CLINICAL-NEUROPHYSIOLOGICAL AND NEUROIMMUNOLOGICAL CHARACTERISTICS OF CHRONIC HEADACHE FORMS

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Abstract

Chronic headache disorders, notably chronic migraine and tension-type headaches, represent a growing neurological concern due to their refractory nature and multidimensional pathophysiology. This research, grounded on a cohort of 315 patients, explores the interplay of neurophysiological and neuroimmunological factors, analyzing EEG markers, heart rate variability (HRV), and cytokine levels including IL-6, TNF-α, and IL-10. Our findings demonstrate distinct EEG profiles and elevated inflammatory markers in chronic migraine cases, supporting the hypothesis of central sensitization and immune dysregulation. Treatment optimization through multimodal approaches, tailored to patients' neurobiological and psychological profiles, yielded significant reductions in attack frequency and improved quality of life.

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

Introduction

Chronic headaches, particularly chronic migraine (CM), constitute a significant global burden, impacting productivity and quality of life. As per the ICHD-3 classification, CM is defined by ≥15 headache days per month for over three months, with at least eight days fulfilling migraine criteria [1]. Traditional explanations of migraine focused on vascular mechanisms, but recent advances highlight a broader framework involving cortical spreading depression, brainstem dysfunction, and immune-inflammatory pathways [2]. Neurophysiological studies, such as EEG, reveal aberrant cortical excitability in CM patients, marked by decreased alpha and increased theta-delta activity, indicative of network instability [3]. Additionally, immunological profiling uncovers elevated levels of IL-6 and TNF-α in CM compared to other headache types, reflecting neuroinflammatory states [4]. Psychological comorbidities, including anxiety and depression, further complicate the clinical picture and may amplify central sensitization through the hypothalamic-pituitary-adrenal axis [5]. In light of this multifactorial pathogenesis, our study investigates clinical,

neurophysiological, and immunological distinctions among chronic headache subtypes and evaluates the efficacy of personalized treatment protocols.

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 ± SD)

Cytokine	Migraine (pg/mL)	Tension-Type (pg/mL)	Normal Range

IL-6	12.8 ± 3.1	5.1 ± 2.0	0–7
TNF-α	18.4 ± 4.2	8.7 ± 3.4	0–8
IL-10	4.2 ± 1.1	9.3 ± 2.8	5–15

Patients with personalized treatment regimens, including immunomodulatory support and CBT, showed a ≥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

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