International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Scholarly Publisher
RS Global Sp. z O.O.
ISNI: 0000 0004 8495 2390

Dolna 17, Warsaw,
Poland 00-773
+48 226 0 227 03
editorial_office@rsglobal.pl

ARTICLE TITLE	CENTRAL SENSITIZATION IN CHRONIC PAIN: NEUROPHYSIOLOGICAL MECHANISMS AND CLINICAL IMPLICATIONS
DOI	https://doi.org/10.31435/ijitss.4(48).2025.4428
RECEIVED	21 October 2025
ACCEPTED	05 December 2025
PUBLISHED	12 December 2025
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

CENTRAL SENSITIZATION IN CHRONIC PAIN: NEUROPHYSIOLOGICAL MECHANISMS AND CLINICAL IMPLICATIONS

Jakub Przerwa *(Corresponding Author, Email: przerwa50@o2.pl)*
7th Navy Hospital in Gdańsk, Gdańsk, Poland
ORCID ID: 0009-0005-4280-2209

ABSTRACT

The definition of central sensitization encompasses enhanced processing and transmission of neural impulses within the central nervous system, ultimately leading to increased pain sensitivity. It is a key mechanism contributing to the development of chronic pain. This phenomenon is of great clinical relevance and plays a role in such conditions as migraine, chronic low back pain, fibromyalgia, and irritable bowel syndrome. The main aim of this review is to present the mechanisms underlying central sensitization, diagnostic methods, and potential therapeutic interventions in patients with chronic pain. Diagnostic tools that allow for the identification of patients with sensitization-related pain, as well as key neurophysiological mechanisms necessary for maintaining central sensitization, are also discussed. Future research should focus on developing therapeutic protocols targeting CS, identifying sensitization biomarkers, and improving diagnostic precision.

KEYWORDS

Central Sensitization, Chronic Pain, Neuroplasticity, Diagnosis, Clinical Implications

CITATION

Jakub Przerwa. (2025). Central Sensitization in Chronic Pain: Neurophysiological Mechanisms and Clinical Implications. *International Journal of Innovative Technologies in Social Science*, 4(48). doi: 10.31435/ijitss.4(48).2025.4428

Methodology

This article is a narrative–analytical review. The analysis included experimental (animal) models, human studies, and concepts related to nociplastic pain. Information regarding synaptic plasticity, alterations in descending modulation, and dysfunction of the antinociceptive system was systematized. Diagnostic tools and the clinical consequences of central sensitization across various conditions were also reviewed.

To this end, a search was conducted in PubMed/MEDLINE, Scopus, Web of Science, and the Cochrane Library. The search covered publications from 2000 to 2025, with particular emphasis on clinical studies, reviews, meta-analyses, and articles in neurobiology and social sciences. Clinical, experimental, and observational studies on central sensitization, neuroimaging and neurophysiological research, biomarker analyses, as well as articles on clinical implications, diagnostic tools, and modern therapeutic methods were included.

Introduction

Chronic pain is a major medical and social problem, affecting up to 30% of the adult population and generating significant social and economic costs [1]. Unlike acute pain, chronic pain has no biological purpose, worsens patient functioning, causes suffering, and is an important factor contributing to depression. Its definition includes a duration of symptoms longer than three months [2].

In the context of chronic pain, central sensitization (CS) is particularly important, representing one of the key mechanisms by which acute pain transitions into chronic pain. CS is defined as a state of increased

excitability of neurons within the central nervous system, leading to exaggerated pain responses to stimuli of normal or even subthreshold intensity [3].

This phenomenon plays a significant role in many conditions where chronic pain is one of the main symptoms, such as fibromyalgia, chronic low back pain, migraine, irritable bowel syndrome (IBS), and chronic fatigue syndrome [4].

Central sensitization is a complex phenomenon involving multiple neurophysiological processes such as glial cell activation, NMDA receptor activation, dysfunction of descending inhibitory pathways, and increased glutamate release [5]. These mechanisms raise important questions regarding their clinical implications in chronic pain. Understanding CS may support differential diagnosis in cases of unclear pain etiology and guide individualized therapeutic interventions targeting CS mechanisms, including pharmacotherapy, cognitive-behavioral therapy, and desensitization-based physiotherapy [6,7].

Mechanisms of Central Sensitization (CS)

Central sensitization encompasses several complex neurophysiological processes such as synaptic plasticity, the wind-up phenomenon, dysfunction of descending inhibitory pathways, and pain potentiation. Neuronal plasticity within the central nervous system is one of the essential mechanisms leading to chronic pain development. Repeated nociceptive stimulation results in excessive activation of NMDA and AMPA receptors in dorsal horn neurons of the spinal cord. This leads to increased calcium influx and the establishment of long-term potentiation (LTP), responsible for pain memory and its persistence independent of ongoing tissue damage [5].

Additionally, pro-inflammatory cytokines (e.g., IL-1β, IL-6, TNF-α) are released, enhancing pain transmission, along with disturbances in noradrenergic and serotonergic pathways originating in the raphe nuclei and locus coeruleus, which constitute the descending inhibitory system [8]. As a consequence, the neuronal excitability threshold is lowered and pain modulation becomes impaired, resulting in two key phenomena: hyperalgesia—an exaggerated response to painful stimuli—and allodynia—pain occurring in response to normally non-painful stimuli such as touch, pressure, or temperature changes [4].

Another important phenomenon is wind-up, in which the repeated activation of C-fiber nociceptors leads to temporal summation of pain signals within the dorsal horn [5]. This results from NMDA receptor activation, increased intracellular calcium, and protein phosphorylation. Clinically, this is associated with pain experienced in the absence of ongoing peripheral nociceptive input, characteristic of many chronic pain conditions.

Neuroimaging studies using fMRI and PET have demonstrated increased activity in brain regions involved in pain processing, including the cingulate cortex, insula, thalamus, and brainstem in patients with CS [9]. EEG and evoked potential studies show increased amplitude and reduced latency in response to painful stimuli, indicating hyperreactivity of central nociceptive structures [3].

Diagnosis of Central Sensitization

Several scales assess symptoms associated with central sensitization, including the Hospital Anxiety and Depression Scale (HADS), Pain Catastrophizing Scale (PCS), and Central Sensitization Inventory (CSI). CSI is the most frequently used tool; it contains 25 items assessing somatic, cognitive, and emotional symptoms (e.g., sleep disturbances, fatigue, sensory hypersensitivity) [4]. However, it should be emphasized that CSI is not a stand-alone diagnostic test but rather a screening tool.

Psychological questionnaires such as HADS and PCS allow identification of emotional–cognitive factors that may intensify CS mechanisms [6,7]. Quantitative Sensory Testing (QST), a standardized set of tests assessing pain thresholds for mechanical, thermal, and electrical stimuli, is also used diagnostically and allows identification of allodynia and hyperalgesia [10].

Current research focuses on identifying biochemical biomarkers of sensitization, such as levels of pro-inflammatory cytokines, neuropeptides (substance P), and neurotrophic factors (BDNF) [8].

Central Sensitization in Clinical Conditions

Studies show that central sensitization is a key pathophysiological mechanism in conditions such as fibromyalgia, chronic low back pain, migraine, and irritable bowel syndrome—where abnormalities in central sensory processing occur independently of peripheral tissue damage, leading to lowered pain thresholds, hyperalgesia, and allodynia [11].

Fibromialgia is the prototypical example of a condition involving CS. It is characterized by chronic, widespread musculoskeletal pain and tender points. Patients show increased activation of cortical pain-processing regions, dysfunction of descending antinociceptive pathways, and elevated glutamate and substance P levels [12].

Central sensitization is also relevant in chronic low back pain (CLBP), where reduced descending inhibition and nociceptive signal summation are frequently observed [13]. This central component often contributes to pain persistence.

In migraine, both peripheral and central sensitization occur. Symptoms such as sound, light, and pain hypersensitivity are linked to CGRP release, activation of the trigeminal nucleus, and alterations in the somatosensory cortex [14]. Sensitization is more pronounced in chronic migraine, explaining its progression from episodic to chronic forms.

In irritable bowel syndrome (IBS), CS plays a role through visceral hypersensitivity, impaired central pain modulation, and dysfunction of the brain–gut axis [15].

Clinical Implications and Therapeutic Management

Understanding the mechanisms of central sensitization is crucial for diagnosis, treatment, and clinical management of chronic pain. It also shifts the perspective on pain from a purely tissue-damage phenomenon toward a more complex biopsychosocial concept [16,17].

Therapy must be individualized. Patients with a central pain component do not achieve satisfactory outcomes when treated solely with peripheral-focused interventions such as massage, mobilization, or physical modalities, which may even exacerbate symptoms [18]. Treatment should instead target central pain modulation through education, neuromodulatory pharmacotherapy, psychological strategies, and graded exercise.

Patient education—pain neuroscience education (PNE)—is essential, as explaining chronic pain mechanisms in simple terms reduces pain-related fear and may decrease symptom severity [19].

Chronic pain syndromes generate substantial healthcare costs—both direct and indirect [20].

A CS-oriented approach may reduce unnecessary expenditures and improve care efficiency.

Pharmacotherapy includes neuromodulatory agents such as SNRIs, TCAs, pregabalin, and gabapentin [21]. NSAIDs have limited efficacy, while opioids are not recommended due to the risk of opioid-induced hyperalgesia and addiction [22].

Non-pharmacological therapies include CBT, mindfulness, ACT, physiotherapy, neuromodulation (TENS, tDCS, rTMS), and emerging technologies such as virtual reality and therapeutic apps. CBT improves coping with pain and normalizes central pain-processing networks [23], while mindfulness and ACT reduce limbic system reactivity [24]. Regular physical activity enhances descending pain inhibition and improves neuroplasticity [25]. Physiotherapy focused on central mechanisms includes functional training and graded exposure.

Digital technologies are gaining importance. Virtual reality enables integration of visual and motor stimuli, modulating pain and reducing fear [26].

Conclusions

Central sensitization is a fundamental mechanism that explains many phenomena observed in chronic pain syndromes [11]. Numerous conditions, including fibromyalgia, IBS, migraine, and chronic low back pain, involve changes within the central nervous system such as increased neuronal excitability, dysfunction of pain-modulation pathways, and neuroplastic disturbances [14].

Understanding CS mechanisms has reshaped pain management, highlighting the need for a biopsychosocial approach [17]. Standard interventions targeting peripheral structures may be insufficient—central modulation is key [4].

Therapeutic strategies include pharmacotherapy (SNRIs, TCAs, anticonvulsants) [21] and non-pharmacological methods such as neuromodulation (TENS, rTMS, tDCS), digital tools, patient education, CBT, and graded-exposure physiotherapy.

Central sensitization is a crucial concept in chronic pain management. Understanding its mechanisms enables accurate diagnosis and implementation of neurophysiology-based therapies. Future research should focus on developing precise CS biomarkers, better understanding neuroplastic mechanisms, and using artificial intelligence tools for therapy personalization.

REFERENCES

1. Cohen, S. P., Vase, L., & Hooten, W. M. (2021). Chronic pain: An update on burden, best practices, and new advances. *The Lancet, 397*(10289), 2082–2097. https://doi.org/10.1016/S0140-6736(21)00393-7
2. Scholz, J., Finnerup, N. B., Attal, N., Aziz, Q., Baron, R., Bennett, M. I., ... & Treede, R. D. (2019). The IASP classification of chronic pain for ICD-11. *Pain, 160*(1), 19–27. https://doi.org/10.1097/j.pain.0000000000001367
3. Woolf, C. J. (2011). Central sensitization: Implications for the diagnosis and treatment of pain. *Pain, 152*(3 Suppl), S2–S15. https://doi.org/10.1016/j.pain.2010.09.030
4. Nijs, J., George, S. Z., Clauw, D. J., Skou, S. T., & Lluch Girbés, E. (2021). Central sensitisation in chronic pain conditions: Latest discoveries and their potential for precision medicine. *The Lancet Rheumatology, 3*(11), e834–e845. https://doi.org/10.1016/S2665-9913(21)00203-0
5. Latremoliere, A., & Woolf, C. J. (2009). Central sensitization: A generator of pain hypersensitivity by central neural plasticity. *The Journal of Pain, 10*(9), 895–926. https://doi.org/10.1016/j.jpain.2009.06.012
6. Yarnitsky, D., Granot, M., Nahman-Averbuch, H., Khamaisi, M., & Granovsky, Y. (2019). Conditioned pain modulation predicts duloxetine efficacy in painful diabetic neuropathy. *Pain, 160*(3), 570–575. https://doi.org/10.1097/j.pain.0000000000001428
7. Clauw, D. J. (2015). Diagnosing and treating chronic musculoskeletal pain based on the underlying mechanism. *Best Practice & Research Clinical Rheumatology, 29*(1), 6–19. https://doi.org/10.1016/j.berh.2015.04.024
8. Ji, R. R., Nackley, A., Huh, Y., Terrando, N., & Maixner, W. (2018). Neuroinflammation and central sensitization in chronic pain. *Nature Reviews Neuroscience, 19*(11), 655–673. https://doi.org/10.1038/s41583-018-0071-2
9. Kosek, E., Cohen, M., Baron, R., Gebhart, G. F., Mico, J. A., Rice, A. S., & Woolf, C. J. (2016). Do we need a third mechanistic descriptor for chronic pain states? *Pain, 157*(7), 1382–1386. https://doi.org/10.1097/j.pain.0000000000000507
10. Treede, R. D., Rief, W., Barke, A., Aziz, Q., Bennett, M. I., Benoliel, R., ... & Wang, S. J. (2019). Chronic pain as a symptom or a disease: The IASP classification of chronic pain for the International Classification of Diseases (ICD-11). *Pain, 160*(1), 19–27. https://doi.org/10.1097/j.pain.0000000000001384
11. Woolf, C. J. (2018). Pain amplification: Central sensitization and neuropathic pain. *Pain, 152*(3), S2–S15.
12. Sluka, K. A., & Clauw, D. J. (2016). Neurobiology of fibromyalgia and chronic widespread pain. *Neuroscience, 338*, 114–129.
13. Arendt-Nielsen, L. (2017). Central sensitization in humans: Assessment and clinical implications. *Pain, 158*(S1), S1–S2.
14. Burstein, R., Noseda, R., & Borsook, D. (2015). Migraine: Multiple processes, complex pathophysiology. *Journal of Neuroscience, 35*(17), 6619–6629.
15. Mayer, E. A., Labus, J. S., Tillisch, K., Cole, S. W., & Baldi, P. (2015). Towards a systems view of IBS. *Nature Reviews Gastroenterology & Hepatology, 12*(10), 592–605.
16. O'Sullivan, P. (2012). It's time for change with the management of non-specific chronic low back pain. *British Journal of Sports Medicine, 46*(4), 224–227.
17. Gatchel, R. J., Peng, Y., Peters, M. L., Fuchs, P. N., & Turk, D. C. (2007). The biopsychosocial approach to chronic pain. *Psychological Bulletin, 133*(4), 581–624.
18. Nijs, J., Van Houdenhove, B., & Oostendorp, R. A. (2014). Recognition of central sensitization in patients with chronic pain: Application of pain neurophysiology in manual therapy practice. *Manual Therapy, 15*(2), 135–141.
19. Moseley, G. L. (2007). Reconceptualising pain according to contemporary pain science. *Physical Therapy Reviews, 12*(3), 169–178.
20. Phillips, C. J. (2009). The cost and burden of chronic pain. *Reviews in Pain, 3*(1), 2–5.
21. Arnold, L. M., Clauw, D. J., & Dunegan, L. J. (2019). Pharmacologic treatment of fibromyalgia and other chronic musculoskeletal pain. *JAMA, 322*(4), 356–366.
22. Volkow, N. D., & McLellan, A. T. (2016). Opioid abuse in chronic pain—misconceptions and mitigation strategies. *New England Journal of Medicine, 374*(13), 1253–1263.
23. Williams, A. C. de C., Eccleston, C., & Morley, S. (2012). Psychological therapies for the management of chronic pain (excluding headache). *Cochrane Database of Systematic Reviews, 11*, CD007407.
24. Cherkin, D. C., Sherman, K. J., Balderson, B. H., Cook, A. J., Anderson, M. L., Hawkes, R. J., Hansen, K. E., & Turner, J. A. (2016). Effect of mindfulness-based stress reduction vs cognitive behavioral therapy on chronic low back pain. *JAMA, 315*(12), 1240–1249.
25. Ellingson, L. D., Stegner, A. J., & Schwabacher, I. J. (2016). Exercise strengthens central nervous system modulation of pain in fibromyalgia. *Pain, 157*(1), 70–79.
26. Mallari, B., Spaeth, E. K., Goh, H., & Boyd, L. (2021). Virtual reality as an analgesic for acute and chronic pain: A systematic review. *Pain Medicine, 22*(1), 82–96.