Neurophysiology of chronic pain: new approaches in treatment and diagnostics

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Abstract. Chronic pain remains a major clinical and social challenge, affecting millions worldwide and significantly reducing quality of life. Recent advances in neurophysiology have shed light on the complex mechanisms underlying chronic pain, including central sensitization, maladaptive neuroplasticity, and the dysregulation of pain modulatory pathways. This growing understanding has led to the development of novel diagnostic and therapeutic approaches that go beyond symptomatic relief to target the root causes of persistent pain. This paper reviews the latest neurophysiological insights into chronic pain and highlights innovative methods for its assessment and treatment. These include functional neuroimaging, neurophysiological biomarkers, and neuromodulation techniques such as transcranial magnetic stimulation (TMS) and spinal cord stimulation (SCS). Pharmacological strategies are also evolving, with increased attention to agents that modulate glial activity, ion channels, and neurotransmitter systems involved in pain transmission.

1 Introduction

Chronic pain is a complex and multifactorial condition that persists beyond the normal healing period, typically lasting for more than three to six months. It affects approximately 20–30% of the global population and imposes a significant burden on individuals, healthcare systems, and society at large. Unlike acute pain, which serves as a protective mechanism in response to tissue injury, chronic pain often persists in the absence of ongoing tissue damage and is increasingly recognized as a disease in its own right.

Understanding the neurophysiology of chronic pain is essential for the development of effective diagnostic and therapeutic strategies. Recent advances in neuroscience have revealed that chronic pain is not merely a symptom, but a manifestation of dynamic changes within the central and peripheral nervous systems.

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These changes include central sensitization, altered synaptic plasticity, impaired descending inhibitory pathways, and neuroinflammatory processes involving glial cells and pro-inflammatory cytokines. Such mechanisms contribute to the amplification and persistence of pain signals, even in the absence of peripheral stimuli.

Traditional treatments for chronic pain—such as non-steroidal anti-inflammatory drugs (NSAIDs), opioids, and physical therapy—often provide limited or temporary relief, and may lead to adverse effects or dependency. As a result, there is a growing need for innovative, mechanism-based approaches that address the underlying neurobiological dysfunctions associated with chronic pain.

This paper aims to explore the latest insights into the neurophysiology of chronic pain and to present emerging diagnostic tools and treatment modalities grounded in contemporary neuroscientific research. By examining the interplay between neuronal circuits, glial activity, and neurochemical signaling, this study seeks to contribute to a more precise and effective framework for chronic pain management.

Crop production is one of the key sectors of the agro-industrial complex and plays an important role in ensuring food security for the country. In the context of climate change, population growth and increasing demand for agricultural products, increasing production efficiency is becoming especially relevant, especially in difficult natural and climatic conditions.

The northern regions of the Russian Federation, characterized by a short growing season, low temperatures, difficult soil conditions and limited infrastructure, require the implementation of innovative solutions for the sustainable development of crop production. However, issues of increasing the efficiency of crop production using modern technologies remain insufficiently studied in relation to other regions with special socio-economic and natural conditions, for example, the Chechen Republic. Despite a more favorable climate compared to traditional northern regions, the republic faces a number of specific problems: a shortage of qualified personnel, limited access to modern technologies, a weak level of technical equipment and insufficient financial support from regional structures. The purpose of this study is to analyze the possibilities of increasing the efficiency of crop production in the northern regions of the Russian Federation and the Chechen Republic using innovative means, such as adapted varieties of agricultural crops, modern agricultural technologies, digitalization of the agro-industrial complex (Fig. 1), small-scale mechanization and plant protection products. Particular attention is paid to the economic feasibility of introducing innovations and their impact on the sustainability of the agricultural sector in various climatic and socio-economic conditions. The study is aimed at identifying successful practices, formulating recommendations for state support, developing a scientific and technical base and training qualified personnel for the sustainable development of crop production in hard-to-reach and mountainous foothill areas. The main problem hindering the effective digital transformation of the agro-industrial complex (AIC) is the insufficient development of the domestic electronic base. In this regard, one of the priority tasks by 2022 was to increase the share of Russian innovative electronic products used in AIC digitalization projects to 37.5%. In order to implement this task, the Ministry of Agriculture and Food of the Russian Federation provided funding for the departmental project on digitalization of the AIC in the amount of 118 billion rubles for the period from 2019 to 2024.

2 Methods and materials

This study is based on a comprehensive review and analysis of recent scientific literature, clinical trials, and neurophysiological studies related to the mechanisms, diagnostics, and treatment of chronic pain. A systematic search was conducted across multiple scientific databases including PubMed, Scopus, Web of Science, and Google Scholar, covering publications from 2015 to 2025. Keywords used in the search included "chronic pain," "neurophysiology," "central sensitization," "neuromodulation," "pain diagnostics," "glial cells," "TMS," and "spinal cord stimulation."

Articles were selected based on their relevance to the neurobiological mechanisms of chronic pain and innovative diagnostic and therapeutic approaches. Priority was given to peer-reviewed publications, clinical trials, meta-analyses, and experimental studies with strong methodological design. Both human and animal model studies were included to provide a comprehensive understanding of pain pathophysiology.

In addition, this study reviewed current clinical guidelines and reports from professional organizations such as the International Association for the Study of Pain (IASP), the American Academy of Neurology (AAN), and the European Federation of Neurological Societies (EFNS), to ensure clinical applicability of the findings.

Analytical methods included qualitative synthesis of evidence and comparative evaluation of new versus traditional diagnostic and treatment modalities. Where applicable, neuroimaging and electrophysiological data were also included to illustrate recent advances in functional diagnostics.

The materials analyzed reflect the interdisciplinary nature of chronic pain research, integrating findings from neuroscience, clinical neurology, pharmacology, and biomedical engineering to provide a holistic perspective on current and emerging approaches in the field.

3. Results

The analysis of recent literature and clinical data has revealed several key developments in the understanding, diagnosis, and treatment of chronic pain, driven by advances in neurophysiology and technology. The results of this study can be grouped into three main domains: neurophysiological mechanisms, diagnostic innovations, and novel therapeutic approaches.

Firstly, current research has significantly advanced the understanding of the neurophysiological basis of chronic pain. Central sensitization was confirmed as a core mechanism, characterized by the heightened responsiveness of neurons in the central nervous system to normal or subthreshold stimuli. Studies showed that long-term potentiation (LTP) of synaptic transmission in the spinal dorsal horn and abnormal thalamocortical activity contribute to persistent pain perception. Moreover, the role of glial cells—especially astrocytes and microglia—has gained increased attention. Activated glial cells release pro-inflammatory mediators that further sensitize neurons and perpetuate chronic pain states.

Secondly, there have been substantial improvements in diagnostic tools. Functional neuroimaging techniques such as fMRI and PET scans have demonstrated altered activity in brain regions associated with pain processing, including the prefrontal cortex, insula, and anterior cingulate cortex. Electroencephalography (EEG) and magnetoencephalography (MEG) have revealed distinctive cortical oscillation patterns in chronic pain patients, suggesting the potential for objective neurophysiological biomarkers. Additionally,

quantitative sensory testing (QST) and laser-evoked potentials (LEPs) have been increasingly used in clinical settings to assess sensory thresholds and central pain modulation.

Thirdly, emerging treatment methods based on neurophysiological insights have shown promising results. Non-invasive neuromodulation techniques such as transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) have been effective in reducing pain in conditions like neuropathic pain, fibromyalgia, and complex regional pain syndrome. Invasive methods such as spinal cord stimulation (SCS) and dorsal root ganglion (DRG) stimulation are also demonstrating long-term pain relief in selected patients. Moreover, pharmacological research has shifted toward targeting neuroinflammation and neuronal excitability, with experimental drugs focusing on glial modulators, ion channel blockers, and cannabinoid receptor agonists.

Overall, the findings highlight a paradigm shift in chronic pain management—from symptomatic treatment to mechanism-based, personalized interventions. These advances underscore the importance of integrating neurophysiological knowledge into clinical practice for more accurate diagnosis and effective long-term treatment.

4. Discussion

The findings of this study affirm that a deeper understanding of the neurophysiological mechanisms underlying chronic pain is crucial for the development of more effective diagnostic tools and treatment strategies. Traditional views of chronic pain as merely a prolonged symptom of injury have been replaced by the recognition of chronic pain as a distinct neurological condition involving complex alterations in both peripheral and central nervous systems. This shift in understanding has profound implications for clinical practice and patient outcomes.

The central role of neuroplasticity in chronic pain has been well-documented across recent studies. Maladaptive changes in synaptic strength, receptor sensitivity, and neural connectivity contribute to persistent pain even in the absence of a clear physical cause. Central sensitization—particularly the hyperexcitability of dorsal horn neurons and cortical reorganization—provides a neurobiological explanation for the amplification of pain and the development of comorbidities such as anxiety, depression, and cognitive dysfunction. The involvement of glial cells and neuroinflammatory processes adds another dimension to our understanding, highlighting that chronic pain is not solely a neuronal disorder but a neuroimmune condition.

From a diagnostic perspective, the emergence of objective biomarkers and advanced neuroimaging techniques represents a significant breakthrough. Functional MRI, EEG-based pain signatures, and quantitative sensory testing are paving the way for earlier and more precise identification of chronic pain syndromes. These tools may eventually allow clinicians to differentiate between subtypes of chronic pain, predict treatment responses, and monitor the effectiveness of interventions—all of which are essential steps toward personalized medicine.

The therapeutic implications of these findings are equally significant. Neuromodulation technologies, such as TMS, tDCS, and SCS, have opened new avenues for non-pharmacological intervention, offering pain relief without the side effects commonly associated with long-term medication use. These techniques not only modulate brain and spinal activity but may also induce long-term changes in neural circuits, making them promising tools for long-term pain management. Moreover, the development of targeted pharmacological agents that influence neuroinflammatory pathways, ion channel activity,

and glial function reflects a more precise, mechanism-driven approach to drug development.

Despite these advances, several challenges remain. Access to specialized diagnostics and neuromodulation therapies is still limited in many regions due to cost, availability, and lack of trained personnel. Furthermore, while research has made significant strides in uncovering pain mechanisms, translating this knowledge into widely accessible treatments remains a gradual process. There is also a need for standardized protocols and larger clinical trials to validate the efficacy and safety of emerging interventions.

In conclusion, this discussion reinforces the importance of a multidisciplinary approach to chronic pain—one that integrates neurophysiology, neuroimaging, clinical neurology, and psychological care. As our understanding of pain mechanisms deepens, it becomes increasingly clear that effective chronic pain management must move beyond symptomatic relief to target the underlying biological processes. Future progress will depend on continued collaboration between researchers, clinicians, and policymakers to ensure that innovations in pain science translate into meaningful improvements in patient care.

3 Conclusion

This study has explored the evolving neurophysiological understanding of chronic pain and examined emerging approaches in its diagnosis and treatment. The evidence reviewed highlights that chronic pain is not merely a symptom, but a complex, multifactorial neurological condition involving dynamic changes in neural networks, central sensitization, neuroinflammation, and glial cell activation. These processes contribute to the persistence and amplification of pain long after the initial cause has resolved, underscoring the need for a paradigm shift in both research and clinical practice. Advances in neuroimaging, electrophysiology, and the identification of neurobiological markers have improved the ability to detect and differentiate chronic pain conditions with greater accuracy. These innovations hold promise for the development of personalized diagnostic protocols, allowing for earlier intervention and better-targeted treatments. Similarly, novel therapeutic methods—such as transcranial magnetic stimulation, spinal cord stimulation, and next-generation pharmacological agents—offer new possibilities for patients who do not respond to conventional therapies.The findings of this study emphasize the importance of interdisciplinary collaboration in addressing the complex nature of chronic pain. Combining neuroscience, clinical medicine, psychology, and bioengineering is essential to develop holistic, individualized treatment strategies that target the underlying mechanisms of pain rather than merely masking its symptoms.

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