Complex regional pain syndrome: are the IASP diagnostic criteria valid and sufficiently comprehensive?

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Abstract

This is a multisite study examining the internal validity and comprehensiveness of the International Association for the Study of Pain (IASP) diagnostic criteria for Complex Regional Pain Syndrome (CRPS). A standardized sign/symptom checklist was used in patient evaluations to obtain data on CRPS-related signs and symptoms in a series of 123 patients meeting IASP criteria for CRPS. Principal components factor analysis (PCA) was used to detect statistical groupings of signs/symptoms (factors). CRPS signs and symptoms grouped together statistically in a manner somewhat different than in current IASP/CRPS criteria. As in current criteria, a separate pain/sensation criterion was supported. However, unlike in current criteria, PCA indicated that vasomotor symptoms form a factor distinct from a sudomotor/edema factor. Changes in range of motion, motor dysfunction, and trophic changes, which are not included in the IASP criteria, formed a distinct fourth factor. Scores on the pain/sensation factor correlated positively with pain duration ($P < 0.001$), but there was a negative correlation between the sudomotor/edema factor scores and pain duration ($P < 0.05$). The motor/trophic factor predicted positive responses to sympathetic block ($P < 0.05$). These results suggest that the internal validity of the IASP/CRPS criteria could be improved by separating vasomotor signs/symptoms (e.g. temperature and skin color asymmetry) from those reflecting sudomotor dysfunction (e.g. sweating changes) and edema. Results also indicate motor and trophic changes may be an important and distinct component of CRPS which is not currently incorporated in the IASP criteria. An experimental revision of CRPS diagnostic criteria for research purposes is proposed. Implications for diagnostic sensitivity and specificity are discussed. © 1999 International Association for the Study of Pain. Published by Elsevier Science B.V.

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1. Introduction

A significant barrier to progress in the understanding and treatment of pain associated with vasomotor and sudomotor abnormalities has been the lack of agreement with regards to diagnostic criteria for these disorders (Janig, 1991; Janig et al., 1991). These disorders have been known in the past by various names, including causalgia, Sudeck’s atrophy, neuroalgodystrophy, shoulder-hand syndrome, and reflex sympathetic dystrophy (RSD), with the latter being most common (Schwartzman and McLellan, 1987; Blumberg, 1991). In 1986, a formal description of the RSD syndrome was published by the International Association for the Study of Pain (IASP; Merskey, 1986), although this description did not provide clear diagnostic criteria or decision rules for determining the presence or absence of the disorder. The lack of formal, standardized diagnostic criteria for RSD resulted in serious problems regarding the comparability of the patient samples across various treatment outcome studies and clinical trials. The limited generalizability of these study results hindered identification of treatments
and treatment sequences which were optimal for RSD patients.

In response to this problem, several proposals were made for more standardized ways of diagnosing RSD (e.g. Blumberg, 1991; Gibbons and Wilson, 1992), although none gained uniform acceptance. More recently, a new set of consensus-based, standardized criteria for diagnosis of these disorders was published by the IASP (Appendix; Merskey and Bogduk, 1994). The new diagnostic entity, Complex Regional Pain Syndrome (IASP/CRPS), is a broad diagnosis designed to encompass the range of pain conditions which can be associated with vasomotor and sudomotor disturbance, and is intended to supersede the variety of previous diagnostic schemes (Stanton-Hicks et al., 1995; Wilson et al., 1996).

Although this move to standardize the criteria was a step forward, the criteria were based entirely on results of a Dahlem-type conference of experts in the field (‘the Orlando conference’; Stanton-Hicks et al., 1995), and have yet to be adequately validated in empirical studies. Results of a recent study in a small sample of CRPS patients suggest that the published criteria may have inadequate specificity (Galer et al., 1998). For example, nearly 40% of patients with diabetic neuropathy met the IASP criteria for CRPS (40% displayed mechanical allodynia, 39% temperature asymmetry, and 28% edema on examination), and might have been misdiagnosed if pathophysiology for diabetic neuropathy were unclear (Galer et al., 1998). Excessive false positives using the current criteria could result in some patients receiving inappropriate treatment. The lack of empirical validation of the IASP/CRPS criteria raises several important questions regarding the diagnosis of CRPS. For example, is it justified to combine edema, vasomotor, and sudomotor signs and symptoms in the same criterion (criterion 3 of IASP/CRPS criteria), or does this contribute to inadequate specificity? Is allowing presence of signs or symptoms to satisfy criteria justified? Are the CRPS criteria sufficiently comprehensive, or are important criteria with treatment implications omitted (Stanton-Hicks et al., 1995, 1998)? Until questions such as these are answered, the full benefits of standardized CRPS criteria cannot be realized (c.f. Merikangas and Frances, 1993).

Statistical pattern recognition methods such as factor analysis and cluster analysis have been used to validate headache diagnostic criteria (Dierh et al., 1982; Drummond and Lance, 1984; Bruehl et al., 1999b), as well as criteria for psychiatric diagnoses (Maes et al., 1992). Similar statistical methods have a clear application to the general issue of chronic pain diagnosis, and to the specific issue of CRPS diagnostic validity as well. Techniques such as factor analysis examine the interrelationships among a set of variables, such as signs and symptoms of CRPS as in the present study. Using factor analysis, subgroups of CRPS signs and symptoms (factors) can be identified which tend to co-vary, and thus group together statistically (i.e. if one sign/symptom in a given factor is present, it is more likely that another sign/symptom in that factor will also be present). These statistically-derived subgroups provide an objective determination of distinct subsets of related signs/symptoms as they present in the clinical setting. If valid, the grouping of signs and symptoms in the various IASP/CRPS criteria (e.g. criterion 3 combines edema, vasomotor, or sudomotor changes) should correspond highly with the objective, statistically-derived groupings of signs and symptoms. If the IASP/CRPS criteria do not correspond well with statistically-derived groupings, this indicates that the diagnostic criteria do not adequately reflect natural groupings between various signs/symptoms as they cluster together in the clinical setting. This latter finding would indicate a lack of internal validity, as the internal structure of the criteria would not accurately reflect signs and symptom subgroups which are objectively detectable in the clinical setting.

The present study used a multisite, prospective CRPS database to test the internal validity of the current IASP/CRPS criteria. If the current criteria are internally valid, it was expected that the statistically-derived groups of signs/symptoms would correspond well with the components of the published criteria. A number of signs and symptoms are currently considered associated with CRPS (e.g. motor changes or trophic changes), but are not used in diagnosis. If these associated signs/symptoms group together statistically into factors distinct from the signs/symptoms currently used in CRPS diagnosis, this might suggest that important areas of dysfunction relevant to CRPS are not reflected in current criteria. Therefore, this study was also used to explore the relationship between current criteria and other clinically-relevant signs and symptoms not currently in the IASP criteria, but which have frequently been reported in the CRPS/RSD literature (Stanton-Hicks, 1990; Stanton-Hicks et al., 1990; Janig and Stanton-Hicks, 1996).

2. Methods

2.1. Subjects

Subjects included a series of 123 patients meeting IASP criteria for CRPS (Merskey and Bogduk, 1994) that presented for evaluation and treatment at the data collection sites. Data collection sites included the University of Washington Medical School (33% of the sample), the Rehabilitation Institute of Chicago (22%), Wright Patterson Air Force Base (11%), University of Wisconsin-Madison (10%), Space Coast Anesthesiology (a private clinic; 10%), the Cleveland Clinic (8%), and Johns Hopkins School of Medicine (7%). All patients received standardized (across sites) criterion-based diagnoses of CRPS based upon the IASP criteria for CRPS as published (see Appendix A for a summary; Merskey and Bogduk, 1994). Objective test results (EMG/Nerve Conduction) were available in 60 patients and were used to distinguish CRPS-Type I (without nerve injury) from CRPS-Type II (with nerve injury).
Within this subsample of 60 patients and using abnormal EMG/Nerve Conduction test results as a conservative diagnostic criterion for CRPS-Type II, 68% of the patients were diagnosed with CRPS-Type I (Merskey and Bogduk, 1994; Baron et al., 1996).

2.2. CRPS database checklist

In order to insure standardized collection of sign and symptom data across sites, a database checklist was created. This CRPS checklist presents a complete list of the signs and symptoms used to diagnose CRPS, as well as other signs/symptoms which are reported to be associated with the disorder in previous literature, but are not used in the IASP diagnostic scheme (see Appendix A; Schwartzman and McLellan, 1987; Stanton-Hicks, 1990; Stanton-Hicks et al., 1990, 1995; Merskey and Bogduk, 1994; Janig and Stanton-Hicks, 1996; Wilson et al., 1996). As recommended by Janig et al. (1991), dichotomous measures (i.e. presence or absence) were used to assess signs and symptoms because of the potential for interrater reliability problems with interval rating scales. Standardized instructions for assessing the signs and symptoms are provided with the checklist to maximize uniform assessment across sites (A copy of the standardized CRPS database checklist and the instructions are available from the corresponding author). Signs and symptoms comprising the checklist are summarized in Table 1.

2.3. Procedures

For all patients meeting IASP diagnostic criteria for CRPS, an evaluation of signs and symptoms was conducted using the CRPS checklist described above. This involved obtaining a patient history to assess subjective symptoms, as well as a physical examination conducted by a study physician to assess objective signs.

Table 1
Frequency of signs and symptoms among CRPS patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Signs (%)</th>
<th>Symptoms (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>‘Burning’ pain</td>
<td>NA</td>
<td>81.1</td>
</tr>
<tr>
<td>Hyperesthesia</td>
<td>NA</td>
<td>65.1</td>
</tr>
<tr>
<td>Temperature asymmetry</td>
<td>56.3</td>
<td>78.7</td>
</tr>
<tr>
<td>Color changes</td>
<td>66.4</td>
<td>86.9</td>
</tr>
<tr>
<td>Sweating changes</td>
<td>24.2</td>
<td>52.9</td>
</tr>
<tr>
<td>Edema</td>
<td>56.1</td>
<td>79.7</td>
</tr>
<tr>
<td>Nail changes</td>
<td>9.3</td>
<td>21.1</td>
</tr>
<tr>
<td>Hair changes</td>
<td>8.5</td>
<td>18.7</td>
</tr>
<tr>
<td>Skin changes</td>
<td>19.5</td>
<td>24.4</td>
</tr>
<tr>
<td>Weakness</td>
<td>56.1</td>
<td>74.6</td>
</tr>
<tr>
<td>Tremor</td>
<td>8.8</td>
<td>23.7</td>
</tr>
<tr>
<td>Dystonia</td>
<td>14.0</td>
<td>20.2</td>
</tr>
<tr>
<td>Decreased range of motion</td>
<td>70.3</td>
<td>80.3</td>
</tr>
<tr>
<td>Hyperalgesia</td>
<td>63.2</td>
<td>NA</td>
</tr>
<tr>
<td>Allodynia</td>
<td>74.0</td>
<td>NA</td>
</tr>
</tbody>
</table>

NA = Not applicable. Items were assessed as objective sign or subjective symptom only.

2.4. Statistical analysis

Principal components factor analysis (PCA) was used for the primary analyses. Principal components factor analysis is a statistical procedure which identifies coherent subsets of variables (factors) within a set of data. Variables within each PCA-derived factor co-vary and thus are correlated highly with one another, but are relatively uncorrelated with variables in other factors. Thus, each factor is relatively independent from the others. Each factor is presumed to reflect some underlying process that produces the observed links between the variables within the factor. PCA results in factor loadings which indicate the degree of correlation between each variable and the various factors generated. For the purposes of this study, a factor loading of 0.50 or greater was required for a variable to be assigned to a given factor. In the context of signs and symptoms of CRPS, PCA was used to identify coherent subsets of signs/symptoms which group together, but which are relatively unrelated to other sign/symptom factors. Such groupings of variables could provide support for the internal validity of the IASP criteria for CRPS, as well as indicate other signs and symptoms that might be appropriate to add to the CRPS criteria. For example, if the signs/symptoms included in IASP/CRPS criterion 3 (i.e. color or temperature asymmetry, edema, sweating asymmetry) are appropriate to treat as a unitary criterion, then these signs/symptoms should all load strongly on the same factor. Varimax rotation was used in all analyses. Determination of the number of factors was based on both examination of scree plots, and theoretical and clinical consistency (Tabachnick and Fidell, 1996).

3. Results

3.1. Demographic and background information

The sample was predominately female (64.5%) and Caucasian (88.7%). The most frequent non-Caucasian group was African-American, comprising 4.3% of the sample. Mean age for the sample was 41.1 years (SD = 10.0). The most common initiating events were surgery (23.7%), crush injuries (18.6%), and fractures (16.1%), with less frequent initiating events including sprains (9.3%), repetitive motion (4.2%), blunt trauma (4.2%), lacerations (3.4%), contusions (3.4%), falls (3.4%), electric shock (1.7%), and venipuncture (1.7%). Only two patients out of the sample reported no clear initiating event. While presence of an initiating event is described in criterion 1, its presence is not required for CRPS diagnosis (Merskey and Bogduk, 1994). CRPS was bilateral in only 4.3% of the cases, with slightly fewer of the unilateral cases occurring on the left side (48.7%). Pain location was also nearly evenly split between upper extremities (48.3%) and lower extremities (50.9%).
consisted of signs and symptoms of motor dysfunction, and signs and symptoms of edema. The final factor consisted of objective signs of asymmetric sweating, symptoms of temperature asymmetry. A third sudomotor/edema reflecting signs and symptoms of color changes and symptoms equally weighted) were derived reflecting the number of signs/symptoms present within each of the four factors described in Table 2. These factor scores were examined as symptoms alone indicated one notable difference in contrast to the combined sign/symptom analyses described above. Specifically, in the symptoms-only analysis, edema loaded on its own separate factor, and sweating displayed its largest loading (although a loading of only 0.53) on the motor/trophic factor. Although in the combined analysis described above both sweating and edema loaded greater than 0.61 on the same unique factor, in the symptoms-only analysis, sweating loaded only 0.40 on the edema factor. Thus, while there are substantial similarities between the results of PCA combining signs and symptoms and PCA using signs or symptoms alone, some differences were apparent. These differences emphasize the importance of replicating these results using a larger, independent set of data.

3.3. Evidence for CRPS stages

Although not the primary purpose of this paper, this study allowed preliminary examination of the issue of whether distinct stages of CRPS exist, something which has been widely accepted regarding RSD in the past (e.g. DeTakats, 1937; Bonica, 1953; Schwartzman and McLellan, 1987). It was hypothesized that if there were distinct stages of CRPS, then there should be a significant relationship between CRPS signs and symptoms, and the duration of the CRPS syndrome. Factor scores (with all signs/symptoms equally weighted) were derived reflecting the number of signs/symptoms present within each of the four factors described in Table 2. These factor scores were examined as...
they related to pain duration. Results of this analysis were mixed (see Table 3). Greater duration of CRPS was related to significantly greater likelihood of abnormalities on the sensory factor. Greater CRPS duration was also related to less likelihood of sweating abnormalities or edema. Although this latter effect is not large, it is statistically significant given the large sample size. There was no significant relationship between CRPS duration and either the vasomotor factor or the motor/trophic factor. This latter finding is surprising given the presumed role of disuse in development of trophic changes (Stanton-Hicks et al., 1995).

### 3.4. CRPS signs/symptoms, test results, and treatment responsiveness

Table 3 also presents correlations between CRPS sign/symptom factor scores, test results, and responses to sympathetic block. Sample sizes for the various objective test results are limited, and these data should be treated as preliminary findings. As might be expected, effectiveness of sympathetic blockade (≥50% decrease in pain) was inversely correlated with pain duration ($r(82) = -0.25$, $P < 0.05$). Of the four sign/symptom factors derived, positive block responses were significantly correlated only with scores on the motor/trophic factor. The direction of this effect was positive, indicating that motor/trophic changes might serve as an indicator of more likely positive sympathetic block response. Such a hypothesis remains to be examined.

Of the test results examined (Table 3), temperature asymmetry assessed using thermography or thermistors displayed the strongest relationships with sign/symptom factors. Bilateral asymmetry of at least 2°C was related positively to scores on both the sensory factor and the vasomotor factor. This latter relationship would be expected given that temperature asymmetry as palpated during the physical exam was one component of this vasomotor factor. Removal of temperature asymmetry from this factor results in this correlation becoming non-significant, although this resulting analysis no longer reflects the pure factors as derived using PCA. Although correlations between the sign/symptom factors, and positive radiographs or bone scans were not statistically significant due to the small sample size, the magnitude of several correlations was similar to that noted for the temperature asymmetry assessments. These correlations were consistent with theoretical expectations, generally indicating directionally greater likelihood of positive results on both tests with progressively higher factor scores, particularly for the motor/trophic factor.

### 4. Discussion

The current IASP criteria for CRPS (IASP/CRPS) reflect a clinical consensus, and have yet to be sufficiently validated (Galer et al., 1998; Bruehl et al., 1999b). Although these criteria represent a step forward in the diagnosis of this syndrome by standardizing the diagnostic process (Stanton-Hicks et al., 1995; Janig and Stanton-Hicks, 1996), initial validation studies raise questions regarding the sensitivity and specificity of the IASP/CRPS criteria (Galer et al., 1998; Bruehl et al., 1999a). To improve diagnosis of CRPS, the current criteria need to be empirically-validated, and modified in accord with results of these validation studies.

There are several types of validity, each of which is important to demonstrate if use of a set of diagnostic criteria is to be justified empirically. Demonstration of the internal validity of diagnostic criteria is one crucial component in developing a useful diagnostic system (Merikangas and Frances, 1993), and this is the focus of the current study. In this study, internal validity reflects the extent to which the signs and symptoms of CRPS relate to each other objectively (i.e. statistically) in a manner consistent with the current, consensus-derived criteria. If the empirically-derived sign/symptom groupings closely match the groupings contained in the current criteria, this would support the internal validity of the criteria.

Results of this study support the validity of treating sensory changes (e.g. allodynia, hyperalgesia, hyperesthesia) as a separate and distinct diagnostic criterion (criterion 2). However, problems in the IASP/CRPS criteria were identified, specifically regarding the way in which signs and symptoms are grouped in criterion 3. Currently, edema, vasomotor changes (i.e. skin color, temperature asymmetry), and sudomotor changes (i.e. sweating) are
combined into a single criterion. Furthermore, presence of only one of these objective signs or subjective symptoms (current or historically) is sufficient to satisfy the criterion. Thus, using a strict interpretation of the IASP/CRPS criteria, a patient with a self-reported history of only edema, subjective hyperalgesia, and ‘continuous pain disproportionate to the inciting event’ in whom no other clear etiology could be identified would be diagnosed with CRPS. Such a patient would likely be physiologically quite different from, and might respond to CRPS treatments quite differently than, a CRPS patient displaying clear objective signs of hyperalgesia and allodynia, temperature asymmetry with color changes, edema, and sudomotor changes.

The results of this study indicate that edema and sweating do group closely together on the same factor, as reflected in the current criteria. However, this sudomotor/edema factor is statistically-distinct from vasomotor signs and symptoms (i.e. skin color changes, temperature asymmetry) which group closely together in a separate factor. These results indicate that it would be appropriate to separate sweating/edema into a criterion distinct from vasomotor signs/symptoms in revised criteria.

Another validity issue relates to whether current criteria adequately reflect the full spectrum of CRPS signs and symptoms relevant to diagnosis, and ultimately to treatment. A number of signs and symptoms commonly associated with CRPS-like syndromes in previous literature have not been included in current criteria (Stanton-Hicks et al., 1990; Stanton-Hicks et al., 1990, 1995; Merskey and Bogduk, 1994; Janig and Stanton-Hicks, 1996). For example, several authors have noted motor dysfunction and range of motion changes as important components of the syndrome (Schwartzman and Kerrigan, 1990; Blumberg, 1991; Galer et al., 1995; Wilson et al., 1996). Trophic changes have also been mentioned frequently as important for the diagnosis of CRPS-like syndromes (Schwartzman and McLellan, 1987; Schwartzman and Kerrigan, 1990; Amadio et al., 1991; Wilson et al., 1996). Results of this study indicate the presence of a factor comprised of signs and symptoms of motor dysfunction (e.g. weakness, dystonia), diminished range of motion, and trophic changes (to hair, nail, or skin). This motor/trophic factor is statistically-distinct from the sensory, vasomotor, and sudomotor/edema components of CRPS.

The clustering together of signs and symptoms of motor, range of motion, and trophic changes could be viewed as consistent with a common link underlying all three. Although disuse would be one possible mechanism underlying these changes, it has also been hypothesized that central nervous system alterations may underlie motor changes in CRPS (Galer et al., 1995). These various hypotheses reflect the fact that there is no definitive understanding of the etiology of these changes associated with CRPS. The absence of adequate data on the pathophysiology of these signs/symptoms in CRPS and the fact that trophic signs may result from simple disuse unrelated to CRPS were reasons that these signs/symptoms were not included in the CRPS criteria (Stanton-Hicks et al., 1995). The results of this study suggest that a data-based re-examination of this issue may be warranted. The question of whether signs and symptoms in this motor/trophic factor are diagnostically useful must be submitted to empirical test.

A preliminary validation study by Galer et al. (1998) in a small sample of diabetic neuropathy and CRPS patients indicated that addition of motor abnormalities and trophic changes to the IASP/CRPS diagnostic criteria did not substantially improve predictive power. However, more recent work using a much larger sample (Bruehl et al., 1999a) suggested that the motor/trophic component of CRPS may be diagnostically useful. The results of the current study support the existence of a motor/trophic factor as one of four primary subsets of CRPS signs and symptoms. Furthermore, this factor was the only one significantly predictive of positive block responses, thus raising the question of whether a clinically useful sign/symptom cluster has been omitted from the IASP criteria. Whether addition of a motor/trophic criterion will enhance diagnostic sensitivity and specificity remains to be determined in future work.

Results regarding two other symptoms not included in current criteria were mixed. Although it is not assessed by criterion 2 of the current diagnostic criteria, patient-reported hyperesthesia (i.e. patient described some type of increased sensitivity to sensory stimulation) loaded quite strongly on the same factor as hyperalgesic signs. This finding would support the addition of hyperesthetic symptoms to criterion 2. ‘Burning’ pain has often been considered characteristic of CRPS (Schwartzman and McLellan, 1987), and its potential diagnostic utility was also considered. ‘Burning’ pain failed to meet the factor loading criterion for any of the four factors extracted from the data, a result consistent with negative findings reported by Galer et al. (1998). Given this finding, addition of ‘burning’ pain as a diagnostic criterion does not appear justified.

Although the primary focus of this study was on the internal validity of the CRPS criteria, more limited information was available addressing one aspect of the external validity of these criteria, specifically their concurrent validity. This form of external validity reflects the extent to which the CRPS criteria (or sign/symptom factors) are associated concurrently with other measures with which they should display an association. As might be expected given the hypothesized role of the sympathetic nervous system in abnormal pain sensation in CRPS (Roberts, 1986; Price et al., 1989), an objective measure thought to reflect sympathetic dysfunction (temperature asymmetry using thermogram or thermistor) was found to correlate significantly with the sensory cluster of symptoms. Objective temperature asymmetry also correlated significantly with the vasomotor cluster of signs and symptoms, although this was confounded to some extent by the inclusion of temperature asymmetry signs on clinical examination as part of this cluster. These relationships are clinically and theoretically
consistently, thus providing support for the concurrent validity of the CRPS sign/symptom factors derived in this study.

A final validity issue addressed in the current study is the distinction between CRPS with (Type II) and without (Type I) a nerve injury. Although clinically such a distinction appears justified, use of a conservative definition of Type I versus Type II (based upon positive or negative EMG/Nerve Conduction findings) indicated no statistically-significant differences in rates of occurrence of any CRPS signs or symptoms, or in rates of positive sympathetic block response. These findings indicate that while this distinction is descriptive, its diagnostic and prognostic utility remain to be proven. It should be noted, however, that EMG/Nerve Conduction findings reflect only dysfunction in large peripheral nerves, and cannot address the issue of whether there are possible sign/symptom differences between patients with and without dysfunction in small nerve fibers. While the external validity information above are intriguing, they should be replicated using larger samples with more complete information on specific test results and block responses than was available in the current study.

4.1. Signs versus symptoms

Results of this study indicated that CRPS symptoms reported by patients were always more frequent than objective signs observed upon examination. This finding could be interpreted as indicating that patients are able to accurately report symptoms which do occur as part of the disorder and are observed at home episodically, but which are not apparent during the physical examination. If this were the case, the patient self-reports could help provide complete assessment of the syndrome being experienced. However, an alternative explanation is that the greater symptom frequencies reflect a tendency for CRPS patients to endorse most symptoms presented to them, thus reflecting response bias. This latter alternative could lead to overdiagnosis of the disorder. The fact that the pattern of frequencies is similar across all signs and symptoms suggests that the former interpretation is more likely. As suggested by the results of Galer et al. (1998), patient self-reports do appear to have utility in characterizing the syndrome.

4.2. Proposed experimental revision of CRPS criteria

Based on the internal validity data provided by this study, a proposed experimental revision of the CRPS criteria for use in future validity research has been developed (Table 4). IASP criterion 1 (presence of an initiating event) was dropped because it is not required for diagnosis even using the current IASP system (Merskey and Bogduk, 1994). Some cases of CRPS appear to be spontaneous, with a portion of these likely the result of an injury which has been forgotten. Failure to have or remember an initial injury does not seem conceptually appropriate for determining whether the patient has CRPS. However, as suggested in previous work (Stanton-Hicks et al., 1995), 'spontaneous' CRPS was quite rare in the current study, with only two out of 123 patients unable to identify any initiating event. Therefore, this proposed change is unlikely to alter significantly the diagnostic process.

Another proposed change is that presence of signs and symptoms be split into separate criteria, with a requirement that both objective and subjective factor-based criteria be fulfilled. Signs and symptoms do not appear to be interchangeable, and symptoms are more frequently reported than the related sign is observed on physical examination. Accuracy of symptom reports may at times be questionable and therefore, allowing a patient to meet CRPS criteria solely based on subjective symptoms may potentially be misleading and problematic.

The four sub-criteria categories included under the sign and symptom criteria were based upon the sign/symptom factor groupings suggested by the analysis presented in Table 2: sensory, vasomotor, sudomotor/edema, and motor/trophic areas. The proposed sign/symptom categories may be the focus of some disagreement among researchers and clinicians. For example, although the proposed modification is similar to current IASP/CRPS criteria, some may question the combination of sweating changes and edema into the same, unique diagnostic category despite a lack of obvious pathophysiologic mechanisms to explain why these two signs/symptoms should group together. Factor analysis using symptoms alone did suggest that these two symptoms may be more unique than was suggested by the combined sign/symptom analysis. However, such differences may also reflect the inaccuracies of symptom reports relative to objective signs. Questions such as this emphasize the importance of replicating the current results in a larger and inde-
Pendent dataset before proposing specific changes to the IASP criteria as they currently exist.

Decision rules for the proposed research criteria (e.g. must have two or more sign factors positive) cannot be empirically validated based upon the data available in this factor analytic study. Such decision rules can only be derived from external validity studies examining the discriminative validity of the proposed revised research criteria. Discriminative validity refers to the ability of the proposed modified CRPS criteria (as well as the current IASP criteria for CRPS) to distinguish between CRPS and non-CRPS neuropathic pain conditions. Work by our research group addressing this external validity issue was used to determine the decision rules in the proposed research criteria presented in Table 4 (Bruehl et al., 1999a). This work is described fully elsewhere (Bruehl et al., 1999a).

The results of this study, as well as work by Galer et al. (1998) and Bruehl et al. (1999a) indicate that while the IASP criteria for CRPS may be quite sensitive, they are not highly specific. In some situations, this balance may prove desirable. For example, in early detection of CRPS, clinicians may be more concerned with the error of failing to diagnose and treat (a sensitivity issue), rather than treating someone for CRPS who may not have it (a specificity issue). In addition to providing high sensitivity, the IASP/CRPS criteria remain the current IASP standard, and should therefore continue to be used for formal diagnostic purposes. It is premature to use the empirically-derived research diagnostic criteria presented herein as a replacement for the IASP criteria in standard clinical practice.

However, the current study and work by Bruehl et al. (1999a) suggest that the proposed modified research criteria have some relative strengths compared to the IASP/CRPS criteria, and may be useful in some situations. Most notably, the proposed research criteria are more specific than the current IASP criteria. Therefore, in situations in which specificity may be equal to or even more important than sensitivity, the proposed research criteria may be useful. For example, many research situations may benefit from a more stringent, yet standardized and empirically-based, means of identifying CRPS samples. Using the proposed research criteria may minimize the risk of including non-CRPS patients in a CRPS research sample. Additional potential advantages of the proposed research criteria are that, relative to IASP/CRPS criteria, the proposed criteria are a more comprehensive reflection of the various components of CRPS that are statistically detectable. Clinically, the proposed research criteria are easy to use, allowing diagnosis to be determined using only ‘bedside’ history and examination. Although diagnosis may be corroborated by use of simple thermometry, no other testing equipment or invasive techniques are required.

Despite the possible benefits of the proposed research criteria over the IASP/CRPS in some situations, it should be noted that this proposal is intended to be only one step in a process of ultimately providing a data-based revision of the official IASP criteria. Additional research and replication are required. It is hoped that research such as this will help provide an empirical basis for these eventual changes.

Appendix A

IASP Diagnostic Criteria for Complex Regional Pain Syndrome (IASP/CRPS).

1. The presence of an initiating noxious event, or a cause of immobilization.
2. Continuing pain, allodynia, or hyperalgesia with which the pain is disproportionate to any inciting event.
3. Evidence at some time of edema, changes in skin blood flow, or abnormal sudomotor activity in the region of pain.
4. This diagnosis is excluded by the existence of conditions that would otherwise account for the degree of pain and dysfunction.

Associated signs and symptoms of CRPS listed in IASP taxonomy but not used for diagnosis:

1. Atrophy of the hair, nails, and other soft tissues,
2. Alterations in hair growth,
3. Loss of joint mobility,
4. Impairment of motor function, including weakness, tremor, and dystonia,
5. Sympathetically-maintained pain may be present.

References


