The American Journal of Medical Sciences and Pharmaceutical Research
ISSN 2689-1026 | Open Access

TYPE Original Research
PAGE NO. 74-76
DOI 10.37547/tajmspr/Volume07Issue06-08

Bridging neurophysiology and immunology in chronic headache: evidence from a clinical cohort study

Akhmedova Dilafruz Bahodirovna

Bukhara State Medical Institute, Uzbekistan

Khodjiyeva Dilbar Tadjiyevna

Bukhara State Medical Institute, Uzbekistan

OPEN ACCESS

SUBMITTED 30 April 2025
ACCEPTED 28 May 2025
PUBLISHED 30 June 2025
VOLUME Vol.07 Issue06 2025

CITATION

Akhmedova Dilafruz Bahodirovna, & Khodjiyeva Dilbar Tadjiyevna. (2025). Bridging neurophysiology and immunology in chronic headache: evidence from a clinical cohort study. The American Journal of Medical Sciences and Pharmaceutical Research, 7(06), 74–76.
https://doi.org/10.37547/tajmspr/Volume07Issue06-08

Abstract: Chronic headache disorders, particularly chronic migraine, present significant diagnostic and therapeutic challenges due to their complex neurobiological underpinnings. This study aims to elucidate the clinical, neurophysiological, and neuroimmunological characteristics of various chronic headache forms and to propose optimized treatment strategies based on individualized assessments. A cohort of patients with chronic migraine and other persistent headache syndromes underwent comprehensive evaluation, including EEG analysis, autonomic testing, and immunological profiling. Our findings reveal distinct neurophysiological markers, such as alterations in cortical excitability and autonomic imbalance, as well as specific immune patterns that correlate with headache severity and frequency. Moreover, personalized treatment protocols, integrating pharmacological, neuro-modulatory, and lifestyle interventions, demonstrated improved therapeutic outcomes compared to standard regimens. These results highlight the necessity of a multimodal diagnostic and therapeutic approach in managing chronic headaches effectively.

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

Introduction: Chronic headaches, particularly chronic migraine, affect a substantial proportion of the global

population, significantly impairing quality of life and functional capacity [1,2]. Despite advances in our understanding of primary headache syndromes, chronic forms remain a complex clinical entity due to their multifactorial etiology involving neurological, immunological, and psychological dimensions [3,4]. Recent evidence underscores the role of central sensitization, dysfunctional cortical excitability, and altered immune responses in perpetuating chronic headache conditions [5,6]. Neuroimaging and electrophysiological studies suggest that hypothalamic and brainstem regions play a pivotal role in migraine pathophysiology, indicating a shift from a purely vascular hypothesis to a neural network dysfunction model [7,8]. However, routine clinical evaluations often overlook these aspects, leading to suboptimal treatment outcomes [9]. The integration of neurophysiological and neuroimmunological assessment tools may offer valuable insights into disease mechanisms and guide targeted therapeutic strategies. This aligns with emerging approaches in precision medicine, emphasizing the role of personalized care in neurological disorders [10]. This study focuses on characterizing these chronic headache forms through detailed clinical and instrumental evaluation, aiming to develop optimized and personalized treatment approaches that address both symptomatic relief and underlying pathophysiology.

METHODS

This observational clinical study included 112 patients aged 18 to 60 years diagnosed with chronic headache forms, primarily chronic migraine, based on the International Classification of Headache Disorders, 3rd edition (ICHD-3) criteria. The cohort was recruited from the neurology departments of regional medical centers between 2021 and 2023. Participants were grouped according to headache subtype and duration, with additional stratification by comorbid factors such as anxiety and sleep disturbances.All patients underwent a comprehensive clinical neurological examination, including detailed headache history, pain intensity assessment using the Visual Analog Scale (VAS), and headache-related disability evaluated through the Migraine Disability Assessment (MIDAS) questionnaire. Neurophysiological investigations comprised resting-state electroencephalography (EEG), brainstem auditory evoked potentials (BAEP), and heart rate variability (HRV) analysis to assess central and autonomic nervous system function. Neuroimmunological evaluation involved serum analysis of pro-inflammatory and anti-inflammatory cytokines (IL-1β, IL-6, IL-10, TNF-α), immunoglobulin profiles (IgG, IgA, IgM), and lymphocyte subset profiling via flow cytometry. Laboratory procedures followed standardized ELISA and immunophenotyping protocols, with samples processed in certified immunology laboratories. Patients received individualized treatment regimens based on clinical and instrumental findings, including pharmacological therapy (antiepileptics, antidepressants, monoclonal antibodies against CGRP), neuromodulation techniques (transcranial magnetic stimulation), and behavioral interventions (CBT, sleep hygiene education). Treatment efficacy was monitored over a 6-month follow-up period through monthly VAS scores, reduction in attack frequency, and patient-reported outcome measures. Statistical analysis was performed using SPSS software (version 25.0), with significance set at $p<0.05$. Parametric and non-parametric tests were applied as appropriate, including ANOVA, chi-square, and Spearman's correlation to explore associations between clinical variables, neurophysiological markers, and immunological parameters.

RESULTS

Among the 112 patients evaluated, 68 (60.7%) were diagnosed with chronic migraine, while 44 (39.3%) presented with other chronic headache forms, including tension-type and mixed-type headaches. The average duration of headache history was 7.4 ± 2.1 years. Clinical assessment revealed a statistically significant higher frequency of severe pain episodes and functional disability in the chronic migraine subgroup ($p<0.01$), with a mean VAS score of 7.9 ± 1.1 and MIDAS score of 32.5 ± 6.4. Neurophysiological findings showed that 74% of chronic migraine patients exhibited diffuse EEG slowing in the alpha range, with increased cortical excitability indicated by enhanced photic stimulation responses. BAEP recordings revealed delayed interpeak latencies (I–V) in 36% of cases, suggesting brainstem dysfunction. HRV analysis demonstrated parasympathetic underactivity and heightened sympathetic tone, particularly in patients with comorbid anxiety.Neuroimmunological profiling identified elevated levels of pro-inflammatory cytokines—especially IL-6 and TNF-α—in chronic migraine patients compared to controls ($p<0.05$), alongside a reduction in regulatory cytokine IL-10. Immunoglobulin analysis showed a moderate increase in IgA and IgG titers, while flow cytometry revealed an imbalance in CD4+/CD8+ T-cell ratios and reduced B-cell populations in a subset of patients with prolonged migraine history.Treatment outcomes indicated that personalized, multimodal interventions led to a ≥50% reduction in headache frequency in 62.5% of patients over six months. Combination regimens incorporating CGRP monoclonal antibodies, neuromodulation, and cognitive behavioral therapy yielded the highest efficacy. Patients receiving

only pharmacological monotherapy showed significantly lower improvement rates ($p<0.01$), underscoring the importance of individualized, integrative treatment approaches.

DISCUSSION

The findings of this study emphasize the multifactorial pathophysiology of chronic headaches, particularly chronic migraine, which is increasingly recognized as a disorder involving complex interactions between neural excitability, autonomic imbalance, and immune dysregulation. The observed EEG alterations, including diffuse alpha slowing and photic hypersensitivity, support existing literature suggesting cortical hyperexcitability as a hallmark of migraine chronification. These neurophysiological disturbances align with previous studies indicating disrupted thalamo-cortical processing and impaired inhibitory control in chronic migraine patients [3].Furthermore, brainstem auditory evoked potential delays and HRV data point to significant dysfunction within the brainstem-autonomic axis, corroborating reports that highlight its role in modulating pain pathways and vascular tone [4]. These disturbances may underlie the persistence and intensification of headache episodes, especially in patients with comorbid anxiety, as supported by our findings.Immunologically, elevated pro-inflammatory cytokines (IL-6, TNF-α) and reduced IL-10 levels indicate an ongoing inflammatory state, potentially contributing to central sensitization and neuronal hyperresponsiveness. Such immune imbalances mirror findings in recent neuroimmunology research that associates migraine with systemic and neurogenic inflammation [5]. The observed T-cell and B-cell profile changes suggest immune exhaustion or compensatory modulation in chronic headache sufferers, though causality remains to be elucidated.Importantly, our study demonstrated that individualized, multimodal treatment regimens—particularly those integrating neuromodulation and behavioral interventions alongside pharmacotherapy—significantly outperformed standard monotherapy approaches. This supports a paradigm shift toward personalized headache management, consistent with emerging clinical guidelines advocating for stratified care models based on neurobiological profiles.However, limitations include a relatively small sample size and the observational design, which may constrain generalizability. Future randomized controlled trials are warranted to validate these findings and further delineate the mechanistic pathways involved in chronic headache disorders.

CONCLUSION

This study provides compelling evidence that chronic headache disorders, especially chronic migraine, are characterized by a confluence of neurophysiological instability, autonomic dysfunction, and immune system dysregulation. The identification of specific EEG changes, brainstem processing delays, and cytokine imbalances underscores the need for a comprehensive diagnostic framework that extends beyond symptomatic assessment. Importantly, the demonstrated efficacy of individualized, multimodal treatment strategies highlights the clinical value of integrating neurophysiological and neuroimmunological findings into therapeutic planning. These insights advocate for a shift toward personalized medicine in chronic headache management, aiming to enhance patient outcomes through targeted interventions. Future investigations, particularly those employing longitudinal and interventional designs, are essential to validate and refine this integrative model.

REFERENCES

Headache Classification Committee of the International Headache Society (IHS). (2018). The International Classification of Headache Disorders, 3rd edition. Cephalalgia, 38(1), 1–211.

10. May, A., & Schulte, L.H. (2016). Chronic migraine: Risk factors, mechanisms and treatment. Nat Rev Neurol, 12(8), 455–464.

Lipton, R.B., et al. (2007). Migraine prevalence, disease burden, and the need for preventive therapy. Neurology, 68(5), 343–349.

Coppola, G., et al. (2019). Neurophysiological correlates of migraine chronification. J Headache Pain, 20(1), 115.

Goadsby, P.J., et al. (2017). Pathophysiology of migraine. Physiol Rev, 97(2), 553–622. https://doi.org/10.1152/physrev.00034.2015

Arumugam, K., et al. (2021). Role of inflammation in migraine. Int J Neurosci, 131(3), 275–285.

Peres, M.F.P., et al. (2001). Hypothalamic involvement in chronic migraine. JNNP, 71(6), 747–751.

Charles, A. (2013). Migraine: A brain state. Curr Opin Neurol, 26(3), 235–239.

Silberstein, S.D., et al. (2021). Pharmacologic treatment for episodic migraine. Neurology, 97(10), 918–932.

Ashina, M. (2020). Migraine. N Engl J Med, 383(19), 1866–1876.