 58 out of 63 patients data were present to show an

Table 1 Functional changes in the arm/hand and leg/foot and pain scores

			T_1 (start of treatment) Mean (SEM, min–max)	T_2 (three months after treatment) Mean (SEM, min–max)	<i>P</i> -value
Arm/hand 37 patients 2 patients lost to follow-up	Radboud Skills Test	Limitation score	21.0 (1.39; 4–32)	5.8 (1.16; 0–30)	<0.0001
		Effort score	7.8 (0.79; 0–16) 9.4 (1.6; 0–60)	2.6 (0.5; 0–10) 60 (6.3; 15–150)	<0.0001 <0.0001
Leg/foot 63 patients	Walking Duration in minutes				
Missing 5 patients	Velocity 7 meters in seconds		16.9 (2.7; 8–137)	8.0 (0.7; 3.8–35)	0.0007
Missing 6 patients	Climbing Stairs 3 steps up and down in seconds		17.3 (2.4; 4.5–97)	7.8 (0.6; 2.7–31)	<0.0001
Pain	VAS		4.9 (0.24; 0–9)	2.7 (0.27; 0–9)	<0.0001

VAS, visual analogue scale; SEM, standard error of the mean.

Radboud Skills Test: Limitation score (0–40). Effort score (0–20): maximum score is functionally poor. Walking: maximum duration of walking possible; time in minutes. Velocity: time in seconds to walk 7 m. Climbing stairs: time in seconds to climb three steps up and down.

increase in walking velocity as seen by a decrease in time to walk 7 m in Table 1. No patient deteriorated functionally during treatment.

Pain

In 76 patients the visual analogue scale score decreased, while in 14 patients it was higher after treatment than before treatment; in 12 patients the visual analogue scale score did not change. Remarkably, in 10 of these 26 patients full functionality was reached, while in 13 partial improvement was noted.

At the end of the study period (three months after treatment) additional physical therapy was needed in 19 patients. This was mainly for persistent contractures, loss of muscle strength or improvement of the general condition of the patient. No patient showed a long-lasting increase in symptoms. Some patients experienced a temporary increase in pain following the treatment session. This, however, did not interfere with functional progress. No other adverse effect was noted in any patient.

Discussion

This study shows that a treatment aimed at maximal functional restoration is safe and effective in

patients with longstanding CRPS-1. Only four patients dropped out due to the pain provocation of the treatment. Conventional treatment of CRPS-1 consists both of physical therapy as well as pharmacological management but in a large group of patients serious impairments can persist.⁵ Physical therapy has always been an important part of the treatment of CRPS-1 although the optimal approach and its efficacy is still undetermined.¹⁵ Despite agreement that early diagnosis and timely physical therapy can lead to better outcomes,² large variations exist in the way physical therapy is prescribed and performed.¹⁴ Usually severe pain provocation during treatment is avoided by using general physical therapeutic or occupational therapeutic principles.^{8,15} Part of this approach is also used in so-called 'graded exposure'. Minimizing pain complaints during this treatment has recently been shown to result in an improved outcome.⁹ Severe spontaneous or provoked pain complaints, however, can be a barrier for the patient and the therapist in regaining the necessary functional improvement.¹⁵

Although pain exposure physical therapy can provoke severe temporary emotional and physical effects and pain, the results appear impressive, especially in these chronic patients. This is even more remarkable considering that 23 patients,

despite the same or increased pain complaints, were able to achieve functional improvement. Due to the fact that many patients are no longer used to seeing and feeling their limbs moving, they frequently show a state of disbelief about the regained control combined with pain at the same time. Crying at that moment, therefore, is not only caused by pain itself. Physical symptoms can present as a temporary swelling which wears off after a few days.

What leads to these positive changes when the induced pain is ignored by both the therapist and the patient? Recently, numerous studies have indicated that early in the development of CRPS-1 extensive changes occur in the central nervous system, in particular the brain.^{6,16,17} These patterns of reorganization consist of shrinkage of the somatotopic area of the affected extremity in the primary somatosensory cortex (S1).⁶ When the syndrome recovers clinically, these changes appear to normalize and the cortical representation is restored.^{16,18} Apart from these somatosensory changes, a disturbance in the normal sensory-motor interaction¹⁹ and a reorganization of various motor circuits as shown by an enlargement of functional magnetic resonance imaging (fMRI) signalling takes place.²⁰ These alterations may lead to extensive changes of the perception of the so-called 'body scheme'.^{7,18,21,22} This underpins that widespread 'central' effects of this 'regional' pain syndrome can be found in the brain. Also, this 'distorted body image' can lead to a delayed recognition of an extremity and a subsequent more extensive and serious loss of control.⁷ Remarkably, there appears to be a close correlation between this sense of 'foreignness' and the pain intensity, as has been shown in numerous neuroimaging studies.^{16,18,23} The occurrence and disappearance of pain appears to be a clinical symptom which is closely linked to these changes in these imaging studies.^{18,24}

These findings may therefore lead to a new therapeutic approach.^{18,23,25} An improvement in this chronic phase of CRPS-1 is still feasible despite the long-lasting complaints and the risk of severe limitations in the future.⁵ Since pain and functional disturbances are major parts of the problem, these will lead to restrictions in the normal use of the affected extremity. The presence of allodynia in CRPS-1 can be determined objectively by fMRI

and appears to be associated with widespread cortical activation beyond the primary somatosensory cortex.^{24,26} Symptoms of allodynia and subsequent fear of movement are reinforced by fear-avoidance cognitions. These reflect the thought that movement will induce more pain and thus cause harm.^{9,27} Finally, the patient's cognitions may be supported by the therapist's ideas that pain-provoking activities may worsen the disease symptoms and consequently the disease.²⁸ When painful activities are thus discouraged this may induce an 'iatrogenic' component in the treatment of CRPS-1, ultimately resulting in a state of 'learned disuse'.²⁹ Also, the presence of a fearful partner or observer can increase the threat value of pain, further adding to this negative affect.³⁰

The rationale for pain exposure physical therapy is, therefore, that this treatment interferes and breaks this vicious cycle and aims mainly at functional restoration. The concomitant pain complaints can therefore be ignored and interpreted as a 'false warning sign' of the nervous system. This is explained extensively to the patients and their partners at various times during the treatment.

Patients are also clearly influenced by cognitive-behavioural effects of the team as a whole. The relative contribution of these components on the total treatment effects remain unclear.

Since the early phase of pain exposure physical therapy can be very painful, we initially considered performing the treatment under regional or general anaesthesia. However, after considering the neuroplastic changes as discussed above, we decided to treat without sedation or concomitant use of analgesics in order to have a rapid restoration of function.

In our experience one of the cornerstones of the success of pain exposure physical therapy is to motivate the patient to undergo both the painful interventions and to keep training and exercising at home. We estimated their motivation in a practical sense. Patients were asked whether they had any idea what they would like to do when their extremity was functioning in a near-normal way. A realistic approach to this question seemed to be a good predictor of achievability. The supportive cooperation of the partner is also necessary since any lack of support could, via operant conditioning, lead to failure of this therapy.³⁰ Although a number of these aspects have been described

extensively by Bruehl and Chung,²⁷ our approach is different since functional restoration is the primary goal of the treatment and pain is ignored. Also, the therapist manipulates the affected extremity from the beginning which is also the difference with the technique described by Watson and Carson¹⁰ where only the patient manipulates and moves the extremity.

A number of drawbacks are present in this case series. Despite the chronic stage situation of the majority of the patients, a control group could have been added to improve the scientific value. However, the 106 patients treated with pain exposure physical therapy in the present study may be considered more or less as their own controls, since they had all undergone several accepted 'standard' therapies for CRPS-1. Therefore, the obtained improvements in these patients clearly indicate that pain exposure physical therapy was either able to reach a higher level of performance or still a lower pain level in comparison with other previous therapies for CRPS-1. It is desirable that a controlled study is undertaken in which new patients are randomized between pain exposure physical therapy and the standard treatment. That study should answer the question whether pain exposure physical therapy is a favourable therapy for recently diagnosed CRPS-1 patients or would be specifically beneficial in only a subgroup of extremely motivated patients. At this moment such a study has started in our hospital (<http://clinicaltrials.gov/ct2/show/NCT00817128>). Finally, another drawback in our study was that blinding of the patients and therapists was impossible due to the pain complaints during treatment. Assessment of the patients was, therefore, not performed by a blinded observer. Future prospective studies should consider these weaknesses.

Although we informed the patients extensively about the experimental nature of the treatment, we did not request the formal consent of an ethical committee. Having undergone a variety of all treatments available for CRPS-1, before, we thought this would not be necessary. Despite the fact that all patients gave written informed consent, in hindsight we should have considered formal ethical approval before the study was performed.

We have described the results of our treatment called pain exposure physical therapy for chronic

CRPS-1 by following a strict physiotherapeutic approach with particular attention to the cognitions and attitudes of the patient and their partner. The main difference from previous treatments is the neglect of the pain complaints aiming primarily at an optimal functional restoration in a motivated patient and partner. We conclude that pain exposure physical therapy as shown in this pilot study is a safe, effective and inexpensive therapy for an otherwise severely debilitating condition.

Clinical messages

- A treatment of longstanding complex regional pain syndrome type I aimed at functional improvement only, without any focus on pain complaints, is safe and can still be effective.
- Despite a temporary increase in pain, ultimately, reduction of it will follow in the majority of patients.

Acknowledgements

The contribution of EN Robertson MD PhD in the preparation of the manuscript is gratefully acknowledged.

References

- 1 Veldman P, Reynen H, Arntz I, Goris R. Signs and symptoms of reflex sympathetic dystrophy: a prospective study of 829 patients. *Lancet* 1993; **342**: 1012–16.
- 2 Birklein F, Riedl B, Sieweke N, Weber M, Neundörfer B. Neurological findings in complex regional pain syndromes-analysis of 145 cases. *Acta Neurol Scand* 2000; **101**: 262–69.
- 3 Mos de M, de Bruijn AGJ, Huygen FJPM, Dieleman JP, Stricker BH, Sturkenboom MC. The incidence of complex regional pain syndrome: a population based study. *Pain* 2007; **129**: 12–20.
- 4 Harden RN, Bruehl SP. Diagnosis of complex regional pain syndrome; signs, symptoms and new empirically derived diagnostic criteria. *Clin J Pain* 2006; **22**: 415–19.

- 5 Vaneker M, Wilder-Smith O, Schrombges P, Oerlemans M. Impairment as measured by ISS do not greatly change between one and eight years after CRPS-1 diagnosis. *Eur J Pain* 2006; **10**: 637–44.
- 6 Maihöfner CA, Handwerker HO, Neundorfer B. Patterns of cortical reorganization in complex regional pain syndrome. *Neurology* 2003; **61**: 1707–15.
- 7 Moseley GL. Why do people with complex regional pain syndrome take longer to recognize their affected hand?. *Neurology* 2004; **62**: 2182–86.
- 8 Oerlemans HM, Oostendorp RA, de Boo T, Goris R. Pain and reduced mobility in complex regional pain syndrome I: outcome of a prospective randomised controlled clinical trial of adjuvant physical therapy versus occupational therapy. *Pain* 1999; **83**: 77–83.
- 9 De Jong JR, Vlaeyen JWS, Onghena P, Cuyper C, den Hollander M, Ruijgrok J. Reduction of pain-related fear in complex regional pain syndrome type 1: The application of graded exposure in vivo. *Pain* 2005; **16**: 264–75.
- 10 Watson HK, Carson L. Treatment of reflex sympathetic dystrophy of the hand with an active 'stress loading' program. *J Hand Surg* 1987; **12**: 779–85.
- 11 Stanton Hicks M, Jänig W, Hassenbusch S, Haddox JD, Boas R, Wilson P. Reflex sympathetic dystrophy: changing concepts and taxonomy. *Pain* 1995; **63**: 127–33.
- 12 Cup E, van de Ven-Stevens L, Corstens-Mignot M. Radboud Skills Test (RST) Een ziektespecifieke functionele handentest voor patiënten met Complex Regionaal Pijnsyndroom aan een bovenste extremititeit. *Ned Tijdschr Ergother* 1999; 152–156.
- 13 Smith TO. How effective is physical therapy in the treatment of complex regional pain syndrome type 1? A review of the literature. *Musculoskeletal Care* 2005; **3**: 181–200.
- 14 Daly AE, Bialocerkowski AE. Does evidence support physiotherapy management of adult Complex Regional Pain Syndrome Type One? A systematic review. *Eur J Pain* 2009; **13**: 339–53.
- 15 Harden RN, Swan M, King A, Costa B, Barthel J. Treatment of complex regional pain syndrome. *Functional restoration. Clin J Pain* 2006; **22**: 420–24.
- 16 Maihöfner CA, Handwerker HO, Neundorfer B, Birklein F. Cortical reorganization during recovery from complex regional pain syndrome. *Neurology* 2004; **63**: 693–701.
- 17 Schwenkreis P, Janssen F, Rommel O *et al.* Bilateral motor cortex disinhibition in complex regional pain syndrome (CRPS) type 1 of the hand. *Neurology* 2003; **61**: 515–19.
- 18 Pleger B, Tegenthoff M, Ragert P *et al.* Sensorimotor returning in complex regional pain syndrome parallels pain reduction. *An Neurology* 2005; **57**: 425–29.
- 19 Turton AJ, McCabe CS, Harris N, Filipovic SR. Sensorimotor integration in Complex Regional Pain Syndrome: a transcranial magnetic stimulation study. *Pain* 2007; **127**: 270–75.
- 20 Maihöfner CA, Baron R, DeCol R *et al.* The motor system shows extensive changes in complex regional pain syndrome. *Brain* 2007; **130**: 2671–87.
- 21 Schwoebel J, Coslett HB, Bradt J, Friedman R, Dileo C. Pain and the body schema: effects of pain severity on mental representations of movement. *Neurology* 2002; **59**: 775–77.
- 22 Förderreuther S, Sailer U, Straube A. Impaired self perception of the hand in complex regional pain syndrome (CRPS). *Pain* 2004; **110**: 756–61.
- 23 Acerra NE, Souvlis T, Moseley GL. Stroke, complex regional pain syndrome and phantom limb pain: can commonalities direct future management? *J Rehabil Med* 2007; **39**: 109–14.
- 24 Maihöfner C, Forster C, Birklein F, Neundorfer B, Handwerker HO. Brain processing during mechanical hyperalgesia in complex regional pain syndrome: a functional MRI study. *Pain* 2005; **114**: 93–103.
- 25 Moseley GL. Graded motor imagery is effective for long-standing complex regional pain syndrome: a randomised controlled trial. *Pain* 2004; **108**: 192–98.
- 26 Maihöfner C, Handwerker HO, Birklein F. Functional imaging of allodynia in complex regional pain syndrome. *Neurology* 2006; **66**: 711–17.
- 27 Bruehl S, Chung O. Psychological and behavioural aspects of complex regional pain syndrome management. *Clin J Pain* 2006; **22**: 430–37.
- 28 Ostelo RWJG, Vlaeyen JWS. Attitudes and beliefs of health care providers: Extending the fear-avoidance model. *Pain* 2008; **135**: 3–4.
- 29 Vlaeyen JWS, Kole-Snijder AMJ, Boeren R, Van Eek H. Fear of movement/(re)injury in chronic low back pain and its relation to behavioral performance. *Pain* 1995; **62**: 363–72.
- 30 Stroud M, Turner J, Jensen M, Cardenas D. Partner responses to pain behaviors are associated with depression and activity interference among persons with chronic pain and spinal injury. *J Pain* 2006; **7**: 91–99.