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FUNCTIONAL–METABOLIC NEUROPHYSIOLOGICAL FEATURES OF DEPRESSIVE STATES IN PATIENTS WITH CHRONIC HEADACHE DISORDERS

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Abstract: Chronic headache disorders are highly prevalent neurological conditions that significantly impair quality of life. Comorbid depressive states exacerbate pain perception, reduce treatment efficacy, and contribute to functional disability. This study investigates the functional and metabolic neurophysiological characteristics of depression in patients with chronic headache disorders. Functional neuroimaging revealed altered activity in the prefrontal cortex, limbic regions, and disrupted connectivity between cortical and subcortical networks. Metabolic assessments demonstrated reduced glucose utilization in key brain regions involved in pain processing and emotional regulation. The severity of depressive symptoms correlated with both functional and metabolic alterations, indicating a neurobiological basis for comorbidity. Findings highlight the importance of early detection and integrated therapeutic strategies targeting both neurological and psychological aspects, which can improve patient outcomes and quality of life.

Keywords: Chronic headache, depression, functional neurophysiology, metabolic changes, neuroimaging, comorbidity, pain perception, emotional regulation.

ФУНКЦИОНАЛЬНО-МЕТАБОЛИЧЕСКИЕ НЕЙРОФИЗИОЛОГИЧЕСКИЕ ОСОБЕННОСТИ ДЕПРЕССИВНЫХ СОСТОЯНИЙ У ПАЦИЕНТОВ С ХРОНИЧЕСКИМИ ГОЛОВНЫМИ БОЛЯМИ

Аннотация: Хронические головные боли являются распространёнными неврологическими расстройствами, значительно ухудшающими качество жизни. Сопутствующие депрессивные состояния усиливают восприятие боли, снижают эффективность лечения и способствуют функциональной инвалидности. В настоящем исследовании изучались функциональные и метаболические нейрофизиологические особенности депрессии у пациентов с хроническими головными болями. Функциональная нейровизуализация выявила изменения активности в префронтальной коре, лимбических областях и нарушение связности между корковыми и подкорковыми сетями. Метаболические исследования показали снижение утилизации глюкозы в ключевых областях мозга, участвующих в восприятии боли и регуляции эмоций. Степень депрессивных симптомов коррелировала с функциональными и метаболическими изменениями, что указывает на нейробиологическую основу коморбидности. Полученные данные подчёркивают важность раннего выявления и комплексных терапевтических стратегий, направленных как на неврологические, так и на психологические аспекты, что может улучшить исходы лечения и качество жизни пациентов.

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Ключевые слова: хроническая головная боль, депрессия, функциональная нейрофизиология, метаболические изменения, нейровизуализация, коморбидность, восприятие боли, регуляция эмоций.

Introduction

Chronic headache disorders represent a significant medical and social problem in modern neurology, as they substantially reduce patients' quality of life and impair functional capacity. In addition to persistent pain, these conditions are frequently associated with emotional and affective disturbances, particularly depressive states. Clinical observations indicate that a considerable proportion of patients suffering from chronic headaches exhibit varying degrees of depressive symptoms, which complicate the clinical course of the disease and reduce the effectiveness of therapeutic interventions. In recent years, increasing attention has been paid to the functional and metabolic neurophysiological mechanisms underlying the comorbidity of chronic headache and depression. Dysregulation of central nervous system neurotransmitter systems, alterations in cerebral metabolic activity, and disturbances in functional neural networks play a crucial role in the pathophysiology of both conditions. In particular, changes in serotonergic, noradrenergic, and dopaminergic pathways are considered key factors influencing pain perception and the development of depressive states. Advances in functional neuroimaging and metabolic assessment techniques have demonstrated abnormal patterns of cortical and subcortical brain activity in patients with chronic headaches. These functional alterations contribute to emotional dysregulation and facilitate the persistence and chronification of pain. Furthermore, dysfunction of the hypothalamic–pituitary–adrenal axis is believed to impair stress-adaptation mechanisms, thereby reinforcing both depressive symptoms and chronic pain processes. Therefore, investigation of the functional–metabolic neurophysiological characteristics of depressive states in chronic headache disorders is of substantial theoretical and clinical importance. A deeper understanding of these mechanisms may support the development of more effective, individualized treatment strategies and promote a comprehensive approach to the management of patients with chronic headache conditions.

Relevance

Chronic headache disorders are among the most common and socially significant conditions encountered in neurological practice. Their prolonged course not only leads to persistent pain but also has a pronounced negative impact on patients' psychoemotional status, contributing to the development of depressive states. The coexistence of chronic headache and depression aggravates disease severity, reduces treatment effectiveness, and complicates rehabilitation processes. At present, depressive states associated with chronic headaches are mainly assessed at the clinical level, while their functional and metabolic neurophysiological mechanisms remain insufficiently investigated. Comprehensive analysis of changes in central nervous system functional activity and cerebral metabolism is essential for a deeper understanding of disease pathophysiology. Therefore, investigation of the functional–metabolic neurophysiological characteristics of depressive states in patients with chronic headache disorders represents a highly relevant scientific and clinical problem.

AIM

The aim of this study is to investigate the functional and metabolic neurophysiological characteristics of depressive states in patients suffering from chronic headache disorders, to

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analyze alterations in central nervous system activity, and to determine their relationship with clinical manifestations.

Main part

Chronic headaches represent one of the most prevalent neurological disorders, significantly affecting patients' quality of life and daily functioning. Epidemiological studies indicate that these headaches are more common in women than men and tend to increase in prevalence with age. According to the World Health Organization, chronic headache disorders are among the leading causes of disability worldwide. Clinically, a chronic headache is characterized by pain occurring at least 15 days per month over a period of three months or longer. The intensity, localization, and frequency of pain episodes vary considerably among individuals. Patients often report additional symptoms, including nausea, photophobia, and phonophobia, which further impair functionality. These headaches are frequently associated with sleep disturbances, fatigue, and mood alterations. Occupational and social impacts are substantial, leading to reduced work productivity and increased healthcare utilization. Risk factors include genetic predisposition, stress, hormonal fluctuations, and lifestyle factors such as sleep deprivation and poor nutrition. Migraine and tension-type headache are the most common forms of chronic headache. Chronic headaches can evolve from episodic patterns due to repeated attacks, central sensitization, and altered pain processing. Early diagnosis and appropriate management are critical to prevent progression and reduce associated disability. Despite advances in treatment, many patients experience inadequate pain relief, highlighting the need for comprehensive evaluation and individualized therapy. Furthermore, comorbid conditions, including anxiety, depression, and other chronic pain syndromes, complicate the clinical course. The socioeconomic burden of chronic headaches extends beyond individual patients, affecting families, workplaces, and healthcare systems. Public health strategies emphasize awareness, early intervention, and education to mitigate the long-term consequences. Comprehensive clinical assessment includes detailed history, neurological examination, and evaluation of psychosocial factors. Advanced diagnostic imaging may be indicated in atypical presentations or when secondary causes are suspected. Understanding epidemiological patterns aids in planning preventive strategies and optimizing treatment outcomes. Overall, the clinical and epidemiological characterization of chronic headaches is essential for effective management, improved patient outcomes, and reduced societal burden.

Chronic headaches develop through complex pathophysiological mechanisms involving both peripheral and central nervous systems. Peripheral sensitization occurs when nociceptors become hyperactive due to repeated stimuli, leading to increased pain signaling. Central sensitization further amplifies pain perception through heightened responsiveness of neurons in the trigeminal and spinal pathways. Neurotransmitter imbalances, particularly involving serotonin, glutamate, and gamma-aminobutyric acid, play a critical role in modulating pain transmission. Dysregulation of the descending inhibitory pain pathways contributes to persistent headache symptoms. Structural and functional alterations in cortical and subcortical regions, including the thalamus, hypothalamus, and somatosensory cortex, have been observed in patients with chronic headaches. Neuroinflammatory processes, including glial activation and cytokine release, may exacerbate neuronal excitability. Hormonal fluctuations, stress, and sleep disturbances can further influence neuronal activity and pain modulation. Over time, these mechanisms lead to the chronification of headaches, making them resistant to conventional treatments. Functional neuroimaging studies have demonstrated altered connectivity between

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pain-processing regions and emotional regulation networks. Genetic factors also contribute to individual susceptibility to chronic headache development. Understanding these pathophysiological mechanisms is crucial for designing targeted therapies and preventing long-term disability. This knowledge informs pharmacological interventions, neuromodulation techniques, and lifestyle-based approaches aimed at modulating central sensitization and restoring neurotransmitter balance. Comprehensive management strategies should consider the interplay between biological, psychological, and environmental factors. Ultimately, elucidating the pathophysiology of chronic headaches enhances both clinical understanding and the potential for personalized treatment approaches.

Depressive states in chronic headache patients are associated with distinct neurobiological alterations. Dysregulation of neurotransmitters such as serotonin, norepinephrine, and dopamine plays a central role in both mood disturbances and pain perception. Functional changes in the limbic system, prefrontal cortex, and hypothalamus contribute to emotional dysregulation. Neuroplasticity deficits reduce adaptive responses to stress and pain. Altered connectivity between cortical and subcortical regions has been observed in neuroimaging studies. These changes reinforce both depressive symptoms and chronic pain. Chronic stress and inflammation may further exacerbate neurochemical imbalances. Understanding these mechanisms is essential for developing targeted interventions. Pharmacological and behavioral therapies aim to restore neurotransmitter balance and improve neural network function. Identifying neurobiological correlates of depression enhances clinical assessment and personalized treatment in chronic headache patients.

Functional alterations in the central nervous system play a critical role in chronic headaches and associated depressive states. Neuroimaging studies demonstrate abnormal activity in the prefrontal cortex, thalamus, and limbic structures. Disrupted connectivity between pain-processing and emotional regulation networks contributes to symptom persistence. Central sensitization increases neuronal excitability, amplifying pain perception. Glial activation and neuroinflammation further exacerbate functional disturbances. These changes correlate with clinical severity and frequency of headaches. Altered inhibitory and excitatory neurotransmission affects both mood and pain modulation. Understanding CNS functional changes informs targeted therapeutic strategies. Neuromodulation and pharmacological interventions aim to restore normal neural activity. Functional assessment is therefore crucial for comprehensive management of affected patients.

Metabolic abnormalities in the brain are closely associated with depressive symptoms in chronic headache patients. Altered glucose metabolism and impaired energy utilization have been observed in cortical and subcortical regions. Neurochemical imbalances disrupt normal neuronal function and synaptic plasticity. Functional imaging shows reduced metabolic activity in the prefrontal cortex and limbic areas. These changes affect mood regulation, stress response, and pain perception. Chronic pain and depression interact through overlapping metabolic pathways. Understanding these mechanisms is essential for optimizing pharmacological treatment. Nutritional and lifestyle interventions may support metabolic recovery. Monitoring metabolic function can guide individualized therapy. Targeting metabolic dysregulation contributes to improved clinical outcomes.

Functional and metabolic brain changes significantly influence the clinical presentation of chronic headache patients. Increased pain sensitivity and reduced tolerance are often observed.

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Depressive symptoms exacerbate perceived pain intensity and frequency. Sleep disturbances, fatigue, and cognitive impairments correlate with neurophysiological alterations. Emotional regulation deficits contribute to anxiety and irritability. These combined effects reduce quality of life and social functioning. Recognizing the clinical impact of functional–metabolic changes is vital for treatment planning. Comprehensive assessment includes neurological, psychological, and metabolic evaluation. Early intervention can prevent symptom progression and chronicity. Integrating functional and metabolic data improves personalized management strategies.

Accurate identification of depressive states in chronic headache patients is essential for effective management. Standardized screening tools, including questionnaires and rating scales, are widely used. Structured clinical interviews provide detailed assessment of mood, cognition, and daily functioning. Neuroimaging and metabolic studies can reveal underlying physiological alterations. Combining clinical and neurophysiological data enhances diagnostic accuracy. Early detection allows timely intervention, improving treatment outcomes. Cognitive-behavioral therapy and pharmacological approaches are tailored to individual needs. Multidisciplinary care supports both psychological and pain-related aspects. Routine monitoring is recommended to track symptom progression. Effective assessment strategies ultimately optimize patient quality of life and clinical response.

Results and Discussion

In the cohort of patients with chronic headache disorders, nearly half exhibited clinically significant depressive symptoms, ranging from mild to severe. Functional neuroimaging consistently revealed hypoactivity in the prefrontal cortex, anterior cingulate cortex, and limbic regions, accompanied by disrupted connectivity between cortical and subcortical networks involved in pain processing and emotional regulation. Metabolic assessments demonstrated reduced glucose uptake and altered energy metabolism in these brain regions. Correlation analyses showed a significant relationship between the severity of depressive symptoms and the degree of functional and metabolic abnormalities. Patients with greater neural disruptions reported higher headache frequency, longer duration of pain episodes, and increased intensity, often accompanied by sleep disturbances, cognitive deficits, and fatigue. These findings indicate that depressive states in chronic headache patients are closely linked to specific neurophysiological changes, supporting a neurobiological basis for the comorbidity. The observed hypoactivity in the prefrontal and limbic regions likely contributes to impaired emotional regulation and heightened pain perception, while metabolic deficits exacerbate both depressive symptoms and headache severity. These results underscore the importance of integrated diagnostic approaches that include both functional and metabolic evaluation to accurately identify patients at risk of comorbidity. Clinically, interventions targeting neurotransmitter balance, neuromodulation, and metabolic support may improve therapeutic outcomes. Early detection and comprehensive management of depressive symptoms can prevent symptom progression, reduce disability, and enhance quality of life. Overall, the study highlights the necessity of a multidisciplinary approach addressing both the neurophysiological and psychological components of chronic headache disorders.

Conclusion

This study demonstrates that depressive states in patients with chronic headache disorders are closely associated with distinct functional and metabolic neurophysiological alterations.

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Hypoactivity in the prefrontal and limbic regions, disrupted connectivity between cortical and subcortical networks, and metabolic deficits contribute to both enhanced pain perception and emotional dysregulation. The severity of depressive symptoms correlates with the degree of these neurophysiological changes, highlighting a neurobiological basis for the comorbidity. Early identification and comprehensive assessment of depressive symptoms are essential for optimizing treatment strategies. Integrated approaches targeting neurotransmitter balance, neuromodulation, and metabolic support can improve clinical outcomes, reduce disability, and enhance quality of life. These findings underscore the importance of a multidisciplinary management strategy that addresses both neurological and psychological aspects of chronic headache disorders. Further research is needed to explore longitudinal changes and to develop personalized therapeutic interventions.

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