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Research Article

Central Sensitization in Patients Attending Physical Therapy for Musculoskeletal Disorders

Louw A[1,2]*, Hartman D[2], Weber B[2], Shuda D[2], Obert C[2], Louw H[3] and Farrell K[2]

[1]Department of Pain Science, Evidence in Motion, USA
[2]Department of Physical Therapy Education Orthopedic Residency, St. Ambrose University, USA
[3]Department of Mathematics, Northwestern College, USA

***Corresponding author:** Louw A, Department of Pain Science, Evidence in Motion, 618 Broad Street, Suite B, Story City, IA 50248, USA

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Abstract

Study Design: Survey study.

Objective: To determine what percentage of patients attending physical therapy with musculoskeletal pain present with central sensitization and which patient factors may be predictive of central sensitization.

Background: Treating pain, especially chronic pain is clinically challenging. It has been suggested that pain be sub-classified as either nociceptive, peripheral neuropathic or central sensitization, to aid clinical decision-making to inform the treatment approach for specific pain conditions.

Methods: A convenience sample of adult patients (18-65) attending PT for musculoskeletal pain were asked to complete a demographic questionnaire and the central sensitization inventory.

Results: Two-hundred and forty-five patients completed the central sensitization inventory, resulting in a mean score of 26.88 ± 15.54. The majority of the patients were classified as "low" in regard to central sensitization scores and nearly one in five patients (n = 39; 17.3%) were classified as "high" in regard to central sensitization scores. The variables of 'being disabled' (β = 13.73), 'currently experiencing feelings of depression' (β = 9.35), and 'identifying as female' (β = 3.60), had the largest partial effects on central sensitization as individual variables.

Conclusions: Approximately one in five patients attending PT for musculoskeletal pain present with a central sensitization inventory score of > 40, suggesting presence of central sensitization. Patients that reported feeling disabled, experiencing feelings of depression and 'identifying as female' were more likely to score > 40 on the central sensitization inventory. Central sensitization is relatively common in patients attending PT for musculoskeletal pain and various patient characteristics may suggest higher potential CSI scores at intake.

Keywords: Central sensitization; Musculoskeletal pain; Physical therapy; Central sensitization inventory

Abbreviations

BMI: Body Mass Index; CNS: Central Nervous System; COVID-19: Corona Virus Disease-2019; CS: Central Sensitization; CSI: Central Sensitization Inventory; PT: Physical Therapy; SD: Standard Deviation; US: United States (of America)

Introduction

Current research suggests that approximately 56 percent of people globally suffer from regular body pain on a weekly basis [1-6]. In the United States (US), it's estimated 116 million American adults are affected by common chronic pain conditions, while 25.3 million suffer from daily chronic pain [7,8]. More alarming is the fact that the chronic pain epidemic seems to be increasing [7,9,10]. Even though the long-term effects of the corona virus disease of 2019 (COVID-19) is yet to be fully understood or realized, it is proposed that it will not only increase the rate of chronic pain, but also intensify the overall pain experience of those already challenged by chronic pain [11,12].

Treating patients with chronic pain poses significant challenges for clinicians. There is evidence that physical therapists (PTs) struggle when treating patients with chronic pain [13,14]. Although it is likely that many factors are involved, it is believed that a significant contribution to this clinical struggle is the lack of training and preparedness for treating chronic pain [13,15]. Not only are many clinicians under-prepared to treat this challenging population, but the pain models they follow are outdated and treatment options that flow out of these models are often ineffective, leading to additional frustration [14].

To help with the clinical challenges with assessing and treating pain, clinicians must develop a greater understanding of the latest science in the study of pain [14]. Recent years have seen an explosion of knowledge related to the underlying biology and physiology of human pain experience - the neuroscience of pain. For example, it is well established that a significant part of a person's pain experience is correlated with the increased sensitization of the central and

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peripheral nervous system [16-18]. Pain, especially chronic pain, is associated with an increased vigilance of the central nervous system (CNS), referred to as central sensitization (CS) [16,19]. CS is defined as an increased responsiveness of nociceptive neurons in the CNS to normal and subthreshold afferent input [19]. Normal, healthy, non-threatening touch is then perceived as a threat and may increase an individual's pain experience. CS can dominate the clinical picture of patients with a variety of medical diagnoses, including many often seen in PT practice (e.g., low back pain [20], shoulder pain [21], neck pain [22], tendinopathies [23]). It is therefore suggested when patients present with pain, especially chronic pain, they be sub-classified as a means to better describe the underlying mechanisms of their pain experience and guide assessment and treatment. Emerging pain science research at minimum divides pain into one of three categories: nociceptive driven pain states, peripheral neuropathic pain states and CS [24,25]. This subclassification of pain has been widely used, expanded upon, and has significant implications for assessment and treatment of patients attending PT [26-29]. A key tenant of this model is even more elementary: identifying patients with or without the clinical presence of CS. CS is such a significant challenge that a clinician should know how to differentiate a patient with or without CS.

CS is not directly measurable in humans and various indirect measures are used to suggest CS [16,30]. There are no medical tests, i.e., scans, bloodwork, nerve conduction tests, etc., that can diagnose CS. Various studies have explored the clinical aspects of CS. For example, Smart et al., used a mechanism-based classification to determine the presence of CS in patients with low back pain with and without radiculopathy, whereby three symptoms and one sign became predictive of CS (sensitivity 91.8%, 95% confidence interval (CI): 84.5-96.4; specificity 97.7%, 95% CI: 95.6-99.0) [28]. Nijs and colleagues, described information obtained from the medical diagnosis, combined with the medical history of the patient, as well as the clinical examination and the analysis of the treatment response in order to recognize CS [16]. Valuable research on measurement of the changes in the nervous system to confirm CS has lately been reported in the literature [31,32]. More recently, there has been a greater focus on the use of the Central Sensitization Inventory (CSI) as a means to quantify the potential presence of CS, with a score over 40 points being suggestive of CS [30,33]. The various options have been combined in a clinical algorithm for the recognition of predominant CS pain in patients presenting with 'musculoskeletal' pain [16], low back pain [34], or post-cancer pain [35,36]. With these algorithms, use of CSI and appropriate clinical reasoning, the modern PT should be able to identify a patient presenting with signs and symptoms associated with CS.

A clinical question, however, remains: how prevalent is CS in PT? Yes, chronic pain is very common, but not all patients with chronic pain present with CS. Some patients present with chronic nociceptive pain, where innervated tissues continue to be the main driver of the pain experience [26]. In others, the peripheral nervous system is the main driver, referred to as peripheral neuropathic pain [27]. Both these - nociceptive and peripheral neuropathic, however, are very commonplace in daily practice and argued to not be as challenging as CS. This study set out to determine the percentage of patients attending PT for musculoskeletal pain that present with potential CS, as measured with the CSI. Additionally, the study aimed to determine which patient characteristics gathered in the intake information at initial evaluation may provide clinical clues as to the potential presence of CS.

Methods

Study design and participants

The study design called for a convenience sample of patients attending outpatient PT to be recruited to complete a survey related to CS. Institutional review board (IRB) approval was obtained from St. Ambrose University or this study. Four private PT clinics participated. Patients with musculoskeletal pain and/or disability, attending PT were asked to participate in the study, by completing an anonymous survey. Participation was entirely voluntary and by agreeing to participate, patients provided informed consent for the study. In order to participate, patients had to present with a primary complaint of musculoskeletal pain and/or disability (no specific duration), over the age of 18 and proficient in reading and writing the English language. Surveys were collected at each clinic over a 4-month period.

Measures

A survey for this study was developed in line with the objectives of the study. The survey consisted of three sections:

Demographics: Data collection included the patient's report on their age, gender, ethnic background, employment status, education background, primary insurance type, social status, if they're experiencing pain at the time of the study, pain rating (numeric pain rating scale), family history of chronic pain, location of pain, amount of sleep per night, amount of exercise per week, if they smoke, weight, height, personal and family history of depression, having had surgery for their condition, been in a motor vehicle collision, having had imaging for their pain and medical providers seen for their pain.

Statements: Four statements on a Likert scale anchored between 0 (strongly disagree) and 6 (strongly agree) were asked and participants were asked to indicate their level of agreement. The statements pertaining to patient beliefs and experiences were based on various beliefs and experiences which have been tied to previous CS studies [37,38]:

- "I am very pleased with the care I have received to date for my issue."
- "I have been wronged by the medical system."
- "I will get better."
- "I am very afraid of moving because it increases my pain."

Central Sensitization Inventory (CSI): The CSI includes 25 questions related to CS. The individual scores each item on a scale of 0 (never) to 4 (always). If the total score is greater than 40, this is considered to indicate the presence of CS [16,30,33]. The CSI is considered a useful and valid measure to screen for patients with CS. It is reported to have strong test-retest reliability as well [30,33]. The internal consistency of the CSI is excellent, with Cronbach's a value ranging from 0.87 to 0.91, and test-re-test reliability has been found to be high. [39,40]. Scores obtained with the CSI showed concurrent validity with a range of relevant measures, including measures of

Table 1: Demographics.

Characteristics	Patients (n = 245)
Mean age (years) (SD)	52.96 (18.38)
Female (%)	149 (60.82)
Race	
• White/Caucasian (%)	216 (88.16)
• African-American/Black (%)	17 (6.94)
• American Indian (%)	6 (2.45)
• Other (%)	6 (2.45)
Employment	
• Full-time (%)	106 (43.27)
• Retired (%)	73 (29.80)
• Part-time (%)	22 (8.98)
• Other (%)	43 (17.95)
Educational background	
• High school diploma (%)	116 (47.35)
• Four-year college degree (%)	67 (27.35)
• Post-graduate degree (%)	33 (13.47)
• Other (%)	29 (11.83)
Social Status	
• Married (%)	136 (55.51)
• Single (%)	65 (26.53)
• Divorced (%)	24 (9.80)
• Other (%)	20 (8.16)
Currently experiencing pain (%)	194 (79.18)
Mean duration of pain for those currently experiencing pain in months (SD)	4.98 (7.34)
Mean pain score (NPRS) for those currently experiencing pain (SD)	3.04 (2.48)
Experienced pain for more than 6 months (%)	57 (23.27)
The three most common areas of pain	
• Knee	80 (32.65%)
• Shoulder	79 (32.24%)
• Lower Back	66 (26.94%)
Mean hours of sleep per night (SD)	6.13 (2.36)
Mean time exercising per week (minutes) (SD)	114.08 (143.40)
Smokers (%)	27 (11.02%)
Mean BMI (SD)	30.47 (8.81)
Self-reported experience of symptoms of depression (%)	80 (32.65)
Immediate family struggle with depression (%)	80 (32.65)
Mean CSI score (SD)	26.88 (15.54)

resilience and negative effect, anxiety, pain catastrophizing, duration and severity of pain, lateralization of pain [41,42].

Upon development of the questionnaire, a first-version was circulated to experts in the management of musculoskeletal pain; management of CS and questionnaire design. Experts were asked to comment, in line with the objectives of the study on the various demographic items potentially associated with CS, clarity and ease of the questionnaire and any grammatical or spelling edits. A convenience sample (n = 6) of patients attending PT with musculoskeletal pain similarly reviewed the questionnaire and provided feedback. Completion of the questionnaire averaged ~8 minutes. Responses were gathered over 30 days. According to Powel, if 70% agreement was obtained by reviewers, the questionnaire would be deemed ready for use [43]. In all, the reviewers agreed with the various questions, made some small grammatical changes, thus deeming the questionnaire ready for the study.

Data analysis

The completed paper survey data was entered into Microsoft Excel™ spreadsheets for data analysis by an independent research assistant. Four separate excel sheets were merged to create one collective database of patient results from different data collection sites. The statistical program RStudio Cloud version 1.4 of RStudio IDE was used in all analyses. Of the original 271 observations, only 245 were used in analysis after outliers were removed from duration of pain being experienced (no pain experienced at the time of the study). Body mass index (BMI) was then calculated for each participant based on their height and weight observations in meters and kilograms. Additionally, two binary variables were created to indicate whether a patient had experienced pain for more than six or twelve months. CSI score was calculated by creating a new variable from the summation of responses from the CSI questionnaire. Demographic data was analyzed and represented as means, standard deviations and percentages.

Results

Demographics

Two-hundred and forty-five patients presenting to PT with musculoskeletal pain completed the surveys (Table 1). The average pain intensity was in the in the lower half of the NPRS (1-5.5 out of 10), and just more than half of the patients experienced pain for longer than 6 months. The majority of patients reported lower back or neck or shoulder pain.

CSI scores

The overall, mean CSI score was 26.88 ± 15.54. The majority of

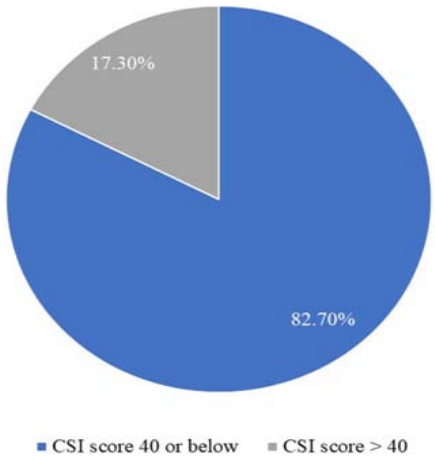

Figure 1: CSI scores in patients attending outpatient physical therapy with musculoskeletal pain and dysfunction.

Table 2: Variable associated with higher CSI scores.

Variable	Coefficient
Disabled	(β = 13.73, p = 0.00)
Depression	(β = 9.35, p = 0.00)
Female	(β = 3.60, p = 0.04)
Immediate family with depression	(β = 3.41, p = 0.05)
Fear of Movement	(β = 1.66, p = 0.00)
Number of healthcare providers seen	(β = 1.51, p = 0.00)
BMI	(β = 0.21, p = 0.03)

the patients were classified as "low" in regard to CSI scores (Figure 1). Nearly one in five patients (n = 39; 17.3%) were classified as "high" in regard to CSI scores.

CSI correlations

CSI scores were analyzed in relationship to patient variables. Multiple linear regressions were used to determine which factors most significantly impacted CSI score. Bayesian Information Criterion (BIC) was used to determine the most accurate model of all demographics. The variables of 'being disabled', 'currently experiencing depression', 'female', and 'having immediate family currently experiencing depression' had the largest partial effects on CSI as individual variables. Not only were these partial effects on CSI the largest in magnitude, they were all positively correlated with CSI score (Table 2).

The multiple linear regression model with the variables listed above regressed on CSI score was found to be statistically significant with $F(7, 237) = 17.68$. Post-hoc power analysis showed a high level of power at nearly 1 with df = 237. This would indicate that the model is highly likely to find an effect on CSI score from the independent variables in the model.

Discussion

Previous studies on patients experiencing chronic pain have explored the presence of CS using the CSI [31,44,45]. This study, however, to our knowledge this is the first study to directly report on the prevalence of CS in all patients attending outpatient PT, not just chronic pain, and determining which factors increase the likelihood of presenting with CS.

In PT there would seem to be two opposing camps emerging as pain science finds its way into academia, scientific presentations, and clinical practice. On the one side, many clinicians take the latest neuroscience of pain and develop a belief that nearly all patients, especially those with chronic pain, present with CS. The belief here is that CS is a very prevalent phenomenon and PT's that don't recognize or address CS may be missing the bigger clinical picture of pain science theory. The results from this study show that approximately one in five patients presenting to outpatient PT present with CS, implying over 80% do not. It is estimated that approximately 25% of patients attending PT present with diagnoses that fit into the peripheral neuropathic category, i.e., cervical and lumbar radiculopathy [46-48]. If we consider the three main pain mechanisms (nociceptive, peripheral neuropathic and CS), the prevalence of CS in this study (20%) and data regarding peripheral neuropathic pain (25%) would thus imply, if pain is divided into one of three dominant pain mechanisms, that 55% of the remaining patients attending PT may fit into the nociceptive-dominant category. The results from this study would thus imply PTs that believe CS is a major factor in PT practice should recognize that more than 80% of people attending PT do not present with CS and acknowledge that tissues (nociceptive) and the peripheral nervous system (peripheral neuropathic) are more prevalent in the clinical presentation of pain, including chronic pain. Many clinicians, with the newfound knowledge of pain science may have forgotten about the powerful nociceptive contributions to a human pain experience [49].

On the flipside, there are PT's that frequently dismiss or downplay the presence of CS. In this scenario, PT's focus their attention of their evaluations and treatments solely on tissue-only contributions to pain. This model is often referred to as the biomedical model [14]. In this model, the sensitization of the peripheral and CNS is not described or recognized as a major player in a patient's pain experience, including chronic pain. This is in direct contrast to emerging pain science indicating various powerful peripheral and central nervous system mechanisms involved in a pain experience [24,50]. The discovery of CS was a major breakthrough in pain neuroscience as it demonstrated that there is no simple relationship between activity in peripheral nociceptors and pain. This realization is likely to have contributed to a change in attitudes of clinicians who would otherwise have diagnosed some patients with chronic pain as "malingerers, liars or hysterical [51]." The results from this study should clearly show biomedically-oriented clinicians that nearly one in five patients attending outpatient PT for a common musculoskeletal disorder present with CS. This would imply that these therapists should in turn learn more about pain and how CS is present in a sub-group of patients and need to be screened, assessed and treating accordingly. CS should be seen as a continuum. Even though it's suggested that a high score of >40 is used as a cut-off [16,30,33], Neblett, et al. has shown CSI severity levels as follow: subclinical = 0 to 29; mild = 30 to 39; moderate = 40 to 49; severe = 50 to 59; and extreme = 60 to 100 [52-54]. Additionally, Cuestas-Vargas et al recently developed a CSI cluster calculator that proposes to classify patients into three groups of CS-related symptom severity: low, medium and high levels of CS-related symptom severity [55].

The CSI, however, is not enough to establish the presence of CS and should be seen as part of the overall screening of patients presenting with pain, especially chronic pain. Additional tests beside clinical history or self-reported symptoms (CSI), should be further explored. Subjectively this may include investigation of pain intensity, pain character, spatial and temporal characteristics, spatial and temporal characteristics, exacerbations of pain, etc. [31]. This concurs with the results from this study whereby other, non-CSI factors, create an overall, patient-centered clinical picture of CS, versus only focusing on a CSI score in excess of 40 points [51]. Similarly, objectively sensory testing such as qualitative sensory testing has been suggested as further ways to explore excitability of different pain pathways or mechanisms and involves a variety of stimulus modalities (thermal, mechanical, chemical, electrical), assessment methods (psychophysics (thresholds, ratings), electrophysiology, imaging), and structures (skin, muscles, joint, and viscera) [31].

Another key part of this study is the correlation between various patient characteristics and presentation of CS. The CSI is not

commonly used in clinical practice as a screening tool and clinicians are advised to use subjective and objective clues to determine the clinical presence of CS [24,28]. It is argued that following a thorough subjective interview and physical examination, the PT should be able to identify various signs and symptoms to determine the appropriate pain mechanism, which in turn should drive decision-making for the treatment. An overlooked aspect of allocating appropriate pain mechanisms would be prior to the actual examination to patients that may or may not present with CS. This may further add significant value to drive the vigor and planning of the physical examination. In this study, self-reporting of being disabled, and feelings of depression, and having immediate family with depression, indicated a higher probability of presenting with a CSI score >40. It is well-established that depression and chronic pain are powerfully linked, making this finding of depression as a marker for possibility of CS an expected finding [56,57]. One in seven patients attending PT for pain present with depression and it's now commonplace for PTs to screen for depression [58], which can be used as a means to alert the PT of the possibility of the clinical presence of CS. This in turn may warrant giving a patient the CSI during the first consultation. Likewise, various studies have linked disability and chronic pain [50]. It can be argued that those who are disabled display higher levels of depression and pain catastrophizing, which in turn may lead to an increased sense of hopelessness, thus fueling the pain experience [59]. This finding is thus not a surprise and clinicians typically are able to recognize this by virtue of a patient's intake forms that often ask patients to divulge their current employment status. The other factor associated with a score >40 in the CSI was 'being female'. This may not come as a surprise since it's well-established females present, in general, with higher rates of chronic pain, experience pain very differently than men, and display higher rates of sensitivity of the nervous system than men [60].

Limitations

The study contains numerous limitations. First, and foremost, the CSI was used to establish the presence of CS. Even though the CSI has been used in numerous studies related to the clinical presence of CS, it has also been challenged in some cases [30]. The score of >40 points is seen as a potential starting point and more in-depth testing and evaluation is needed to come to the clinical conclusion of the presence of CS. Second, the results of this study can only be applied to the clinics involved in this study, along with the diagnoses included in these results and tied to the local geography. Larger scale studies will be needed to determine if these results are present at scale in various regions, diagnoses and clinical settings. The results can only be interpreted in adults aged 18-65 and not extrapolated to those under 18 or over 65. Additionally, depression and disability were not directly measured and only based on patient self-reports.

Conclusion

Approximately one in five patients attending outpatient PT for musculoskeletal pain present with CS, based on their CSI score. Patient report of feeling disabled and depressed, as well as being female and having immediate family with depression increases the odds of presenting to PT with CS.

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