

NEUROPHYSIOLOGICAL AND NEUROIMMUNE PROFILING OF CHRONIC HEADACHE DISORDERS

Akhmedova Dilafruz Bahodirovna

Associate Professor, Bukhara State Medical Institute

E-mail: doctordilya81@mail.ru, dilafruz_axmedova@bsmi.uz

ORCID: 0009-0000-0960-137X

Abstract: Chronic headache disorders particularly chronic migraine and chronic tension-type headache — are emerging as a major neurological burden due to their persistent course and complex, multifactorial pathophysiology. Based on a cohort of 315 patients, the present study examines the integrated neurophysiological and neuroimmunological mechanisms underlying these conditions. Comprehensive assessment included EEG-based functional markers, heart rate variability (HRV) indices, and cytokine profiling (IL-6, TNF- α , IL-10). The results revealed a distinct pattern of EEG dysregulation and heightened pro-inflammatory cytokine activity in chronic migraine, indicating pronounced central sensitization alongside immune imbalance. These findings support the model in which sustained nociceptive input and neuroimmune activation jointly maintain chronicity. Implementation of individualized, multimodal treatment strategies aligned with each patient's neurobiological and psychophysiological characteristics led to marked reductions in headache frequency and meaningful improvements in overall quality of life.

Keywords: Chronic headache, migraine, neurophysiology, neuroimmunology, optimization, treatment

Introduction

Chronic headaches, particularly chronic migraine (CM), constitute a major global health burden due to their high prevalence, impact on productivity, and detrimental effects on quality of life. According to the ICHD-3 criteria, CM is characterized by ≥ 15 headache days per month for more than three months, with at least eight days meeting migraine-specific diagnostic features [1]. While early theories emphasized predominantly vascular mechanisms, contemporary research supports a more integrative pathophysiological model involving cortical spreading depression, dysregulation within brainstem pain-modulating circuits, and activation of immune-inflammatory pathways [2]. Neurophysiological investigations further substantiate these mechanisms. EEG analyses in CM patients consistently demonstrate altered cortical excitability, reflected by attenuated alpha activity and increased theta-delta power, which collectively signify impaired thalamocortical rhythm regulation and global network instability [3]. Complementing these findings,

immunological assessments reveal substantially elevated pro-inflammatory cytokines, particularly IL-6 and TNF- α , in CM compared to other chronic headache subtypes, underscoring the contribution of persistent neuroinflammation to disease chronicity [4]. The clinical phenotype is further complicated by psychological comorbidities such as anxiety and depression, which may potentiate central sensitization through dysregulation of the hypothalamic–pituitary–adrenal axis and maladaptive stress responses [5]. Given this multidimensional pathogenesis, the present study aims to delineate the clinical, neurophysiological, and immunological distinctions across chronic headache forms and to assess the therapeutic efficacy of individualized, multimodal treatment strategies.

Materials and Methods

This cross-sectional study involved 315 patients aged 18 to 60 years with chronic headache syndromes who attended Carmen Plus Clinic (Bukhara, 2021–2024). The sample included 117 patients with chronic tension-type headache, 151 with migraine (76 with aura, 75 without), and 47 with medication-overuse headache. Diagnostic categorization adhered to the International Classification of Headache Disorders, 3rd edition (ICHD-3) [1]. Patients underwent comprehensive evaluations, including neurological and psychiatric examinations, EEG analysis, heart rate variability (HRV) testing, and immunological blood screening. Psychological state was assessed using the HADS scale, while quality of life was measured using SF-36 and HALT questionnaires. EEG signals were recorded under resting and photic stimulation conditions, and cytokines (IL-6, TNF- α , IL-10) were measured via ELISA [4]. Treatment regimens were individualized based on clinical and laboratory profiles and included pharmacological therapy, non-pharmacological interventions (CBT, biofeedback), and, where indicated, neuromodulation. Data were analyzed using SPSS v25.0; significance was set at $p < 0.05$.

Results

Demographic distribution showed a female predominance (71%) and a peak incidence in the 25–44 age group.

Table 1. Distribution of Patients by Headache Type

Headache Type	Number of Patients	Percentage (%)
Chronic Tension-Type Headache	117	37.1%
Migraine with Aura	76	24.1%
Migraine without Aura	75	23.8%
Medication-Overuse Headache	47	14.9%

Clinically, migraine groups reported higher VAS scores (7.8 ± 1.2) and MIDAS grades compared to tension-type cases (VAS: 5.2 ± 1.3). HRV parameters indicated

elevated sympathetic tone in migraine and medication-overuse subgroups. Notably, IL-6 and TNF- α levels were significantly elevated in chronic migraine (12.8 pg/mL and 18.4 pg/mL, respectively), compared to tension-type headache (5.1 and 8.7 pg/mL) [4,5]. IL-10 was higher in tension-type cases, suggesting anti-inflammatory balance.

Table 2. Serum Cytokine Levels (Mean $\pm$ SD)

Cytokine	Migraine (pg/mL)	Tension-Type (pg/mL)	Normal Range
IL-6	12.8 $\pm$ 3.1	5.1 $\pm$ 2.0	0–7
TNF- α	18.4 $\pm$ 4.2	8.7 $\pm$ 3.4	0–8
IL-10	4.2 $\pm$ 1.1	9.3 $\pm$ 2.8	5–15

Patients with personalized treatment regimens, including immunomodulatory support and CBT, showed a $\geq 50\%$ reduction in headache frequency in 63% of cases, outperforming monotherapy outcomes [6].

Table 3. EEG Features by Headache Type

EEG Parameter	Migraine with Aura	Tension-Type Headache
Alpha rhythm amplitude	Decreased	Preserved
Theta wave activity	Increased	Normal
Visual evoked response	Enhanced	Stable

EEG patterns revealed increased slow-wave activity in migraine with aura, while tension-type patients showed stable alpha rhythms.

Discussion

The study confirms the heterogeneity of chronic headache disorders and underscores the importance of a multidimensional diagnostic approach. The EEG abnormalities observed in migraine patients are consistent with cortical hyperexcitability theory and may help predict chronification risk [3]. Elevated cytokines such as IL-6 and TNF- α reinforce the role of systemic inflammation in headache pathogenesis [4]. These findings align with literature describing neurogenic inflammation and cytokine-driven neuronal sensitization as pivotal mechanisms in chronic migraine development [5]. Furthermore, psychological assessments highlight the necessity of incorporating mental health screening into routine headache management. The superior efficacy of multimodal therapies, especially those integrating psychological support, suggests a synergistic effect on pain modulation

and autonomic balance [6,7]. Our findings advocate for adopting precision medicine in headache care, matching therapy to pathophysiological markers.

Conclusion

Chronic headache disorders, particularly chronic migraine, exhibit distinct clinical, neurophysiological, and immunological profiles that justify individualized management strategies. EEG and cytokine markers such as IL-6 and TNF- α serve as valuable indicators of disease severity and treatment response. Multimodal approaches that integrate neurological, immunological, and psychological dimensions demonstrate superior outcomes, reducing headache frequency and improving life quality. These results support a paradigm shift toward integrated, biomarker-informed care models in neurology.

References:

1. Akhmedova D. B., Xodjiev D. T. Analysis of the prevalence of headaches among the population in bukhara region //ACADEMICIA: An International Multidisciplinary Research Journal. – 2021. – Т. 11. – №. 3. – С. 431-433.
2. Ходжиева Д. Т., Ахмедова Д. Б. Гирудотерапия тарихи ва илмий асослари //Журнал" Медицина и инновации". – 2021. – №. 3. – С. 143-146.
3. Ахмедова Д. Б. СУРУНКАЛИ ЗЎРИҚИШДАГИ БОШ ОҒРИҚЛАРИДА БЕМОР НЕЙРОПСИХОЛОГИК ҲОЛАТИГА ДАВОЛАШ ЧОРАЛАРИНИНГ ТАЪСИРИНИ ҚИЁСИЙ БАҲОЛАШ //Academic research in educational sciences. – 2021. – Т. 2. – №. 10. – С. 408-413.
4. Ходжиева Д. Т., Ахмедова Д. Б. Турли генезли бош оғриқларида беморларни олиб боришга дифференциал ёндашув ва реабилитация усуллари тақомиллаштириш //журнал неврологии и нейрохирургических исследований. – 2022. – Т. 3. – №. 4.
5. Bakhodirovna A. D. Analysis of Side Effects of Drugs Used in the Treatment of Chronic Tension-Type Headache //international journal of inclusive and sustainable education. – 2022. – Т. 1. – №. 4. – С. 54-55.
6. Ахмедова Д. Б. Сурункали зўриқишдаги бош оғриғи ва мигренда олий нерв фаолияти бузилиши //журнал неврологии и нейрохирургических исследований.–2021.–№. SPECIAL. – Т. 1.