The Central Sensitization Inventory (CSI): Establishing Clinically-Significant Values for Identifying Central Sensitivity Syndromes in an Outpatient Chronic Pain Sample

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Abstract: Central sensitization (CS) is a proposed physiological phenomenon in which central nervous system neurons become hyperexcitable, resulting in hypersensitivity to both noxious and nonnoxious stimuli. The term central sensitivity syndrome (CSS) describes a group of medically indistinct (or nonspecific) disorders, such as fibromyalgia, chronic fatigue syndrome, and irritable bowel syndrome, for which CS may be a common etiology. In a previous study, the central sensitization inventory (CSI) was introduced as a screening instrument for clinicians to help identify patients with a CSS. It was found to have high reliability and validity (test-retest reliability = .82; Cronbach’s alpha = .88). The present study investigated a cohort of 121 patients who were referred to a multidisciplinary pain center, which specializes in the assessment and treatment of complex pain and psychophysiological disorders, including CSSs. A large percentage of patients (n = 89, 74%) met clinical criteria for one or more CSSs, and CSI scores were positively correlated with the number of diagnosed CSSs. A receiver operating characteristic analysis determined that a CSI score of 40 out of 100 best distinguished between the CSS patient group and a nonpatient comparison sample (N = 129) (area under the curve = .86, sensitivity = 81%, specificity = 75%).

Perspective: The CSI is a new self-report screening instrument to help identify patients with CSSs, including fibromyalgia. The present study investigated CSI scores in a heterogeneous pain population, with a large percentage of CSSs, and a normative nonclinical sample to determine a clinically relevant cutoff value.

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Key words: Central sensitization inventory (CSI), central sensitivity syndrome, fibromyalgia, chronic widespread pain, irritable bowel syndrome.

Central sensitization (CS) is a proposed physiological phenomenon in which dysregulation in the central nervous system causes neuronal dysregulation and hyperexcitability, resulting in hypersensitivity to both noxious and non-noxious stimuli. The presence of CS has been demonstrated in central sensitivity syndrome (CSS) populations by comparing the pain thresholds of CSS patients to the thresholds of pain-free controls to various stimuli (such as electrical, pressure, cold, and heat). Objective measures of CS, which complement subjective self-report, include brain imaging and nociceptive spinal reflex tests. CS is associated with allodynia, hyperalgesia (excessive sensitivity to a normally painful stimulus), expansion of the receptive field (pain extending beyond the area of peripheral nerve supply), and unusually prolonged pain after a painful stimulus has been removed (usually throbbing, burning, tingling, or numbness). CS has been proposed as the root etiology for CSSs, which refer to a group of medically indistinct disorders for which no organic cause can be
In its initial comprehensive evaluation, the CSI was found to be psychometrically sound, with a high degree of test-retest reliability and internal consistency (Pearson’s r = .817; Cronbach’s alpha = .879). Evaluation of the construct validity of the CSI in 4 samples (3 within a work-related injury population and 1 nonclinical normative sample) confirmed that fibromyalgia patients (with increased tenderness to palpation, suggesting the most CS) scored the highest on the CSI; chronic widespread pain patients, without fibromyalgia (with less tenderness to palpation, suggesting less CS), and chronic low back pain patients (without chronic widespread pain, suggesting less CS) scored somewhat lower; and the non-clinical normative population (with presumably minimal to no CS) scored the lowest (P < .05).

The goals of the present study were 3-fold: 1) to determine if CSI scores are associated with the presence of 1 or more CSSs in a group of patients seeking outpatient multidisciplinary pain management treatment; 2) to determine if the self-reported diagnoses on Part B of the CSI correspond with actual physician diagnosis; and 3) to establish a clinically relevant cutoff score for predicting the presence of a CSS, using a receiver operating characteristic (ROC) analysis.

**Methods**

**Subjects**

Data were collected from 268 consecutive patients referred to an interdisciplinary pain clinic specializing in the assessment and treatment of complex pain and psychophysiological disorders, including CSSs. Eighteen patients were eliminated from the total sample based on the following exclusion criteria: 1) age over 70 and/or 2) diagnosis of specific medical conditions that can negatively affect the central nervous system, including cancer, brain or spinal cord injury, neurological disease or injury, and multiple sclerosis. The remaining 250-subject total sample was then randomly assigned to 2 groups of 121 and 129 subjects, utilizing the “approximately 50% of all cases” function in SPSS v.18 (SPSS, Inc, Armonk, NY). The first group of 121 subjects was used in this study to establish a clinically relevant cutoff score for the CSI, and the second group of 129 subjects was used in another study. Of the 121 subjects used in the current study, 89 (74%) were diagnosed with 1 or more CSSs.

Upon arrival at the initial appointment, all patients completed a self-administered CSI as well as self-reported documentation of current and past symptoms and disorders. It should be noted that because all the data used in the present study were part of the patients’ standard medical files, the study was granted exemption from institutional review board review. A comprehensive interview was conducted by a single psychiatrist (H.C.) with extensive experience and training in the diagnosis of mental illness, chronic pain conditions, and CSSs. Specifically, subjects were evaluated for presenting complaints, current and past medications, medical and psychiatric history, and current medical and psychiatric diagnosis, based upon all available diagnostic tests.

### Table 1. Prevalence of CSSs (Diagnosed by a Physician) and CSI Scores in the CSS Patient Sample (n = 89 [73.6%])

<table>
<thead>
<tr>
<th>DIAGNOSIS</th>
<th>N (%)</th>
<th>M (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tension headache/migraines</td>
<td>47 (39)</td>
<td>55.6 (13.1)</td>
</tr>
<tr>
<td>Myofascial pain syndrome</td>
<td>47 (39)</td>
<td>49.6 (15.0)</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>38 (31)</td>
<td>57.7 (13.0)</td>
</tr>
<tr>
<td>Irritable bowel syndrome</td>
<td>18 (15)</td>
<td>60.7 (13.6)</td>
</tr>
<tr>
<td>Temporomandibular joint disorder</td>
<td>14 (12)</td>
<td>66.1 (12.9)</td>
</tr>
<tr>
<td>Posttraumatic stress disorder</td>
<td>14 (12)</td>
<td>56.0 (14.7)</td>
</tr>
<tr>
<td>Adult onset</td>
<td>10 (8.3)</td>
<td>52.8 (13.3)</td>
</tr>
<tr>
<td>Childhood onset</td>
<td>4 (3.3)</td>
<td>64.0 (17.0)</td>
</tr>
<tr>
<td>Restless leg syndrome</td>
<td>10 (8)</td>
<td>53.9 (12.9)</td>
</tr>
<tr>
<td>Chronic fatigue syndrome</td>
<td>5 (4)</td>
<td>66.8 (15.0)</td>
</tr>
<tr>
<td>Interstitial cystitis</td>
<td>5 (4)</td>
<td>55.0 (17.1)</td>
</tr>
<tr>
<td>Complex regional pain syndrome</td>
<td>3 (2)</td>
<td>66.3 (11.4)</td>
</tr>
<tr>
<td>Multiple chemical sensitivity</td>
<td>1 (1)</td>
<td>75 (-)</td>
</tr>
</tbody>
</table>

Abbreviations: M, mean; SD, standard deviation.

*46 of these 89 patients had more than 1 CSS diagnosis.
The area under the curve (AUC) was used to examine patient sample and the nonpatient comparison sample.

Measures

The presence or absence of each CSS in Table 1 was determined by symptom complaints and physical examination, using established clinical diagnostic criteria, including tender point evaluations for subjects with chronic widespread pain to diagnose fibromyalgia. Subjects with PTSD were divided into 2 groups—those who developed PTSD as an adult (adult onset) and those with childhood onset—as research suggests that those with childhood PTSD onset may develop more CS due to developmental changes in the brain and the increased length of time that CS has to develop from childhood to adulthood.12,19

A nonpatient comparison sample included undergraduate students at The University of Texas at Arlington who were not currently in treatment for chronic pain. All nonpatient subjects provided written informed consent, approved by the institutional review board at The University of Texas at Arlington. The initial nonpatient sample had 131 subjects. Two subjects were excluded because they failed to respond to 3 or more items on the CSI, resulting in a total sample of 129 participants.

Prevalence of CSSs

The prevalence rates and mean CSI scores of all 11 CSSs are presented in Table 1. Of the total 121-patient sample, 74% (n = 89) were diagnosed with a CSS by the physician. The most frequent CSSs diagnosed were tension headaches/migraines and myofascial pain syndrome (39%), followed by fibromyalgia (31%), IBS (15%), and TMD and PTSD (12%). Of the 89 CSS patients, 46 (51%) had more than 1 CSS diagnosis. Of the 43 patients with a sole CSS diagnosis, a high percentage had myofascial pain syndrome (n = 20). Subjects with myofascial pain syndrome had the lowest CSI scores (mean = 50), and subjects with chronic fatigue syndrome had the highest CSI scores (mean = 67). Because 51% of CSS subjects were diagnosed with more than 1 CSS, these data do not allow one to determine clearly which individual CSSs were associated with higher and lower CSI scores.

Comparison Among the CSS Patient Group, Non-CSS Patient Group, and Nonpatient Comparison Group

As shown in Table 2, significant demographic differences were found among the CSS patient group, the non-CSS patient group, and the nonpatient comparison group. The CSS patient group was more likely to be Caucasian and had a significantly higher mean age than the nonpatient comparison group (P < .001). There was no race or age difference between patient groups. The CSS patient group was significantly more likely to be female than both the non-CSS patient group and the nonpatient comparison group (P < .001). In addition, the CSS patient group exhibited significantly higher mean CSI scores than the non-CSS patient group and the nonpatient comparison group (P < .001), and the non-CSS patient group had a significantly higher mean

Results

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and referring physician notes. The presence or absence of a psychiatric disorder was determined by the DSM-IV-TR.1

The 11 disorders listed in Table 1 have been shown in previous studies to have a CS component and have been included in the CSS family by other authors.15,42,45 The presence or absence of each CSS in Table 1 was determined by symptom complaints and physical examination, using established clinical diagnostic criteria, including tender point evaluations for subjects with chronic widespread pain to diagnose fibromyalgia. Subjects with PTSD were divided into 2 groups—those who developed PTSD as an adult (adult onset) and those with childhood onset—as research suggests that those with childhood PTSD onset may develop more CS due to developmental changes in the brain and the increased length of time that CS has to develop from childhood to adulthood.12,19

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Measures

Part A of the CSI assesses 25 health-related symptoms common to CSSs. Responses are recorded about the frequency of each symptom, with a Likert scale from 0 (never) to 4 (always), resulting in a total possible score of 100. Higher scores are associated with a higher degree of self-reported symptomology. Part B asks if subjects have previously been diagnosed with 1 or more specific diagnoses, including 7 CSSs (tension headaches/migraines, fibromyalgia, irritable bowel syndrome, restless leg syndrome, TMD, chronic fatigue syndrome, and multiple chemical sensitivities) and 3 CSS-related related disorders (depression, anxiety/panic attacks, and neck injury). Subjects are asked 1) if they have previously been diagnosed by a doctor with each of the disorders; and 2) what year they were diagnosed.

Total scores from CSI Part A and self-reported diagnosis from CSI Part B were collected from all patient and nonpatient comparison subjects. In addition, the presence or absence of all CSS diagnoses was recorded for each patient.

Statistical Methods

The data were analyzed using SPSS v.18. Pearson's correlation was used to determine correlations between the number of CSS diagnoses and CSI scores, and between different CSSs. Kappa was calculated as a measure of agreement between the CSI Part B and the CSS diagnoses. To develop a clinically relevant cutoff point, ROC analyses47 were conducted, using both the CSS patient sample and the nonpatient comparison sample. The area under the curve (AUC) was used to examine the ability of the CSI to discriminate between the CSS patient and nonpatient groups. The AUC is useful in 1) evaluating the discriminatory ability of a test to correctly identify a disease and nondisease state; and 2) determining an optimal cutoff point to discriminate between “diseased” and “nondiseased” patients. As has been recommended previously,46 interpretation of the AUC ranges from .5 (for a test that shows no ability to discriminate between subject groups) to 1.0 (for a test that discriminates perfectly between subject groups), with a general satisfactory level of .7. Finally, the sensitivity (the proportion of true positives that are correctly identified) and specificity (the proportion of the true negatives correctly identified) were used to determine an ideal cutoff value for the CSI. The sensitivity and specificity are dependent on the cutoff value used, and there is a tradeoff between sensitivity and specificity. The higher the sensitivity, the lower the specificity, and vice versa. A minimum acceptable level for both sensitivity and specificity is 75%.31 The cutoff value in this study was determined at the point that maximized sensitivity while maintaining a minimum specificity of 75%.

Results

Prevalence of CSSs

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As shown in Table 2, significant demographic differences were found among the CSS patient group, the non-CSS patient group, and the nonpatient comparison group. The CSS patient group was more likely to be Caucasian and had a significantly higher mean age than the nonpatient comparison group (P < .001). There was no race or age difference between patient groups. The CSS patient group was significantly more likely to be female than both the non-CSS patient group and the nonpatient comparison group (P < .001). In addition, the CSS patient group exhibited significantly higher mean CSI scores than the non-CSS patient group and the nonpatient comparison group (P < .001), and the non-CSS patient group had a significantly higher mean

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of the total 121-patient sample, 89 (74%) were diagnosed with 1 or more CSSs (see Table 3). Patients with multiple CSS diagnoses scored higher on the CSI than those with fewer CSS diagnoses. The number of CSS diagnoses and the CSI scores were significantly correlated ($r = .51$, $P < .001$), with a large effect size ($r^2 = .26$). Although the nonpatient comparison subjects were not evaluated by a physician for CSSs in this study, it should be noted that 19% (n = 24 of 129 subjects) reported a CSS on CSI Part B. When those subjects were removed from the analysis in an attempt to create a more homogeneous sample, the physician (on a different patient).

### Identification of a Clinically Significant Cutoff Value

The ROC analysis compared the CSS patient group (n = 89) with the nonpatient comparison group (N = 129). Only patients with 1 or more CSSs were included in this analysis. The AUC and standard errors for the CSI were .86 and .03, with a significance level of .05. As shown in Table 6, the sensitivity (the proportion of true positives, or correctly identifying patients with a CSS) and specificity (the proportion of true negatives, or correctly identifying nonpatient comparison subjects) were dependent on the cutoff scores used. The optimal CSI value of 40 was identified as showing the highest sensitivity level (81%) with an acceptable level of specificity (75%). The lower cutoff scores increased the sensitivity but decreased the specificity (below 75%). Conversely, the higher cutoff scores increased the specificity but decreased the sensitivity. As noted previously, a subset of the nonpatient comparison subject (n = 24 of 129 subjects) reported a CSS on CSI Part B. When those subjects were removed from the analysis in an attempt to create a more homogeneous sample, the physician (on a different patient).
sample, the specificity increased to 79% from 75%, while the sensitivity remained at 81%, using the same cutoff score of 40.

Additional ROC analyses were also performed in an attempt to increase the screening accuracy of the CSI. It was observed that a relatively large number of patients diagnosed with myofascial pain syndrome had a sole diagnosis (n = 20 out of 47, or 43%) of myofascial pain syndrome. Mean CSI scores for those subjects with a sole diagnosis of myofascial pain syndrome (mean = 39.7) were similar to patients without a CSS (mean = 40.9), and significantly lower than patients with both myofascial pain syndrome and 1 or more additional CSS diagnosis (CSI, mean = 57.0). When patients with a sole diagnosis of myofascial pain syndrome were excluded from the analysis, the AUC increased to .91 (SE = .02), and the sensitivity increased up to 91% with the cutoff value of 40. The specificity remained at 79%.

Discussion

As reviewed earlier, the CSI is a self-report scale designed to alert healthcare providers that presenting symptoms may be related to CS, and thus the possibility of a CSS should be considered. Part A of the CSI assesses 25 health-related symptoms common to CSSs, with total scores ranging from 0 to 100. Part B asks about previous diagnoses, including 7 separate CSSs. In a previous study, the construct validity of the CSI was evaluated in 3 clinical samples within a work-related injury population and a normative sample. Fibromyalgia patients (with presumably the most CS) scored the highest on the CSI; chronic widespread pain patients, without fibromyalgia, and chronic low back pain patients (both with presumably less CS) scored somewhat lower; and a nonclinical normative sample (with presumably minimal to no CS) scored the lowest (P < .05).

The present study further investigated the construct validity of the CSI in a sample of patients referred to a multidisciplinary pain center, specializing in the assessment and treatment of complex pain and psychophysiological disorders, including CSSs. Most of the 121 subjects studied (74%) met criteria for at least 1 CSS, 18

Table 4. Correlation Among CSS Diagnoses and CSS-Relevant Diagnoses in the CSS Patient Sample

<table>
<thead>
<tr>
<th>MPS</th>
<th>TH/M</th>
<th>F</th>
<th>IBS</th>
<th>TMD</th>
<th>PTSD^C</th>
<th>PTSD^A</th>
<th>RLS</th>
<th>CRPS</th>
<th>CFS</th>
<th>IC</th>
<th>MCS</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPS</td>
<td>–</td>
<td>–</td>
<td>.20*</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>TH/M</td>
<td>–</td>
<td>–</td>
<td>.03</td>
<td>.48**</td>
<td>.37**</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>F</td>
<td>.19*</td>
<td>.35**</td>
<td>.20*</td>
<td>.43**</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>IBS</td>
<td>–</td>
<td>.06</td>
<td>.14</td>
<td>.07</td>
<td>.05</td>
<td>.24**</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>TMD</td>
<td>.19*</td>
<td>–</td>
<td>.06</td>
<td>.11</td>
<td>.14</td>
<td>.13</td>
<td>.10</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<tr>
<td>PTSD^C</td>
<td>.06</td>
<td>–</td>
<td>.03</td>
<td>.44**</td>
<td>.19*</td>
<td>.06</td>
<td>.44**</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>PTSD^A</td>
<td>.06</td>
<td>–</td>
<td>.03</td>
<td>.20*</td>
<td>.19*</td>
<td>.06</td>
<td>.44**</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>RLS</td>
<td>.13</td>
<td>.25**</td>
<td>.19*</td>
<td>.30**</td>
<td>.17</td>
<td>–</td>
<td>.06</td>
<td>.02</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>CRPS</td>
<td>–</td>
<td>–</td>
<td>.02</td>
<td>.01</td>
<td>.08</td>
<td>.11</td>
<td>–</td>
<td>.03</td>
<td>.14</td>
<td>.05</td>
<td>–</td>
</tr>
<tr>
<td>CFS</td>
<td>.01</td>
<td>.26**</td>
<td>.31**</td>
<td>.03</td>
<td>.44**</td>
<td>.19*</td>
<td>.06</td>
<td>.24**</td>
<td>–</td>
<td>.03</td>
<td>–</td>
</tr>
<tr>
<td>IC</td>
<td>.09</td>
<td>.26**</td>
<td>.22*</td>
<td>.26**</td>
<td>.19*</td>
<td>–</td>
<td>.04</td>
<td>.09</td>
<td>.19*</td>
<td>.03</td>
<td>.04</td>
</tr>
<tr>
<td>MCS</td>
<td>–.07</td>
<td>.12</td>
<td>.14</td>
<td>.22*</td>
<td>.25**</td>
<td>–</td>
<td>.02</td>
<td>.03</td>
<td>.30**</td>
<td>.02</td>
<td>.44**</td>
</tr>
</tbody>
</table>

**Abbreviations:** MPS, myofascial pain syndrome; TH/M, tension headaches/migraines; F, fibromyalgia; C, childhood onset; A, adult onset; RLS, restless leg syndrome; CRPS, complex regional pain syndrome; CFS, chronic fatigue syndrome; IC, interstitial cystitis; MCS, multiple chemical sensitivity.

**NOTE.** Significant level: *<.05, **<.001.

Table 5. Agreement Between CSI Part B Self-Report Within the CSS Patient Sample (n = 70*) and CSS Diagnosis by Physician

<table>
<thead>
<tr>
<th>CSS</th>
<th>CSI PART B N (%)</th>
<th>AGREEMENT (KAPPA)</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Restless leg syndrome</td>
<td>19 (16)</td>
<td>.42</td>
<td>.00</td>
</tr>
<tr>
<td>Chronic fatigue syndrome</td>
<td>12 (11)</td>
<td>.19</td>
<td>.03</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>35 (30)</td>
<td>.70</td>
<td>.00</td>
</tr>
<tr>
<td>TMD</td>
<td>17 (15)</td>
<td>.44</td>
<td>.00</td>
</tr>
<tr>
<td>Tension headaches/migraines</td>
<td>45 (39)</td>
<td>.71</td>
<td>.00</td>
</tr>
<tr>
<td>Irritable bowel syndrome</td>
<td>25 (22)</td>
<td>.71</td>
<td>.00</td>
</tr>
<tr>
<td>Multiple chemical sensitivities</td>
<td>1 (1)</td>
<td>.00</td>
<td>.92</td>
</tr>
</tbody>
</table>

*19 of the 89 total CSS subjects failed to complete CSI Part B.
(Kappa is a measure of agreement between 2 variables. Kappa value: poor, 0–19; fair, 20–39; moderate, 40–59; good, 60–79; excellent, 80–100.

Table 6. CSI Cutoff Scores, Comparing Patients Diagnosed With a CSS (n = 89) and Nonpatient Comparison Subjects (N = 129)

<table>
<thead>
<tr>
<th>CUTOFF SCORES</th>
<th>SENSITIVITY*</th>
<th>SPECIFICITY†</th>
<th>AREA UNDER THE CURVE‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>39</td>
<td>83%</td>
<td>74%</td>
<td>.86** (.81–.91)</td>
</tr>
<tr>
<td>40</td>
<td>81%</td>
<td>75%</td>
<td>.86** (.81–.91)</td>
</tr>
<tr>
<td>41</td>
<td>80%</td>
<td>76%</td>
<td>.87** (.82–.92)</td>
</tr>
<tr>
<td>42</td>
<td>76%</td>
<td>78%</td>
<td>.87** (.82–.92)</td>
</tr>
<tr>
<td>43</td>
<td>76%</td>
<td>81%</td>
<td>.87** (.82–.92)</td>
</tr>
<tr>
<td>44</td>
<td>73%</td>
<td>81%</td>
<td>.87** (.82–.92)</td>
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<tr>
<td>37</td>
<td>87%</td>
<td>73%</td>
<td>.87** (.82–.92)</td>
</tr>
<tr>
<td>38</td>
<td>85%</td>
<td>75%</td>
<td>.87** (.82–.92)</td>
</tr>
<tr>
<td>39</td>
<td>83%</td>
<td>78%</td>
<td>.87** (.82–.92)</td>
</tr>
<tr>
<td>40</td>
<td>81%</td>
<td>79%</td>
<td>.87** (.82–.92)</td>
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<td>41</td>
<td>80%</td>
<td>80%</td>
<td>.87** (.82–.92)</td>
</tr>
<tr>
<td>42</td>
<td>76%</td>
<td>82%</td>
<td>.87** (.82–.92)</td>
</tr>
</tbody>
</table>

**NOTE.** CSI cutoff scores, comparing patients diagnosed with a CSS (n = 89) and nonpatient comparison subjects, excluding those who reported a CSS on CSI part B (n = 105).

*Sensitivity: The proportion of actual positives which are correctly identified.†Specificity: The proportion of negatives which are correctly identified.‡Area under the curve: Excellent, .90–1.00; Good, .80–.90; Fair, .70–.80; Poor, .60–.70; Fail, .50–.60.

**Significant at P < .001.
of those, 38% met criteria for more than 1 CSS, which is similar to previous studies. There were significantly more female subjects in the CSS group, which also confirms previous studies that have found female gender to be a risk factor for many CSSs. Of those patients diagnosed with a CSS, the most frequent diagnoses were tension headaches/migraines (39%), myofascial pain syndrome (39%), fibromyalgia (31%), IBS (15%), TMD (12%), PTSD (12%), and restless leg syndrome (8%). Chronic fatigue syndrome (4%), interstitial cystitis (4%), chronic regional pain syndrome (2%), and multiple chemical sensitivities (1%) were diagnosed relatively infrequently. Patients with multiple CSS diagnoses scored higher on the CSI than those with fewer CSS diagnoses. The number of CSS diagnoses per patient, and the CSI scores, were also highly correlated, indicating support for the construct validity of the CSI.

In order to identify a clinically meaningful cutoff score, CSI scores were compared between the CSS patient group (n = 89) and a nonpatient comparison group (N = 129), using an ROC analysis. A cutoff score of 40 on the CSI yielded good sensitivity (correctly identifying CSS subjects) and specificity (correctly identifying the nonpatient comparison subjects). Although a physician assessment for CSSs was not available for the nonpatient comparison group, it was noted that a subset of nonpatient subjects (n = 24 of 129) reported a CSS on the CSI Part B. When these patients were removed from the ROC analysis, specificity increased from 75% to 79%, and sensitivity remained at 81%, with the same cutoff score of 40.

There was good agreement between the patient self-report on CSI Part B and the physician's diagnosis of fibromyalgia, tension headaches/migraines, and IBS, and moderate agreement with restless leg syndrome and TMD. There was poor agreement between patients and the physician on chronic fatigue syndrome. This disorder may be unfamiliar to patients, and it may be endorsed due to symptoms of general fatigue, as fatigue is a common symptom of CSSs.

Most CSS diagnoses in this study population were significantly correlated with multiple other CSSs, as has been demonstrated in other previous studies. The core CSSs, including IBS, TMD, fibromyalgia, and chronic fatigue syndrome (as well as restless leg syndrome), correlated well with each other and had the highest number of correlations with other CSSs (6 or more correlations each). Interstitial cystitis and multiple chemical sensitivities were somewhat less correlated with other CSSs (4–5 correlations each), although the number of subjects with these diagnoses was relatively low. Myofascial pain syndrome and PTSD (childhood onset) had few correlations (2–3 each). Chronic regional pain syndrome and PTSD with adulthood onset did not significantly correlate with any other CSS diagnoses.

Though the number of subjects was small, childhood-onset PTSD (n = 4) had higher CSI scores (CSI, mean = 64.0) and more correlations with other CSS in this sample than subjects with adult-onset PTSD (n = 10; CSI, mean = 52.8). It is possible that subjects with childhood PTSD onset may develop more CS due to developmental changes in the brain and the increased length of time that CS has to develop from childhood to adulthood. There is evidence that childhood abuse can cause long-lasting neurobiological changes, especially affecting hypothalamic-pituitary-adrenal regulation. Several studies link childhood psychosocial trauma to the development of a CSS (specifically fibromyalgia), although this association is complex and the quality of previous studies weakens these conclusions.

Some controversy exists about whether myofascial pain syndrome and chronic regional pain syndrome are caused by peripheral or central mechanisms, and this may explain why those disorders correlated less with other CSSs. In particular, myofascial pain syndrome seemed to differ from other CSSs in this study. A relatively large number of patients diagnosed with myofascial pain syndrome had a sole diagnosis of myofascial pain syndrome (43% of the myofascial pain syndrome sample). Myofascial pain syndrome correlated poorly with other CSSs, and mean CSI scores for subjects with a sole diagnosis of myofascial pain syndrome (CSI, mean = 39) were similar to patients without a CSS (mean = 40.9), and significantly lower than myofascial pain syndrome patients with 1 or more additional CSS diagnosis (CSI, mean = 57.0). Eliminating those patients with a sole diagnosis of myofascial pain syndrome from the ROC analysis increased sensitivity from 81% to 91% without decreasing specificity. Although myofascial pain syndrome has previously been classified as a CSS, subjects in this study with a sole diagnosis of myofascial pain syndrome appeared more similar to patients without a CSS. As noted earlier, peripheral pain mechanisms are clearly implicated in myofascial pain syndrome. As with low back pain, for instance, perhaps myofascial pain syndrome is primarily a peripheral disorder that may develop CS over time. It is possible that some proportion of patients with a sole diagnosis of myofascial pain syndrome in the current study developed minimal CS and associated symptoms, explaining why removal of this subgroup increased sensitivity.

As in most clinical studies of this type, there were some limitations. First, a single psychiatrist (H.C.) diagnosed all patients. Although standard criteria were used to determine CSS diagnosis, additional physician confirmation was not performed. Second, there may have been differences in the degree of CS associated with each CSS diagnosis in the present sample. However, specific tests of CS were not performed in this study. Third, while the total number of patients in the CSS group (n = 89) yielded sufficient power for analysis, some CSSs were not well represented in this sample. Fourth, CSS diagnosis data from nonpatient control subjects, collected from the CSI Part B, were self-report only and did not represent all possible CSSs or include a physician evaluation. It is unknown whether a physician would have confirmed the self-reported CSS diagnoses, or would have made additional CSS diagnoses, within the...
nonpatient comparison sample. Finally, since results of this study are based on 1 patient sample in an interdisciplinary pain clinic, these findings may not generalize to other CSS patient samples, and cutoff scores may differ.

In conclusion, most CSS diagnoses in this study significantly correlated with other CSSs, providing further support for the interrelatedness of these disorders and the probability that they are related to a common etiology. CSI scores were highly associated with the presence of a diagnosed CSS, and the presence of increased numbers of CSSs was correlated with higher CSI scores. Separately, CSS diagnoses on the CSI Part B corresponded well between patient self-report and physician diagnoses. Good sensitivity (81%) and specificity (79%) values were found, with a cutoff score of 40, indicating that 81% of CSS patients were correctly identified as having a CSS, and 79% of the nonclinical comparison sample were correctly identified as lacking a CSS. Removing those subjects with a sole diagnosis of myofascial pain syndrome raised the sensitivity to 91%. Some false positives were identified (non-CSS subjects who were identified as having a CSS), and it should be noted that the mean CSI score for non-CSS patients was 40.9, which is slightly higher than the 40-point cutoff score that best distinguished between the CSS patients (CSI, mean = 52.4) and control subjects (CSI, mean = 30.9).

Although non-CSS patients in this study were not diagnosed with a CSS, they did have chronic pain, were seeking treatment for their pain, and reported more symptoms on the CSI than the nonpatient controls. Although the CSI cutoff score of 40 distinguished well between CSS patients and nonpatient comparison subjects in this study, it is unknown if it will distinguish well between CSS and non-CSS chronic pain subjects. A follow-up study by our group, with a similar cohort of chronic pain patients, will analyze the ability of the CSI to identify patients with a CSS and to distinguish patients without a CSS, using the 40-point cutoff score. Nevertheless, overall, the current study provides evidence that the CSI is a valid screener for CSSs and that a cutoff score of 40 provides a clinically relevant guide to alert healthcare professionals to the possibility that a patient's symptom presentation may indicate the presence of a CSS. These important clinical findings warrant future replication with a larger sample size and multiple physicians' diagnoses.

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References


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