Convergent validity of the Dutch central sensitization inventory: associations with psychophysical pain measures, quality of life, disability, and pain cognitions in patients with chronic spinal pain

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Convergent Validity of the Dutch Central Sensitization Inventory: Associations with Psychophysical Pain Measures, Quality of Life, Disability, and Pain Cognitions in Patients with Chronic Spinal Pain

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Abstract

Objective: Symptoms of Central Sensitization (CS) have been described in patients with chronic spinal pain (CSP). Although a gold standard to diagnose CS is lacking, psychophysical pain measures are often used. The Central Sensitization Inventory (CSI) is proposed as an alternative method and indirect tool for evaluation of CS symptomatology. The aim of the current study was to evaluate the convergent validity of the CSI by investigating the association with psychophysical pain measures and self-reported measures of current pain intensity, quality of life, disability, and catastrophizing in CSP patients.

Methods: One-hundred-and-sixteen patients with non-specific CSP were included in the present study. Patients completed the CSI, were subjected to pressure pain thresholds (PPT), a conditioned pain modulation (CPM) paradigm, and completed questionnaires for current pain intensity, quality of life, pain disability, and pain catastrophizing.

Results: Higher CSI scores were weakly correlated with lower PPTs ($-.276 \leq r \leq -.237$; all $p \leq .01$) and not with CPM efficacy ($r=.017$; $p=.858$). Higher CSI scores were moderately correlated with higher current pain intensity ($r=.320$; $p<.001$), strongly correlated with lower physical ($r=-.617$; $p<.001$) and emotional ($r=-.635$; $p<.001$) quality of life, and moderately correlated with higher pain disability ($r=.472$; $p<.001$), and higher pain catastrophizing ($r=.464$; $p<.001$).

Conclusion: The CSI was weakly associated with PPTs and not with CPM efficacy in CSP patients. Moderate to strong associations were found with current pain intensity, quality of life, disability, and catastrophizing. The current results illustrate that the CSI does not reflect a direct measure of CS, yet is a representation of general distress, possible originating from CS symptoms.

Keywords: central sensitization; central sensitization inventory; pressure pain threshold; conditioned pain modulation; chronic low back pain; chronic neck pain

Introduction

The perception of pain is the result of several mechanisms and interactions between the periphery and the central nervous system. Dysregulations of ascending and descending pathways have been observed in chronic pain patients, resulting in clinical signs as allodynia, hyperalgesia, hypersensitivity, increased or prolonged aftersensations and temporal summation to noxious and non-noxious stimuli.[1,2] Extended high frequency stimulation of neurons has been found to cause long lasting cellular changes because of elevated cell responsiveness, a diminished working of the inhibitory cells and network sprouting.[3,4] This increase in excitability and synaptic working in the central nociceptive pathways is called central sensitization (CS), which is known to be present in multiple chronic pain disorders.[1,5–7] In this regard, subgroups of patients with chronic low back pain (CLBP) and chronic neck pain (CNP), have shown abnormal central pain processing.[8–12]

Objectifying CS symptomatology is a major challenge requiring standardized protocols. Although a gold standard is lacking, psychophysical pain measures such as pressure pain thresholds (PPT) or conditioned pain modulation (CPM) are commonly used methods for the evaluation of CS symptoms. The objective of these testing procedures is to evaluate the efficacy of pain mechanisms by investigating patients' responses to sensory stimuli.[13,14] Widespread changes in nociceptive function have often been quantified by PPTs, in which the perceived pain rating is observed during mechanically induced pressure stimuli.[15,16] Using PPT measurements, primary (i.e., at symptomatic level) and secondary (i.e., at remote locations) hyperalgesia, an increased sensitivity to painful stimuli, can be quantified.

Regarding primary hyperalgesia in patients with chronic spinal pain (CSP), Imamura et al. (2013) showed decreased PPTs in patients with CLBP in the lumbar region,[17] while general hyperalgesia was reported in patients with chronic whiplash associated disorders (CWAD).[11,18] Mixed results were found in chronic idiopathic neck pain patients.[10,8] In addition, the efficacy of inhibitory nociceptive

mechanisms can be evaluated using a conditioned pain modulation (CPM) paradigm. Activation of CPM reduces neuronal activity of the spinal cord dorsal horn, decreasing pain and hyperalgesia.[6,19–22] The CPM effect occurs when a painful test stimulus is inhibited by a secondary conditioning stimulus.[23] A commonly applied conditioning stimulus is the cold pressor test, involving the immersion of the hand in cold water.[24] When comparing the test stimulus values (e.g. PPTs) before and after or during the conditioning stimulus, the degree of CPM can be quantified. Efficacy of the CPM mechanism has been shown malfunctioning in CWAD patients[25,26] and varying results were found regarding CLBP patients.[24,27–29]

Given the time-consuming nature of experimental pain protocols and the lack of feasibility for clinical practice, the Central Sensitization Inventory (CSI) has been developed as an indirect tool for CS-symptomatology evaluation.[30] In clinical practice, this tool may help identify patients whose presenting symptoms are related to CS, and be a guidance in developing a specific treatment approach. The CSI has been used to assess self-reported signs of CS and overlapping symptoms related to CS, using 25 items scored on a temporal Likert scale, with higher scores denoting more CS symptomatology.[30] Previous studies tested the CSI on samples of chronic pain patients including a variety of disorders, e.g. fibromyalgia, chronic widespread pain, and CLBP,[30–35] which showed associations with self-report measures of pain, function, and psychological correlates.[31,34,35] Concerning accuracy, the CSI showed to be a valid instrument screening the presence of CS symptoms.[30,36] Yet the chances of false positives are relatively high when evaluating patients who suffer from pain that originates from a combination of pain systems (including nociceptive pain and neuropathic pain) and psychophysiological disorders, since false-positive patients in an earlier study were characterized by increased perceived pain-related disability, and higher incidents of past abuse.[36] On the other hand, using the CSI to evaluate patients with CSP is specifically interesting since almost a quarter of the patients with CLBP and CNP will develop chronic widespread pain, depending on several risk factors which are assessed with the CSI.[37]

The chance of a false positive outcome is likely a consequence of multiple items that refer to symptoms that are existent in, yet not restricted to CS. For instance, the English and Dutch versions of the CSI consist of comparable factor structures, with factors referring to general disability and physical symptoms, higher central sensitivity, headache/jaw symptoms, urological and dermatological symptoms, or emotional distress.[30,32] This indicates that the CSI should not be used as a sole screening instrument for CS, but is a feasible addition to a comprehensive screening protocol. Moreover, it suggests that the CSI relates to the outcome of instruments evaluating pain intensity, quality of life, pain disability, or pain cognitions. Regarding the latter, pain catastrophizing is an important cognitive-affective response to pain, which influences the experience of pain[38] and the degree of descending nociceptive modulation,[39] and is therefore implicated to have an effect on CS symptomatology.

To date, the Dutch CSI has not been compared with psychophysical pain measures and self-reported measures in a sample of patients with CSP. Therefore, the present study aimed to investigate whether CSI scores were related to psychophysical pain measures, as proxies for CS, and self-reported measures of pain intensity, quality of life, pain disability, and pain catastrophizing. Consequently, the convergent validity of the CSI was explored by analysing the association of the Dutch version of the CSI with these self-reported measures in a sample of CSP patients. Negative associations of the CSI with PPT and CPM values were hypothesized. Furthermore, given the factor structure of the CSI, that has been described previously,[30,32] it was hypothesized that CSI scores would be associated with measures of pain intensity, quality of life, disability and pain catastrophizing.

Materials and Methods

Study design and participants

The present cross-sectional study reports baseline data from a randomized clinical trial (ClinicalTrials.gov Identifier: NCT02098005).[40] The dataset included 120 male and female patients with non-specific CSP (including CLBP, chronic idiopathic neck pain, failed back surgery (e.g. more than three years ago, anatomically successful operation without symptom disappearance) and CWAD). All patients were recruited through advertisements in primary care facilities, medical physician practices, social media and advertisement distribution around the university hospitals of Ghent and Brussels (Belgium). Data collection took place from March 2014 until January 2016.

The patient group included 56 subjects with CLBP and 64 subjects with CNP (of which 13 with CWAD). Patients were included if they were native Dutch-speaking patients between 18 and 65 years old; experienced non-specific low back or neck pain for at least 3 times a week over a minimum period of 3 months and were seeking for care at the time of recruitment. Included patients were not following therapy for their spinal pain, were on stable medication, and did not start new treatments in the 6 weeks prior to study participation.

Patients were excluded when having chronic widespread pain or with a history of back or neck surgery in the past 3 years, osteoporotic vertebral fractures, neuropathic pain, rheumatologic diseases, or concomitant therapies (i.e., rehabilitation, alternative medicine or therapies). Considering the use of magnetic resonance imaging in the comprehensive clinical trial, patients with contra-indications for magnetic resonance imaging were excluded, as were patients who were pregnant or had given birth in the year prior to study enrolment. Patients were instructed to refrain from alcohol, caffeine and nicotine 24 hours prior to assessments. Pain medication intake was discouraged 48 hours to the assessments. In the 3 days before assessments, patients were instructed not to perform intensive physical activity. Each patient signed for informed consent prior to study enrolment. The study was approved by the medical ethics committees of the University Hospitals of Ghent (registration number: 2013/1133) and Brussels (registration number: 2013/385).

Measurements

Central Sensitization Inventory

The CSI was collected using an online form. The CSI consists of 2 parts, of which part A includes 25 items about CS related symptoms, scored on a 5-point Likert scale from 0 to 4.[30] Higher total scores reflect higher CS symptomatology, whereas a 40-point score out of 100 was described as the cut off value indicative for CS.[30,33,36] Part B evaluates previously diagnosed CS-related disorders, which was not considered for analysis in the present study. The original English CSI showed excellent construct validity and test-retest reliability.[30,33,36] The Dutch version of the CSI showed a good discriminative power and excellent test-retest reliability.[32]

Pressure pain thresholds

The PPTs were determined unilaterally, i.e. at the most painful body side or at the side of the dominant hand in case of equally painful body sides. Pressure was applied with a constant rate of 1 $kg/cm^2/s$[41,42] by the use of a digital algometer, equipped with a 1 cm^2 tip (Wagner Instruments, Greenwich, CT, USA).[41,42] PPTs were defined as the transition point of minimum pressure that induced an unpleasant sensation. Both symptomatic and asymptomatic body locations were investigated. For the CLBP patients, the symptomatic level was marked at the lower back, 5 cm lateral to the spinous process of L3.[41] In CNP, PPTs were measured at the upper trapezius muscle at the shoulder, more specifically midway between C7 and the lateral border of the acromion.[43] PPTs for secondary hyperalgesia were measured at the hand (i.e., muscle web between thumb and index finger)[44] and the quadriceps muscle at the upper leg (i.e., middle between anterior superior iliac spine and upper patella border). The order of PPT measurements was randomised to avoid order effects. PPTs were determined twice at each test site and the final PPT was calculated as the mean of these 2 measurements in units of kilogram-force (kg/cm^2). PPT algometry is considered reliable.[45]

Cold Pressor Test - Conditioned Pain Modulation

The efficacy of descending nociceptive inhibition was evaluated using a CPM paradigm based on a cold pressor test with a refrigerated circulating bath (Versacool, Thermo Fischer Scientific, Newington NH) kept at 12°C as conditioning stimulus. Prior to this test, patients had to submerge their hand, contralateral to the PPT measurements, in water at room temperature (22°C ± 1°C) for 1 minute as a procedure of standardization. During the subsequent cold pressor test, patients were asked to immerse their hand up to the wrist in the cold-water bath for 2 minutes with continuously extended fingers and not making any hand movements during immersion. After 30s, PPT measurements at the upper leg were measured and used as test stimulus. Consistent with the prior measurements, the average of 2 consecutive measurements was taken for analysis. PPTs before the cold pressor test were subtracted from the PPTs during the cold pressor test to obtain a continuous measure of CPM ($\Delta kg/cm^2$), with more negative values indicating less nociceptive inhibition (i.e. PPTs after cold pressor test lower than before cold pressor test) and more positive values indicating more nociceptive inhibition. Patients were encouraged to keep their hand in the water for 2 minutes, but could retract their hand if the pain became intolerable and the elapsed time was registered.

Self-reported pain intensity, quality of life, disability, and pain cognitions

Patients rated their current pain intensity on an **11-point numeric rating scale (NRS-11)**. The score ranges from 0-10 with 0 representing 'no pain at all' and 10 representing 'worst pain'.

Health-related quality of life was evaluated with the **Short Form – 36 items (SF-36),**[46] which consists of 8 different health concepts, including physical functioning, role limitations due to physical health, bodily pain, general health, vitality, social functioning, role emotional, and mental health. Each subset ranges from 0-100 points, with higher scores indicating a better health. The 8 health concepts can be summarized in both the physical component score and the mental component score, representing physical and emotional quality of life, respectively.[47] Again, higher scores represent

better self-reported health. The Dutch language version of the SF-36 has been shown valid and reliable in community and chronic disease populations.[48]

The **Pain Disability Index (PDI)** is a concise questionnaire to evaluate the interference of pain with participation in daily life activities.[49] Patients were asked to rate their level of disability on a rating scale from 0 (no disability) to 10 (total disability), resulting in a maximum score of 70, with higher scores representing greater disability due to pain. The Dutch version of the PDI, which was used in the present study, has been shown to be valid and reliable in a sample of patients with musculoskeletal pain.[50]

Pain cognition, and more specific pain catastrophizing, was assessed with the **pain catastrophizing scale (PCS)**. It consists of 13 items assessing different thoughts and feelings associated with the experience of having pain, scored on a 5-point Likert scale.[51] Three subscale scores can be calculated, referring to rumination, magnification, and helplessness. Here, only the total score was used. Higher scores reflect more pain catastrophizing. The Dutch language version of the PCS showed to have a good reliability and validity.[52]

Statistical analyses

All statistical analyses were performed using SPSS Statistics v23 (IBM Corp., Armonk, NY, USA). Normality of the data was evaluated by the skewness, kurtosis, histograms, and Q-Q plots. Group differences among CLBP and CNP for descriptive statistics, total CSI scores, PPTs, CPM, and self-reported questionnaires were evaluated using independent-samples *t* tests in case of normal distributions. The Levene's test was performed to test for equality of variances. In case of non-normal distributed data, the Mann-Whitney U test was used. In case of no differences between CLBP and CNP, associations of the CSI with the other outcome measures were calculated on the total CSP group with Pearson correlation coefficients for parametric variables (r_P) and Spearman's correlation

coefficients (r_S) for non-parametric variables. Absolute significant correlation coefficients were considered clinically relevant only if ≥.30, according to the suggestion of Cohen (1992).[53] Statistical significance was set at .05.

Results

Descriptive statistics

Data of psychophysical pain measurements were missing in 4 subjects (2 CLBP, 2 CNP), resulting in a total of 116 participants that were included in the analyses (54 CLBP patients and 62 CNP patients). Descriptive data concerning gender, age, body length, weight, and pain duration are presented in *Table 1*.

CSI, psychophysical pain measures, and self-reported questionnaires across patients with CLBP, CNP, and the total CSP group

Details of CSI total scores, psychophysical pain measures, and self-reported questionnaires are shown in *Table 2*. No statistical differences between patients with CLBP and CNP for each of the evaluated measures.

Associations of the CSI with psychophysical pain measures and self-reported measures of pain intensity, quality of life, pain disability, and pain catastrophizing

Considering the lack of differences between CLBP and CNP patients on any of the outcome measures, correlation analyses were carried out on the aggregated study population. Results of correlation analyses of the CSI with psychophysical pain measures and self-reported questionnaires are presented in *Figure 1*.

Higher CSI total scores were weakly correlated with lower PPTs (*Fig 1*$^{A\text{-}D}$; $-.276 \leq r \leq -.237$; all $p \leq .01$) and not correlated with lower CPM efficacy (Fig 1^{E}; $r = .017$; $p = .858$). However, higher CSI total scores showed a moderate correlation with current higher pain intensity (*Fig 1*^{F}; $r = .320$; $p < .001$)

and strong correlations with lower physical (*Fig 1*^{G}; r = -.617; $p < .001$) and emotional (*Fig 1*^{H}; r = -.635; $p < .001$) quality of life. Lastly, higher CSI total scores showed moderate correlations with higher pain disability (*Fig 1*^{I}; r = .472; $p < .001$) and higher pain catastrophizing (*Fig 1*^{J}; r = .464; $p < .001$).

Discussion

This study aimed at investigating the convergent validity of the CSI by assessing its association with psychophysical pain measures (i.e., PPT and CPM), self-reported measures of pain intensity, quality of life, pain disability, and pain catastrophizing in patients with CSP. It was hypothesized that higher CSI total scores would be associated with lower PPTs, representing pressure hyperalgesia, as well as impaired CPM efficacy, representing dysfunctional descending nociceptive modulation.[4,9,12,33] Furthermore, higher CSI total scores were expected to be associated with higher pain intensity, higher pain catastrophizing, and lower quality of life, given the identified constructs within the CSI based on previous studies.[30,32] The present study revealed that higher CSI total scores in patients with CSP were weakly associated with lower PPTs and not with CPM efficacy. Furthermore, higher CSI total scores were strongly associated with lower physical and emotional quality of life; and were moderately associated with higher current pain intensity, higher pain disability, and higher pain catastrophizing in patients with CSP.

When evaluating the results of the correlational analyses, the CSI marginally reflects direct alterations in central nociceptive processing, as reflected by pressure pain algometry and CPM. However, symptoms related to CS, and reflected by measures of pain intensity, quality of life, pain disability, and pain catastrophizing, show a stronger relationship with the CSI. When considering the original development of the CSI, it was designed 'to assess key somatic and emotional complaints often associated with central sensitivity syndromes'.[30] In this respect, the current results confirm the validity of the CSI as a tool to assess CS symptomatology within a construct of general distress. Based

on findings that CS is not a key factor in most of the patients with CSP, the CSI should not be administered as an isolated measure, but is a useful addition to comprehensive protocols in diagnosing CS. This is supported by the finding that the CSI is not very specific due to the high risk of false positives when evaluating patients with complex pain and psychophysiological disorders.[36]

In that respect, evaluating the presence of CS and associated mechanisms may not be straightforward among CSP populations. The current negative correlations between PPTs and CSI show a weak association between CSI scores and pressure sensitivity in the current sample of CSP patients. However, earlier studies revealed that potential differences in pain pathophysiology may exist between patient populations with idiopathic neck pain, CWAD, or CLBP.[10,11,8,54,55] Compared to the well-known presence of CS in patients with CWAD,[11,56] research on the presence of CS in idiopathic neck pain is rather ambiguous.[10,8,57] A recent systematic review by Malfliet et al. (2015) concluded that CS is not a characteristic feature of idiopathic neck pain, but can be present in some individuals.[8] Likewise, the systematic review and meta-analysis of Marcuzzi et al. (2015) found no evidence for pain hypersensitivity in idiopathic neck pain.[54] Although different studies described the contribution of CS to CLBP,[12,58] the relationship remains controversial.[20] For example, Meeus et al. (2010) found no evidence for abnormal central processing and hyperalgesia in CLBP.[59] The study reported an increase of PPTs after submaximal aerobic exercise, suggesting normal exercise induced activation of pain inhibition. Diers et al. (2007) also showed no significant PPT differences between CLBP and healthy controls.[60] As in patients with CNP, altered central nociceptive processing seems present only in subgroups of patients with CLBP.[61,62]

In addition to the association with PPTs, the current study also aimed at investigating the association of the CSI with CPM efficacy, which is a measure of descending nociceptive inhibition.[24] Negative CPM values, representing lower PPTs during the cold pressor test compared with the condition without the cold pressor test, were expected to correlate with higher CSI scores.[1] In the present study, most patients exhibited positive CPM scores, as the conditioning stimulus led to diminished

pressure sensations in most patients. It should be noted that overall a marginal CPM effect was seen, given the positive difference value of approximately 1. Previous research found no evidence of an impaired CPM efficacy in patients with chronic idiopathic neck pain.[8] In CWAD patients, however, an impaired CPM efficacy has been found.[18,25] In CLBP patients, varying results were found, with (partially) intact,[24] impaired,[27] or varying CPM efficacy.[28,29] Considering these previous findings, it is very likely that the current sample of CSP patients is relatively heterogeneous with respect to CPM efficacy. This could have led to the lack of differences between CLBP and CNP on CPM efficacy, yet also to the absence of an association with the CSI total score.

Hence it appears that the CSI may, to a certain degree, identify symptoms of altered nociceptive processing in patients with CLBP and CNP. Within these patients, the CSI did not show a substantial association with the degree of pressure hyperalgesia, given the negligible correlations with PPTs. The CSI was not representative of the degree of nociceptive inhibition, as it showed no association with CPM efficacy.

When considering the second hypothesis, it was expected that, based on previously identified factor structures of the CSI,[30,32] the CSI would be associated with measures of pain intensity, quality of life, pain disability, and pain catastrophizing. Whereas higher current pain intensity, pain disability, and pain catastrophizing showed a moderate association with higher CSI total scores, both lower physical and emotional quality of life were strongly associated with higher CSI total scores. Although these characteristics are not specific to patients with CS, the CSI was stronger associated with these measures than with PPTs and CPM efficacy. This confirms the underlying factor structure of the Dutch CSI,[32] of which the factor 'General disability and physical symptoms', might explain the associations with the SF-36 and PDI in the current study. The association with the PCS might be explained by the factor 'Emotional distress'. This is furthermore supported by a recent study that compared the CSI with other self-reported measures in a sample of people with chronic pain, which not only demonstrated a direct relationship between psychological distress and the CSI, but also an

indirect relation between pain catastrophizing and the CSI mediated by psychological distress.[63] Although individual CSI items do not directly reflect pain catastrophizing, some of the included items deal with psychological states that are strongly associated with pain catastrophizing, such as anxiety (item 3), insomnia (item 12), or depression (item 16).[64,65]

Limitations and strengths

Some limitations need to be considered when interpreting the current results. First, it would have been interesting to include a sample of healthy controls and a group of patients with CS as main underlying pathology (such as fibromyalgia). This would have provided understanding about the associations between the CSI and the other outcome measures among groups and possible different associations between groups. As the current data was part of baseline assessments from a comprehensive RCT, no healthy controls or additional patient groups were included. Notwithstanding, CS has been proven to contribute to the clinical presentation in subgroups of the CSP population,[8–12] which is represented by the current patient sample. Furthermore, the CSI seems specifically relevant for screening patients with CSP, since this patient group is at relative high risk of developing chronic widespread pain.[37]

A second consideration is the location of PPT measurements. In both CLBP and CNP, the PPT measurement locations included standardized locations at the lumbar region and the trapezius muscle. PPTs at the trapezius served as a primary hyperalgesia site in CNP patients, whereas this site served as secondary hyperalgesia site for the CLBP group and vice versa. Measurements at the upper thigh and hand, however, served as secondary hyperalgesia sites in both groups. Because of this, primary and secondary hyperalgesia were not differentiated between patients with CLBP and CNP.

The CSI was not associated with CPM efficacy based on the cold pressor test as conditioning stimulus in the current study. Although this a reliable protocol, the scientific literature describes many alternative CPM protocols, including suprathreshold conditioning stimuli,[66] which may possibly lead to different results. In addition, the limited range of the CPM metric may have underestimated the

association between CPM efficacy and the CSI. Again, including a sample of healthy controls and a group of patients with CS as main underlying pathology would be interesting to increase the range of the CPM metric.

The included measures to evaluate nociceptive processing in the current study are a selection of available methods to detect altered nociceptive processing. Although a gold standard to detect CS is lacking, several other tests and combinations of tests can be used to examine altered central nociceptive processing related to CS.

Nevertheless, the current study included a large patient sample, which allows for better deduction of the results with regard of using the CSI in the clinical practice. Furthermore, no previous studies have evaluated the convergent validity of the Dutch CSI with psychophysical pain measures and self-reported measures of pain intensity, quality of life, pain disability, and pain catastrophizing in a sample of patients with CSP.

Recommendations for further research

The current work evaluated the association of the CSI with pressure sensitivity and nociceptive inhibition. As mentioned in the limitations, several other measures to assess altered central nociceptive processing have been developed. For example, it has been shown that patients with spinal pain can be differentiated based on sensory responsiveness, as assessed with measures of pressure and thermal pain sensitivity and temporal summation protocols.[66] Future studies with the CSI should therefore also take these and other psychophysical pain measures into account.

Early recognition of CS symptoms is considered key in the management of CSP in order to prevent persistent pain complaints and transition into a chronic pain state.[67] For patients with regional pain in the neck or back, and when other disorders are excluded, a high CSI score might be indicative of developing persistent pain. Particularly since almost a quarter of patients with regional neck or back pain develops chronic widespread pain.[37] Consequently, the CSI should be considered in prospective longitudinal studies, aimed at detecting risk factors for developing a chronic pain state in patients

with CLBP and CNP. Similarly, evaluation of the CSI in detecting progression from rehabilitation of chronic pain states seems valuable.

Conclusion

The current results indicate that the CSI shows a weak association with pressure sensitivity and not with CPM efficacy in patients with CSP. However, moderate to strong associations were found with respect to measures of pain intensity, quality of life, pain disability, and pain catastrophizing. This confirms the original development goal of the CSI, which is 'assessing key somatic and emotional complaints often associated with central sensitivity syndromes' [30]. The current results furthermore illustrate that the CSI does not reflect a direct measure of CS, yet is a representation of general distress originating from CS symptoms. Future research on the CSI should focus on comparison with other relevant measures to detect altered central nociceptive processing, the ability of the CSI to recognize early symptoms of developing chronic pain states, and the assessment of progression in the rehabilitation of chronic pain patients.

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Table 1: Demographics and differences between patients with CLBP and CNP[a]

	CSP *(n = 116)*	**CLBP** *(n = 54)*	**CNP** *(n = 62)*	**Statistical Difference between CLBP and CNP**
Females *(% total)*	72 (62.1)	31 (57.4)	41 (66.1)	$\chi(115) = 116$, $p = .456$
Age *(years)*	39.92 (12.52)	41.24 (13.04)	38.77 (12.05)	$t(114) = 1.059$, $p = 292$
Length *(centimeters)*	172.12 (9.93)	172.54 (10.26)	171.75 (9.70)	$t(113) = .420$, $p = .675$
Weight *(kilograms)*	70.07 (14.17)	72.56 (13.13)	67.87 (14.79)	$t(113) = 1.791$, $p = .076$
Pain duration *(months)*[b]	82 (130.5)	114 (141.5)	74 (92.5)	$U = 1390.5$, $p = .199$

[a] Values are mean (SD) unless otherwise indicated
[b] Displayed as median (interquartile range)
Abbreviations: CLBP = chronic low back pain patients; CNP= chronic neck pain patients

Table 2: Mean values (standard deviation) and group differences of CSI, psychophysical pain measures and self-reported questionnaires among CLBP and NP patients

	CSP *(n = 116)*	**CLBP** *(n = 54)*	**CNP** *(n = 62)*	**Statistical difference between CLBP and CNP**
CSI	40.09 (11.49)	39.06 (11.61)	40.98 (11.41)	$t(114) = .901$, $p = .370$
$PPT_{lower\ back}$ *(kg/cm²)*[a]	5.04 (2.77)	4.62 (1.99)	5.40 (3.26)	$t(102.9) = 1.563$, $p = .121$
$PPT_{trapezius}$ *(kg/cm²)*	4.32 (2.29)	4.25 (1.82)	4.39 (2.64)	$t(108.5) = .323$, $p = .747$
PPT_{leg} *(kg/cm²)*	5.22 (2.54)	5.23 (2.15)	5.20 (2.85)	$t(114) = .066$, $p = .947$
PPT_{hand} *(kg/cm²)*	3.61 (1.86)	3.72 (1.51)	3.51 (2.13)	$t(114) = .586$, $p = .559$
CPM *(Δkg/cm²)*[b]	.98 (1.36)	1.00 (1.48)	.96 (1.25)	$t(107) = .140$, $p = .889$
NRS-11[a] (/10)	5 (4)	5 (3)	5 (3)	$U = 1603.5$, $p = .692$
SF-36 PC (/100)	229.01 (74.08)	222.64 (77.43)	234.56 (71.20)	$t(114) = .863$, $p = .390$
SF-36 MC (/100)	279.92 (71.26)	280.91 (68.42)	279.05 (74.18)	$t(114) = .140$, $p = .889$
PDI (/70)	21.73 (14.11)	23.70 (14.62)	20.02 (13.52)	$t(114) = 1.1411$, $p = .161$
PCS (/52)	16.71 (10.17)	17.41 (12.07)	16.10 (8.21)	$t(91.4) = .674$, $p = .502$

[a] Displayed as median (interquartile range)
[b] Missing value in 7 patients due to inability of maintaining their hand immersed in the cold water
Abbreviations: CLBP = chronic low back pain patients; CNP= chronic neck pain patients; CSI= central sensitization inventory; PPT= pressure pain threshold; CPM= conditioned pain modulation; NRS-11 = numeric rating scale - 11 items; SF-36 PC = short form – 36 items, physical component score; SF-36 MC = short form – 36 items, mental component score; PDI = pain disability index; PCS = pain catastrophizing scale.

Figure 1**.** Correlation coefficients of CSI total scores, with experimental pain measures (A. PPT lower back; B. PPT trapezius; C. PPT leg; D. PPT hand; E. CPM) and self-reported questionnaires (F. NRS; G. SF-36 PC; H. SF-36 MC; I. PDI; J. PCS)**.** Abbreviations: r_P = Pearson correlation coefficient; r_S = Spearman's correlation coefficient; CSI = central sensitization inventory; PPT= pressure pain threshold *(kg/cm²)*; CPM= conditioned pain modulation (*Δkg/cm²*); NRS-11 = numeric rating scale - 11 items; SF-36 PC = short form – 36 items, physical component score; SF-36 MC = short form – 36 items, mental component score; PDI = pain disability index; PCS = pain catastrophizing scale. * Correlation is significant at the .05 level; ** Correlation is significant at the .01 level; *** Correlation is significant at the .001 level