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Brush-evoked allodynia predicts outcome of spinal cord stimulation in Complex Regional Pain Syndrome type 1

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ABSTRACT

Background: Spinal cord stimulation (SCS) has proven to be an effective however an invasive and relatively expensive treatment of chronic Complex Regional Pain Syndrome type 1(CRPS-1). Furthermore, in one third of CRPS-1 patients, SCS treatment fails to give significant pain relief and 32–38% of treated patients experience complications. The aim of the current study was to develop effective prognostic factors for prediction of successful outcome of SCS.

Methods and results: The study population consisted of 36 chronic CRPS patients enrolled in a randomized controlled trial of SCS efficacy. We analyzed various prognostic factors in the group of patients treated with SCS and compared baseline values of possible predictors of outcome in the successfully treated and the not successfully treated group. Success was defined as Patient Global Perceived Impression of Change score of at least "much improved" and pain reduction of at least 2.5 on a visual-analogue scale (VAS score 0–10). Univariate analyses showed that patient age, duration of the disease, localization of the disease, intensity of the pain, and the presence of mechanical hypoesthesia did not predict SCS success. The mean and maximum value of brush-evoked allodynia proved to be statistically significant predictors of outcome. Using Receiver-Operating Characteristic (ROC) curve analyses of maximum allodynia values, the diagnostic sensitivity for successful SCS was 0.75 and the specificity 0.81.

Conclusion: Brush-evoked allodynia may be a significant negative prognostic factor of SCS treatment outcome after 1 year in chronic CRPS-1.

1. Introduction

CRPS-1 is a syndrome that describes an array of painful conditions that are characterized by a continuing regional pain which is seemingly disproportionate in time or degree to the usual course of any known trauma or other lesion, as defined by the clinical diagnostic criteria of the International Association for the Study of Pain (IASP) (Merskey, 1994). Common symptoms in CRPS-1 patients are the presence of pain, edema, trophic changes and sensory disturbances, with mechanical hypoesthesia being present in 74% and mechanical allodynia in 85% of cases (Kemler et al., 2000b; Maihofner and Birklein, 2007; Maihofner et al., 2006).

Spinal cord stimulation (SCS) is an accepted, effective therapy for chronic pain in Complex Regional Pain Syndrome (CRPS) patients who fail to improve with medication, physical therapy or less invasive procedures and who require additional or more aggressive pain therapy (Grabow et al., 2003; Taylor et al., 2006). It is considered general practice in SCS treatment to begin with a test stimulation period of about one week with an external stimulating device before a permanent SCS device is implanted. Both test stimulation and subsequent implantation of a SCS device are invasive procedures, with common complications such as electrode displacement and pain from the pulse generator pocket, requiring reoperation. These complications are reported in 31–38% of patients within the first 2 years of stimulation (Kemler et al., 2004; Kumar et al., 2006).

About two thirds of CRPS-1 patients undergo implantation of a permanent spinal cord stimulating system (Kemler et al., 2001; North et al., 1991; Spiegelmann and Friedman, 1991). The effect of the permanent SCS on pain may gradually decline over time (Farrar et al., 2001; Kemler et al., 2008; Kumar et al., 1998).

There have been few reports on the prognostic factors in successful stimulation in CRPS-1 (Sindou et al., 2003; Smits et al.,

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2006; Taylor et al., 2006). Absent or significantly altered neural conductivity in the dorsal column-lemniscal system as measured by somatosensory evoked potentials (SSEPs) was a negative predictor of SCS success in patients with intractable chronic neuropathic pain (Sindou et al., 2003). A differential effect of SCS related to the severity of the allodynia was reported in an experimental neuropathic pain model in rats (Smits et al., 2006). In this model SCS led to a better and faster pain relief in mildly allodynic rats than in those with severe allodynia.

The present study is part of our participation in a randomized controlled trial of SCS efficacy for CRPS patients out of which demographic criteria and a variety of reliable and validated pain and sensory measurement were used to asses changes in outcome in the SCS treated group (Kemler et al., 2001).

For identification of predictors for successful pain relief after SCS treatment, we analyzed pretreatment responses to the above mentioned criteria and correlated each with the reported pain status after trial stimulation and after 1 year of SCS treatment. Special attention was paid to two clinically useful and common sensory characteristics in CRPS-1, namely mechanical hypoesthesia and brush-evoked allodynia.

2. Methods

2.1. Patients

The study population was drawn from a series of 54 consecutive CRPS-1 patients who underwent a randomized trial of SCS at the University Medical Centre of Maastricht, The Netherlands (Kemler et al., 2000a). Of these trial patients only the 36 patients treated with SCS were considered for this study.

Patients were eligible for the study if they were between 18 and 65 years old and met the diagnostic criteria for CRPS-1 established by the IASP with impaired function and symptoms beyond the area of trauma (Table 1) (Merskey, 1994).

Additional criteria for enrolment included disease which was clinically restricted to one hand or foot and affected the entire hand or foot, and which had lasted for at least 6 months. Furthermore, patients should not have a sustained response to standard therapy (6 months of physical therapy, sympathetic blockade, transcutaneous electrical nerve stimulation, and pain medication), and suffer a mean pain intensity of at least 5 cm on a visual-analogue scale from 0 (no pain) to 10 cm (worst imaginable pain).

Exclusion criteria were the presence of Raynaud's disease, current or previous neurologic abnormalities unrelated to reflex sympathetic dystrophy, another condition affecting the function of the diseased or contra lateral extremity, a blood-clotting disorder, or use of an anticoagulant drug, and implanted cardiac pacemaker. The study was approved by the Medical Ethics Committee of Maastricht University Medical Centre, Maastricht, The Netherlands. All patients gave written informed consent prior to inclusion in the study.

Of the 36 patients, 24 patients were responders to SCS trial therapy and subsequently underwent implantation of a permanent SCS device. In 12 patients the trial stimulation was unsuccessful and the percutaneous trial electrode was removed. All 36 patients received a standardized physical therapy program.

2.2. Materials

All 36 patients considered for this study had a trial stimulation period of at least one week of home-testing during which pain had to be scored in a pain diary, three times a day (Jensen and McFarland, 1993). If there was less than 50% pain reduction, patients were considered non-responders, and subsequently the test electrode was removed. A spinal cord stimulator was implanted permanently if the visual-analogue score for the intensity of pain during the last four days of the testing period was at least 50% lower than the baseline score, or if there was a score of at least 6 (“much improved”) on a seven-point scale for patients global impression of change (PGIC). PGIC is a seven-point ordinal scale, used after treatment, as an external criterion of clinically important change. A score of 4 means no change in the condition, and scores >4 denotes an improvement indicating “improved”, “much improved” and “very much improved”, and a score of 3 or less means a worsening, “ minimally worse”, “much worse”, “very much worse” (Forouzanfar et al., 2003). PGIC measures are valid indicators of important change in CRPS patients (Farrar et al., 2001; Forouzanfar et al., 2003).

2.3. Implantation of the Spinal Cord Stimulator System

After the prophylactic administration of cefuroxime (1500 mg given intravenously), the patient was placed in the prone position and a 5-cm vertical midline incision was made in the skin overlying the thoracic spine (if the hand was affected) or the lumbar spine (if the foot was affected). An electrode (model 3487A, Medtronic) was implanted in a fashion similar to the implantation of the temporary lead and was fixed with special clips. The patient was then placed in a lateral position, and a sedative was adminis-

Table 1
Diagnostic criteria for CRPS-1 in the study related to implant effect.[a]

	R.I.[b] *N* = 20 (%)	N.N. *N* = 12 (%)	N.I. *N* = 4 (%)	Total 36 (%)
Absolute criteria				
Pain	20	12	4	
Impaired function	20	12	4	
Symptoms beyond the area of trauma	20	12	4	
Relative criteria				
Cold, warm, or intermittently cold/warm	15 (75)	8 (67)	4 (100)	27 (75)
Edema	16 (80)	10 (83)	4 (100)	30 (83)
Increased nail growth	8 (40)	8 (67)	3 (75)	19 (53)
Increased hair growth	4 (20)	2 (17)	2 (50)	8 (22)
Hyperhidrosis	15 (75)	10 (83)	2 (50)	27 (75)
Abnormal skin color	18 (90)	11 (92)	4 (100)	33 (92)
Hypoesthesia	14 (70)	6 (50)	1 (25)	21 (58)
Hyperalgesia	15 (75)	11 (92)	4 (100)	30 (83)
Mechanical or thermal allodynia or both	15 (75)	11 (92)	4 (100)	30 (83)

[a] All the absolute criteria, together with at least three of the relative criteria, were required for this study.
[b] R.I., responders implanted; N.N., non-responders not implanted; N.I., non-responders implanted.

tered (1 mg of propofol per kilogram of body weight). A pulse generator (Itrel III, model 7425, Medtronic) was implanted subcutaneously in the left lower anterior abdominal wall and connected to the electrode by a tunnelled extension lead (model 7495-51/66, Medtronic). After the skin had been closed, the pulse generator was activated (rate, 85 Hz; pulse width, 210 μs) with the use of a console programmer (model 7432, Medtronic). The patient could control the intensity of stimulation by adjusting the amplitude from 0 to 10 V with a programmer (model 7434-NL, Medtronic). The patient remained in the hospital for 24 h after the implantation, during which time two doses of cefuroxime (750 mg each) were given intravenously. If no change in the position of the electrode was evident on an X-ray film obtained the following day, the patient was discharged.

2.4. Physical therapy

Physical therapy, which both groups of patients received, consisted of a standardized program of graded exercises designed to improve the strength, mobility, and function of the affected hand or foot. Pain during the exercises was considered acceptable, but if it had not returned to the pre-session level within 24 h, the intensity of the exercises was reduced. Physical therapy was administered for 30 min twice a week, with a minimum of two days between sessions. The total duration of the physical therapy was 6 months, starting after the second assessment. To ensure standardization, selected physical therapists were trained to provide the program of exercises. The coordinating physical therapist from our institution visited the other therapists regularly to make sure the treatment was uniform.

2.5. Data collection and follow up

Outcome measures were assessed at baseline. The effect of SCS on pain intensity VAS and PGIC was measured at 1, 3, 6, and 12 months after implantation.

2.6. Methods

Semmes–Weinstein pressure filaments (Smith and Nephew Rolyan Inc., Germantown, WI) were used to measure mechanical detection thresholds (i.e. mechanical hypoesthesia). Measurements at hands and feet were done at nine standardized sites. This procedure has been described earlier (Kemler et al., 2001). Hands were examined in sitting position, while the feet were examined in the supine position. Subjects were required to keep their eyes closed while being tested.

We classified the amount of mechanical hypoesthesia into four categories of intensity according to the Semmes–Weinstein conversion tables. These categories are: normal sensibility, diminished sensibility to light touch, diminished protective sensation and loss of protective sensation.

Brush-evoked allodynia was assessed by transiently stroking the skin of subject's hands and feet with a soft standardized brush at nine sites (Kemler et al., 2001). This procedure is not painful in normal subjects. If the procedure was perceived as painful, this signifies the presence of allodynia and subjects were asked to verbally rate the evoked pain on a numerical rating scale (NRS) from 0 to 10 (0 = no pain and 10 = worst imaginable pain). The mean brush-evoked allodynia was then calculated by dividing the total score by nine.

Demographic characteristics, spontaneous pain VAS, localization of the CRPS-1, duration of the disease, medication use, Semmes–Weinstein QST measurements and brush-evoked allodynia were all measured before implantation as baseline values. Subjects were tested in a quiet room maintained at 21–23 °C and after having received explanation of the procedure.

2.7. Statistical analysis

Patients who in the first year of their treatment with SCS had a sustained effect on their pain reduction, as defined by pain reduction of at least 2.5 on their VAS score and/or a PGIC score of "much improved" or "very much improved" in at least 3 out of the 4 follow up assessments are considered to be successfully treated (Forouzanfar et al., 2003). Implanted patients with significant decline in pain reduction during the evaluation period as defined by not meeting the above mentioned criteria for successful treatment are considered to be unsuccessfully treated with SCS.

The frequency of occurrence at baseline of the different possible predictors of SCS outcome was determined in the successful and in the non-successful group. The predictive performance of allodynia (maximum value and average of nine measurements), hypoesthesia, age, gender, localization of the disease, duration of the disease, and baseline intensity of the pain was investigated. Due to the limited number of patients this analysis was done with a univariate logistic regression analysis. This way only two statistically significant predictors ($p < 0.10$) remained and these were entered in a multivariate logistic regression model with a forward stepwise procedure. The results of this regression analysis were used to construct a ROC curve and calculate an Area Under the Curve (AUC). Non-parametric testing, i.e. Mann–Whitney, was used for the hypoesthesia and allodynia parameters due to the non-symmetrical distribution of results. Analyses were performed with the Statistical Package for the Social Sciences, version 16.0 (SPSS Inc., Chicago, IL). Two-tailed p values of less than 0.05 were considered statistically significant.

3. Results

Thirty-six patients, aged 40–65 years, 22 women and 14 men, with chronic CRPS-1 in one extremity, who had been referred to our department and took part in the previously described randomized clinical trial and who subsequently underwent SCS trial stimulation were part of this predictor study.

All 36 chronic CRPS-1 patients underwent SCS trial stimulation with a screening electrode. Following the trial period 12 patients did not receive a permanent implant due to insufficient pain reduction. Twenty-four patients received an implant after a positive trial.

Table 1 shows the diagnostic criteria for CRPS-1 as assessed in this study in relation to implant effect. There are no differences between the separate groups in all aspects of the absolute and relative criteria for CRPS-1.

Baseline characteristics and the distribution of patients in relation to treatment effect are shown in Table 2. Furthermore, it shows the results of the chi square tests for patient age, gender, disease duration, localization of the disease, allodynia, hypoesthesia and pain intensity measured by the success rate of SCS after trial stimulation and 1 year of SCS treatment. The average age of patients included in this study was 40, SD 11.7, range 21–65 years. The lower limb was affected in 14 patients and 22 patients had upper limb involvement. The mean duration of the disease was 40 months, SD 27.5, range 9–120. The mean patient baseline pain intensity VAS score was 71 mm, SD 15, range 50–90. Chi square analysis showed no significant correlation between age, location of the affection, baseline pain intensity VAS score, gender, and success of SCS. Medication use included peripheral analgesics like non-steroidal anti-inflammatory drugs and acetaminophen, antidepressants and antiepileptic drugs and weak opioids like

Table 2
Baseline characteristics of 36 CRPS-1 patients in relation to implant effect.

Characteristic		Implant effect				*P* values	
		Trial effect (*N*%)		1 year effect (*N*%)		Trial	1 year
		Successful *N* = 24	Unsuccessful *N* = 12	Successful *N* = 20	Unsuccessful *N* = 16		
Age	⩽40	15 (65%)	8 (35%)	13 (65%)	7 (35%)	0.81	0.20
	>40	9 (69%)	4 (31%)	7 (44%)	9 (56%)		
Gender	Male, *N* = 14	9 (64%)	5 (36%)	6 (43%)	8 (57%)	0.81	0.22
	Female, *N* = 22	15 (68%)	7 (32%)	14 (64%)	8 (36%)		
Localization	Arm	15 (68%)	7 (32%)	12 (55%)	10 (45%)	0.81	0.88
	Leg	9 (64%)	5 (36%)	8 (57%)	6 (43%)		
Disease duration in months	<40	15 (68%)	7 (32%)	13 (62%)	8 (38%)	0.45	0.36
	⩾40	9 (64%)	5 (36%)	7 (47%)	8 (53%)		
Pain intensity	VAS ⩽ 7.1	12 (75%)	4 (25%)	12 (57%)	9 (43%)	0.34	0.20
	VAS > 7.1	12 (60%)	8 (40%)	8 (53%)	7 (47%)		
Allodynia	Absent	14 (88%)	2 (12%)	13 (81%)	3 (19%)	0.06	0.017
	Moderate	2 (50%)	2 (50%)	2 (50%)	2 (50%)		
	Severe	8 (50%)	8 (50%)	5 (31%)	11 (69%)		
Hypoesthesia	Absent/light[a]	11 (69%)	5 (31%)	8 (50%)	8 (50%)	0.81	0.55
	Severe[b]	13 (65%)	7 (35%)	12 (60%)	8 (40%)		

[a] Normal sensibility or diminished sensibility to light touch.
[b] Diminished sensibility or loss of protective sensation.

tramadol or buprenorphine. Thirteen out of twenty allodynia patients used one or more of these drugs and ten out of sixteen patients in the non-allodynia group. Only one patient used oral morphine sulfate and two used an antidepressant or antiepileptic. So there was no clinical relevant difference in the use of medication between the groups. Our data indicate that the absence or presence of hypoesthesia, light or severe, does not predict SCS outcome (*P*, 0.55). In our patient sample, only allodynia was significantly correlated with success of treatment after 1 year. A trend could be seen after the trial period towards the negative association of allodynia and treatment success (*P*, 0.06). The difference in success rate after 1 year (Mann–Whitney test) is statistically significant (*P*, 0.017) between the groups with and without allodynia. In the successfully treated group five patients had severe allodynia (5/20; 25%) compared to 11 patients in the not successfully treated group (11/16; 69%).

After 1 year, 20 out of the 24 (83%) SCS-implanted patients maintained their significant pain reduction.

Of the 24 patients who underwent definitive implantation, four showed a significant loss of pain reduction after 1 year. These four patients together with the 12 patients not receiving a permanent implant were considered to be unsuccessfully treated after 1 year (16/36 patients; 41%). Table 3 shows the baseline characteristics of the unsuccessfully treated group in separate categories and combined. Of the 4 patients implanted but longer term non-responding to SCS treatment, 3 patients suffered severe allodynia. In all other aspects the baseline variables did not differ.

The univariate logistic regression analysis shows that the maximum value as well as the mean value of brush-evoked allodynia are statistically significant predictors of outcome after SCS trial and even more significant after 1 year of SCS treatment. These two predictors were entered in a multivariate logistic regression model with a forward stepwise procedure. The result of this regression analysis were used to construct a ROC curve and calculate an Area Under the Curve (AUC) and is displayed in Fig. 1. The corresponding tables belonging to Fig. 1 show that the cutoff point can be set at a brush-evoked allodynia pain intensity NRS score of 2.5 with a sensitivity of 0.75 and a specificity of 0.81.

4. Discussion

Spinal cord stimulation is an established and effective treatment option for controlling chronic pain in CRPS-1 patients, but it is also an invasive and expensive therapy. The selection of optimal candidates is a very important factor for increasing SCS treatment success rates. In this study we showed that the presence of brush-evoked allodynia may be a negative predictor for successful SCS treatment.

Not every patient achieves an acceptable reduction of pain following treatment with SCS. Patients with paraplegic pain, stump

Table 3
Baseline characteristics of CRPS-1 patients non-responding to SCS therapy.

Characteristic		Non-responders after 1 year of treatment		
		^{N}I. *N* = 4	^{N}N. *N* = 12	^{N}C. *N* = 16
Age, mean(SD) range		46 (9) 33–55	41 (14) 21–65	42 (13) 21–65
Disease duration in months, mean (SD) range		39 (29) 11–76	43 (24) 14–99	42 (24) 11–99
Pain intensity VAS in mm, mean (SD) range		75 (11) 60–85	72 (12) 54–95	73 (12) 54–95
Gender, *N* (%)	Male	3 (75%)	5 (42%)	8 (50%)
	Female	1 (25%)	7 (58%)	8 (50%)
Localization, *N* (%)	Arm	3 (75%)	7 (58%)	10 (63%)
	Leg	1 (25%)	5 (42%)	6 (37%)
Allodynia, *N* (%)	Absent	1 (25%)	2 (17%)	3 (19%)
	Moderate	0 (0%)	2 (17%)	2 (12%)
	Severe	3 (75%)	8 (66%)	11 (69%)
Hypoesthesia, *N* (%)	Absent/light[a]	3 (75%)	5 (42%)	8 (50%)
	Severe[b]	1 (25%)	7 (58%)	8 (50%)

^{N}I., non-responders implanted. ^{N}N., non-responders not implanted. ^{N}C., combined group of non-responders.
[a] Normal sensibility or diminished sensibility to light touch.
[b] Diminished sensibility or loss of protective sensation.

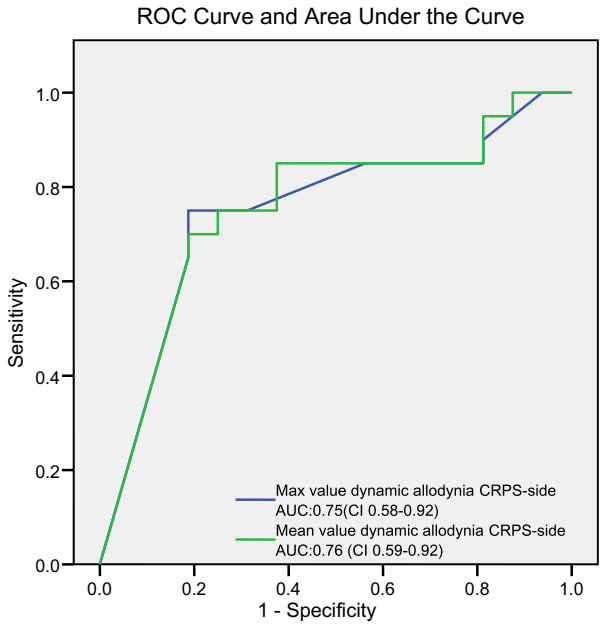

Fig. 1. ROC curve and Area Under the Curve of the maximal and mean value of the brush-evoked allodynia measurements on the CRPS effected limb in patients after 1 year of SCS treatment.

pain, and phantom limb pain do not respond to SCS, whereas patients having pain attributable to failed back syndrome, ischemic lower limb pain, painful peripheral neuropathy or CRPS-1 in general do (Kumar et al., 1998). In patients with failed back syndrome who have undergone surgical procedures it has been demonstrated that, with a shorter duration of the pain syndrome, greater rates of success could be achieved (Kumar et al., 1998). In the present study with chronic CRPS-1 patients, we could not confirm this correlation between disease duration and SCS success. Others found that increased patient age was inversely correlated with SCS success, in a patient population consisting mainly of failed back surgery syndrome; however, in our population of CRPS-1 patients we observed no effect of patient age on outcome (Burchiel et al., 1995).

SCS has evolved as a clinical application of Melzack and Wall's gate-control theory (Melzack and Wall, 1965). The general mechanism of pain relief by SCS is still understood in these gating terms. The pain alleviating effect is generally seen to be caused by activation of large-diameter afferents in the dorsal columns. The fact that chronic neuropathic pain patients, even those with severe hypoesthesia, can still show a successful response to SCS might be explained by the presence of remaining intact large fibers in the dorsal column which can be recruited for stimulation. Pain in an affected extremity provoked by the normally non-painful stimulus of a brush is regarded as a sign of central sensitization (Vaneker et al., 2005). Our results show that brush-evoked allodynia seems to be associated with a lower chance of achieving long-term pain reduction with SCS treatment. This phenomenon is probably due to central sensitization which makes it difficult to suppress the total experienced pain, both spontaneous and evoked, even when stimulating the spinal cord dorsal columns. Central sensitization on spinal level occurs in the dorsal horn and is probably caused by repetitive high frequency stimulation of peripheral C-fibres leading to an amplification and prolongation of the response of the dorsal horn neurons, a phenomenon called 'wind up'. This process may be linked to increased release of substance P and the excitatory neurotransmitter glutamate, mediated through voltage gated N-calcium channels, leading to postsynaptic *N*-methyl-D-aspartate (NMDA) receptor interaction and hyperexcitability. Furthermore the amount of inhibitory neurotransmitter Gamma-aminobutyric acid (GABA) and GABAergic interneurones within the spinal cord may increase or decrease the output of the dorsal horn. These mechanisms cause increased sensitivity to pain (hyperalgesia) and input from non-nociceptive Aß-fibres to be perceived as pain (allodynia) (Baron, 2009; D'Mello and Dickenson, 2008). So far, neurochemical and electrophysiological evidence from experimental studies has suggested that the effects of SCS on the dorsal columns are mediated centrally in the dorsal horns of the spinal cord, by altering the release of neurotransmitters (e.g. increased release of GABA) and suppression of hyperexcitable Wide Dynamic Range neurons (WDR) (Cui et al., 1996). In experimental SCS the amount of pain relief is related to the severity of allodynia (Smits et al., 2006; Yakhnitsa et al., 1999). The non-response to SCS in animals with severe allodynia may well relate to a severe form of central neuropathic derangement and may imply a disability to produce appropriate amounts of GABA, either alone or accompanied by the increased loss of inhibitory interneurons. In this scenario modulation of dorsal horn neurons by SCS could have either little or no effect. Other animal studies showed that the combination of SCS with pharmacological therapy, in rats not responsive to SCS, can become effective when combined with intrathecal or intravenous medication like baclofen, adenosine, gabapentin and pregabalin (Wallin et al., 2002).

None of these medications were being used by the described patients. CRPS patients who fulfil the criteria for SCS are rather scarce and, although the sample sizes of our study are small, we consider the present study of interest because it can provide new insights into pain mechanism and treatment in CRPS-1 patients. Because of these small sample sizes we adjusted our statistical tests for small and non-parametric data.

In the most ideal situation, when comparing different possible predictors, all patients in one group should have undergone exactly the same treatment. In this study 12 patients who did not show pain reduction after one week of trial stimulation and the 4 patients who did receive an implant but showed significant loss of pain reduction after 1 year were both considered non-responders. These 16 patients were compared to the responder group where all patients received an SCS implant. Because both groups did not receive exactly the same treatment which is preferable in predictor studies, we analyzed the groups according to success of the trial versus failure of the trial and the association with allodynia. This reflects widely accepted routine clinical practice where patients indeed have the device removed, or permanent stimulating treatment is not considered, if they do not have significant pain reduction after the trial period.

To our knowledge the predictive effect of mechanical allodynia on the outcome of SCS therapy in neuropathic pain syndromes such as CRPS-1 has never been investigated. We tested for brush-evoked allodynia in nine standardized places of the hand or foot and calculated the mean. However, the ROC curve shows that brush-evoked allodynia at the area of maximal pain is an equally effective indicator as the average of nine individual allodynia measurements. This has clinical relevance since the attention of clinician and patient in routine clinical assessment of CRPS-1 patients is typically directed towards the area of maximal pain and allodynia. As in diabetic neuropathy, severe hypoesthesia of the plantar aspect of the foot can easily be detected by bed side testing using the 10 g filament and severe hypoesthesia of the hand and dorsal aspect of the foot can easily be detected using the 4 g filament (Perkins et al., 2001). We showed that there was no correlation between the severity of hypoesthesia and the success of SCS. Hence testing for the presence of hypoesthesia, despite its importance in the diagnosis of CRPS-1, seems to be of no value in predicting SCS success.

In conclusion, there seems to be a good chance (81%) of achieving and maintaining successful pain reduction for more than 1 year with SCS if allodynia is absent before stimulation is started. If brush-evoked allodynia is shown with a minimal intensity of 2.5 on a NRS scale, the chance of achieving successful stimulation is significantly lower (31%). This does not necessarily mean that patients with allodynia should be denied a test spinal cord stimulation since there still is a 31% chance of achieving successful pain reduction. However, if there is any doubt about satisfactory pain reduction in a patient with allodynia after the trial phase, it is probably better not to proceed with a definitive implant.

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