Central Sensitization Symptom Severity and Patient-Provider Relationships in a Community Setting

Xiao Jing Wang¹, Jon O. Ebbert¹, Elizabeth A. Gilman¹, Jordan K. Rosedahl¹, Priya Ramar¹, and Lindsey M. Philpot¹

Abstract
Introduction: Central sensitization syndromes (CSS) comprise an overlapping group of clinical conditions with the core feature of “pain arising as a direct consequence of a lesion or disease affecting the somatosensory system.” Patients with CSS are known to have challenging interactions with healthcare providers contributing to psychological distress and increased healthcare utilization. CSS symptom severity has been associated with psychologic comorbidities, but little is known about how symptom severity relates to provider interactions. Methods: We performed a cross-sectional survey among patients with CSS in our primary care practices to examine the relationship between CSS symptom severity and experiences with doctors. Results: A total of 775 respondents completed the survey (775/5000; 15.5%) with 72% reporting high CSS symptom severity. About 44% of respondents had a prior diagnosis of fibromyalgia, 72% had migraines, and 28% had IBS. Patients with high CSS symptom severity were more likely to report that doctor(s) had often/always told them that they don’t need treatment when they feel like they do (OR = 3.6, 95% CI 1.9-7.5), that doctor(s) often/always don’t understand them (OR = 3.1, 95% CI 1.9-5.4), and that doctor(s) often/always seem annoyed with them when compared with respondents with low-moderate CSS symptom severity (OR = 4.8, 95% CI 2.2-12.5). Patients with high CSS symptom severity were at greater than 5 times odds of reporting being told that their symptoms were “all in their head” when compared to patients with low-moderate symptom severity (OR = 5.4, 95% CI 3.3-9.0). Conclusion: Patients with CSS spectrum disorders experience frequent pain and decreased quality of life. A high degree of CSS symptom severity is associated with negative experiences with healthcare providers, which deters the establishment of a positive provider-patient relationship. Further research is needed to help understand symptom severity in CSS and harness the power of the therapeutic alliance as a treatment modality.

Keywords
chronic pain, central nervous system sensitization, surveys and questionnaires, cross sectional study

Introduction
Central sensitization (CS) is defined by the International Association for the Study of Pain as “pain arising as a direct consequence of a lesion or disease affecting the somatosensory system.”¹ Central sensitization syndromes (CSS) comprise an overlapping group of clinical conditions the core feature of which is CS.² CSS include clinically common conditions such as migraine headaches,³ irritable bowel syndrome (IBS),⁴ and fibromyalgia.²,⁵,⁶

Previous research has identified that patients with CSS have challenging interactions with the healthcare system and healthcare providers. Qualitative interviews of patients who met criteria for fibromyalgia suggest that they feel invalidated and unsupported in their condition,⁷ and experience significantly more objective discounting and lack of understanding compared to patients with rheumatoid arthritis.⁸ We have observed in our own work that patients with chronic migraine express lower satisfaction with medical care and advice than patients with episodic migraine.⁹ Patients with IBS report humiliating encounters

¹Mayo Clinic, Rochester, MN, USA
Corresponding Author:
Lindsey M. Philpot, Mayo Clinic, 200 1st Street SW, Rochester, MN 55905, USA.
Email: Philpot.Lindsey@mayo.edu
with healthcare providers feeling like their symptoms are being trivialized or dismissed.\textsuperscript{10} 

Strong relationships exist between symptom severity and psychosocial variables such as depression.\textsuperscript{11} However, if the severity of CSS negatively impacts relationships between patients and healthcare providers then the ability to address CSS symptoms and psychosocial factors will be compromised. Little is known about the degree to which CSS symptom severity is associated with negative healthcare experiences.

To assess the relationship between CSS symptoms severity and negative interactions with healthcare providers, we analyzed data from a community sample of patients with CSS conditions migraine headaches, IBS, and fibromyalgia.

**Methods**

**Setting, Study Design, and Sample**

We performed a cross-sectional assessment within the community patient population of our Mayo Clinic Health System primary care practices. The Mayo Clinic Health system is a large, integrated healthcare delivery system that serves community populations in southern Minnesota, northeastern Iowa, and western Wisconsin. The Mayo Clinic Health System serves approximately 600,000 patients each year and employs over 1,000 physicians and 15,000 employees.

The study team utilized a cross-sectional survey approach to assess the relationship between CSS symptom severity and experiences with healthcare providers. An electronic survey was built in partnership with the Mayo Clinic Survey Research Center and deployed via Qualtrics Survey Software (Provo, UT). Invitations to participate in the study were sent via patient-provided E-mail and an opt-out link was provided for individuals who did not want to be contacted further. Two reminder E-mails were sent to non-responders who did not opt-out of participation 7 and 10 days following initial invitation for study participation.

To target patients with CSS, we sampled those who were greater than 18 years of age with a documented diagnosis of migraine headache (ICD-10 G43.*), IBS (ICD-10 K58.*), or fibromyalgia (ICD-10 M79.7) within their medical chart between January and August of 2020, and who had an assigned primary care doctor within our Mayo Clinic Health System clinical practice sites. In adherence with local legal requirements, only individuals who indicated interest in participating in clinical research were eligible for sampling. We identified 22,211 individuals who were eligible for inclusion within our study. Previous experience by the research team within this population indicates an approximately 20% response rate to electronic survey investigations. To target 1000 survey responses for our analyses, we performed a simple random sample of 5000 individuals to contact for participation within this study.

This study was reviewed and approved by the Mayo Clinic Institutional Review Board (IRB# 20-008119).

**Measures**

The study team compiled a set of questionnaires to be administered electronically to assess our study aims. The 2-part Central Sensitization Inventory was created as a patient self-report tool to assess the presence and severity of symptoms related to CSS.\textsuperscript{12} Since development in 2011, the Central Sensitization Inventory has been adopted into clinical practice and research as a measurement tool to proxy the experiences of patients.\textsuperscript{13} The inventory is comprised of 25-items requesting the respondent to indicate “how often” he/she experiences the 25-items on a 5-point frequency Likert scale (Never, Rarely, Sometimes, Often, Always). The second portion of the Central Sensitization Inventory assesses for previous diagnosis of 10 conditions and is used for clinical assessment purposes. The present study exclusively utilizes the first portion of the inventory instrument. Previous research has grouped the first portion of responses on the Central Sensitization Inventory to represent patients with low, moderate, and high CSS-related symptom severity.\textsuperscript{14} We have adopted this approach within our analyses.

To investigate the healthcare experiences of our study population, we developed a set of 8 questions based on our clinical experience and a review of the relevant literature. The constructs we were most interested in investigating are those we have heard qualitatively from our patients with CSS, including report of difficult interactions with healthcare providers related to their CSS, difficulty in feeling heard or understood by providers when discussing their CSS, and feelings of dismissal of their symptoms related to their CSS.

In addition to our primary measures, we also asked patients to validate the presence of our 3 main CSS conditions (migraine, IBS, fibromyalgia), to report on how often they experienced pain (chronic pain defined as pain on most or every day), and to rate their overall health on a 5-point Likert scale (Poor, Fair, Good, Very Good, Excellent). Our electronic survey tool included the EuroQol 5-dimension (EQ-5D) scale to understand patient-reported quality of life.\textsuperscript{15} The EQ-5D index score is provided and can be interpreted as figures closer to zero indicating poorer quality of life, and numbers closer to one indicating higher quality of life. From the medical record we collected patient age at time of surveying, gender, marital status, race, and ethnicity.

**Statistical Analyses**

Descriptive statistics were calculated among our respondent population for patient demographic characteristics, patient clinical indications, patient report of chronic pain and
self-rated health, and EQ-5D index by CSS severity. Responses to our healthcare experiences question set were also reported by CSS severity group. We report median and interquartile ranges for continuous and index variables and assess for differences between CSS severity groups with the Mann-Whitney U-test. Categorical variables were summarized as frequency (n) and proportion (%) and differences between CSS severity groups were assessed using the Chi Square test of Independence unless the test assumptions were not met, then the Fisher Exact test was utilized. Associations between CSS severity group and patient reported experiences were assessed using crude odds ratios, and associated 95% confidence intervals were calculated as our primary measure of effect. Associations were considered statistically significant if \( P < .05 \) and 95% confidence intervals did not span the null value. All data management and statistical analyses were performed using Statistical Analysis Software (SAS) Version 9.4 (Cary, NC).

Results

In total, 775 individuals responded to our electronic survey (response rate 775/5000 = 15.5%). Findings of our survey assessment by CSS symptom severity are outlined in Table 1. Across our response population, 10.6% felt that doctor(s) never or rarely take their symptoms seriously and 7.0% felt that they never or rarely have positive interactions with doctor(s) (Table 2). Overall, 12.0% of our respondents felt that doctor(s) often or always tell them that they don’t need treatment when they feel like they do. When compared with individuals in the low or moderate CS-related symptom severity group, individuals within the high CS symptom severity group had significantly lower patient ages (47.0 vs. 52.5 years, \( P = .0226 \)) and lower self-rated health (44.0 vs. 57.3, \( P = .0034 \)).

### Table 1. Patient Characteristics by Central Sensitization Symptom Severity (N = 775).

| Central sensitization symptom severity | Low (N = 31) | Medium (N = 186) | High (N = 558) | \( P \) value |
|---------------------------------------|-------------|-----------------|---------------|--------------|
| **Patient age, Median (IQR)**         | 45.0 (34.0, 63.0) | 52.5 (39.0, 63.0) | 47.0 (36.0, 59.0) | .0226        |
| **Gender**                            |             |                 |               |              |
| Female                                | 27 (87.1%)  | 154 (82.8%)    | 510 (91.4%)   | .0045        |
| Male                                  | 4 (12.9%)   | 32 (17.2%)     | 48 (8.6%)     |              |
| **Marital status**                    |             |                 |               |              |
| Divorced/separated/widowed            | 1 (3.2%)    | 17 (9.1%)      | 105 (18.8%)   | .0034        |
| Life partnership/married              | 22 (71.0%)  | 129 (69.4%)    | 320 (57.3%)   |              |
| Single                                | 8 (25.8%)   | 40 (21.5%)     | 133 (23.8%)   |              |
| **Race**                              |             |                 |               |              |
| African American                      | 0 (0.0%)    | 0 (0.0%)       | 5 (0.9%)      | .5475        |
| Asian                                 | 0 (0.0%)    | 4 (2.2%)       | 7 (1.3%)      |              |
| Other                                 | 0 (0.0%)    | 3 (1.6%)       | 16 (2.9%)     |              |
| White                                 | 31 (100.0%) | 179 (96.2%)    | 530 (95.0%)   |              |
| **Ethnicity**                         |             |                 |               |              |
| Hispanic or Latino                    | 0 (0.0%)    | 3 (1.6%)       | 10 (1.8%)     | .1960        |
| Not Hispanic or Latino                | 31 (100.0%) | 182 (97.8%)    | 529 (94.8%)   |              |
| Other                                 | 0 (0.0%)    | 1 (0.5%)       | 19 (3.4%)     |              |
| **Patient reported condition**        |             |                 |               |              |
| Fibromyalgia                          | 0 (0.0%)    | 37 (19.9%)     | 305 (54.7%)   | <.0001       |
| Migraine                              | 26 (83.9%)  | 134 (72.0%)    | 395 (70.8%)   | .2872        |
| Irritable bowel syndrome              | 5 (16.1%)   | 46 (24.7%)     | 166 (29.7%)   | .1354        |
| Chronic pain (most/every day)         | 6 (19.4%)   | 114 (63.3%)    | 498 (91.5%)   | <.0001       |
| Missing                               | 0           | 8               | 15            | <.0001       |
| **Self-rated health**                 |             |                 |               |              |
| Missing                               | 0           | 8               | 15            | <.0001       |
| Excellent                             | 11 (35.5%)  | 6 (3.4%)       | 5 (0.9%)      |              |
| Very good                             | 12 (38.7%)  | 54 (30.3%)     | 59 (10.9%)    |              |
| Good                                  | 7 (22.6%)   | 87 (48.9%)     | 236 (43.5%)   |              |
| Fair                                  | 1 (3.2%)    | 29 (16.3%)     | 193 (35.5%)   |              |
| Poor                                  | 0 (0.0%)    | 2 (1.1%)       | 50 (9.2%)     |              |
| **EQ-5D index, Median (IQR)**         | 0.9 (0.9, 1.0) | 0.8 (0.7, 0.9) | 0.6 (0.3, 0.7) | <.0001       |

Abbreviations: EQ-5D, EuroQol 5-dimension scale; IQR, interquartile range.
severity group were at increased odds of reporting that doctor(s) had often or always told them that they don’t need treatment when they feel like they do (OR = 3.6, 95% CI 1.9-7.5). Overall, 18.1% of respondents reported that doctor(s) often or always don’t understand them; respondents within the high CS symptom severity group were at increased odds of reporting that doctor(s) often or always don’t understand them when compared with low and moderate CS-related symptom severity respondents (OR = 3.1, 95% CI 1.9-5.4). Just under 10% (9.4%) of respondents indicated doctor(s) often or always seem annoyed with them. Respondents with high CS symptom severity were at increased odds of reporting that doctor(s) often or always seem annoyed with them when compared with respondents with low and moderate CS symptom severity (OR = 4.8, 95% CI 2.2-12.5).

Among respondents, 27.4% felt that they had been told by doctor(s) that their symptoms are “all in their head,” including 37.4% of CSS patients with high CS symptom severity profiles. CSS patients with high CS symptom severity were at greater than 5 times the odds of reporting being told that their symptoms were “all in their head” when compared with CSS patients with low and moderate CS symptom severity profiles (OR = 5.4, 95% CI 3.3-9.0). Over half of our respondents indicated being told by a doctor that their symptoms were attributable to stress (55.5%), and nearly one-third of respondents indicated that interactions with healthcare provider(s) had made them question their own intuition about their health (30.2%).

**Discussion**

We observed that patient perceptions of their interactions with healthcare providers vary based on severity of CSS symptoms they experience. Patient degree of CS symptom
severity impacts patient report of overall self-rated health and quality of life. Patients with high degrees of CS-related symptom severity had increased odds of feeling that doctor(s) do not understand them, and that doctor(s) often or always seem annoyed with them. We observed that over half of our CSS respondents reported being told by doctor(s) that their symptoms were attributable to stress. Additionally, CSS patients with high CS symptom severity were also at increased odds of being told that their symptoms are “all in their head.”

Our findings are consistent with previous publications in a population of patients with CSS. We provide quantitative data for previously reported experiences among patients with fibromyalgia who face challenges establishing therapeutic relationships with healthcare providers. This can lead to frustration for both patients, who suffer a large burden of disease from decreased quality of life, and providers, who are limited in what they are able to provide these patients in terms of diagnosis or treatment, leading to frustration and increased burnout. Providers often underestimate the severity of CSS symptoms and their impact on patient quality of life and consider patients to have less severe symptoms with a greater psychological contribution. Patients with functional gastrointestinal (GI) disorders are more likely to be perceived as less reasonable, less disabled, and were less likely compared to patients with organic GI disorders while those with fibromyalgia report frustrations from lack of a clear diagnosis, adequate counseling, and education by providers. This is particularly key in education around the use of antidepressant medications for pain as this can both provide confusion and a sense of invalidation to patients. Lack of diagnosis can lead to patients continuing to seek answers with increased healthcare utilization.

Strong therapeutic relationships with healthcare providers are key to management and clinical improvement of CSS disorders. Positive patient perceptions of healthcare interactions in primary care led to improvement in discomfort and better emotional health with fewer diagnostic tests and referrals. Positive provider-patient relationships in IBS have been associated with fewer return visits for IBS related symptoms, all decreasing healthcare utilization. Empathy in the patient relationship not only improves patient satisfaction and decrease rates of malpractice suits, but also improves clinical outcomes including medication adherence. A strong therapeutic alliance can enhance placebo or nocebo effect, impacting therapeutic benefit of the limited available array of recommended medications. On the provider side, positive patient interactions can lead to enhanced work satisfaction and resilience.

Prior literature shows that symptom severity in patients with CSS has been associated with higher rates of co-morbidities, greater psychologic distress, poorer physical function, and greater health-care utilization, requiring more intervention than among individuals with mild or moderate symptoms. Our findings further the literature by providing evidence that perceptions of negative interactions with healthcare providers increase with increased symptom severity. The paradox of increased challenges in this cohort of CSS patients is remarkable since a patient-provider therapeutic alliance is needed the most in this population. In patients with psychological comorbidities, a strong therapeutic alliance becomes even more critical in order for patients to undergo integrative therapeutic approaches for their concomitant anxiety/depression. CSS patients overall have limited directed medication options and has the potential for the greatest benefit from therapeutic relationships and psychotherapy techniques which rely on strong provider-patient alliance. Further studies should focus on advancing our understanding of the factors contributing to CSS severity and improving provider training in communications in the care of CSS patients.

Our study has several limitations. First, our response rate was 15.5% and was lower than our previous surveys conducted among patients with migraine headaches. Additionally, our response population was predominately female and of White race, which is consistent with national prevalence estimates of patients with CSS. Second, our sample may be biased toward patients with more severe symptoms and more difficult interactions with healthcare providers. We are unable to assess for the prevalence of underlying mental and other medical conditions due to the blinded nature of our study. Strengths of our work include the unique population, the use of a validated instruments and the inclusion of a spectrum of central sensitization disorders.

Conclusion

Patients with CSS experience frequent pain and diminished quality of life. A high degree of CS symptom severity is associated with more negative experiences with healthcare providers, deterring establishment of a positive provider-patient relationship. A positive relationship between provider and patient can enhance patient experience and facilitate healing, as well as provide benefit to providers, improving work-satisfaction and decreasing burnout. Patients with CSS often face limited therapeutic options, and further research is needed to help understand symptom severity in CSS and harness the power of the therapeutic alliance as a treatment modality.

Acknowledgments

We thank Libby J. Hammond and Christina M. Smith (Mayo Clinic Survey Research Center) for their help in planning, testing, and implementing the survey.
Declaration of Conflicting Interests
The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: JOE is a consultant for Nesmah outside the current work. The remaining authors (XJW, EAG, JKR, PR, LMP) report no disclosures.

Funding
The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This study was funded by the Mayo Clinic Alix College of Medicine and Science.

ORCID iD
Lindsey M. Philpot https://orcid.org/0000-0002-0462-6233

References
1. Nijs J, Leysen L, Vanlauwe J, et al. Treatment of central sensitization in patients with chronic pain: time for change? Expert Opin Pharmacother. 2019;20(16):1961-1970.
2. Yunus MB. Fibromyalgia and overlapping disorders: the unifying concept of central sensitivity syndromes. Semin Arthritis Rheum. 2007;36(6):339-356.
3. Burstein R, Levy D, Jakubowski M. Effects of sensitization of trigeminovascular neurons to triptan therapy during migraine. Rev Neurol (Paris). 2005;161(6-7):658-660.
4. Chalaye P, Goffaux P, Bourgault P, et al. Comparing pain modulation and autonomic responses in fibromyalgia and irritable bowel syndrome patients. Clin J Pain. 2012;28(6):519-526.
5. Arendt-Nielsen L, Graven-Nielsen T. Central sensitization in fibromyalgia and other musculoskeletal disorders. Curr Pain Headache Rep. 2003;7(5):355-361.
6. Woolf CJ. Central sensitization: implications for the diagnosis and treatment of pain. Pain. 2011;152(suppl 3):S2-S15.
7. Kool MB, van Middendorp H, Boeije HR, Geenen R. Understanding the lack of understanding: invalidation from the perspective of the patient with fibromyalgia. Arthritis Rheum. 2009;61(12):1650-1656.
8. Kool MB, van Middendorp H, Lumley MA, et al. Lack of understanding in fibromyalgia and rheumatoid arthritis: the Illness Invalidation Inventory (3*I). Ann Rheum Dis. 2010;69(11):1990-1995.
9. Young NP, Philpot LM, Vierkant RA, et al. Episodic and chronic migraine in primary care. Headache. 2019;59(7):1042-1051.
10. Hakanson C. Everyday life, healthcare, and self-care management among people with irritable bowel syndrome: an integrative review of qualitative research. Gastroenterol Nurs. 2014;37(3):217-225.
11. Neblett R, Hartzell MM, Mayer TG, Cohen H, Gatchel RJ. Establishing clinically relevant severity levels for the central sensitization inventory. Pain Pract. 2017;17(2):166-175.
12. Mayer TG, Neblett R, Cohen H, et al. The development and psychometric validation of the central sensitization inventory. Pain Pract. 2012;12(4):276-285.
13. Scerbo T, Colasurdo J, Dunn S, Unger J, Nijs J, Cook C. Measurement properties of the central sensitization inventory: a systematic review. Pain Pract. 2018;18(4):544-554.
14. Cuesta-Vargas AI, Neblett R, Nijs J, et al. Establishing central sensitization-related symptom severity subgroups: a multicountry study using the central sensitization inventory. Pain Med. 2020;21(10):2430-2440.
15. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. Ann Med. 2001;33(5):337-343.
16. Chen AT, Swaninathan A. Factors in the building of effective patient-provider relationships in the context of fibromyalgia. Pain Med. 2020;21(1):138-149.
17. Dixon-Woods M, Critchley S. Medical and lay views of irritable bowel syndrome. Fibromyalgia and other musculoskeletal disorders. J Clin Med. 2018;7(1):3.
18. Chaitoff A, Sun B, Windover A, et al. Associations between physician empathy, physician characteristics, and standardized measures of patient experience. Acad Med. 2017;92(10):1464-1471.
19. Lacy BE, Rosemore J, Robertson D, Corbin DA, Grau M, Crowell MD. Physicians’ attitudes and practices in the evaluation and treatment of irritable bowel syndrome. Scand J Gastroenterol. 2006;41(8):892-902.
20. Dalton CB, Drossman DA, Hathaway JM, Bangdiwala SI. Perceptions of physicians and patients with organic and functional gastrointestinal diagnoses. Clin Gastroenterol Hepatol. 2004;2(2):121-126.
21. Moayyedi P, Mearin F, Azpiroz F, et al. Irritable bowel syndrome diagnosis and management: A simplified algorithm for clinical practice. United European Gastroenterol J. 2017;5(6):773-788.
22. Di Palma JA, Herrera JL. The role of effective clinician-patient communication in the management of irritable bowel syndrome and chronic constipation. J Clin Gastroenterol. 2012;46(9):748-751.
23. Stewart M, Brown JB, Donner A, et al. The impact of patient-centered care on outcomes. J Fam Pract. 2000;49(9):796-804.
24. Owens DM, Nelson DK, Talley NJ. The irritable bowel syndrome: long-term prognosis and the physician-patient interaction. Ann Intern Med. 1995;122(2):107-112.
25. Lucassen P, Olesen F. Context as a drug: some consequences of placebo research for primary care. Scand J Prim Health Care. 2016;34(4):428-433.
26. Drossman DA, Whitehead WE, Toner BB, et al. What determines severity among patients with painful functional bowel disorder? Am J Gastroenterol. 2000;95(4):974-980.
27. Halpert A. Irritable bowel syndrome: patient-provider interaction and patient education. J Clin Med. 2018;7(1):3.
28. Walitt B, Nahin RL, Katz RS, Bergman MJ, Wolfe F. The prevalence and characteristics of fibromyalgia in the 2012 national health interview survey. PLoS One. 2015;10(9):e0138024.