

# CHAPTER 3

## **Development of a symptoms questionnaire for Complex Regional Pain Syndrome and potentially related illnesses: the TREND Symptoms Inventory**

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### **Abstract**

*Objective:* To develop a questionnaire to evaluate symptoms of Complex Regional Pain Syndrome type 1 (CRPS 1), fibromyalgia (FM) and repetitive strain injury (RSI), to determine the test-retest reliability and investigate concurrence in the clinical manifestations of CRPS 1 and FM.

*Design:* The TREND (Trauma RElated Neuronal Dysfunction) Symptom Inventory (TSI) questionnaire was developed by determining the content validity and the practical use of the questionnaire. Furthermore, the test-retest reliability was assessed on two identical questionnaires filled out with an 7 days interval by CRPS 1 and FM patients.

*Setting:* Outpatient pain clinic of the ... medical center.

*Participants:* Twenty-six CRPS 1 and 42 FM patients (mean age 54.0 and 45.4, respectively).

*Interventions:* Not applicable.

*Main outcome:* Test-retest reliability calculated with Intra Class Correlation (ICC).

*Results:* Reliability scores were good for the whole questionnaire, its categories and domains ( $ICC > 0.75$ ) for both CRPS 1 and FM patients. Sensory complaints (except for change in cold perception), motor complaints, visceral complaints (diarrhea and incontinence), were reported by both CRPS 1 and FM patients. Change in cold perception, discoloration, change in skin temperature, change in sweating behavior, change in severity of edema during exercise and tropic changes of skin were reported significantly more often by CRPS 1 patients, whereas complaints of the (upper/lower) back, constipation, urine retention and experiencing a dry mouth were reported significantly more often by FM patients.

*Conclusion:* The TSI questionnaire is a reliable instrument with good content validity, which can be used in the evaluation of similarities and differences between CRPS 1 and FM. Systematic evaluation of symptoms of CRPS 1 and potentially related illnesses may provide a better basis for future research into the underlying mechanism(s).

## Introduction

Complex Regional Pain Syndrome type 1 (CRPS 1), fibromyalgia (FM), and repetitive strain injury (RSI) are chronic pain disorders with unknown pathophysiologic mechanisms. For these illnesses no gold standard and no objective measurement instrument for diagnosis is available, therefore diagnosis is based on history and observation of clinical manifestations. Similarities between these disorders have been described in different studies. Martin-Lavin suggested that FM may reflect a generalized CRPS (1). He proposed that both CRPS and FM are sympathetically maintained pain syndromes in which ongoing sympathetic hyperactivity sensitizes the primary nociceptors and induces pain and allodynia. This author claimed that the sympathetic state may also be responsible for other clinical features (e.g. chronic pain, allodynia, paresthesias, vasomotor instability, response to sympathetic blockade and emotional response to chronic pain), seen in both CRPS and FM, although more widespread in FM. Tenderness at palpation as seen in FM patients, may reflect a state of generalised allodynia, according to the author (2).

Macfarlane et al. considered forearm pain associated with RSI, as a regional manifestation of a widespread pain/FM-type syndrome (3). In a population based prospective study, in which the epidemiology of diffuse forearm pain was examined, Macfarlane et al. found that forearm pain commonly co-occurred with other regional musculoskeletal pain syndromes (shoulder, low back pain) or with chronic widespread pain. The authors hypothesized that forearm pain may be one feature of a wider process of somatisation, like FM. Based on systematic literature analysis, Marinus and Van Hilten (4) suggested that CRPS, FM and RSI may evolve through a common pathway. These authors found that patients with CRPS and FM share similarities with respect to demographic characteristics, and particularly occurrence of sensory symptoms. Furthermore, although less distinct, similarities were found for motor, autonomic and trophic changes and for systemic symptoms. In addition, they have hypothesized that several other features, such as risk factors, age at onset and gender distribution may be similarly distributed in these complaints. This review, however, also identified methodological differences between studies which limits the possibilities of comparison between studies. Furthermore, similar symptoms may have been reported differently, making accurate comparison of the symptoms difficult.

To overcome abovementioned limitations, a uniform systematic evaluation which addresses the clinical manifestations and demographic characteristics of patients with CRPS 1 and potentially related syndromes like FM and RSI is necessary. Furthermore, possible associations between CRPS 1 and these syndromes may

contribute to a better understanding of the involved underlying pathophysiologic mechanism(s) of these disorders. In order to compare disease characteristics of CRPS 1 patients with syndromes like FM and RSI, a questionnaire was developed. In this study, the development of the questionnaire is described, and the test-retest reliability of this TREND (Trauma RElated Neuronal Dysfunction) Symptom Inventory (TSI) questionnaire for CRPS 1 and FM patients is evaluated. Furthermore, clinical manifestations of CRPS 1 and FM will be compared.

## **Methods**

### *Development of the questionnaire:*

Over a period of 2 years (2003-2004) a generic questionnaire for the evaluation of signs and symptoms was developed in three sequential stages, during which the content validity, other clinimetric properties and the practical use of the questionnaire were addressed.

In the first stage of development, literature was searched for studies that evaluated the clinical spectrum described for CRPS, FM and RSI. Literature was obtained from Medline, Pubmed and the Cochrane database over the period between 1980 and 2003, whereby the following search terms were used: Complex Regional Pain Syndrome, CRPS, PTD, RSD, Posttraumatic Dystrophy, Reflex Sympathetic Dystrophy, Sudeck Dystrophy, Dystonia; Repetitive Strain Injury, Refractory Cervicobrachial Pain Syndrome, Cumulative Trauma Disorder, work related upper limb disorders, occupational overuse syndrome, occupational cervicobrachial disorder, work related upper extremity musculoskeletal disorders, chronic upper limb pain; Fibromyalgia, Fibromyalgia syndrome, Fibrositis. These search terms were subsequently combined with the following keywords: epidemiology; female, male, women, men; incidence, prevalence, occurrence; age; gender, sex; hereditary, heredity; risk factors; disease course, longitudinal course, symptoms, signs. After screening of 526 publications, 240 articles were included.

Based on aforementioned reviews, the second phase was started, which led to the development of the first trial version of the questionnaire. A 47-item set list was constructed, which was divided into domains reflecting the presence of sensory, autonomic, motor, tropic and visceral symptoms. Clinical signs were evaluated in the extremity in which the complaints started. The provisional item list was first tested as a standardized interview-questionnaire in 19 CRPS 1 and 5 FM patients, in order to improve the quality and content of the questionnaire and to remove redundant items.

As features such as neck and back problems were only marginally addressed in abovementioned version of the questionnaire, a new search was performed with spine, spinal column as additional keywords. This resulted in a 57-item interview-questionnaire, in which the frequency and severity of sensory, autonomic, motor and trophic symptoms were assessed both in the extremity in which complaints first started as well as in the upper back/neck and lower back regions. The interrater reliability between 3 interviewers was good (mean ICC = 0.90; n = 38 CRPS 1 patients), whereas the intrarater reliability with a 2 week interval was moderate (mean ICC = 0.70; n = 12 CRPS 1 patients), which was due to changes in complaints over the evaluation period. As the frequency and severity data showed high agreement (mean ICC = 0.89), these questions were combined to reduce redundancy. Finally, the questionnaire was adapted to be used as a written questionnaire, which could be completed by patients.

In this final version of the TSI questionnaire, complaints were evaluated in all extremities, resulting in a questionnaire with 164-items. The TSI questionnaire, is a Dutch questionnaire, which consists of ten categories. Category 1 + 2 (9 items): address general (disease) characteristics (medication use, disease duration, cause of complaints and other disorders). Category 3, 4, 5 and 6 (128 items) address sensory, autonomic, trophic and motor symptoms in the right arm, left arm, right leg, and left leg, respectively. Category 7 and 8 (12 items) address the neck/upper back and lower back. Category 9 (1 item) consists of a body picture to record the region of complaints. Category 10 (14 items) addresses the visceral domain and includes a miscellaneous domain for symptoms that do not fit in the aforementioned categories. Questions addressed the frequency of complaints and response options were presented on an ordinal scale (1-4). A preliminary translation of a section of the questionnaire, can be found in appendix 1.

### *Study population*

CRPS 1 patients were recruited at the outpatient pain clinic of the ... medical center. CRPS 1 patients had to meet the following inclusion criteria: 1. Diagnosis of CRPS 1 according to the IASP criteria (5); 2. Minimum age of 18 years; 3. Command of the Dutch language; 4. No history of psychiatric abnormalities as registered in the patient's medical record.

FM patients were recruited from a FM patient organization. The diagnosis of FM had to be made by a specialist or general practitioner and patients had to meet inclusion criteria 2-4.

### *Test-retest reliability*

Patients received two identical questionnaires in order to test the test-retest reliability. Both patient groups received the first questionnaire with an accompanying letter with instructions, in addition to oral instructions. Patients were requested to fill out the questionnaire alone on the day of receipt, and to return it in the following week. The second questionnaire was sent by mail after 7 days with the request to complete it exactly seven days after completing the first. To control for possible changes in general health and/or the specific complaints of the patient, an additional 5-point rating scale evaluating changes in general health, and CRPS 1 or FM complaints was completed together with the second questionnaire. To assess whether the questionnaire was user-friendly, a short questionnaire, inquiring after the clarity of questions and response options, and the terminology used in the questionnaire, was added.

### *Statistical analysis*

The data were processed and analyzed with SPSS 11. Questions with regard to patients' general (disease) characteristics were not included in the test-retest analyses. Test-retest reliability between first and second measurement was calculated for all individual items using the Intra Class Correlation coefficient (ICC) (6;7), which were subsequently used to calculate the mean overall test-retest reliability, the mean category reliability (i.e., body areas) and the mean domain reliability (type of symptom). The following cut-off-points were used: <0.50 poor reliability, 0.50-0.75 moderate reliability, >0.75 good reliability(6;7). Test-retest reliability of the questionnaire was determined for the entire study sample and for CRPS 1 and FM patients separately.

To determine the measurement error for each domain of the questionnaire, the standard error of measurement ( $SEM = \sigma\sqrt{1-ICC}$ ) was calculated in patients who reported no change of complaints and/ or general health status. Additionally, differences scores for patients reporting change of complaints of the extremities or general health status were compared to the SEM. Patients with scores exceeding the range of the confidence interval of the SEM were considered to have a 'true' change of complaints. To compare the reported clinical manifestations of CRPS 1 patients with the reported clinical manifestations of FM patients the Fisher's exact test was used. Patient characteristics of CRPS 1 patients and FM patients were evaluated using the Student T test, Mann-Whitney U test and Fisher's exact test. P-values < 0.05 were considered significant.

## Results

The questionnaire was sent to 35 CRPS 1 and 54 FM patients. Twenty-five CRPS 1 patients and 41 FM patients filled out the first and second questionnaire (response rate of 77% for CRPS 1 and 76% for FM). Patient characteristics are displayed in Table 1. Two CRPS 1 and 4 FM patients only completed the first questionnaire and could not be included in the test-retest analysis.

CRPS 1 patients were significantly older than FM patients (mean: 54.0 vs. 45.4 years,  $p=0.009$ ). The median duration of complaints was significantly longer for FM than for CRPS 1 patients (5.0 vs. 2.3 years,  $p=0.001$ ).

The onset of CRPS 1 was of a traumatic origin in most of the cases (92%), FM more frequently occurred spontaneously (45%). FM complaints were predominantly present in more than one extremity (73% in 4 extremities), whereas most CRPS 1 patients (67%) experienced complaints in one limb.

The total number of missing data was limited; 1.5% and 0.8% for CRPS 1 and FM patients, respectively.

**Table 1: patient characteristics**

	CRPS 1 (N=27)	FM (N=45)
Men/women	5/22	2/43
Age (years)	54.0 (16.4)*	45.4 (10.3)**
Duration of complaints (years)	2.3 (0.7-4.8) <sup>§</sup>	5.0 (3.0-14.0) <sup>§§</sup>
<b>Onset</b>	<b>%</b>	<b>%</b>
Fracture	40	5
Bruise	12	-
Sprain	4	5
Overuse	4	29
Operation	24	-
Spontaneous	8	45
Other	8	19
<b>Affected body area</b>	<b>%</b>	<b>%</b>
1 extremity	67	4
2 extremities	22	9
3 extremities	7	11
4 extremities	4	73
Neck/upper back	41	100
Lower back	24	93

\*Mean (SD). <sup>§</sup>Median (Inter quartile range).

\*\* $p<0.05$ , Student T test. <sup>§§</sup> $p<0.05$ , Mann-Whitney U test.

The ICC for the whole questionnaire was good for both CRPS 1 and FM patients. Category and domain ICC's were good for CRPS 1, FM and for the entire sample (see table 2).

For patients reporting improvement of complaints, 4 out of 6 indicated to have improved a lot. Two out of 14 patients reporting deterioration of complaints reported to have deteriorated a lot. For patients reporting change of general health, 3 out of 6 patients reported to have improved a lot, and 2 out of 23 patients reported to have deteriorated a lot (not shown in table). For the remainder of patients reporting change in either complaints or health, the changes were moderate.

**Table 2: Mean overall, category and domain ICC for test-retest reliability of the TSI questionnaire for CRPS 1+FM and CRPS 1 and FM**

	<b>CRPS1</b>	<b>FM</b>	<b>CRPS1 + FM</b>
<b>Overall*</b>	0.93	0.83	0.90
<b>Category<sup>§</sup></b>			
Right arm	0.97	0.82	0.91
Left arm	0.92	0.75	0.89
Right leg	0.92	0.86	0.92
Left leg	0.92	0.87	0.91
Neck/up back	0.87	0.82	0.91
Low back	0.89	0.81	0.89
No body region	0.91	0.85	0.88
<b>Domain<sup>#</sup></b>			
Sensory	0.92	0.83	0.90
Autonomic	0.96	0.84	0.92
Motor	0.93	0.82	0.90
Back	0.88	0.81	0.90
Visceral	0.91	0.86	0.87
Miscellaneous	0.91	0.84	0.90

\*All test items. <sup>§</sup>The test items are divided in 10 categories; the categories address the onset and course of complaints and symptoms located to a specific body area and exists of domains. <sup>#</sup>Type of complaints that fall into a specific level.

The SEM values per domain, the number of patients with scores that exceeded the SEM confidence interval, the highest possible domain scores and the mean domain scores are reported in table 3. In general, SEM values were small compared to the domain sum scores and ranged from 3.5% (visceral) to 8.3% (motor).



**Table 3: Standard error of measurement per domain and number of patients with scores exceeding the SEM confidence interval**

Domain	Total domain score*	No change extremities				No change health					
		Mean (SD) <sup>§</sup>	ICC <sup>#</sup>	SEM <sup>¶</sup>	N <sup>‡</sup>	N <sup>§</sup>	N <sup>¶</sup>	Mean (SD) <sup>§</sup>	ICC <sup>#</sup>	SEM <sup>¶</sup>	N <sup>‡</sup>
Sensory	152	75.74(37.74)	0.92	10.67	2	3	70.20(36.20)	0.93	9.58	3	4
Autonomic	64	18.72(10.20)	0.92	2.88	3	1	17.86(9.84)	0.95	2.20	3	3
Motor	96	51.16(27.14)	0.92	7.97	2	3	47.34(27.53)	0.93	7.28	2	3
Back	18	11.74(4.61)	0.95	1.03	2	6	11.00(4.98)	0.92	1.40	3	6
Visceral	20	7.98(1.94)	0.87	0.69	1	3	7.93(1.91)	0.93	0.50	2	5
Miscell.	8	4.18(1.37)	0.91	0.41	0	4	4(1.41)	0.91	0.42	2	4

\*Highest possible domain score. <sup>§</sup>Mean domain score for patients reporting no change of extremities or general health. <sup>#</sup>Domain ICC for patients reporting no change of extremities or general health. <sup>¶</sup>Standard error of measurement. <sup>‡</sup>Number of patients with true improvement of complaints. <sup>§</sup>Number of patients with true worsening of complaints. <sup>¶</sup>Number of patients with true improvement of general health. <sup>¶</sup>Number of patients with true worsening of general health.

Table 4 shows the type of complaints reported by CRPS 1 and FM patients. The frequency of sensory complaints (except for change of cold perception), motor complaints, diarrhoea, incontinence, urgency to void, and dry mouth and eyes was not significantly different between CRPS 1 and FM patients. Changes in cold perception, complaints of the autonomic domain, (except for edema and changes in edema during rest) were reported significantly more often by CRPS 1 patients. Complaints of the back, and constipation and urinary retention were reported significantly more often by FM 1 patients.

**Table 4: Type of complaints present in CRPS 1 and FM patients**

	CRPS 1(%)	FM(%)	p*
<b>Complaints sensory domain</b>			
Pain	96	100	0.38
Paresthesias	81	91	0.27
Allodynia	58	38	0.14
Hypaesthesia	4	2	1.00
Hyperaesthesia	59	33	0.05
Change of cold perception	81	53	0.02
Change of warmth perception	48	33	0.23
Change of pain during exercise	92	98	0.55
Change of pain during rest	35	56	0.14
Change of pain during humid weather	62	76	0.28
Change of pain during cold weather	65	62	1.00
Change of pain during hot weather	56	51	0.80
Change of pain during dry weather	16	31	0.25

	CRPS 1(%)	FM(%)	p*
<b>Complaints autonomic domain:</b>			
Discoloration	92	47	0.000
Edema	89	73	0.14
Change in sweating	77	36	0.001
Change of skin temperature	93	71	0.01
Change of edema during exercise	74	47	0.03
Change of edema during rest	33	38	0.90
<b>Complaints motor domain:</b>			
Loss of strength	96	100	0.38
Coordination problems	96	100	0.38
Dystonia	82	84	0.75
Tremor	70	71	1.00
Myoclonia	44	56	0.47
Decreased range of movement	89	96	0.38
<b>Complaints back domain:</b>			
Pain in neck/upper back	52	100	0.000
Decreased range of movement neck/upper back	46	96	0.000
Pain in lower back	30	93	0.000
Decreased range of movement lower back	24	87	0.000
<b>Complaints visceral domain:</b>			
Diarrhea	58	67	0.46
Constipation	36	73	0.005
Incontinence	31	38	0.61
Urgency to void	50	64	0.32
Urine retention	0	18	0.02
<b>Complaints tropic domain</b>			
Tropic change of skin	73	36	0.003
<b>Complaints miscellaneous domain</b>			
Dry mouth	62	84	0.04
Dry eyes	65	76	0.42

\*Differences between clinical manifestations of CRPS 1 and FM patients analyzed with Fisher's exact test.

Eighty percent of the CRPS 1 patients and 68% of the FM patients indicated that the questions were clear. However, both CRPS 1 and FM patients indicated to have difficulties categorizing body regions (for instance whether the shoulder belonged

to the arm or upper back). All CRPS 1 patients and 98% of FM patients indicated to have no difficulties with the response options of the multiple-choice questions. Eighty-eight percent of the CRPS 1 patients and 95% of the FM patients indicated to have no problems with the use of specific terms in the questionnaire. CRPS 1 patients completed the questionnaire in 18 minutes; FM patients in 22 minutes.

## **Discussion**

The purpose of this study was to establish the reliability of the TSI questionnaire, an instrument developed to evaluate symptoms, general health status and demographic characteristics of CRPS 1 and potentially related illnesses such as FM. The extensive literature search for symptoms of the involved conditions assures adequate content validity. Additionally, the high ICC scores found for the whole questionnaire, categories and domains indicate that the TSI is a reliable questionnaire for evaluation of generic symptoms in CRPS 1 and FM.

The TSI questionnaire provides the possibility to assess complaints reported by CRPS 1 and FM patients in a uniform and reliable fashion, and to compare reported complaints between the disorders systematically. Using the TSI, hypotheses proposed in previous studies (FM reflecting a generalized form of CRPS (8) and, CRPS and FM having a common disease pathway (9)) could be evaluated further. Furthermore, systemic evaluation of complaints in CRPS 1 and FM patients and in patients with other conditions (such as RSI) may provide insight into which symptoms are shared by these conditions and which symptoms are specific for a particular syndrome, which ultimately may lead to a better understanding of underlying disease mechanisms.

The small SEM scores found in this study reflects its potential to detect differences between serial assessments. Although only a small number of patients showed change that exceeded the SEM, one should take into account that changes in complaints and general health reported by the patients were generally small. The ability to detect these small differences may hint at the instrument's potential for responsiveness, although this still needs to be established more thoroughly. Furthermore, the majority of CRPS 1 and FM patients had no difficulties filling out the questionnaire, and reported no problems concerning the clarity of the response options and terminology used in the questionnaire. Additionally, missing data were limited and high response rates (77% and 83% for CRPS 1 and FM respectively) were obtained. This, together with the limited time required to complete the questionnaire, suggests that the TSI questionnaire is useful in clinical practice.

In addition to the high reliability of the questionnaire we also found differences between CRPS 1 and FM in the frequency of reported complaints. Hyperaesthesia and changes in cold perception, tended to be reported more by CRPS 1 patients. Possibly, these differences can be related to the neuropathic nature of the complaint of CRPS 1, which has been suggested in literature (10). As these findings are not consistent over other neuropathic symptoms (frequencies for other sensory indices were not significantly different between groups) these differences should be considered as artifacts in this study. Studies using larger patient samples might give more insight whether the differences found between both complaints for hyperaesthesia and cold perception are consistent and can be related to differences in disease mechanisms.

Autonomic disturbances were reported significantly more often by CRPS 1 patients compared to FM patients, with the exception of edema. This higher occurrence rate of autonomic symptoms might be expected in CRPS 1 patients (11), but it is surprising that the frequency of edema and change in skin temperature was high in FM patients as well, although one should realize that subjective joint swelling has been described in FM patients, but could not be confirmed during clinical examination (12;13). Temperature changes in FM could be explained by a Raynaud-like phenomenon which has been found in FM patients (14;15). Whether or not the vasomotor abnormalities found in CRPS 1 are comparable to the Raynaud-like phenomena in FM has to be investigated.

Constipation and urine retention were reported significantly more frequently by FM patients compared to CRPS 1 patients. Despite these differences, the frequency of visceral complaints in the CRPS 1 group was substantial (31-58%), with the exception of urine retention. Visceral complaints have been reported in FM literature (16) and in CRPS 1 patients with generalized symptoms (17). In our sample, however, the majority of CRPS 1 patients reporting visceral complaints had localized symptoms (i.e. in one extremity), which suggests that visceral complaints might be an (overlooked) problem for CRPS 1 patients in general, and could be an indication of a more generalized disease mechanism in CRPS 1.

Neck and back complaints are frequently reported in FM patients (18), but little is known about the occurrence of these problems in CRPS 1 patients. The prevalence of reported neck and low back pain in our sample of CRPS 1 patients (52% and 30%, respectively) are higher than those reported in the general population (21% neck pain and 27% low back pain)(19). Possibly, these neck and back problems could be caused by changes in functional use of the limb which might affect neck and lower back functioning, or as a result of a functional neuromuscular relationship

between lower back and lower limb on the one hand, and neck and upper limb on the other hand. Although no solid explanation of this occurrence can be provided at this point, the high frequencies suggest that neck and back problems in CRPS 1 patients should be evaluated more thoroughly in future studies.

Further differences between both groups comprise the occurrence of tropic changes, experiencing a dry mouth, onset of the complaint (more spontaneous in FM and more traumatic in CRPS 1), the number of affected limbs (more limbs affected in FM), age distribution (CRPS 1 patients are older than FM patients) and the disease duration (longer duration in FM). Although these findings and the overlap of symptoms found between both groups may be suggestive for the hypothesis that FM is a generalized form of CRPS 1, it is not possible to conclude this at this point in time. Despite above mentioned differences between both patient groups, the overall picture of the TSI data is that of concurrence rather than difference between CRPS 1 and FM.

### *Study limitations*

The TSI questionnaire is divided in domains which represent complaints on sensory, autonomic, motor, tropic and visceral level. The grouping of domains was based on experience of physicians in the field and on thorough search of the literature. As the sample size of this study was limited we did not perform statistical analysis (i.e. factor analysis, cluster analyses) to identify theoretical dimensions or domains in this study.

FM patients were recruited from a patient organization. Therefore, no information was available on the criteria used to diagnose FM in these patients. Furthermore, it is not known whether the diagnosis FM was still accurate at time of filling out the questionnaire. Although we have tried to increase the uniformity of this subgroup by including only those patients which were diagnosed by their general practitioner or specialist, we do find that diagnosing the patients according to the criteria established by the American College of Rheumatology (20) would have been more accurate.

With regard to the significant difference found between CRPS 1 and FM for reported complaints, we cannot rule out the possibility of chance finding (type 1 error). However, we expect the occurrence of type 1 error to be limited because of the small number of patients used. Furthermore, the small number of clinically significant differences argue against controlling for type 1 error.

In addition, complaints reported in this questionnaire were not verified by a physician. Although the validity of patient responses should be assessed in future research, the variable nature of some of the symptoms (such as temperature difference, and

pain) and the subjective nature of sensory abnormalities will present problems for objective assessment of all the items in the questionnaire. On the other hand, the fact that the questionnaire is patient-based, provides the possibility to surpass the temporary character of various complaints, and assess symptoms which would otherwise remain obscured at clinical examination. Therefore, we do think that a patient-based evaluation of complaints associated with CRPS 1 and disorders like FM will provide more insight in the possible differences and overlap in features reported by different patients.

### Conclusion

The TSI questionnaire is a reliable and practical instrument which can be used for the evaluation of symptoms and complaints in CRPS 1 and FM patients. Our study found many parallels and some dissimilarities between the reported symptoms of CRPS 1 and FM patients. The enhanced knowledge of reported symptoms in CRPS 1 and FM could contribute to the development of new clinical criteria for the diagnosis of the disorders.

More research is needed in which the TSI is tested in a large group of patients with CRPS 1 and syndromes like FM and other potentially related illnesses like RSI. Thorough comparison of similarities and differences in symptoms between CRPS 1 and these other syndromes may contribute to a better understanding of the involved underlying pathophysiologic mechanism(s) of the disorders.

### Appendix:

#### Category 3

*Questions below inquire about complaints and symptoms in the right arm*

1. Do you have complaints of the right arm?  
Yes continue with question 2   
No, continue with next category
2. Can you specify when the complaints of the right arm started?  
About.....months and..... years ago
3. If you cannot move your right arm as intended, please specify when this started  
About.....months and..... years ago
4. Please specify how the complaints of the right arm started  
fracture  overload  wrench   
sprain  operation  twisting   
bruise  spontaneous  other.....

*Questions below inquire about:  
The frequency of complaints in the right arm  
The complaints of last week*

	never	occasionally	frequently	always
5. How often do you experience pain in your right arm?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. How often do you experience tingling in your right arm?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. How often do you experience discoloration of the skin of your right arm?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. How often do you experience a change of sweating of your right arm?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. How often do you experience swelling of your right arm?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. How often do you experience a change of skin temperature of the right arm?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11. How often do you experience loss of strength in your right arm?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
12. How often do you have difficulties in directing movements of your right arm?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13. How often do you experience cramps in your right arm?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
14. How often do you experience abnormal posture of hand due to muscle cramps in your right arm?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
15. How often do you experience trembling of your right arm?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
16. How often do you experience abrupt unexpected movements of your right arm?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
17. How often do you experience decreased range of movements of the right arm?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

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