

Pain-Related Fear, Perceived Harmfulness of Activities, and Functional Limitations in Complex Regional Pain Syndrome Type I

Jeroen R. de Jong,^{*,1} Johan W. S. Vlaeyen,^{1,†} Jantha M. de Gelder,[‡] and Jaap Patijn[§]

^{*}Department of Rehabilitation, University Hospital Maastricht, Maastricht, The Netherlands.

[†]Department Clinical Psychological Science, Maastricht University, Maastricht, The Netherlands.

[‡]Department of Psychology, University of Leuven, Leuven, Belgium.

[§]Department of Pain Management and Research, University Hospital Maastricht, Maastricht, The Netherlands.

Abstract: Numerous studies have shown that pain-related fear is one of the strongest predictors of pain disability in patients with chronic musculoskeletal pain, and there is evidence that the reduction of pain-related fear through an exposure treatment can be associated with restoration of functional abilities in patients with complex regional pain syndrome type I (CRPS-I). These findings suggest that pain-related fear may be associated with functional limitations in neuropathic pain as well. The aim of the current study was to test whether the debilitating role of pain-related fear generalizes to patients with CRPS-I. The results of 2 studies are presented. Study I includes a sample of patients with early CRPS-I referred to an outpatient pain clinic. In Study II, patients with chronic CRPS who are members of a patients' association were invited to participate. The results show that in early CRPS-I, pain severity but not fear of movement/(re)injury as measured with the Tampa Scale for Kinesiophobia was related to functional limitations. In patients with chronic CRPS-I, however, perceived harmfulness of activities as measured with the pictorial assessment method significantly predicted functional limitations beyond and above the contribution of pain severity. Not fear of movement/(re)injury in general, but the perceived harmfulness of activities appears a key factor that might be addressed more systematically in the clinical assessment of patients with CRPS-I. These results support the idea that pain-related fear might be a promising concept in the understanding of pain disability in patients with neuropathic pain.

Perspective: This is the first study showing that perceived harmfulness of activities contribute to the functional limitations in CRPS-I. The current findings may help clinicians customizing cognitive-behavioral treatments for patients with chronic neuropathic pain.

© 2011 by the American Pain Society

Key words: Complex regional pain syndrome type I (CRPS-I), pain-related fear, perceived harmfulness, pain severity, functional limitations.

There is general consensus that the pathophysiology of complex regional pain syndrome type I (CRPS-I) is still unknown, and that the contribution of biopsychological interactions to the development and

maintenance of CRPS-I symptoms is unclear.⁵² During the last decade, biopsychosocial models have been introduced and successfully applied in chronic pain research.^{49,55} One particular model that has gained wide interest among pain researchers and clinicians is the fear-avoidance model.^{30,53} Patients who (mis)interpret pain catastrophically are likely to become fearful about their pain and its consequences, and to engage in protective avoidance behaviors that are adaptive in acute pain, but paradoxically worsen the pain problem later on. Although pain-related fear has repeatedly been shown to be associated with persistent pain and functional limitations in musculoskeletal pain conditions,²⁸ the role of pain-related fear in CRPS-I has never been tested systematically. In 1 study, however, CRPS-I patients responded successfully to an exposure in vivo treatment aimed at the reduction of pain-related fear. This replicated single case experimental study showed

Received June 3, 2010; Revised June 1, 2011; Accepted June 17, 2011.

Supported by the Esperance Foundation, affiliated to the Dutch association for Patients of Post-Traumatic Dystrophy (Nederlandse Vereniging van Posttraumatische Dystrofie Patienten) and the Department of Pain Management and Research of the University Hospital Maastricht. Participation of J.W.S. Vlaeyen was supported by the NWO Social Sciences Research Council of the Netherlands, VICI Grant No. 453-04-003, and an Odysseus Grant by the Fund for Scientific Research (FWO) Flanders, Belgium.

The authors have no conflicts of interest to report.

Address reprint requests to Jeroen R. de Jong, Department of Rehabilitation, University Hospital Maastricht, PO Box 5800, 6202 AZ Maastricht, The Netherlands. E-mail: jeroen.dejong@mumc.nl

1526-5900/\$36.00

© 2011 by the American Pain Society

doi:10.1016/j.jpain.2011.06.010

that, as compared with baseline and education, exposure in vivo treatment produced relevant decreases in self-reported pain-related fear, pain severity, and increased functional abilities.¹² These findings are in line with other studies suggesting that nociceptive and neuropathic pain conditions share cognitive and affective characteristics.¹¹ Taken together, the current literature suggests that the impact of pain-related fear on functioning is not restricted to patients with nociceptive pain, but is also relevant in patients with neuropathic pain, and CRPS-I in particular.¹⁸

Therefore, the aim of the current studies was to test whether the debilitating role of pain-related fear generalizes to patients with CRPS-I. We predicted that pain-related fear is significantly associated with functional limitations, over and beyond the effects of pain severity.

Methods

The role of pain-related fear in CRPS-I was investigated in 2 independent cross-sectional studies. Study I used data collected by the pain clinic of the University Hospital Maastricht; pain-related fear was measured with the Tampa Scale for Kinesiophobia (TSK),^{33,40} a self-report measure focused on the general fear that painful movement might be a sign of (further) injury. In Study II, the data was collected from chronic CRPS-I patients who were members of the Dutch association for patients with CRPS. In this study, a pictorial measure of perceived harmfulness of activities²⁹ was used in addition to TSK. The Medical Ethics Committee of Maastricht University approved both studies.

Study I

Participants

In this study, 79 CRPS-I patients who visited the outpatient clinic of the Pain Management and Research Center (PKC) of the University Hospital Maastricht for the first time from 2004 to 2006 were included. The diagnosis of CRPS-I was made according to the criteria formulated by Veldman et al⁵⁰ and based on physician evaluation of objective symptoms. Veldman et al's criteria were initially developed for the description of CRPS I in the acute phase of the disease and are formulated as follows: 1) At least 4 out of 5 signs or symptoms; pain, difference in skin color, oedema, difference in skin temperature, and active range of motion; 2) signs and symptoms present in an area larger than might be expected of the initial trauma; and 3) increased signs and/or symptoms during or after exercise.

Procedure

Once the first appointment at the pain clinic of the Maastricht University Hospital was scheduled, patients were sent a booklet with a series of questionnaires at home. They were asked to complete and return the questionnaires a few days before the first meeting with the anaesthesiologist. These data served as additional diagnostic information which was added to the case history and physical examination. At this point, patients gave

their informed consent that the questionnaire data could be used for research purposes.

Measures

Sociodemographics. By means of the above-mentioned booklet, data were available on age, gender and pain duration.

Functional Limitations. One of the most widely used generic health status measures is the Short Form Health Survey (SF-36).⁵⁴ The SF-36 was developed in the late 1980s, and is translated and validated for use among Dutch-speaking residents of the Netherlands.¹ SF-36 includes 36 questions and standardized response choices, organized into 8 multi-item scales.⁵⁴ For this study we used the scale "limitations in physical activities because of health problems." The raw scale scores were linearly converted to a 0 to 100 scale, with higher scores indicating higher levels of functioning. The SF-36 has shown to be a reliable and valid instrument, with a mean Cronbach's alpha of .84 across scales and samples.⁴⁸ Cronbach's alpha of the subscale in our sample of CRPS-I patients was .73.

Pain-Related Fear. The Dutch language version of the Tampa Scale for Kinesiophobia (TSK-DV)^{19,20,26} was used. The TSK-DV measures one's belief that activities which increase pain indicate serious injury and hence should be avoided.^{20,40} The TSK-DV consists of 17 statements that are rated on a 4-point scale (1 = strongly agree, 4 = strongly disagree). Sample items are "Pain always means I have injured my body" and "If I were to try to overcome it, my pain would increase." The total score was calculated after inversion of items 4, 8, 12, and 16, which were phrased in reversed key. The total score varies between 17 and 68. The Dutch version of the TSK has shown to be sufficiently reliable and valid.⁴⁰ Cronbach's alpha of the total score in our sample of CRPS-I patients was .94.

Pain Severity. Four visual analogue scales (VAS), consisting of 10-cm horizontal lines anchored at the left and the right with the words "no pain at all" and "worst pain experienced" were used.³² The VAS referred to the present pain, experienced average pain of the last week, and the lowest and highest experienced pain. Because the statistical analyses showed the same results for these different VAS scales, we report on average pain (VAS-average pain).

Statistical Analyses. The obtained data were analyzed with the SPSS v.15.0 (SPSS Inc., Chicago, IL). The analyses included pain-related fear and pain severity in predicting functional and role limitations. Multiple regression analyses were carried out with functional limitations as dependent variable. Gender and age were entered into the first step to control for sociodemographic variables. Next, pain-related fear was entered, and pain severity in the third step.

Results Study I

Sociodemographics

A summary of the sociodemographics is displayed in Table 1. Seventy-nine patients with CRPS-I with an average age of 43.9 years (SD = 13.5, range 16–80) were included in the analyses. CRPS-I involved the upper

extremities in 39% (4 men and 27 women), the lower extremities in 44% (12 men and 23 women), and both the upper as well as the lower extremities in 16% (1 man and 12 women) of the patients. In total, 78% is female. In 48.1% of the patients the duration of the CRPS-I symptoms was less than 1 month. Thirty-five percent had pain duration between 1 and 6 months. The remaining 21.4% of the patients had pain for longer than 6 months (range 7 months–26 years).

Variable Information

The mean TSK score, as measure for pain-related fear, was 43.68 (SD = 8.70, range 20.0–63.0). Compared with normative data about the TSK in chronic low back pain (CLBP), patients or a mixed group of patients with chronic pain,^{33,51} 52.7% scored below or on the same level, as the reported median. This suggests that the level of fear of movement/(re)injury of the CRPS-I group in Study I is comparable with that of the the average chronic pain population. The mean score of the experienced average pain was 7.34 (SD = 1.73, range 1.4–10.0). In addition, patients reported a mean present pain of 6.91 (SD = 2.12, range 0–10.0), mean highest experienced pain score of 8.87 (SD = 1.07, range 5.9–10.0), and mean lowest experienced pain score of 4.94 (SD = 2.12, range .1–10.0).

Regression Analyses

The results of the multiple regression analysis are displayed in Table 2. Adding pain-related fear to the model in which age and gender were already included explained an additional 19% of the variance. When pain severity was added to these predictors, they accounted for 51% of the total variance. Step 3 (F (change) = 18.87, $P < .01$) in the regression model did improve our ability to predict general physical health. Pain severity ($\beta = -.479$, $P < .01$) but not pain-related fear (TSK) contributed significantly to the prediction of functional limitations.

Conclusion

In contrast to what was expected, pain-related fear was not a significant predictor of functional limitations in this sample of early diagnosed CRPS-I patients admitted to the University Hospital. However, fear was measured with the TSK, which might be too global a measure of pain-related fear. A novel measure of pain-related fear is the Photograph Series of Daily Activities (PHODA),^{27,29,15} which more specifically measures the perceived harmfulness of a series of movements and activities presented by photographs. Another explanation could be that the measure of functional disability was too generic, and not specific enough for patients with CRPS-I. Measures that are specifically developed for patients with CRPS might be more appropriate. Furthermore, CRPS-I patients who were referred to the pain clinic might have been a highly selected group with early symptoms, and in whom avoidance behavior might still have an adaptive function. Therefore, to examine the role of more CRPS-specific variables for disability and pain-related fear with a different cohort of patients with CRPS-I, Study II was set up.

Table 1. The Sociodemographics for the Patients in Study I and II

	Study I (N = 79)	Study II (N = 107)
Age (years)		
Mean	43.9	48.5
Standard deviation	13.5	11.3
Range	16–80	23–65
Gender (% female)	78%	89%
CRPS-I upper extremities (%)	39%	24%
CRPS-I lower extremities (%)	44%	39%
CRPS-I both extremities (%)	16%	37%
Pain Duration		
<1 Month (%)	48.1%	1%
1–6 Months (%)	35%	0%
>6 Months (%)	21.4%	99%

Abbreviation: CRPS-I, complex regional pain syndrome type I.

Study II

Study II was carried out among members of the Dutch association for patients of posttraumatic dystrophy (Nederlandse Vereniging van Posttraumatische Dystrofie Patienten [NVPDP]), and used more specific measurement tools to test the role of pain-related fear and pain severity on functional limitations in chronic CRPS-I patients.

Procedure

A sample of 400 NVPDP members was randomly selected using the computer program PEPI 3.0,² and contacted by mail. A package including patient information, informed consent form, a body pain chart, a letter of recommendation by the patients' association, and stamped addressed envelopes were sent to them. Body pain charts, developed by A.J. Kresch (<http://www.kickas.org/painmap.shtml>), were used to indicate the body location where participants felt most severe pain. The instruction was to mark with a cross the body location

Table 2. The Results of the Multiple Regression Analysis of Study I With Functional Limitations as Outcome Measure

MODEL STEPS	B	SE B	β	R^2	F CHANGE
Step 1				.029	.969
Gender	8.591	6.945	.150		
Age	-.163	.226	-.087		
Step 2				.008†	.547
Gender	10.488	7.426	.184		
Age	-.151	.228	-.081		
Pain-related fear (TSK)	.257	.347	.096		
Step 3				.210†	18.873*
Gender	4.560	6.716	.080		
Age	-.152	.202	-.082		
Pain-related fear (TSK)	.242	.308	.091		
Pain severity (VAS-average pain)	-6.761	1.556	-.479*		

Abbreviations: TSK, Tampa Scale for Kinesiophobia; VAS, visual analogue scale. * $P < .01$.

†For steps 2 and 3, the value of the R^2 is the Adjusted R^2 .

where the most intense pain was felt. This information was used to decide which set of questionnaire(s) was to be sent to the participants (upper versus lower extremities) to measure functional and role limitations. Depending on the affected limb, different versions of disability instruments were completed.

The participants returned their informed consent forms and the body pain chart in the preaddressed envelopes to the Maastricht University. They also indicated their preference for either the on-line or the off-line paper-and-pencil version of the questionnaires. Participants who were able to use the Internet received a personal code by e-mail. These codes gave access to an Internet-based electronic environment²⁴ enabling completion of the questionnaires online. The answers were registered and transformed to the computer program Statistical Package for the Social Sciences (SPSS). Respondents who were not able to complete the questionnaires on-line were sent print copies of the questionnaires by postal mail with a free return address envelope.

Participants

Four of the randomly selected NVPDP members lived in foreign countries and were excluded from participation. In total, 396 members were contacted, of whom 121 (30.6%) gave their informed consent to participate. Four of these respondents gave their informed consent too late, 1 participant was not able to complete the on-line version of the questionnaires, and another patient failed to provide his gender. Eight participants failed to complete the whole set of questionnaires, resulting in a final sample of 107 (27%) respondents for the purpose of the current analyses.

Measures

Functional Limitations. The functional limitations were measured by 2 questionnaires. The first is the Radboud Skills Questionnaire (RASQ),³⁷ which was completed by CRPS-I patients with upper extremity pain. The RASQ was used to score the patient's ability to perform activities of daily living in the normal manner. The activities are described in 45 items which are divided into 6 domains: 1) personal care; 2) household activities; 3) recreational activities; 4) social activities; 5) other activities; and 6) work. Each of the items can be scored on a 5-point Likert scale (1 = normal, 5 = I do not perform the activity anymore as a result of CRPS-I). There is an extra score of 9 when the item is deemed not applicable. The patient indicates the effort performing the activity by choosing the corresponding number. Different scores are computed by summing up scores of the relevant items, divided over the number of items of the relevant scale, minus the number of items in which the category not applicable was chosen. For this study the total score was converted into a 0 to 10 score. The questionnaire has been found reliable in CRPS patients, with good agreement between the outcomes for test-retest and interobserver reliability studies as established with the method of Bland and Altman.^{5,37}

For patients with CRPS-I lower extremity pain, the Dutch Walking Ability Questionnaire (WAQ) was

included.⁴¹ The 3 domains that were used in this study are: 1) walking inside the house; 2) walking outside; and 3) rising and sitting down. The questionnaire is a combination of the original form of the Walking Stairs Questionnaire, and a shortened version of the Questionnaire Rising and Sitting Down.⁴² Response options are presented in a dichotomous fashion (yes or no). Following Perez et al,³⁸ the score of each of the domains was calculated by adding up the total number of affirmative responses. These scores were then converted into a 0 to 10 total score for each scale, by dividing the score of each scale by the total number of items of that particular scale, and subsequently multiplying the outcome by 10. For the item, "I do not walk inside/outside due to my dystrophy," a total score of 10 was used. Items that suggest difficulties with walking due to other reasons than CRPS were excluded from the total score calculation. In terms of test-retest reliability as expressed by Spearman's r (range .79–.90 and .85–.89, respectively) and the intraclass correlation coefficient (range .78–.84 and .84–.87, respectively) the Walking Stairs Questionnaire and the Questionnaire Rising and Sitting Down form a reliable tool for measuring activity limitation of patients with CRPS-I of a lower extremity. Patients who had lower as well as upper extremity CRPS-I (37%) filled in both the RASQ and the WAQ.

Pain-Related Fear. The TSK is a brief questionnaire that measures fear of movement/(re)injury.³³ Although psychometric studies have supported the reliability and validity of the TSK,^{20,40,45} limitations are such that it does not provide more specific information about which movements or activities are feared or avoided. Therefore, the PHODA^{15,25,27,46} was included as well. The PHODA consists of a number of photographs of various daily life activities. Patients are requested to indicate to what extent they perceive these daily activities to be harmful on a VAS fear thermometer. Support has been found for both the reliability and validity of a computer version of PHODA.²⁹

Two parallel forms of PHODA were used. PHODA-UE¹⁵ was used for the upper extremities, and PHODA-LE²⁵ for the lower extremities. For this study, a shortened computer version of PHODA-UE and PHODA-LE was developed, consisting of 40 pictures. For every basic movement category, activities were selected with variable degrees of rated harmfulness. Participants were instructed to watch each photograph carefully and to try to imagine performing that activity. The expected harmfulness of these activities is rated on a VAS, consisting of a 100-mm horizontal line anchored at the left and right by the words not harmful and very harmful. Each photograph is given a rating according to its position on the VAS. A mean total score ranging from 0 to 100 is calculated as the sum of each rating divided by 40. To test the predictive value of the PHODA in the hierarchical regression analyses, PHODA-UE or PHODA-LE were used depending on the affected limb.

Pain. The Dutch translation of the Neuropathic Pain Scale (NPS)¹⁷ measures the distinct pain qualities associated with neuropathic pain. The NPS consists of 10 items.

Two items assess the global dimensions of pain intensity and pain unpleasantness. Seven items contain the words intense, sharp, hot, dull, cold, and itchy to characterize the patient's pain, and the word sensitive to describe the patient's pain reaction to light touch (eg, clothing). One item describes the temporal sequence of pain as constant with intermittent increases, intermittent, or constant with fluctuation. Each item was rated on a 0 to 10 numerical rating scale. Galer and Jensen¹⁷ provided preliminary support for the discriminant and predictive validity of the NPS items.

Statistical Analyses. The obtained data were analyzed with SPSS v.15.0. Because functional limitations were measured differently in patients with CRPS-I in the lower and upper extremities, analyses were performed in 2 groups: lower extremity group and upper extremity group, by which patients who had CRPS-I in the lower as well as the upper extremity were added to both groups. Pearson correlation coefficients showed that the RASQ and the WAQ were highly correlated in the sample of patients who had CRPS-I in both the lower and upper extremity (Pearson $r = .62$, $P < .01$). Descriptive statistics of each questionnaire were generated to evaluate the completeness of the data, and to characterize the score distributions, including scale ranges, means, and standard deviations. In the case of missing data, means replacement methods were used if 90% of relevant data was present.

Multiple regression analyses were carried out with functional and role limitations as dependent variable. Gender and age were entered into the first step to control for sociodemographics. Next, pain-related fear was entered, and pain severity was entered in the third step. Regression analyses were repeated in each group separately with the TSK or PHODA as a measure for pain-related fear.

Results Study II

Sociodemographics

The sociodemographics for the patients in Study II are displayed in Table 1. One hundred and seven members of the Dutch association for patients with CRPS-I (89% women) with an average age of 48.5 years (SD = 11.3, range 23–65) were included in the analyses. Fifty-three respondents completed the questionnaires online and 54 respondents completed paper versions of the questionnaires. CRPS-I involved the upper extremities in 24% (6 men and 20 women), the lower extremities in 39% (4 men and 38 women), and both extremities in 37% (2 men and 37 women) of the respondents. The average duration of the CRPS-I symptoms was estimated at 8.14 years (SD = 4.65, range 0–22 years). In only 1 patient was the duration of the CRPS-I symptoms less than 1 month, and 1 patient reported a pain duration between 1 and 6 months. The remaining patients had pain for longer than 6 months.

Variable Information

The mean TSK score of the patients was 37.69 (SD = 8.20, range 19.0–59.0). Compared with normative data of the TSK in a mixed group of patients with chronic pain, 65% scored below or on the same level as the reported median.³⁶ The mean PHODA score was 48.02 (SD = 20.66, range 6.25–94.05). Compared with normative data of the PHODA in CLBP patients,²⁹ 50% scored below or on the same level as the reported median. This suggests that the level of pain-related fear, as measured with the PHODA, of the CRPS-I group in Study II is comparable with the average CLBP population. Furthermore, the mean NPS score, as measure for pain severity, was 50.16 (SD = 17.46, range 7.00–90.70).

Table 3. The Results of the Multiple Regression Analysis of Study II in Lower and Upper Extremities CRPS-I Patients With Functional Limitations as Outcome Measure and the TSK as Measure for Pain-Related Fear

MODEL STEPS	LOWER EXTREMITIES					UPPER EXTREMITIES				
	B	SE B	β	R^2	F CHANGE	B	SE B	β	R^2	F CHANGE
Step 1				.083	3.292*				.035	1.086
Gender	2.464	1.199	.235			.274	.342	.103		
Age	.051	.026	.221			-.012	.011	-.141		
Step 2				.045‡	.016				-.004‡	.576
Gender	2.453	1.211	.234*			.284	.344	.107		
Age	.051	.027	.222			-.013	.011	-.150		
Pain-related fear (TSK)	-.004	.034	-.014			.011	.014	.097		
Step 3				.149‡	9.870‡				.427‡	45.425‡
Gender	1.747	1.164	.167			.062	.262	.023		
Age	.063	.025	.274*			.010	.009	.114		
Pain-related fear (TSK)	-.024	.033	-.081			-.005	.011	-.044		
Pain severity (NPS)	.055	.017	.351‡			.035	.005	.717‡		

Abbreviations: CRPS-I, complex regional pain syndrome type I; TSK, Tampa Scale for Kinesiophobia; NPS, Neuropathic Pain Scale.

* $P < .05$.

‡ $P < .01$.

†For steps 2 and 3 the value of the R^2 is the adjusted R^2 .

Table 4. The Results of the Multiple Regression Analysis of Study II in Lower and Upper Extremities CRPS-I Patients With Functional Limitations as Outcome Measure and the PHODA as Measure for Pain-Related Fear

MODEL STEPS	LOWER EXTREMITIES					UPPER EXTREMITIES				
	B	SE B	β	R ²	F CHANGE	B	SE B	β	R ²	F CHANGE
Step 1				.076	2.780				.036	1.104
Gender	2.394	1.232	.233			.264	.345	.099		
Age	.049	.028	.209			-.013	.011	-.148		
Step 2				.197†	13.538†				.256†	21.051†
Gender	2.121	1.134	.206			.360	.299	.135		
Age	.045	.026	.192			-.016	.010	-.184		
Pain-related fear (TSK)	.052	.014	.395†			.022	.005	.510†		
Step 3				.228†	3.766				.490†	27.525†
Gender	1.766	1.127	.172			.156	.251	.058		
Age	.053	.026	.225*			.002	.009	.022		
Pain-related fear (TSK)	.043	.015	.328†			.011	.004	.267*		
Pain severity (NPS)	.035	.018	.221			.029	.006	.575†		

Abbreviations: CRPS-I, complex regional pain syndrome type I; PHODA, Photograph Series of Daily Activities; TSK, Tampa Scale for Kinesiophobia; NPS, Neuropathic Pain Scale.

* $P < .05$

† $P < .01$.

‡For steps 2 and 3 the value of the R² is the adjusted R².

Regression Analyses

Lower Extremity CRPS-I Group. Table 3 shows the results of the multiple regression analysis of the lower extremity CRPS-I group in which the TSK was used as measure for pain-related fear. The demographic variables gender and age were entered in Step 1 and explained 29% of the variance in functional limitations. The variable pain-related fear entered in step 2 explained an additional 29% of the variance, and for pain severity in step 3, this was an addition of 44% of the variance. Inclusion of the predictor pain severity in the model (step 3) improved the ability to predict the outcome variable (F [change] = 9.87, $P < .01$). Of the variables, age ($\beta = .274$, $P < .05$) and pain severity ($\beta = .351$, $P < .01$) were significantly related to the function in which the level of functional and role limitations was predicted.

In an additional multiple regression analysis, the PHODA, as a measure for pain-related fear, was entered in step 2 (Table 4). As a consequence, this explained an additional 48% of variance in functional limitations. For pain severity in step 3, this was 52%. Unlike the analysis described above, in which the TSK was used as measure for pain-related fear, pain-related fear improved the ability to predict the outcome variable rather than the inclusion of pain severity (F [change] = 13.54, $P < .01$). In addition, the multiple regression analysis showed that pain-related fear ($\beta = .328$, $P < .01$) and age ($\beta = .225$, $P < .05$), and not pain severity, were significantly related to functional limitations.

Upper Extremity CRPS-I Group. Table 3 also shows the results of the multiple regression analysis of the upper extremity CRPS-I group in which the TSK was used as measure for pain-related fear. Adding gender and age in step 1 explained 19%, pain-related fear in step 2 explained 21%, and pain severity in step 3 explained 68% of the variance in functional limitations. Inclusion of pain

severity in the model (step 3) improved the ability to predict the outcome variable (F (change) = 45.43, $P < .01$). Of the variables, only pain severity ($\beta = .717$, $P < .01$) was significantly related to functional limitations.

When PHODA, as a specific measure for pain-related fear, was entered in step 2 of the regression model (Table 4) this explained an additional 54% of variance in functional limitations. Adding pain severity in step 3 explained 72%. Inclusion of the predictors pain-related fear (F (change) = 21.05, $P < .01$) and pain severity (F (change) = 27.53, $P < .01$) improved the ability to predict the outcome variable. Contrary to the previous multiple regression analysis, not only pain severity ($\beta = .575$, $P < .01$), but also pain-related fear ($\beta = .267$, $P < .05$) was significantly related to functional limitations.

Conclusion

Study II showed that the higher pain-related fear, when measured with a pictorial fear of activity scale (PHODA) and not with TSK, the higher impact on the experienced functional limitations. Contrary to Study I, the role of pain severity was different in both CRPS-I subsamples. When the PHODA was entered in the regression model in patients with lower extremity CRPS-I, only pain-related fear, and not pain severity, was a significant predictor of functional limitations.

Discussion

The primary aim of this study was to investigate the role of pain-related fear on functional limitations in CRPS-I patients. Two studies were carried out. In Study I, data of patients with early CRPS-I who visited an outpatient pain clinic for the first time were used. Pain-related fear was measured with TSK, a self-report measure of fear of movement/(re)injury. The results of Study I

showed that pain severity affected functional limitations more than any other variable. In Study II, members of the Dutch Association for CRPS-I Patients completed a series of questionnaires. To measure pain-related fear, a pictorial fear of activity scale (PHODA) was used. The results demonstrated that pain-related fear, only when measured with the PHODA, was associated with functional limitations, above and beyond the contribution of pain severity. Moreover, pain severity was also a predictor for functional limitations in Study II. However, in the subgroup of patients with CRPS-I in the lower extremities, only pain-related fear, and not pain severity, was a predictor of functional limitations.

To the current knowledge of the authors, both studies are the first to specifically examine the role of pain-related fear in relation to functional limitations in a group of CRPS-I patients. By using motor imagery in CRPS patients, Moseley et al³⁴ showed that change in pain and swelling was related to pain catastrophizing and pain-related fear, which they interpreted in a way that pain-related fear affects motor processes and pain even when the individual has no intention to actually execute the movement. Another possible mechanism that is suggested to underlie CRPS-I, and as such may be associated with pain-related fear, is disuse or deconditioning, that may develop in an effort to avoid persistent pain.⁵¹ One idea is that operantly conditioned disuse of the affected extremity, reinforced by the avoidance of actual pain, or by the reduced anxiety of anticipated worsening of pain, may prevent desensitization. This may eliminate the normal tactile and proprioceptive input from the extremity that is necessary to restore normal central processing.^{7,44} Disuse is also suggested as a trigger of hyperalgesia and allodynia in the affected extremity, which subsequently may interact with pathophysiological mechanisms. A vicious cycle is perpetuated in which altered central processing leads to increased pain, provoking catecholamine release that further stimulates the nociceptive input maintaining central processing alterations.^{8,11} It is possible that pain-related fear is a mechanism that underlies and contributes to this disuse through its associated avoidance behavior, and that this may help maintain the primary features of CRPS-I. These, of course, are speculations that still await scientific scrutiny.

It is remarkable that both studies demonstrated that TSK as a measure of pain-related fear does not significantly predict functional limitations in patients with CRPS-I. These results are not consistent with previous research among patients with musculoskeletal pain in which TSK was shown to be associated with pain disability, and often more so than pain itself.^{10,28} Although there is a lack of consensus among researchers, CRPS-I is thought to be a neuropathic pain disorder.²³ Therefore, TSK might not be suitable for measuring pain-related fear in neuropathic pain disorders such as CRPS-I. However, the mean score and the standard deviation of the TSK in Study I did not deviate that much from the scores in studies among chronic back patients, in which the TSK predicts the level of disabilities.¹⁶

In contrast to the weak association between TSK and functional disability, pictorial measure of perceived

harmfulness of activities (PHODA) appeared to be a significant predictor for reported functional limitations in CRPS-I patients. It is possible that as compared with general verbal statements such as the ones used in TSK, visualized activities are more salient, making it easier for patients to imagine executing the pain-eliciting activity. There is evidence that exposure to pictures with a negative valence elicit not only lower pain tolerance¹³ but also fear responses such as increased startle potentiation⁴³ and neurocognitive changes.⁹ As the PHODA was not included in Study I, we do not know whether perceived harmfulness of activities is also a predictor of disability in patients with early CRPS-I who are admitted to a specialized pain clinic of the university hospital.

In patients with chronic low back pain, Leeuw et al²⁹ found that a short electronic version of the PHODA appeared to be significantly related to the TSK. However, the relatively modest correlation coefficients suggest that there is conceptual overlap between the PHODA and TSK, but that PHODA measures unique aspects as well that are distinct from TSK. Another explanation for the presence of the significant relationship between the PHODA and functional limitations in Study II might be a degree of criterion contamination. However, 1 argument against this possibility is that the instructions for both measures were quite different. For the measurement of functional limitations, patients were requested to reflect on the ability to perform activities of daily living in a habitual manner. For the PHODA, participants indicated the expected harmfulness of activities represented by the pictures.

Finally, several limitations of both studies should be mentioned. First, the present studies are limited by their cross-sectional design. Positive correlations or regression weights may not be confused with causal effects. Second, the results are based on a relatively small number of CRPS-I patients. Third, because only 27% of the initially recruited sample actually participated in the study, there may be a potential impact of selection bias. However, even with a high participation rate, nonresponse can cause a significant bias if the nonresponders are a relatively homogeneous group that differs markedly from the responders.⁴ Unfortunately, and due to the study logistics, we do not have information about the characteristics of the nonresponders in our study. Fourth, the studies are impeded by the use of self-report measures only, which are subject to self-serving biases. Fifth, the 2 CRPS-I samples differed in duration of the condition. Study I consisted primarily of early CRPS-I patients while Study II included chronic CRPS-I patients. Although most of the data supporting the association between pain-related fear and functional disability is gathered in patients with chronic pain,⁵³ there is accumulating evidence that in (sub)acute pain disorders pain-related fear is not only related to pain and disability, but that it may be a key factor in the development of chronicity and long-term disability.^{16,18,21,22,31,47,49} Therefore, we do not think that differences in pain duration between both samples have affected our results adversely.

Finally, a further point of consideration is the fact that no gold standard for the diagnosis of CRPS-I has

been established, because a single pathophysiological mechanism explaining the variety of features observed in CRPS-I is lacking. Only the criteria set by the International Association for the Study of Pain is officially recognized to be used for formal diagnosis of CRPS-I. Other sets of diagnostic criteria are from Veldman et al⁵⁰ and Bruehl et al.⁶ Perez et al³⁹ found a lack of agreement between the different diagnostics sets for CRPS-I as well as differences in clinical appearances between patients meeting the different criteria. This may have profound consequences for the clinical profile of a study population. In Study I, the diagnosis of CRPS-I is made based on the criteria of Veldman et al, while in Study II, the participants declared themselves to be diagnosed with CRPS-I. Despite the choice for any of the criteria sets used in a study remains arbitrary,³⁹ the current research results could be better translated if the diagnostic criteria for both studies were uniform.

In sum, the current studies show pain severity affects functional limitations in CRPS-I patients. In addition, pain-related fear when measured with a pictorial fear of activity scale (PHODA) is a unique predictor of functional limitations among CRPS-I patients with longstanding pain who are not seeking care in a specialized university pain clinic. However, it is not clear what CRPS-I patients with a high pain-related fear score actually fear. Study I and II provide data to start qualitative studies to address the current concerns of CRPS-I patients. Despite the need for replications in a larger CRPS-I sample, these studies support the idea that pain-related fear in CRPS-I patients deserves more research attention. Such research may contribute to a better understanding of a poorly understood, painful, and disabling disorder.³⁵

What are the clinical implications of these results? If pain-related fear is indeed relevant for the understand-

ing of functional limitations, it could be an important treatment target in CRPS-I. Treatments that are based on the fear-avoidance model of pain do not primarily aim at pain relief, but at extinguishing pain-related fear, and the expectancy that certain movements or activities may lead to further body harm. Because of remarkable similarities between pain-related fear and fear/phobias in general, and the success of exposure-based treatments in patients with anxiety disorders, a similar treatment was developed for application in fearful chronic pain patients⁵² and patients with chronic CRPS-I.¹² The most essential step in this approach consists of graded exposure to the situations the patient has identified as dangerous or threatening. In addition, beliefs are challenged by the use of behavioral experiments. Thus, in patients with chronic CRPS-I, it seems appropriate to assess not only pain severity, but also the perceived harmfulness of functional activities. For those who fear that certain movements or activities will increase body harm, a cognitive-behavioral treatment approach is available showing promising results¹² (see³ and¹⁴ for recent reviews).

Acknowledgments

We are grateful for the efforts of the volunteers of the Dutch association for Patients of Post-Traumatic Dystrophy (Nederlandse Vereniging van Posttraumatische Dystrofie Patienten); to Rosanne Janssen who designed the computer program EMIUM, which was instrumental in the realization of Study II; to Eric Schouten who helped with the statistical analysis; and to Elke Vermeulen for her assistance in the data collection of Study I. We also thank all participants for completing the questionnaires.

References

1. Aaronson NK, Muller M, Cohen PDA, Essink ML, Fekkes M, Sanderman R, Sprangers MA, te Velde A, Verrips E: Translation, validation and norming of the Dutch language version of the SF-36 Health Survey in community and chronic disease populations. *J Clin Epidemiol* 51: 1171-1181, 1998
2. Abramson JH, Gahlinger PM: Computer Programs for Epidemiologists. London, UK, Brixton Books, 1999
3. Bailey KM, Carleton RN, Vlaeyen JW, Asmundson GJ: Treatments addressing pain-related fear and anxiety in patients with chronic musculoskeletal pain: A preliminary review. *Cogn Behav Ther* 39:46-63, 2010
4. Bergstrand R, Vedin A, Wilhelmsson C, Wilhelmsen L: Bias due to non-participation and heterogenous sub-groups in population surveys. *J Chronic Dis* 36:725-728, 1983
5. Bland JM, Altman DG: Statistical methods for assessing agreement between two methods of clinical measurement. *The Lancet* 8:307-310, 1986
6. Bruehl S, Harden RN, Galer BS, Saltz S, Bertram M, Backonja M, Gayles R, Rudin N, Bhugra MK, Stanton-Hicks M: External validation of IASP diagnostic criteria for complex regional pain syndrome and proposed research diagnostic criteria. *International Association for the Study of Pain. Pain* 81:147-154, 1999
7. Bruehl SP: Psychological interventions, in Wilson PR, Stanton-Hicks M, Harden RN (eds): *CRPS: Current Diagnosis and Therapy*. Seattle, WA, IASP Press, 2005
8. Bruehl SP: Do psychological factors play a role in the onset and maintenance of CRPS? in Harden RN, Baron R, Jänig W (eds): *Complex Regional Pain Syndrome, Progress in Pain Research and Management, Vol. 22*. Seattle, WA, IASP Press, 2001
9. Bublatzky F, Flaish T, Stockburger J, Schmäzle R, Schupp HT: The interaction of anticipatory anxiety and emotional picture processing: An event-related brain potential study. *Psychophysiology* 47:687-696, 2010
10. Crombez G, Vlaeyen JW, Heuts PH, Lysens R: Pain-related fear is more disabling than pain itself: Evidence on the role of pain-related fear in chronic back pain disability. *Pain* 80: 329-339, 1999
11. Daniel HC, Narewska J, Serpell M, Hoggart B, Johnson R, Rice AS: Comparison of psychological and physical function in neuropathic pain and nociceptive pain: Implications for cognitive behavioral pain management programs. *Eur J Pain* 12:731-741, 2008

12. De Jong JR, Vlaeyen JWS, Onghena P, Cuypers C, Den Hollander M, Ruijgrok J: Reduction of pain-related fear in complex regional pain syndrome type I: The application of graded exposure in vivo. *Pain* 116:264-275, 2005
13. De Wied M, Verbaten MN: Affective pictures processing, attention, and pain tolerance. *Pain* 90:163-172, 2001
14. den Hollander M, de Jong JR, Volders S, Goossens ME, Smeets RJ, Vlaeyen JW: Fear reduction in patients with chronic pain: A learning theory perspective. *Expert Rev Neurother* 10:1733-1745, 2010
15. Dubbers AT, Vikström MH, De Jong JR: The Photograph series of Daily Activities (PHODA-UE): Cervical Spine & Shoulder. CD-rom version 1.2: Hogeschool Zuyd, University Maastricht and Institute for Rehabilitation Research (iRv), The Netherlands, 2003
16. Fritz JM, George SZ: Identifying psychosocial variables in patients with acute work-related low back pain: The importance of fear-avoidance beliefs. *Phys Ther* 82:973-983, 2002
17. Galer BS, Jensen MP: Development and preliminary validation of a pain measure specific to neuropathic pain: The Neuropathic Pain Scale. *Neurology* 48:332-338, 1997
18. Gheldof E, Crombez G, Van den Bussche E, Vinck J, Van Nieuwenhuysse A, Moens G, Mairiaux P, Vlaeyen JW: Pain-related fear predicts disability, but not pain severity: A path analytic approach of the fear-avoidance model. *Eur J Pain* 14:870.e1-870.e9, 2010
19. Goubert L, Crombez G, Vlaeyen JWS, Van Damme S, Van den Broeck A, Van Houdenhove B: The Tampa Scale for Kinesiophobia: Psychometric characteristics and standardization (translated from Dutch). *Gedrag en Gezondheid* 28:54-62, 2000
20. Goubert L, Crombez G, Van Damme S, Vlaeyen JWS, Bijttebier P, Roelofs J: Confirmatory factor analysis of the Tampa Scale for Kinesiophobia: Invariant two-factor model across low back pain patients and fibromyalgia patients. *Clin J Pain* 20:103-110, 2004
21. Heneweer H, Aufdemkampe G, van Tulder MW, Kiers H, Stappaerts KH, Vanhees L: Psychosocial variables in patients with (sub)acute low back pain: An inception cohort in primary care physical therapy in The Netherlands. *Spine* 32:586-592, 2007
22. Heuts PH, Vlaeyen JW, Roelofs J, de Bie RA, Aretz K, van Weel C, van Schayck OC: Pain-related fear and daily functioning in patients with osteoarthritis. *Pain* 110:228-235, 2004
23. Jänig W, Baron R: Complex Regional Pain Syndrome: Mystery explained? *Lancet Neurol* 2:687-697, 2003
24. Janssen R: Electronic Measurement Instrument: EMIUM. Department of Medical, Clinical and Experimental Psychology, University Maastricht, the Netherlands, 2005
25. Jelinek S, Germes D, Leyckes N, De Jong JR: The Photograph series of Daily Activities (PHODA-LE): Low Extremities. CD-rom version 1.2: Hogeschool Zuyd, University Maastricht and Institute for Rehabilitation Research (iRv). The Netherlands, 2003
26. Kori SH, Miller RP, Todd DD: Kinesiophobia: A new view of chronic pain behaviour. *Pain Management* 3:35-43, 1990
27. Kugler K, Wijn J, Geilen M, De Jong JR, Vlaeyen JWS: The Photograph series of Daily Activities (PHODA). CD-rom version 1.0, Institute for Rehabilitation Research and School for Physiotherapy Heerlen, The Netherlands, 1999
28. Leeuw M, Goossens MEJB, Linton SJ, Crombez G, Boersma K, Vlaeyen JWS: The fear-avoidance model of musculoskeletal pain: Current state of scientific evidence. *J Behav Med* 30:77-94, 2007
29. Leeuw M, Goossens MEJB, van Breukelen GJP, Boersma K, Vlaeyen JWS: Measuring perceived harmfulness of physical activities in patients with low back pain: The Photograph Series of Daily Activities – Short electronic Version. *J Pain* 8:840-849, 2007
30. Leeuw M, Houben RMA, Severeijns R, Picavet HSJ, Schouten EGW, Vlaeyen JWS: Pain-related fear in low back pain: A prospective study in the general population. *Eur J Pain* 11:256-266, 2007
31. Linton SJ: A review of psychological risk factors in back and neck pain. *Spine* 25:1148-1156, 2000
32. Melzack R: The McGill Pain Questionnaire: Major properties and scoring methods. *Pain* 1:277-299, 1975
33. Miller RP, Kori SH, Todd DD: The Tampa Scale for Kinesiophobia: Unpublished report, Tampa, FL, 1991
34. Moseley GL, Zalucki N, Birklein F, Marinus J, van Hilten JJ, Luomajoki H: Thinking about movement hurts: The effect of motor imagery on pain and swelling in people with chronic arm pain. *Arthritis Rheum* 59:623-631, 2008
35. Nelson DV: Treating patients with complex regional pain syndrome, in Turk DC, Gatchel RJ (eds): *Psychological Approaches to Pain Management. A Practitioner's Handbook*. New York, NY, Guilford Press, 2002, pp 470-488
36. Nicholas MK, Asghari A, Blyth FM: What do the numbers mean? Normative data in chronic pain measures. *Pain* 134:158-173, 2008
37. Oerlemans HM, Cup EHC, De Boo T, Goris RJA, Oostendorp RAB: The Radboud skills questionnaire: Construction and reliability in patients with reflex sympathetic dystrophy of one upper extremity. *Disabil Rehabil* 22:233-245, 2000
38. Perez RS, Roorda LD, Zuurmond WW, Bannink II, Vranken JH, de Lange JJ: Measuring perceived activity limitations in lower extremity complex regional pain syndrome type I (CRPS I): Test-retest reliability of two questionnaires. *Clin Rehabil* 16:454-460, 2002
39. Perez RS, Collins S, Marinus J, Zuurmond WW, de Lange JJ: Diagnostic criteria for CRPS I: Differences between patient profiles using three different diagnostic sets. *Eur J Pain* 11:895-902, 2007
40. Roelofs J, Sluiter JK, Frings-Dresen MH, Goossens M, Thibault P, Boersma K, Vlaeyen JW: Fear of movement and (re)injury in chronic musculoskeletal pain: Evidence for an invariant two-factor model of the Tampa Scale for Kinesiophobia across pain diagnoses and Dutch, Swedish, and Canadian samples. *Pain* 131:181-190, 2007
41. Roorda LD, Roebroek ME, Lankhorst GJ, Van Tilburg TG, Bouter LM: Measuring functional limitations in rising and sitting down: Development of a questionnaire. *Arch Phys Med Rehabil* 77:663-669, 1996
42. Roorda LD, Roebroek ME, Lankhorst GJ, Van Tilburg TG: The walking ability questionnaire: Hierarchical scales to measure disabilities in rising and walking (in Dutch). *Revalidata* 18:34-38, 1996
43. Smith JC, Bradley MM, Lang PJ: State anxiety and affective physiology: Effects of sustained exposure to affective pictures. *Biol Psychol* 69:247-260, 2005

10 The Journal of Pain

44. Stanton-Hicks M, Baron R, Boas R, Gordh T, Harden N, Hendler N, Koltzenburg M, Raj P, Wilder R: Consensus report: Complex regional pain syndromes: Guidelines for therapy. *Clin J Pain* 14:155-166, 1998
45. Swinkels-Meewisse IE, Roelofs J, Verbeek AL, Oostendorp RA, Vlaeyen JW: Fear of movement/(re)injury, disability and participation in acute low back pain. *Pain* 105:371-379, 2003
46. Trost Z, France CR, Thomas JS: Examination of the photograph series of daily activities (phoda) scale in chronic low back pain patients with high and low kinesiophobia. *Pain* 141:276-282, 2009
47. Turk DC, Okifuji A: Psychological factors in chronic pain: Evolution and revolution. *J Consult Clin Psychol* 70:678-690, 2002
48. Van der Zee KI, Sanderman R: Het meten van de algemene gezondheidstoestand met de RAND-36. Een handleiding. Groningen, Noordelijk Centrum voor Gezondheidsvraagstukken, 1993
49. Vangronsveld KL, Peters M, Goossens M, Vlaeyen J: The influence of fear of movement and pain catastrophizing on daily pain and disability in individuals with acute whiplash injury: A daily diary study. *Pain* 139:449-457, 2008
50. Veldman PHJM, Reynen HM, Arntz IE, Goris RJA: Signs and symptoms of reflex sympathetic dystrophy: Prospective study of 829 patients. *The Lancet* 342:1012-1016, 1993
51. Verbunt JA, Seelen HA, Vlaeyen JW, van de Heijden GJ, Heuts PH, Pons K, Knottnerus JA: Disuse and deconditioning in chronic low back pain: Concepts and hypotheses on contributing mechanisms. *Eur J Pain* 7:9-21, 2003
52. Vlaeyen JW, de Jong JR, Leeuw M, Crombez G: Fear reduction in chronic pain: graded exposure in vivo with behavioral experiments, in Asmundson GJ, Vlaeyen JW, Crombez G (eds): *Understanding and Treating Fear of Pain*. New York, NY, Oxford University Press, 2004
53. Vlaeyen JW, Morley S: Cognitive-behavioral treatments for chronic pain: What works for whom? *Clin J Pain* 21:1-8, 2005
54. Ware JE, Sherbourne CD: The MOS 36-Item Short-Form Health Survey (SF-36). *Med Care* 30:473-483, 1992
55. Wilson PR, Stanton-Hicks M, Harden N: CRPS: Current Diagnosis and Therapy. *Progress in Pain Research and Management*, vol. 22. Seattle, WA, IASP Press, 2005