

Mechanistic Insights into Acupuncture for the Prevention and Treatment of Migraine

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Abstract: *Migraine is a highly prevalent neurological disorder that imposes substantial burdens on individual-patient health and public healthcare systems worldwide. A large proportion of patients with migraine seek symptom relief through complementary and alternative medicine (CAM), with Traditional Chinese Medicine (TCM) being the most frequently preferred option. Acupuncture has been widely adopted in the clinical management of migraine and demonstrates reliable therapeutic benefits. This review synthesizes contemporary evidence regarding the mechanistic basis underlying acupuncture-mediated migraine prophylaxis and treatment. Acupuncture exerts its therapeutic effects via multiple pathways: modulating neuropeptides and associated neurotransmitters, suppressing neurogenic inflammation, mitigating central sensitization, and reshaping functional brain-network connectivity. Overall, this work aims to provide a scientific rationale for optimizing TCM-oriented clinical strategies for migraine management.*

Keywords: Acupuncture, Migraine, Neuroinflammation, Functional brain network, Mechanism of action.

1. Introduction

Migraine is a recurrent, throbbing headache typically accompanied by symptoms such as nausea, vomiting, photophobia, and phonophobia. In a subset of patients, the onset is preceded by visual, sensory, or motor auras. It is recognized as one of the most prevalent primary headache disorders worldwide [1]. The latest version of the International Classification of Headache Disorders (ICHD-3) classifies more than 250 distinct headache phenotypes into four major groups: primary headaches, secondary headaches, painful cranial neuropathies and other facial pains, and miscellaneous headaches, with migraine constituting a major subgroup within primary headaches [2]. Globally, migraine affects approximately 1 billion individuals, contributing to 42 million years lived with disability (YLDs). Epidemiological data indicate a prevalence of approximately 14%. Characterized by chronic relapsing episodes, migraine disproportionately affects females, particularly among women aged 15 to 49 years. It severely impairs patients' quality of life and generates considerable socioeconomic burdens [3-5]. Conventional management of migraine encompasses acute treatments, prophylactic therapies, and non-pharmacological interventions. Currently prescribed medications include acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs), β -blockers, antiepileptic drugs, tricyclic antidepressants, and calcium channel blockers [6]. Nevertheless, limited therapeutic responses, frequent adverse events, and various contraindications, these pharmacological agents fail to fully satisfy unmet clinical demands among people living with migraine.

Acupuncture, a cornerstone of TCM, is extensively used in clinical practice for the treatment of migraine. As a complementary and alternative therapy for migraine and other pain disorders, acupuncture is gaining increasing recognition in Western countries, and cumulative clinical evidence supports its efficacy and safety profiles [7, 8]. With the advancement of evidence-based medicine, a growing body of systematic reviews has evaluated the efficacy and safety of acupuncture in migraine management. Nonetheless, many

such reviews suffer from notable methodological limitations, which may weaken the robustness of available evidence and mislead patients, clinicians, and health policy stakeholders. To date, relatively mature guidelines for the diagnosis and treatment of migraine have been established in China, validating the reliable efficacy of TCM interventions for this condition [9]. The present review systematically summarizes recent mechanistic research advances concerning acupuncture for migraine prevention and treatment, intending to lay a solid foundation for future basic investigations and real-world clinical applications.

2. Pathophysiological Mechanisms of Migraine

Although the precise pathogenesis of migraine remains to be fully elucidated, accumulating evidence has established that key elements—including genetic predisposition, the trigeminovascular system (TGVS), inflammatory responses, cortical spreading depression (CSD), and central sensitization—exert profound influences on its initiation and progression [10, 11]. From a pathophysiological perspective, the TGVS is regulated by the brainstem and diencephalic nuclei. Within this system, efferent nerve fibers innervate the meningeal vasculature, whereas afferent fibers transmit nociceptive signals to the trigeminal nucleus caudalis (TNC). The activation of these neural circuits subsequently generates perceptible meningeal inflammation and vasodilation, ultimately triggering headache [12, 13].

CSD is widely considered a key trigger event in migraine, which can activate the TGVS and prompt the release of vasoactive neuropeptides, such as calcitonin gene-related peptide (CGRP) and substance P (SP), from trigeminal afferent terminals, thereby inducing neurogenic inflammation [14]. This inflammatory cascade leads to meningeal vasodilation, increased vascular permeability, and plasma protein extravasation, which collectively stimulate intracranial pain-sensitive structures to generate nociceptive signals. Under persistent stimulation by these chronic nociceptive signals, the central nervous system undergoes neuroplastic remodeling. This results in an abnormal increase

in the excitability and a reduction in the threshold of nociceptive pathways, consequently prompting central sensitization [15]. Central sensitization further amplifies pain perception and renders patients hypersensitive to sensory stimuli, which not only exacerbates the severity of headache attacks but also increases their frequency. Furthermore, aberrant signaling pathways involving various neurotransmitters (e.g., 5-hydroxytryptamine, glutamate, and dopamine), together with disrupted connectivity and dysregulation of large-scale functional brain networks including the default mode network (DMN) and the pain matrix, exert complex yet pivotal effects on migraine initiation, maintenance, and chronification.

3. Modulation of Neuropeptides and Associated Neurotransmitters

The pathogenesis of migraine involves complex neurovascular dysregulation, characterized by a pathophysiological cascade propagating from peripheral triggers to the central nervous system. Upon activation of the trigeminovascular system (TGVS), sensory nerve endings release various vasoactive neuropeptides, including calcitonin gene-related peptide (CGRP), substance P (SP), and pituitary adenylate cyclase-activating polypeptide (PACAP). These neuropeptides act on cerebral blood vessels to induce vasomotor dysfunction, while simultaneously activating peripheral nociceptors, which amplifies pain signal transduction and culminates in migraine attacks. In addition to neuropeptides, neurotransmitters such as 5-hydroxytryptamine (5-HT), glutamate, and γ -aminobutyric acid (GABA) actively participate in the activation of the trigeminovascular pathway [16, 17]. Acupuncture intervention can reverse aberrant neural signaling cascades, thereby blocking the initiation and progression of migraine, and ultimately achieving therapeutic efficacy by alleviating headache and reducing recurrence.

Xu et al. [18] performed electroacupuncture (EA) experiments on a rat model of migraine and demonstrated that EA significantly decreased the plasma levels of vasoactive peptides, including PACAP, CGRP, and SP, which may contribute to lowered migraine recurrence risk. Endothelin (ET) and nitric oxide (NO), which are released by vascular endothelial cells, participate in blood flow regulation by modulating vasomotor function, with NO acting as an intermediate mediator in CGRP-mediated vasodilation. A systematic review [19] showed that acupuncture not only reduces NO release but also significantly downregulates CGRP and SP, an effect linked to inhibited meningeal vasodilation. Another study [20] revealed that shallow acupuncture with high-frequency twisting manipulation significantly increased patient β -endorphin (β -EP) levels. This suggests that acupuncture can activate the mesolimbic analgesic pathway, upregulate the functioning of the endogenous opioid peptide system, elevate the pain threshold, and produce morphine-like analgesic effects, thereby effectively alleviating migraine symptoms.

4. Suppression of Neurogenic Inflammation

Neurogenic inflammation represents one of the major initiating drivers in migraine onset. During this inflammatory

response, the activation of microglia and macrophages triggers the release of abundant pro-inflammatory cytokines from immune cells, such as interleukin (IL)-6, tumor necrosis factor (TNF)- α , and IL-1. This cascade leads to meningeal vasodilation, plasma protein extravasation, and mast cell degranulation, which collectively exacerbate the positive feedback loop of neuroinflammation. Consequently, peripheral nociceptive signals are transmitted to the central nervous system, prompting central sensitization and allodynia, which eventually drive the development and progression of characteristic clinical manifestations of migraine [21].

Experimental studies have demonstrated that acupuncture exerts therapeutic effects in migraine through its anti-inflammatory properties. In a single-blind, double-dummy, randomized controlled trial [22], a 12-week course of acupuncture therapy maintained its efficacy for up to 24 weeks, showing superior efficacy to topiramate in treating chronic migraine, with no serious adverse events reported. Inflammatory processes are intricately involved in the initiation and maintenance of migraine attacks. Activated microglia release pro-inflammatory cytokines such as IL-1 β , TNF- α , and IL-6, which mediate the inflammatory cascade [23]. Animal studies in rats have confirmed that acupuncture can mitigate neuroinflammatory responses in migraine by reducing matrix metalloproteinase-2 (MMP-2) activity and modulating CB1 receptor-mediated regulation of inflammatory mediators, including the inhibition of prostaglandin E2 (PGE2) release and the downregulation of IL-1 β and cyclooxygenase-2 (COX-2) protein levels in the trigeminal ganglion [24]. Furthermore, the IL-1 β /COX-2/PGE2 inflammatory pathway is involved in CGRP release during the activation of the trigeminovascular system in migraine. Further research indicated that EA can suppress IL-1 β /COX-2 inflammatory signaling in the trigeminal ganglion, reduce PGE2 synthesis and release, and inhibit CGRP release in a rat model of migraine [25]. Zhou et al. [26] established a model of recurrent migraine-like rats via seven repeated dural infusions of inflammatory soup (IS). Their EA experiments demonstrated that EA regulates the Toll-like receptor 4/nuclear factor- κ B (TLR4/NF- κ B) pathway, thereby reducing microglial activation and downregulating CGRP, ionized calcium-binding adapter molecule 1 (Iba-1), and microglia-mediated inflammatory cytokines. Additionally, another study [27] confirmed that acupuncture treatment significantly upregulated hsa-miR-550a-3-5p and inhibited platelet endothelial cell adhesion molecule-1 (PECAM-1), thereby reducing the transendothelial migration of inflammatory cells and the release of inflammatory cytokines, which ultimately alleviated migraine symptoms. Zhou et al. [28] also established a rat migraine model using repeated dural stimulation with IS, confirming that EA alleviates allodynia and central sensitization in migraine rats by inhibiting microglial activation and inflammation associated with the P2X4R and NLRP3/caspase-1/IL-1 β inflammatory pathways.

5. Attenuation of Central Sensitization

Central sensitization refers to the persistent hyperexcitability of central nociceptive neurons coupled with reduced pain thresholds. Clinically, it manifests as cutaneous allodynia during migraine attacks and serves as the core pathological

node in the transition of migraine from episodic to chronic states [29]. Persistent peripheral nociceptive input, neuroinflammatory mediators, and excitatory neurotransmitters collectively induce neuroplastic changes in wide dynamic range (WDR) neurons within the trigeminal cervical complex (TCC). Once the sensitized state is established, the functional activity of sensory pathways is enhanced, and the central nervous system maintains a state of hyperreactivity. Acupuncture can reverse central neuronal hyperexcitability through multiple pathways, blocking the plastic remodeling of nociception and inhibiting the chronification of migraine. Brain-derived neurotrophic factor (BDNF) is a key molecule in neuroplasticity and development, and is upregulated by factors associated with inflammatory activation; studies have shown that acupuncture can modulate BDNF levels in migraine [30]. Glutamate, the primary excitatory neurotransmitter in the central nervous system, is closely linked to central sensitization during migraine development [31]. High levels of glutamate bind to its receptors (NMDA and AMPA/KA receptors), facilitating calcium influx and intracellular signaling, which increases excitotoxicity, disrupts normal neurotransmission, and leads to neuronal damage or even cell death. Gao et al. [32] experimentally demonstrated that EA alleviates migraine by effectively reducing circulating glutamate concentrations. Currently, a systematic consensus regarding the specific mechanisms by which acupuncture modulates key effector molecules in the process of central sensitization in migraine has not yet been established. Existing clinical studies focus heavily on the observation of therapeutic effects post-acupuncture, and additional molecular-level investigations are required to fully unpack these regulatory mechanisms.

6. Regulation of Functional Brain-Network Connectivity

Traditional mechanistic studies have focused primarily on localized molecular changes within the brainstem and trigeminal pathways. However, advancements in neuroimaging, particularly functional magnetic resonance imaging (fMRI), have propelled migraine mechanism research into the realm of brain networks. Migraine is now conceptualized not as a pathology of a single brain region, but as coordinated dysfunction across multiple intrinsic functional brain networks. These include the default mode network (DMN), salience network (SN), descending pain modulatory system (DPMS), thalamocortical sensory network, and visual-related networks, involving functional abnormalities in brain regions such as the cingulate cortex, caudate nucleus, thalamus, and cerebellum. In particular, limbic system regions (including the cingulate cortex, amygdala, and parahippocampal gyrus) are key areas of brain dysfunction in migraine patients, and these abnormalities are thought to be associated with emotional, cognitive, and autonomic dysfunctions [33, 34]. Acupuncture may modulate migraine symptoms through interactions between different brain regions. In a retrospective study involving 112 participants [35], fMRI scans and region of interest (ROI)-based analysis focusing on pain-processing brain regions demonstrated that acupuncture modulates neural activity in the frontal, parietal, and limbic regions, as well as nociceptive processing-related brain areas, thereby improving

migraine symptoms. In a pre-post study of 41 migraine patients, Yang et al. [36] found that migraine relief after acupuncture was correlated with baseline gray matter (GM) volume in the parietal, frontal, and occipital lobes, with longitudinal GM-volume increases in the left hemisphere observed after treatment. Furthermore, Li et al. [37] experimentally demonstrated that acupuncture treatment significantly increases the resting-state functional connectivity between the periaqueductal gray (PAG) and the rostral anterior cingulate cortex/medial prefrontal cortex (rACC/mPFC), thereby enhancing the activity of the DPMS and alleviating pain perception.

Moreover, patients with migraine frequently exhibit decreased gut microbiota diversity, reduced abundance of beneficial bacteria, and an increased proportion of harmful bacteria. This dysbiosis of the gut microbiota drives gut metabolite dysregulation, disrupts the intestinal barrier and the blood-brain barrier, activates the TGVs and central neuroinflammation, and subsequently triggers or exacerbates migraine [38, 39]. Research indicates [40] that acupuncture may exert anti-migraine effects by regulating the *Lactobacillus*-metabolite-inflammation axis, restoring gut homeostasis, alleviating pain and neuroinflammation, and reducing the production of harmful metabolites.

Energy metabolism may also represent a critical factor in the pathogenesis and progression of migraine, characterized by either increased energy demand (cortical hyperexcitability) or reduced energy supply (mitochondrial dysfunction) [41]. Studies have shown that following acupuncture stimulation at Baihui (GV20), Shenting (GV24), bilateral Benshen (GB13), Shuaigu (GB8), and Fengchi (GB20) acupoints, the expression levels of key proteins and metabolites, such as α -D-glucose, flavin adenine dinucleotide (FAD), biliverdin reductase B (BLVRB), and L-glutamate, were significantly altered. The glycolytic/gluconeogenic and riboflavin metabolism pathways were significantly enhanced, thereby regulating cerebral glucose metabolism, correcting the energy supply-demand imbalance following migraine attacks, and attenuating abnormally elevated neuronal excitability [42].

7. Discussion and Conclusion

Due to the complex pathophysiological mechanisms of migraine, single-target pharmacological agents possess inherent limitations. Acupuncture, with its multi-target and peripheral-central coordinated regulation advantages, can simultaneously modulate key pathological processes, including neuropeptides and related transmitters, neurogenic inflammation, central sensitization, and functional brain networks. It addresses both acute pain relief and interictal prophylaxis, and blocks the chronification of migraine, thereby demonstrating the unique therapeutic advantages of acupuncture. Although this review summarizes the current research on the mechanisms of acupuncture in treating migraine, the precise mechanisms remain to be fully elucidated. Future investigations integrating multi-omics datasets (proteomics, metabolomics, genomics, transcriptomics, lipidomics, immunomics, radiomics) are urgently required to comprehensively decode acupuncture-mediated anti-migraine mechanisms. With the development of neuroimaging techniques, which have revealed structural

and functional brain abnormalities in migraine patients, functional MRI and other modalities should be routinely utilized to evaluate the central effects of acupuncture in these patients. Although basic research has accumulated substantial cellular, animal, and neuroimaging evidence, challenges such as insufficient protocol standardization, animal model limitations, fragmented mechanism elucidation, and lagging clinical translation persist. In the future, high-quality, evidence-based clinical trials combined with multidisciplinary translational basic research will be essential to further delineate the complete signaling pathways of acupuncture, establish individualized and precise acupuncture protocols, and ultimately establish acupuncture as an indispensable component of the standardized, full-course prevention and management system for migraine.

References

- [1] HUANG Y, NI N, HONG Y, et al. Progress in Traditional Chinese Medicine for the Treatment of Migraine [J]. The American journal of Chinese medicine, 2020,48(8): 1731-1748.
- [2] Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition [J]. Cephalalgia: an international journal of headache, 2018,38(1): 1-211.
- [3] GBD D A I C. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019 [J]. Lancet (London, England), 2020,396(10258): 1204-1222.
- [4] STOVNER L J, HAGEN K, LINDE M, et al. The global prevalence of headache: an update, with analysis of the influences of methodological factors on prevalence estimates [J]. The journal of headache and pain, 2022,23(1): 34.
- [5] ASHINA M, KATSARAVA Z, DO T P, et al. Migraine: epidemiology and systems of care [J]. Lancet (London, England), 2021,397(10283): 1485-1495.
- [6] ASHINA M, BUSE D C, ASHINA H, et al. Migraine: integrated approaches to clinical management and emerging treatments [J]. Lancet (London, England), 2021,397(10283): 1505-1518.
- [7] ZHAO L, ZHANG F W, LI Y, et al. Adverse events associated with acupuncture: three multicentre randomized controlled trials of 1968 cases in China [J]. Trials, 2011,12: 87.
- [8] ZHAO L, CHEN J, LI Y, et al. The Long-term Effect of Acupuncture for Migraine Prophylaxis: A Randomized Clinical Trial [J]. JAMA internal medicine, 2017,177(4): 508-515.
- [9] Neurologists Branch of the Chinese Medical Doctor Association, Headache and Sensory Disorders Professional Committee of China Research Hospital Association, Zhao D, et al. Chinese guidelines for the diagnosis and treatment of migraine 2022 edition [J]. Chinese Journal of Pain Medicine, 2022,12(28): 881-898.
- [10] ASHINA M, TERWINDT G M, AL-KARAGHOLI M A M, et al. Migraine: disease characterisation, biomarkers, and precision medicine [J]. Lancet (London, England), 2021,397(10283): 1496-1504.
- [11] KHAN J, ASOOM L I A, SUNNI A A, et al. Genetics, pathophysiology, diagnosis, treatment, management, and prevention of migraine [J]. Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie, 2021,139: 111557.
- [12] KARSAN N. Pathophysiology of Migraine [J]. Continuum (Minneapolis, Minn.), 2024,30(2): 325-343.
- [13] AKERMAN S, HOLLAND P R, GOADSBY P J. Diencephalic and brainstem mechanisms in migraine [J]. Nature reviews. Neuroscience, 2011,12(10): 570-584.
- [14] DALKARA T, KAYA Z, ERDENER Ş E. Unraveling the interplay of neuroinflammatory signaling between parenchymal and meningeal cells in migraine headache [J]. The journal of headache and pain, 2024,25(1): 124.
- [15] PULEDDA F, SILVA E M, SUWANLAONG K, et al. Migraine: from pathophysiology to treatment [J]. Journal of neurology, 2023,270(7): 3654-3666.
- [16] IYENGAR S, JOHNSON K W, OSSIPOV M H, et al. CGRP and the Trigeminal System in Migraine [J]. Headache, 2019,59(5): 659-681.
- [17] PIETRA A D, KUBURAS A, RUSSO A F. PACAP versus CGRP in migraine: From mouse models to clinical translation [J]. Cephalalgia: an international journal of headache, 2025,45(9): 3331024251364242.
- [18] XU X, LIU L, ZHAO L, et al. Effect of Electroacupuncture on Hyperalgesia and Vasoactive Neurotransmitters in a Rat Model of Conscious Recurrent Migraine [J]. Evidence-based complementary and alternative medicine: eCAM, 2019,2019: 9512875.
- [19] SU P, XIE X, XU Y, et al. Effectiveness of acupuncture in migraine rats: A systematic review [J]. PloS one, 2023,18(1): e0280556.
- [20] FENG X X, HUANG K Y, CHEN L, et al. Clinical efficacy of the shallow puncture and more-twirling acupuncture method in migraine treatment and its effects on serum 5-HT and β -EP levels [J]. Technology and health care: official journal of the European Society for Engineering and Medicine, 2023,31(S1): 533-540.
- [21] REDUCHA P V, EDVINSSON L, HAANES K A. Could Experimental Inflammation Provide Better Understanding of Migraines? [J]. Cells, 2022,11(15): 2444.
- [22] LIU L, CHEN Q, ZHAO L, et al. Acupuncture plus topiramate placebo versus topiramate plus sham acupuncture for the preventive treatment of chronic migraine: A single-blind, double-dummy, randomized controlled trial [J]. Cephalalgia: an international journal of headache, 2024,44(6): 3331024241261080.
- [23] EDVINSSON L, HAANES K A, WARFVINGE K. Does inflammation have a role in migraine? [J]. Nature reviews. Neurology, 2019,15(8): 483-490.
- [24] ZHAO L, LIU L, XU X, et al. Electroacupuncture Inhibits Hyperalgesia by Alleviating Inflammatory Factors in a Rat Model of Migraine [J]. Journal of pain research, 2020,13: 75-86.
- [25] ZHANG H, ZHANG X M, ZONG D D, et al. miR-34a-5p up-regulates the IL-1 β /COX2/PGE2 inflammation pathway and induces the release of CGRP via inhibition of SIRT1 in rat trigeminal ganglion neurons [J]. FEBS open bio, 2021,11(1): 300-311.
- [26] ZHOU M, PANG F, LIAO D, et al. Electroacupuncture at Fengchi (GB20) and Yanglingquan (GB34) Ameliorates Paralysis through Microglia-Mediated

- Neuroinflammation in a Rat Model of Migraine [J]. *Brain sciences*, 2023,13(4): 541.
- [27] WU Z, WANG D, YAO J, et al. Acupuncture Upregulates hsa-miR-550a-3-5p Targeting PECAM1 To Reduce Transendothelial Migration of Inflammatory Cells and Alleviate Migraine [J]. *Journal of molecular neuroscience: MN*, 2025,76(1): 4.
- [28] ZHOU M, PANG F, LIAO D, et al. Electroacupuncture improves allodynia and central sensitization via modulation of microglial activation associated P2X4R and inflammation in a rat model of migraine [J]. *Molecular pain*, 2024,20: 17448069241258113.
- [29] JI R R, NACKLEY A, HUH Y, et al. Neuroinflammation and Central Sensitization in Chronic and Widespread Pain [J]. *Anesthesiology*, 2018,129(2): 343-366.
- [30] BORKUM J M. Harnessing migraines for neural regeneration [J]. *Neural regeneration research*, 2018,13(4): 609-615.
- [31] VIKELIS M, MITSIKOSTAS D D. The role of glutamate and its receptors in migraine [J]. *CNS & neurological disorders drug targets*, 2007,6(4): 251-257.
- [32] GAO Z, LIU X, YU S, et al. Electroacupuncture at Acupoints Reverses Plasma Glutamate, Lipid, and LDL/VLDL in an Acute Migraine Rat Model: A (1) H NMR-Based Metabolomic Study [J]. *Evidence-based complementary and alternative medicine: eCAM*, 2014,2014: 659268.
- [33] BORKUM J M. Harnessing migraines for neural regeneration [J]. *Neural regeneration research*, 2018,13(4): 609-615.
- [34] KE J, YU Y, ZHANG X, et al. Functional Alterations in the Posterior Insula and Cerebellum in Migraine Without Aura: A Resting-State MRI Study [J]. *Frontiers in behavioral neuroscience*, 2020,14: 567588.
- [35] TIAN Z, GUO Y, YIN T, et al. Acupuncture Modulation Effect on Pain Processing Patterns in Patients With Migraine Without Aura [J]. *Frontiers in neuroscience*, 2021,15: 729218.
- [36] YANG X J, LIU L, XU Z L, et al. Baseline Brain Gray Matter Volume as a Predictor of Acupuncture Outcome in Treating Migraine [J]. *Frontiers in neurology*, 2020,11: 111.
- [37] LI Z, LIU M, LAN L, et al. Altered periaqueductal gray resting state functional connectivity in migraine and the modulation effect of treatment [J]. *Scientific reports*, 2016,6: 20298.
- [38] AURORA S K, SHREWSBURY S B, RAY S, et al. A link between gastrointestinal disorders and migraine: Insights into the gut-brain connection [J]. *Headache*, 2021,61(4): 576-589.
- [39] GAMIL N M, GHORAB R M, ELSADAWY R Z, et al. A review on gut microbiota and migraine severity: a complex relationship [J]. *Inflammopharmacology*, 2026,34(1): 285-308.
- [40] SUN S, XU L, WANG Y, et al. Acupuncture Alleviates Neuroinflammation in Chronic Migraine by Modulating Lactobacillus and Its Metabolite Pathways [J]. *Pain research & management*, 2026,2026(1): e5189419.
- [41] BORKUM J M. Brain Energy Deficit as a Source of Oxidative Stress in Migraine: A Molecular Basis for Migraine Susceptibility [J]. *Neurochemical research*, 2021,46(8): 1913-1932.
- [42] LIU L, LI W, WANG L, et al. Proteomic and metabolomic profiling of acupuncture for migraine reveals a correlative link via energy metabolism [J]. *Frontiers in neuroscience*, 2022,16: 1013328.