Journal of Multidisciplinary Healthcare

Dovepress
Taylor & Francis Group

Open Access Full Text Article

REVIEW

Acupuncture's Regulatory Role in Glial Cells and Their Interactions for Antidepressant Effects: A Review of Research Progress

Jing Cao[1,2,*], Lian Yang[3,4,*], Deguang Ding[2], Xiaolei Zhang[2], Nana Ding[3], Fengmin Ding[1], Qinglai Bian[1], Jiaxu Chen[1,3,5]

[1]School of Basic Medicine, Hubei University of Chinese Medicine, Wuhan, Hubei, 430070, People's Republic of China; [2]Hubei Provincial Hospital of Traditional Chinese Medicine, Wuhan, Hubei, 430065, People's Republic of China; [3]Guangzhou Key Laboratory of Formula-Pattern of Traditional Chinese Medicine, School of Traditional Chinese Medicine, Jinan University, Guangzhou, Guangdong, 510000, People's Republic of China; [4]Affiliated Hospital of Xiangnan University, Chenzhou, Hunan, 423000, People's Republic of China; [5]School of Traditional Chinese Medicine, Beijing University of Chinese Medicine, Beijing, 100029, People's Republic of China

*These authors contributed equally to this work

Correspondence: Qinglai Bian; Jiaxu Chen, Email 756402872@qq.com; chenjiaxu@hotmail.com

Abstract: The clinical management of depression presents significant challenges. While acupuncture has shown efficacy in alleviating depressive symptoms, the underlying mechanisms through which it exerts its antidepressant effects remain incompletely understood. Recent research has underscored the crucial role of glial cells in the pathophysiology of depression. This discovery opens a novel and promising avenue for investigating the mechanisms underlying acupuncture's antidepressant actions. Based on clinical evidence supporting the use of acupuncture in treating depression, this article reviews recent studies on how acupuncture influences the glial cell network. This is the first review of studies examining the effects of acupuncture on glial cells in depression. The review encompasses several key aspects, including microglial polarization and associated inflammatory signaling pathways, the role of astrocytes in maintaining metabolic homeostasis, the processes of oligodendrocyte differentiation and myelin repair, as well as the intricate interactions among these three types of glial cells. However, this paper also has certain limitations, such as the majority of mechanistic evidence deriving from animal models, and due to the heterogeneity of acupuncture protocols and the lack of human causal data.

Keywords: acupuncture, depression, microglia, astrocytes, oligodendrocytes

Introduction

Depression is a highly disabling mental disorder,[1] clinically characterised by low mood and anhedonia, often accompanied by sleep disturbances and cognitive impairment,[2] severely affecting patients' social functioning and quality of life.[3] The pathogenesis of depression is complex, with no unified scientific consensus currently established. Most studies suggest associations with neuroinflammation, immune dysregulation, neurotrophic factor deficiency, and myelin damage.[4–6] Antidepressants remain the mainstream treatment, yet many patients exhibit poor response to existing medications or cannot tolerate their side effects, compelling the urgent need for more effective and safer intervention strategies. Meta-analyses of multiple randomised controlled trials indicate that acupuncture exhibits holistic, multi-targeted regulatory effects in treating depression, demonstrating significant efficacy[7] with a low incidence of adverse reactions.[8] It represents an effective complementary or alternative therapy,[9] however, the specific cellular pathway networks and interaction mechanisms through which it exerts its "holistic, multi-target" regulatory effects remain to be systematically elucidated. Most studies suggest its effects relate to reducing neuroinflammation, regulating immune imbalances, and restoring neurotrophic factors.[10–12] Glial cells, the most abundant cells in the nervous system, participate in immune and inflammatory responses, promote neurogenesis and synaptic plasticity, and maintain the neuronal microenvironment.[13] Their dysfunction directly leads to neuroinflammation, neurotrophic deficiency, and myelin damage. Recent studies indicate

https://doi.org/10.2147/JMDH.S581593
Received: 14 November 2025
Accepted: 25 January 2026
Published: 11 February 2026

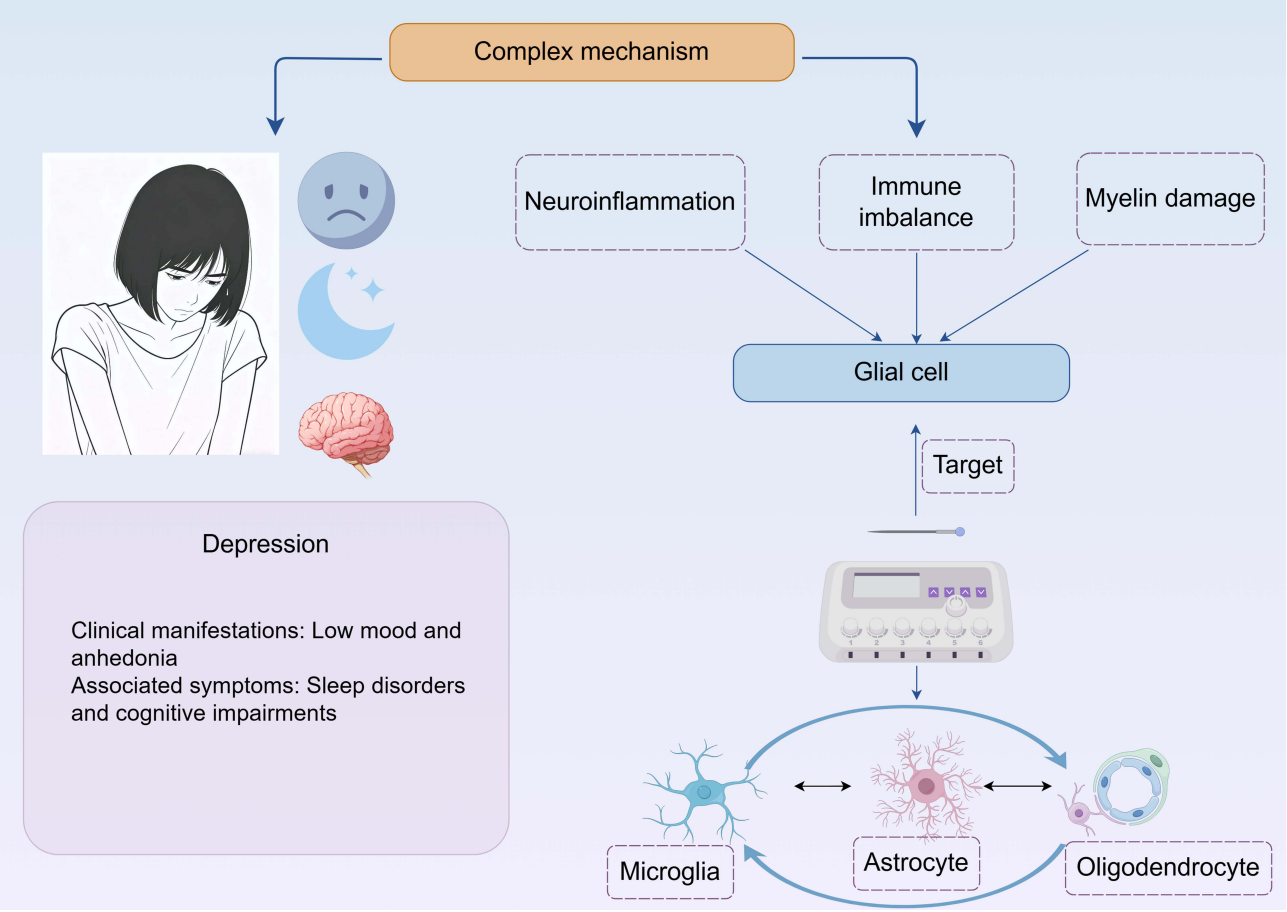

Figure 1 Current Status of Depression Onset and Treatment.

that glial cells represent a novel target for the antidepressant mechanism of acupuncture,[14] as illustrated in Figure 1. Existing research predominantly focuses on individual glial cell types, failing to adequately elucidate how acupuncture modulates the dynamic interactive network comprising microglia, astrocytes, and oligodendrocytes. It is precisely this network that plays a pivotal role in sustaining the pathological cycle of depression. This review does not examine acupuncture's effects on a single glial cell type in isolation, but rather emphasises its holistic regulation of the glial cell interaction network. The onset and progression of depression stem from a vicious cycle formed between different glial cell types. Therefore, elucidating how acupuncture disrupts this harmful network and restores beneficial interactions better captures its "multi-target" therapeutic essence than studying its effects on individual cells. This represents a crucial advancement in understanding its integrated regulatory mechanisms. Although acupuncture treatment is associated with restored glial cell function and alleviated depressive symptoms, much of the evidence primarily reveals strong correlations rather than establishing clear causal sequences within clinical settings. Whether these mechanistic findings can be fully translated to human pathological mechanisms remains to be elucidated in depth; consequently, caution is warranted when interpreting direct causal relationships in clinical applications.

A systematic review of this field remains lacking. This paper therefore focuses on three glial cell types and their interactions, summarising current research on acupuncture's antidepressant effects through glial cell regulation. This provides a foundation for deepening our understanding of the modern biological mechanisms underlying acupuncture's antidepressant properties.

Search Strategy and Selection Criteria

This narrative review synthesises existing evidence linking acupuncture, depression, and glial cell regulation. To ensure comprehensiveness and objectivity, a literature search was conducted across major databases, including PubMed, Web of

Science, and CNKI, covering publications from January 2000 to November 2025. The search strategy employed keyword combinations including "acupuncture", "depression", "microglia", "astrocytes", "oligodendrocytes", and "neuroinflammation".

Inclusion criteria were stratified by study type to encompass diverse dimensions of the review: (1) Clinical evidence: High-quality studies, such as randomised controlled trials (RCTs) and meta-analyses, were selected to evaluate the therapeutic efficacy and safety of acupuncture; (2) Mechanistic evidence: Preclinical studies—particularly those employing specific inhibitors or genetically modified animal models—were included to elucidate molecular mechanisms and cellular interactions. The selection of specific signalling pathways (TLR4/NF-κB) and acupoints (GV20, ST36) was based on their citation frequency in high-quality literature and the robustness of experimental data, ensuring a focus on targets with the strongest scientific validation.

Clinical Application of Acupuncture in Treating Depression

Acupuncture is widely used in clinical practice to treat depression. Many randomized controlled trials and meta-analyses have shown that it is effective. It can be used alone for mild to moderate depression, or together with other treatments for more severe cases. By selecting specific acupoints, acupuncture helps regulate mental state and relieve depressive symptoms. Its clinical efficacy is evidenced not only by improved scores on the Hamilton Depression Rating Scale but also by the alleviation of common related symptoms such as insomnia and anxiety. Acupuncture is thought to work by regulating neurotransmitters like serotonin and norepinephrine, and by reducing inflammation in the body.

These proven clinical effects provide a practical basis for further studying how acupuncture influences glial cells to treat depression. Selected recent studies from 2024–2025 are listed in Table 1.

Glial Cells and the Pathogenesis of Depression

Microglia and Neuroinflammation

Neuroinflammation is an inflammatory reaction that happens in the central nervous system. It is mainly characterized by the activation of microglia and the release of pro-inflammatory cytokines. This process is now considered a key mechanism in depression. There is a two-way relationship between depression and neuroinflammation. On one hand, neuroinflammation

Table 1 Clinical Application of Acupuncture in the Treatment of Depression

Author/Year	Document Type/ Research Subject	Intervention Plan	Primary Outcome Measure	Conclusions and Findings
Wang Dongli et al[15] /2025	Clinical Observation / 30 Cases of Neurogenic Bladder with Anxiety and Depression Following Spinal Cord Injury	Acupuncture: Baihui (GV20), Yintang (GV29), Sanyinjiao (SP6), etc., once daily; Navel therapy: Shenque (CV8), once daily; Continuous treatment for 4 weeks.	Indicators: HAMA, HAMD, urodynamic parameters. Results: Overall response rate of 93.3%. Significant reduction in HAMA and HAMD scores and residual urine volume, with improvement in maximum urinary flow rate.	This demonstrates the efficacy of integrated acupuncture and medication for comorbid affective disorders.
Hao Moujia et al[8] /2025	Meta-analysis / 52 randomized controlled trials (RCTs), 5277 patients with depressive disorders	Comprehensive analysis indicates that the plan encompasses multiple interventions, including acupuncture and electroacupuncture.	Indicators: HAMD score, clinical non-response rate, 5-HT levels, adverse reactions. Results: Acupuncture significantly improved HAMD scores, reduced clinical non-response rates, elevated 5-HT levels, and demonstrated good safety.	Provides the highest level of evidence for acupuncture in treating depression.

(*Continued*)

Table 1 (Continued).

Author/Year	Document Type/ Research Subject	Intervention Plan	Primary Outcome Measure	Conclusions and Findings
Gao Yuyan et al[16] /2025	RCT / 75 patients with post-stroke depression (PSD)	Electroacupuncture for Calming the Mind and Relieving Depression: Select points including Shenmen (HT7) and Neiguan (PC6). Apply sparse-dense wave (2/20 Hz) once daily for 8 consecutive weeks.	Indicators: HAMD, NIHSS, hs-CRP, IL-6, Hcy. Results: Significant improvement in depressive symptoms and neurological function, reduction in inflammatory markers, with superior efficacy compared to the sham acupuncture group.	The study revealed the mechanisms by which acupoint selection in the Heart Sutra demonstrates anti-inflammatory and antidepressant effects.
Liu Jingjing et al[17] /2025	RCT / 119 patients with post-stroke depression	Acupuncture: Baihui (GV20), Yintang (GV29), once every other day; combined with Chinese herbal medicine; treatment duration: one month.	Indicators: HAMD, NIHSS, NE, 5-HT levels. Results: Overall response rate: 96.67%. Demonstrated superiority over the conventional Western medicine group in improving depression scores, neurological function, and neurotransmitter levels.	This demonstrates the efficacy of acupuncture in treating depression and the advantages of integrating traditional Chinese and Western medicine.
Li H, Wu H, Cui J[18] /2025	RCT / 60 patients with chronic insomnia and mild depression	Acupuncture: Zhaohai (KI6), Shenmen (HT7), etc.; combined with bamboo moxibustion on abdominal and Governor Vessel points, three times weekly for four consecutive weeks.	Indicators: PSQI, HAMD-17, ISI, serum GABA. Results: Overall response rate was 96.7%. The treatment group demonstrated superior efficacy compared to the acupuncture-only group in reducing PSQI, HAMD-17, ISI, and FAI scores, as well as increasing GABA levels.	This study demonstrates the synergistic therapeutic effect of combining acupuncture with moxibustion for chronic insomnia complicated by mild depression.
Li Zhongxian et al[19] /2025	Clinical Observation: 24 Patients with Co-occurring Depression and Insomnia	Integrated Acupuncture: Needle Baihui (GV20) and Neiguan (PC6); Apply moxibustion to Zhongwan (CV12) and Qihai (CV6); Retain needles at Xinshu (BL15). Administer treatment every other day for 6 weeks.	Indicators: PSQI, HAMD-17, fMRI, serum NE, CORT, etc. Results: Significant improvement in sleep and depression scores post-treatment, elevated serum NE, decreased CORT, and enhanced functional connectivity between the right locus coeruleus and left inferior frontal gyrus.	The role of integrated therapy has been demonstrated at the levels of imaging and biochemistry.
Zhang Xi[20] /2025	RCT / 90 patients with mild to moderate depression	"Electroacupuncture for Qi Regulation": Apply at Zhongwan (CV12)-Guanyuan (CV4) and Hegu (LI4)-Taichong (LR3) points using continuous wave (2 Hz) at 3 sessions per week, combined with medication for 8 weeks.	Indicators: HAMD-17, PSQI, WHOQOL-BREF, SERS. Results: The "electroacupuncture with qi regulation + medication" group demonstrated superior outcomes compared to both the "sham electroacupuncture + medication" group and the "medication alone" group in improving depression, sleep, quality of life, and reducing medication dosage and side effects.	This demonstrates the synergistic effect of acupuncture as a complementary therapy.

(*Continued*)

Table 1 (Continued).

Author/Year	Document Type/ Research Subject	Intervention Plan	Primary Outcome Measure	Conclusions and Findings
Xu Kun et al[7] /2024	RCT / 64 patients with mild to moderate depression	Electroacupuncture for Regulating Qi and Relieving Depression: Select points including Baihui (GV20) and Shenting (GV24). Connect Baihui to Yintang with electroacupuncture needles. Apply continuous wave (2 Hz). Administer 3 times weekly for 8 weeks.	Indicators: HAMD-17, PHQ-9, SAS, SF-36. Results: The electroacupuncture group demonstrated significantly greater improvement in depressive and anxious symptoms and quality of life compared to the sham acupuncture group.	The antidepressant value of acupuncture at points along the Governor Vessel has been confirmed.
Lu Jiajing et al[21] /2024	RCT / 76 patients with post-stroke depression (PSD)	Acupuncture Points: Shangxing (GV23), Baihui (GV20), Shenting (GV24), Fengchi (GB20), Shuigu (GB8) Supplementary Points: Tai Chong (LR3), He Gu (LI4), Qu Chi (LI11), Nei Guan (PC6), Yang Ling Quan (GB34), Zu San Li (ST36), Tai Xi (KI3) 5 sessions per week, for 4 consecutive weeks.	Indicators: HAMD, MBI, 5-HT, NE, gut microbiota. Results: The acupuncture group demonstrated superiority over the control group in reducing HAMD scores, improving activities of daily living, and regulating neurotransmitters.	Acupuncture may exert antidepressant effects by regulating the gut-brain axis.

can cause depressive symptoms. It does this by increasing pro-inflammatory cytokines and activating the HPA axis (a key stress response system). This affects neurotransmitter systems and disrupts normal brain chemical metabolism. As a result, levels of serotonin (5-HT) decrease, and neurotoxic substances are produced. These changes eventually lead to symptoms such as loss of pleasure and persistent low mood.[22] On the other hand, depressive symptoms can also worsen inflammation. This is closely related to microglial function.[23] Under normal conditions, microglia are in a resting state (called M2), which helps maintain balance in the central nervous system. However, chronic stress or signals from inflammation in the body can activate microglia.[24] When activated, they switch from the M2 state to a pro-inflammatory state (M1). In this state, microglia release more pro-inflammatory cytokines, which further increases neuroinflammation. At the same time, activated microglia trigger a series of downstream effects. These involve the neuroendocrine system, monoamine neurotransmitters, and oxidative stress pathways.[25] They also suppress the birth of new neurons in important brain regions like the hippocampus and prefrontal cortex, promote cell death, and disrupt synaptic plasticity.[26] Together, these changes impair normal brain function and mood regulation. Therefore, the shift of microglia from the M2 to the M1 state is a central process through which neuroinflammation causes or worsens depression.

Astrocytes and Neurological Homeostatic Dysregulation

An imbalance in neurological homeostasis is a key pathological mechanism in depression. This includes problems in synaptic, mitochondrial, and retinoid homeostasis.

Disruption of synaptic homeostasis can harm emotional and cognitive functions.[27] Research on how this imbalance leads to depressive symptoms is relatively clear, especially regarding monoamine neurotransmitters like serotonin (5-HT), norepinephrine (NE), and dopamine (DA).[28–30] However, there is still limited evidence on the role of GABAergic and glutamatergic systems.

Mitochondrial homeostasis imbalance contributes to depression by causing energy shortages in key brain regions. This happens through problems in aerobic oxidation, mitochondrial formation, and autophagy.[31] How mitochondria interact with other cell components such as the endoplasmic reticulum still needs more study.

Otto LR et al found that depressed patients have significantly higher serum retinol levels compared to healthy people.[32] This suggests that disrupted retinol homeostasis also plays a role in depression. Retinol may affect mood by influencing neurotransmitter balance in brain regions like the hippocampus, hypothalamus, and orbitofrontal cortex,[33] though this area of research is still in early stages.

Astrocytes are the most common and largest type of glial cell in the nervous system. They perform many important functions, including structural support, nutrient supply, ion balance regulation, blood-brain barrier maintenance, and signal transmission. They also help start immune responses, release cytokines, repair nerve damage, and—most importantly—maintain overall homeostatic balance in the brain.[34]

When astrocytes do not function properly, they can disrupt this balance and contribute to depression. For example: Astrocytes normally remove glutamate from synapses using special transporters. If this process fails, glutamate builds up and causes excitotoxicity, which damages synapses and neurons. Since this process is energy-dependent, impaired transport further disrupts cellular energy metabolism.[35] Astrocytes help release neurotrophic factors such as BDNF. If this function is impaired, it affects the survival, development, and synaptic plasticity of neurons in areas like the hippocampus and prefrontal cortex. This can lead to abnormal connections in brain networks.[36] Malfunction of the Cx43 gap junction protein in astrocytes disrupts communication between neurons and glial cells. This can cause abnormal neurotransmitter activity and interfere with electrical signaling, making synaptic imbalance worse.[37] Astrocytes also supply energy to neurons through processes such as the lactate shuttle. If they cannot perform this role, neurons may not get enough energy. Moreover, mitochondrial problems in astrocytes themselves can worsen the brain's energy crisis.[38] Some studies also suggest that astrocyte dysfunction might affect mood through the retinoic acid signaling pathway, though the exact mechanisms are still unclear.[39]

In summary, when astrocytes do not work correctly, they disrupt synaptic function, energy metabolism, and cell signaling. Together, these effects contribute significantly to the development of depression.

Oligodendrocytes and Myelin Damage

Myelin helps regulate information transmission within neural circuits[40] and is involved in the development of depression. Studies have shown that people with depression often have significant white matter damage and loss of myelin in the brain.[41] When myelin is damaged, it can reduce the efficiency of communication between different brain regions. This may contribute to the development of mood disorders[42] and is considered a key neuropathological feature of depression. Brain imaging studies also support this. They show that the white matter tracts connecting the prefrontal cortex to limbic areas—such as the corpus callosum and anterior cingulate cortex—are often less intact in depressed patients.[43] This damage slows down neural signaling and disrupts coordination between brain regions.[44] As a result, the prefrontal cortex has less control over the amygdala, which can lead to increased negative emotions. Based on these findings, Hoogenboom WS et al suggested that specific white matter abnormalities may explain why some people experience long-term, treatment-resistant depression. The study also noted that these structural differences can vary between men and women.[45] Oligodendrocytes are the cells responsible for producing myelin and maintaining white matter integrity.[46] When oligodendrocytes do not function properly, it can lead to reduced myelin formation or even demyelination, as seen in mouse studies.[47,48] In addition, chronic stress or neuroinflammation can prevent oligodendrocyte precursor cells (OPCs) from maturing properly, which may worsen depression.[49] Given these findings, researchers such as Tan Hui have suggested that antidepressant treatments may work in part by promoting myelin regeneration and improving white matter integrity.[50] For example, Adili A et al used phosphodiesterase 4 (PDE4) inhibitors to raise cAMP levels in the brain. This treatment promoted the differentiation of oligodendrocyte progenitor cells and facilitated myelin repair.[51] Together, this evidence indicates that oligodendrocytes—through their role in myelin maintenance and repair—are importantly involved in both the development and treatment of depression.

The relationship between the three types of glial cells and depression is summarized in Table 2.

Glial Cell Interactions and Vicious Cycles

Depression arises from interactions between microglia, astrocytes, and oligodendrocytes,[52,53] with the relationship between microglia and astrocytes being particularly critical. When microglia are activated (M1), they release

Table 2 The Role of Three Types of Glial Cells in Depression

Cell Type	Primary Function	Relationship with Depression	Key Mechanisms Mediating the Onset and Progression of Depression
Microglia	Maintain central nervous system stability	Induces neuroinflammation, exhibiting a bidirectional relationship with depression	1. Phenotypic conversion; 2. Release of inflammatory mediators; 3. Impairment of neural plasticity.
Astrocyte	Maintains synaptic, energy, and neurotransmitter homeostasis while providing neurotrophic support.	Induces multiple homeostatic imbalances, leading to depression.	1. Glutamate homeostasis disruption; 2. Loss of neurotrophic support; 3. Inadequate energy support; 4. Signal transduction disorder.
Oligodendrocyte	Form and maintain myelin sheaths to ensure the integrity of white matter and the efficiency of nerve conduction.	Dysfunction and loss lead to myelin damage and reduced white matter integrity.	1. Myelin synthesis is impaired; 2. Nerve conduction is delayed;

inflammatory factors that are not only neurotoxic but also impair astrocytic glutamate uptake. This happens through downregulation of the angiotensin II type 2 receptor (AT2), which can push astrocytes into a neurotoxic A1 phenotype.[54] In turn, impaired astrocytes release fewer anti-inflammatory factors and more pro-inflammatory factors. This further activates microglia and sustains neuroinflammation, creating a cycle of damage.[55] Both microglia and astrocytes also harm oligodendrocytes. The inflammatory substances they release prevent OPCs from maturing properly and can cause existing oligodendrocytes to die.[56] As a result, myelin production decreases and white matter integrity is damaged. Additionally, when astrocytes do not function normally, they fail to provide adequate metabolic and neurotrophic support to oligodendrocytes, which worsens myelin damage.[57] Oligodendrocyte injury also affects microglia. Damage to oligodendrocytes and breakdown of myelin produce substances that are detected by microglia. Together with iron buildup caused by ferroportin 1 (FPN1) deficiency, this further activates microglia and increases neuroinflammation.[58] This creates a vicious cycle.

In summary, glial cell pathology in depression is a dynamic and interconnected process involving multiple cell types. Figure 2 summarizes the roles of microglia, astrocytes, and oligodendrocytes in neuroinflammation, homeostatic imbalance, and myelin damage. Because these three glial cell types play such important roles in depression, we next examined how acupuncture can influence them to produce antidepressant effects. We found that acupuncture—based on the holistic principles of Traditional Chinese Medicine—can intervene at multiple targets and shows considerable potential as a treatment for depression.

Acupuncture Modulates Glial Cells for Antidepressant Effects

Suppression of Microglial Activation and Regulation of Neuroinflammation

One of the core mechanisms of acupuncture in antidepressant treatment is that acupuncture can regulate the phenotypic transformation of microglia and their key signaling pathways, thereby achieving the effect of inhibiting neuroinflammation. Multiple studies have shown that electroacupuncture stimulation at acupoints such as Baihui (GV20), Dazhui (GV14), Zusanli (ST36), Quchi (LI11), Shangxing (GV23), and Fengfu (GV16) can down-regulate pro-inflammatory factors such as IL-1β, IL-18, TNF-α, and IL-6, and inhibit M1-type transformation; at the same time, it can up-regulate and increase anti-inflammatory factors such as Arg-1, IL-4, and IL-10, promote M2-type transformation, reverse microglial activation, thereby reducing hippocampal neuroinflammation and repairing neuronal injury.[59–63] However, whether there are differences in the anti-inflammatory effects mediated by different acupoint combinations in terms of onset efficiency, action intensity, or downstream signaling pathways has not been confirmed. In addition, acupuncture can also inhibit the abnormal phagocytic activity of microglia (down-regulate the expression of MERTK and LAMP2), and protect synaptic structure and neural network function.[64–66] For example, Li W et al found that electroacupuncture

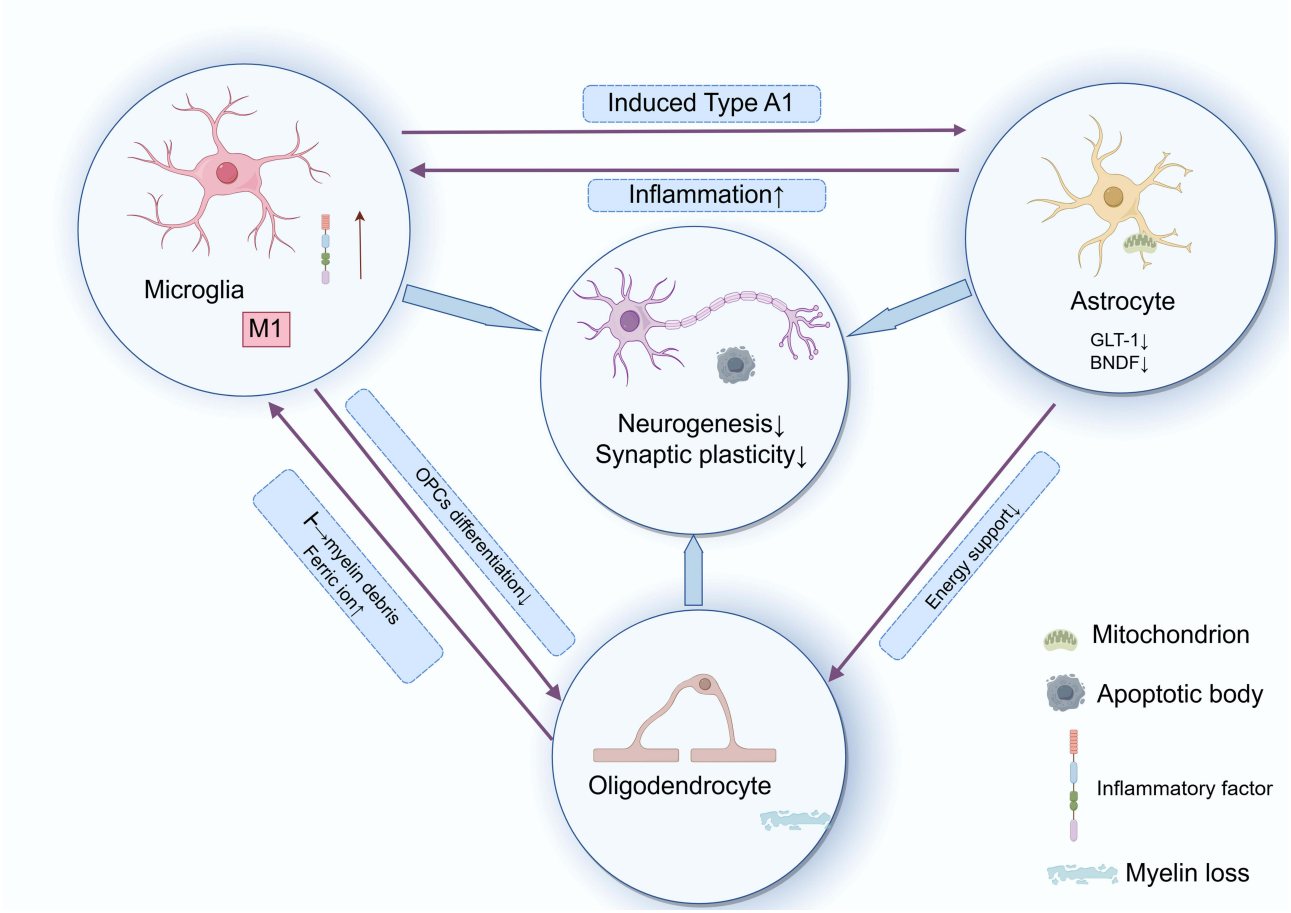

Figure 2 The Vicious Cycle of Glial Cells in Depression. The figure illustrates reciprocal interactions among microglia, astrocytes, and oligodendrocytes under inflammatory conditions, forming a self-reinforcing cycle that contributes to neuroinflammation, impaired synaptic plasticity, and myelin loss. An upward arrow (↑) indicates increased activity or expression, while a downward arrow (↓) denotes decreased activity or expression. A solid purple arrow represents specific intercellular interactions under inflammatory conditions. An inhibitory arrow (⊣→) indicates a directional suppressive effect on the indicated cellular processes or functions.

stimulation at GV20 and ST36 can down-regulate the expression of MERTK, a molecule related to phagocytic function, and LAMP2, a lysosomal marker, thereby reducing the phagocytosis of PSD-95-positive synaptic structures, and ultimately improving neural circuit function and emotional behavior.[67]

The above phenotypic transformation is regulated by multiple signaling pathways, and acupuncture can regulate these key signaling pathways. Acupuncture at GV20 and Yintang (GV29) can inhibit the classic inflammatory pathway TLR4/MyD88/NF-κB, promote the expression of anti-inflammatory factors such as IL-10 and Arg-1.[68] Stimulating acupoints of the Liver Meridian such as Ququan (LR8) and Zhongfeng (LR4), as well as Yingu (KI10), can also inhibit the cGAS-STING-NLRP3 pathway, down-regulate the expression of NLRP3 and Caspase-1,[69,70] thereby reducing the release of pro-inflammatory factors such as IL-1β and IL-18, and alleviating pyroptosis. However, the study by Huang Wentao et al pointed out that acupuncture at Baihui (GV20) and Yintang (GV29) can activate the IL-4-JAK1-STAT6 anti-inflammatory pathway, promote the transformation of microglia to M2 type, and simultaneously inhibit pro-inflammatory signals such as TNF/NF-κB/mTOR.[71] Cao S pointed out that electroacupuncture stimulation at Zusanli (ST36), Tianshu (ST25), and Taichong (LR3) can inhibit HMGB1-mediated inflammatory reaction and pyroptosis pathway (NLRP3/CASP-1/GSDMD), reduce the release of inflammatory factors, and improve synaptic plasticity.[72] In addition, in the sleep deprivation model, electroacupuncture can also regulate clock genes (Bmal1/Clock), inhibit the activation of NF-κB pathway, and reverse the M1 polarization of microglia.[73] To sum up, acupuncture can inhibit microglial activation by regulating multiple signaling pathways, improve neuroinflammation and promote the formation

of anti-inflammatory microenvironment, thereby exerting antidepressant effect, which reveals the multi-target characteristics of acupuncture, as shown in Figure 3.

It is worth noting that the regulatory effect of electroacupuncture is related to its stimulation parameters (such as frequency, waveform, intensity) and the selection of acupoints.[68] Zusanli (ST36), Baihui (GV20), and Yintang (GV29) are high-frequency acupoints. Electroacupuncture with different frequencies may have different effects in the treatment of Depression. However, there is currently no consensus on the optimal combination of electroacupuncture parameters for different depression models. Systematically exploring the influence of parameters such as frequency and intensity on glial cell transformation will be an important direction for future research on acupuncture for antidepressant therapy.

Restoring Astrocyte Function and Neuromicroenvironmental Homeostasis

Acupuncture promotes the secretion of multiple neurotrophic factors by astrocytes, such as brain-derived neurotrophic factor (BDNF),[74] fibroblast growth factor 2 (FGF2),[75] transforming growth factor-β (TGF-β),[76] and glial cell-derived neurotrophic factor (GDNF),[14] thereby restoring their energy-supplying function and exerting antidepressant effects. Scholars hold differing views on acupoint selection and underlying mechanisms. Yao Z noted that electroacupuncture stimulation at Baihui (GV20) and Yintang (GV29) upregulates hippocampal FGF2 expression, enhances astrocyte activity, and ameliorates depression-like behaviour in the chronic unpredictable mild stress (CUMS) model, indicating the FGF2-astrocyte axis as a key mechanism in electroacupuncture's antidepressant effects.[75] Li P's research indicates that acupuncture at Shangxing (GV23) may influence neurotrophic factors in the nervous system by regulating gut microbiota and metabolites,[77] or directly modulate factors such as TGF-β to participate in the antidepressant process.[78]

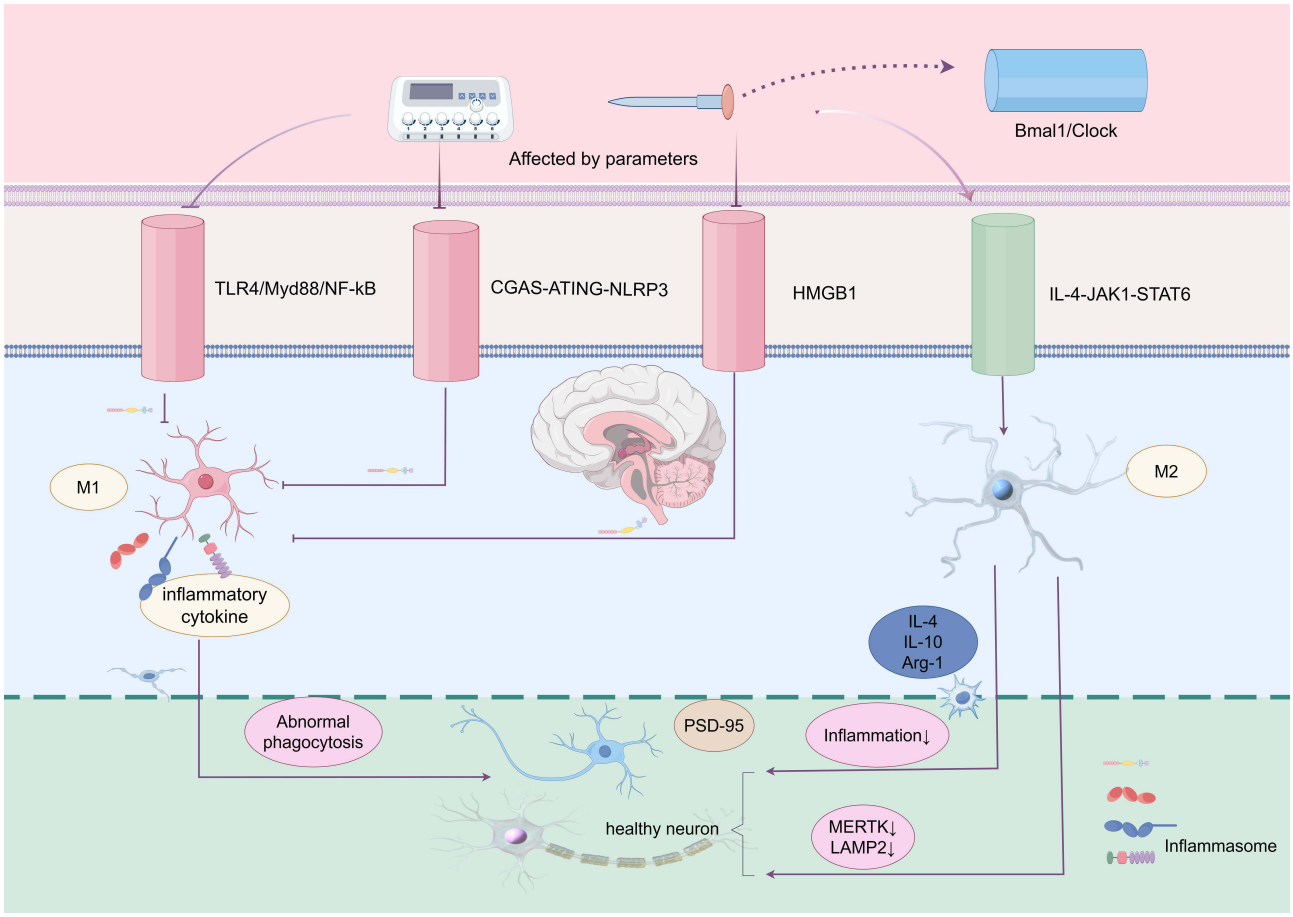

Figure 3 Acupuncture Modulates Neuroinflammation by Inhibiting Microglia Through Multiple Target Points. The figure illustrates the regulatory effects of acupuncture on microglial activation and neuroinflammation, highlighting its role in promoting anti-inflammatory microglial polarization, reducing aberrant inflammatory responses, and preserving synaptic integrity through multi-target mechanisms.

https://doi.org/10.2147/JMDH.S581593

Building upon this, Wang Wei further indicated that multiple neurotrophic factors secreted by astrocytes can activate downstream receptors such as TrkB/GFRα and signal pathways including CREB/MAPK, thereby mitigating neuronal damage, promoting neuronal regeneration, and exerting antidepressant effects.[79]

The function of astrocytes extends beyond providing nutritional support, playing a crucial role in maintaining the homeostasis of the neuroinflammatory microenvironment. Acupuncture modulates astrocyte function through multiple targets, restoring glutamate metabolic balance in depressive models and thereby reshaping the neuroinflammatory microenvironment. Luo et al demonstrated that electroacupuncture stimulation at Tai Chong (LR3) and He Gu (LI4) significantly reduced glutamate levels in the hippocampus and prefrontal cortex, while upregulating glutamine synthetase (GS) and glutamate transporter (GLT-1/GLAST) expression within astrocytes, thereby mitigating excitotoxicity.[80] Building upon this, Cai M and Lai LF discovered that electroacupuncture stimulation of Baihui (GV20), Yintang (GV29), Dazhui (GV14) further regulates glutamate homeostasis and NMDA receptor subtype balance by increasing NR2A and decreasing NR2B expression. This inhibits the CaMKII-Bax-caspase3 apoptotic pathway while promoting Bcl-2 expression, thereby enhancing neuronal survival and synaptic plasticity.[81,82] To investigate its metabolomic evidence, Xu Xuejiao et al discovered that acupuncture modulates metabolites such as L-glutamate and taurine, influencing aminoacyl-tRNA biosynthesis and amino acid metabolic pathways to protect neurotransmission.[83] Furthermore, acupuncture can regulate astrocytic transformation via the ERK1/2-Cx43 pathway, suppressing Cx43 expression and restoring neuromicroenvironmental homeostasis.[84] Notably, acupuncture may exhibit distinct regional specificity in modulating glial cells across different brain areas. For instance, Wu Zonglin et al demonstrated that electroacupuncture at ST36 (Zusanli) and SP6 (Sanyinjiao) alleviates pain sensitisation and anxiety-like behaviour in SNI-induced mice by regulating the dorsal raphe nucleus-basolateral amygdala neural circuit;[85] while Zhang C et al indicated that electroacupuncture at Baihui (GV20) and Zusanli (ST36) effectively ameliorates neuroinflammatory responses and synaptic structural damage in the hippocampus;[86] Jiang Shuo et al demonstrated that electroacupuncture at Hegu (LI4) and Taichong (LR3) aids in repairing morphological abnormalities and structural damage in hippocampal astrocytes of chronic stress-induced depression model rats.[87] Although these mechanisms support acupuncture's role in restoring neuroinflammatory homeostasis, its direct regulation of astrocytic ion balance and the specific effects of different acupoints warrant further investigation.

The role of acupuncture in regulating astrocyte function to restore neuroinflammatory homeostasis is summarized in Figure 4.

Promoting Oligodendrocyte Regeneration and Myelin Repair

Acupuncture exerts antidepressant effects by promoting oligodendrocyte proliferation and differentiation while inhibiting apoptosis,[88] thereby ameliorating myelin damage. Research indicates that electroacupuncture stimulation at Zusanli (ST36) and Taixi (KI3) significantly promotes OPC proliferation and induces their differentiation into mature oligodendrocytes, via mechanisms involving upregulation of the Olig2 transcription factor and suppression of DNA-binding inhibitor 2 (Id2) expression.[89] Concurrently, electroacupuncture at ST36 and KI3 suppresses endoplasmic reticulum stress and mitochondrial apoptosis pathways, safeguarding existing oligodendrocytes. This enhances myelin basic protein (MBP) expression, ultimately promoting myelin repair and motor function recovery.[90] Restored myelin integrity ensures efficient neural signal transmission, thereby enhancing brain function and alleviating emotional distress.[91] Severe depression is frequently accompanied by cognitive impairment. In a study investigating electroacupuncture intervention for cognitive deficits in vascular dementia caused by myelin damage, Liu C noted that stimulating Baihui (GV20) and and Shenting (GV24) may mitigate inflammation by inhibiting NF-κB activation, thereby promoting OPC differentiation and myelin repair. This improved learning and memory functions in rats with vascular dementia, suggesting electroacupuncture may enhance myelin regeneration by regulating the NF-κB signalling pathway, thus alleviating cognitive impairment.[92] Although the aforementioned studies were conducted in spinal cord injury demyelination models and vascular dementia models, given the close association between oligodendrocyte dysfunction and impaired white matter integrity in depression, coupled with acupuncture's capacity to promote myelin regeneration, we propose that acupuncture-targeted modulation of oligodendrocytes may offer novel therapeutic targets for depression treatment.

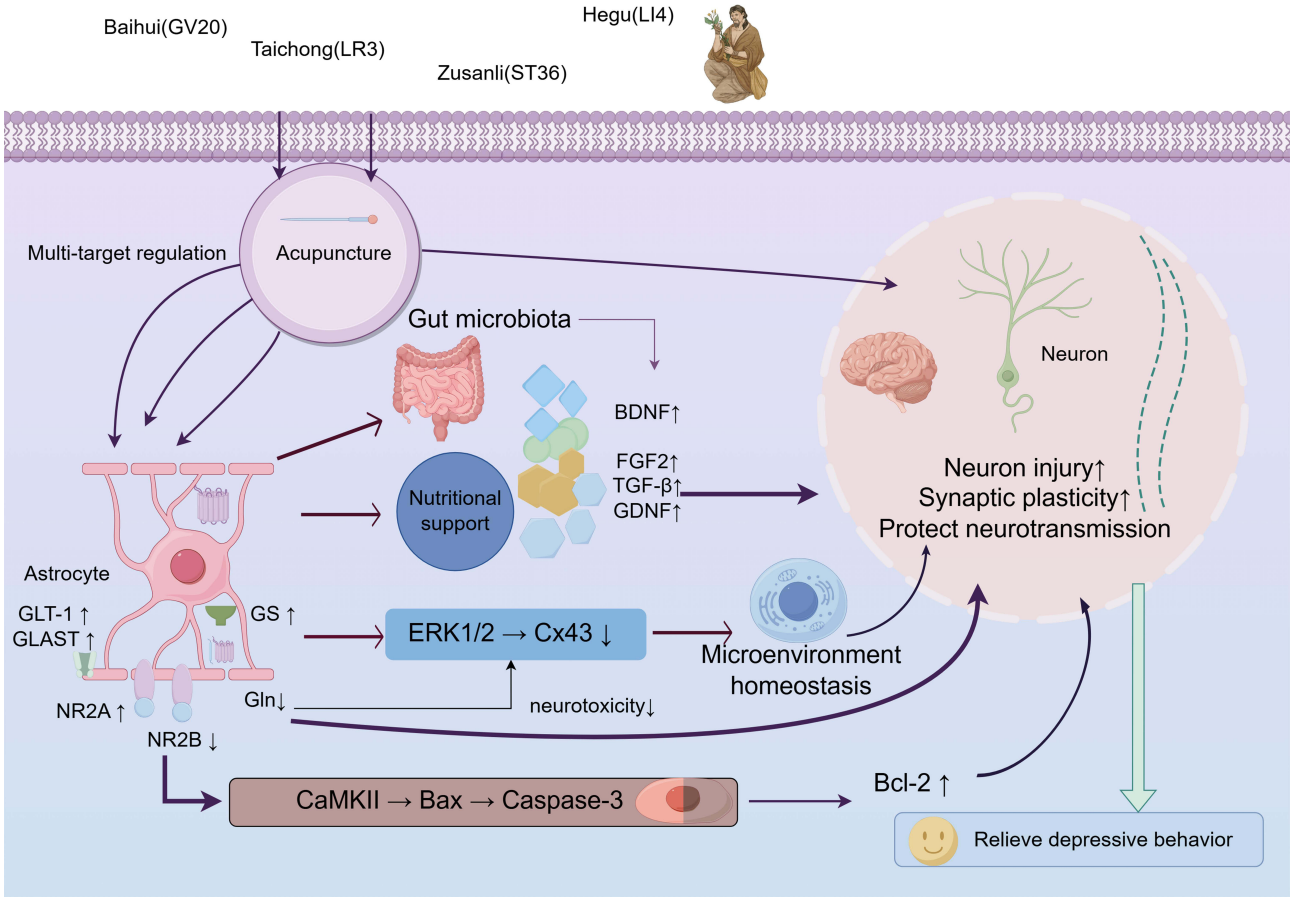

Figure 4 Mechanism of Acupuncture in Regulating Astrocyte Function to Restore Microenvironmental Homeostasis. The figure illustrates the regulatory effects of acupuncture on astrocyte function and neuromicroenvironmental homeostasis. Acupuncture enhances neurotrophic support, maintains glutamate metabolic balance, and protects synaptic plasticity and neuronal survival through integrative, multi-target actions.

In summary, one important way acupuncture may help treat depression is by regulating oligodendrocytes and promoting the repair of myelin. This process is illustrated in Figure 5.

Regulation of Glial Cell Interactions by Acupuncture

Acupuncture Modulation of Microglia-Astrocyte Interactions

The communication between microglia and astrocytes is very important in depression. These two types of cells work together in a closely connected network, and their interaction affects both neuroinflammation and the balance of neural function.[93,94] When microglia become activated (M1), they release substances such as IL-1α, TNF, and C1q. These signals can cause nearby astrocytes to change into a neurotoxic A1 phenotype, which worsens inflammation and damages neurons.[95] Acupuncture can help reduce this damaging cycle. It suppresses the overactivation of microglia and decreases the release of pro-inflammatory factors. This prevents astrocytes from transitioning into the neurotoxic A1 phenotype. At the same time, acupuncture increases the expression of GLT-1, a glutamate transporter in astrocytes. This helps restore normal glutamate levels and supports the release of anti-inflammatory factors.[96,97] These changes also provide better support to microglia, improving their function and strengthening protective interactions between the two cell types. Overall, acupuncture helps relieve depression and protect the brain by regulating both microglia and astrocytes. It blocks their harmful interactions while encouraging their beneficial cooperation. Targeting this microglia-astrocyte communication may be a specific and effective approach for acupuncture in treating depression. However, more research is needed to understand how acupuncture promotes the shift of microglia to the M2 type and astrocytes to the A2 type.

https://doi.org/10.2147/JMDH.S581593

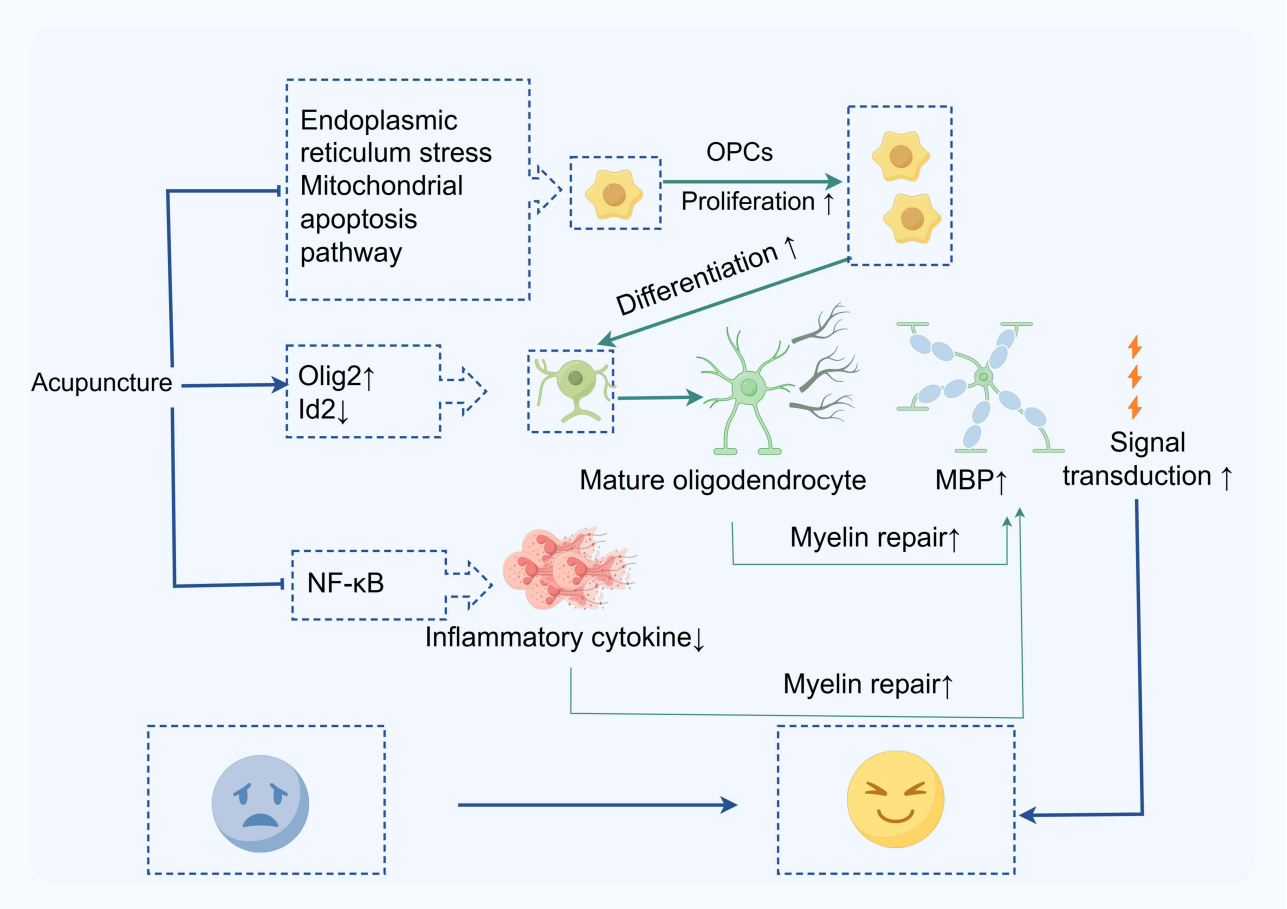

Figure 5 Mechanism of Acupuncture in Promoting Oligodendrocyte Regeneration and Myelin Repair. The figure illustrates the regulatory effects of acupuncture on oligodendrocyte regeneration and myelin repair. By promoting OPC proliferation and differentiation while inhibiting apoptosis and inflammatory responses, acupuncture contributes to restored myelin integrity and improved neural function.

So far, most studies have looked at microglia and astrocytes separately. There is still limited understanding of how acupuncture affects the communication between them. Future research should focus more on how acupuncture regulates these cellular interactions to produce antidepressant effects. This is expected to provide new insights and inform novel treatment strategies for depression.

The way acupuncture regulates microglia-astrocyte interactions is summarized in Figure 6.

Potential Regulatory Effects of Acupuncture on Oligodendrocytes via the Glial Network

Under disease conditions, astrocytes and microglia can harm OPCs. They do this by releasing inflammatory cytokines, which reduce OPC survival and prevent them from maturing.[98] Microglia also release exosomes that may influence myelin regeneration through the Nrf2 signaling pathway in OPCs.[99] Currently, there is limited evidence showing how microglia and astrocytes directly control oligodendrocyte function. Oligodendrocytes are mostly seen as cells that react to inflammation and injury. However, they may also help regulate their environment by releasing certain signals or metabolites—though this needs more study.

So far, few studies have directly examined how acupuncture affects oligodendrocytes. It is also unclear whether oligodendrocytes send feedback signals to other glial cells. Still, a key way acupuncture may help treat depression is by shifting the glial network from a diseased state back to a healthy one.[100] By calming overactive microglia and harmful astrocytes, acupuncture can reduce their damaging effects on oligodendrocytes. At the same time, it encourages microglia and astrocytes to take on helpful roles (such as M2 and A2), which increases the release of neurotrophic factors and

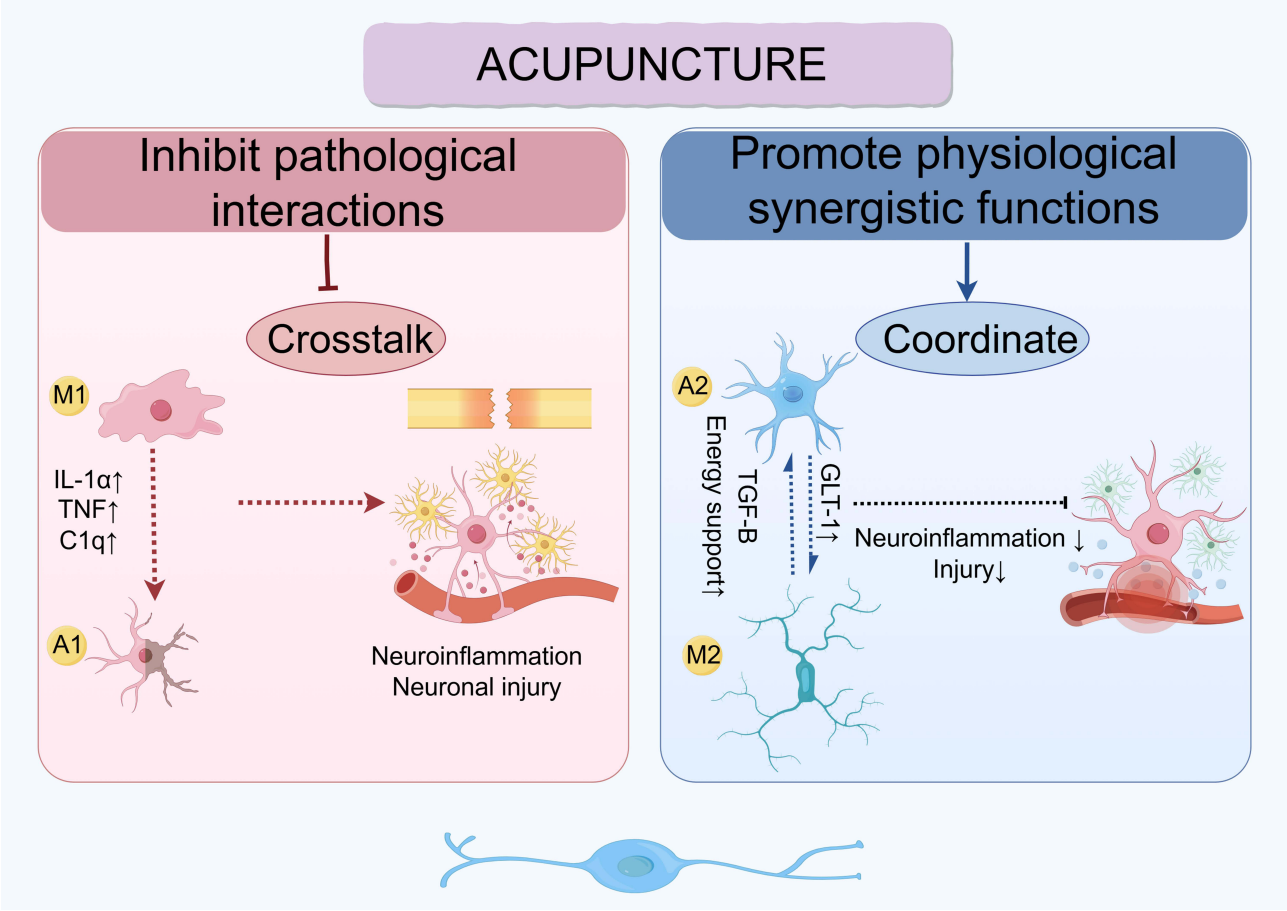

Figure 6 Acupuncture synergistically regulates the antidepressant effects of microglia-astrocyte interactions. The figure illustrates the regulatory effects of acupuncture on microglia–astrocyte interactions. Acupuncture suppresses pathological inflammatory crosstalk and promotes coordinated, neuroprotective cooperation between microglia and astrocytes. In the figure, dashed arrows (⇢) indicate hypothesized connections based on current evidence, and the symbol "⊣" denotes an inhibitory effect.

antioxidants. This creates a healthier environment for OPCs to develop and produce myelin. In this way, acupuncture indirectly supports oligodendrocyte function by first improving how microglia and astrocytes interact. This reflects the holistic way acupuncture may work against depression. Future research should focus on whether acupuncture directly affects signaling pathways in oligodendrocytes, and how these cells communicate with other glial cells. This will help us better understand the full picture of how acupuncture helps repair myelin and improve mood.

The potential ways acupuncture may regulate oligodendrocytes are shown in Figure 7.

Acupuncture's Holistic Regulation of Upstream Signaling Pathways

Acupuncture produces antidepressant effects by regulating common signaling pathways that influence all three types of glial cells. These pathways include those involved in inflammation, neuroprotection, metabolism, stress response, and epigenetic regulation. Reducing neuroinflammation is an important first step. Research shows that acupuncture can inhibit several key inflammatory pathways, such as NF-κB, NLRP3/caspase-1/IL-1β, and TLR4/MyD88. For example, Li M et al found that acupuncture lowers activity in the NF-κB pathway, which reduces the release of pro-inflammatory factors like TNF-α and IL-1β in microglia.[101] This also helps restore normal function in astrocytes and reduces inflammation-related damage to oligodendrocytes.[102] Chen Y et al further showed that acupuncture suppresses the NLRP3 inflammasome pathway. This reduces pyroptosis (a type of inflammatory cell death) in microglia and decreases their harmful effects on astrocytes and oligodendrocytes.[103,104] Acupuncture also affects the TLR4/MyD88 pathway, which helps block NF-κB from entering the cell nucleus. This enhances the overall anti-inflammatory response.[105] In addition to reducing inflammation, acupuncture supports nerve repair by activating neurotrophic and cell-protective

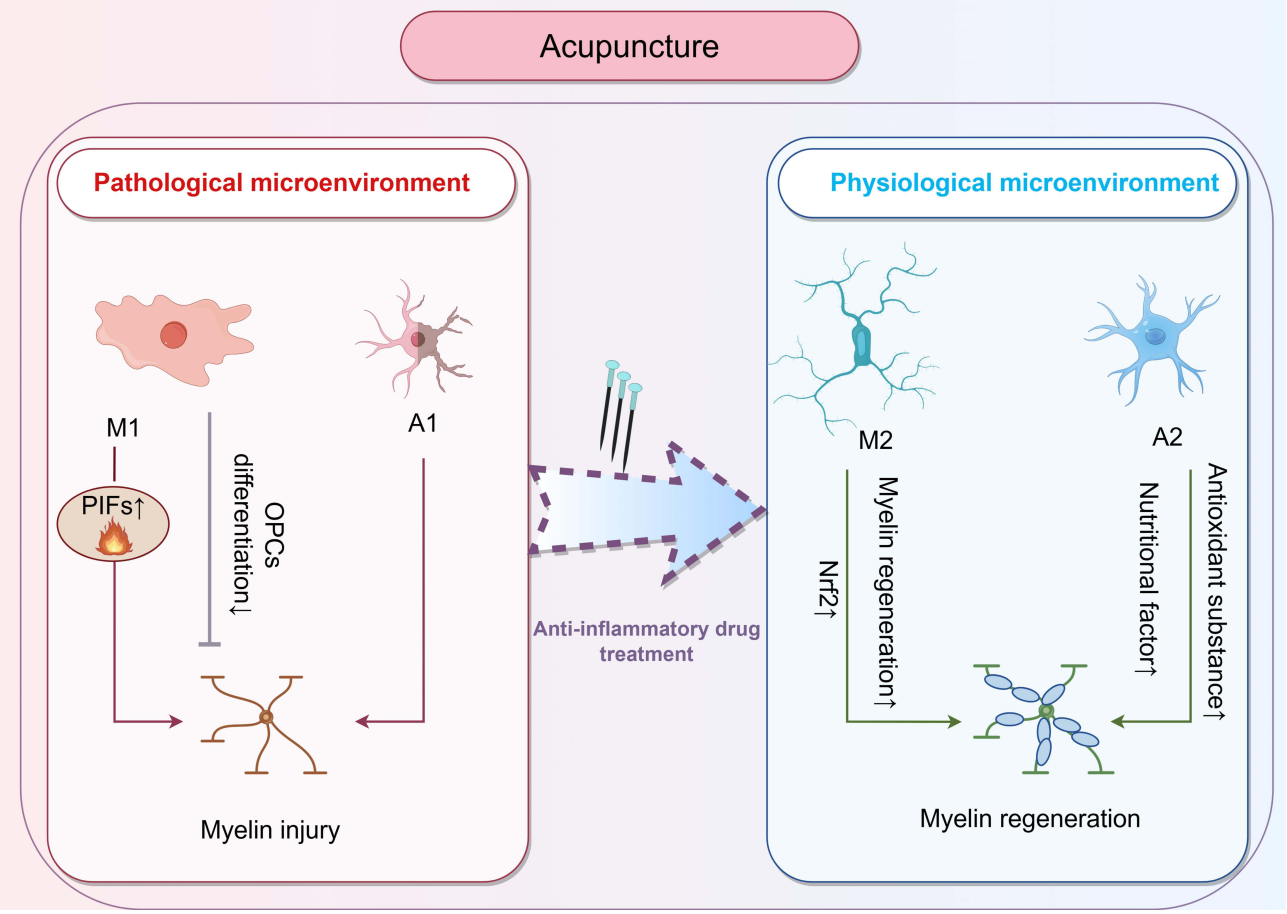

Figure 7 Acupuncture indirectly regulates oligodendrocyte function by reshaping the glial microenvironment. The figure illustrates how acupuncture may indirectly regulate oligodendrocyte function through modulation of the glial network. By suppressing pathological inflammatory interactions and promoting protective glial phenotypes, acupuncture contributes to a microenvironment favorable for myelin regeneration.

pathways. A central pathway is BDNF-TrkB signaling. When this pathway is activated, it improves the ability of astrocytes to support neurons.[106,107] It also triggers downstream signals such as PI3K/Akt and MAPK/ERK, which help neurons survive, strengthen synapses, and assist oligodendrocytes in producing myelin.[108,109] Unlike the "inhibitory" effect on inflammatory pathways, acupuncture "activates" these protective pathways. The two actions work together: reducing inflammation creates a better environment for repair, while neurotrophic signals directly stimulate regeneration. Acupuncture also helps glial cells better cope with stress. It activates the Nrf2/ARE pathway, which increases antioxidant capacity in astrocytes and microglia.[110] At the same time, it helps restore balance in cellular autophagy through the mTOR pathway, improving mitochondrial function.[111] These changes support glial cells by reducing oxidative stress and improving energy use. Recent studies also suggest that acupuncture may produce long-term benefits through epigenetic mechanisms. For instance, it can reduce HDAC activity and lower DNA methylation near the BDNF gene. This leads to sustained increases in helpful substances such as BDNF, IL-10, and IGF-1.[112] Such lasting changes in gene activity may help explain why acupuncture can have prolonged antidepressant effects. However, most evidence so far comes from animal or cell studies. More research is needed to confirm whether these epigenetic changes also occur in humans and whether they contribute to long-term recovery from depression.

In summary, acupuncture works through multiple pathways—reducing inflammation, activating repair, supporting metabolism, and influencing gene regulation—to relieve depressive symptoms. These combined actions are illustrated in Figure 8.

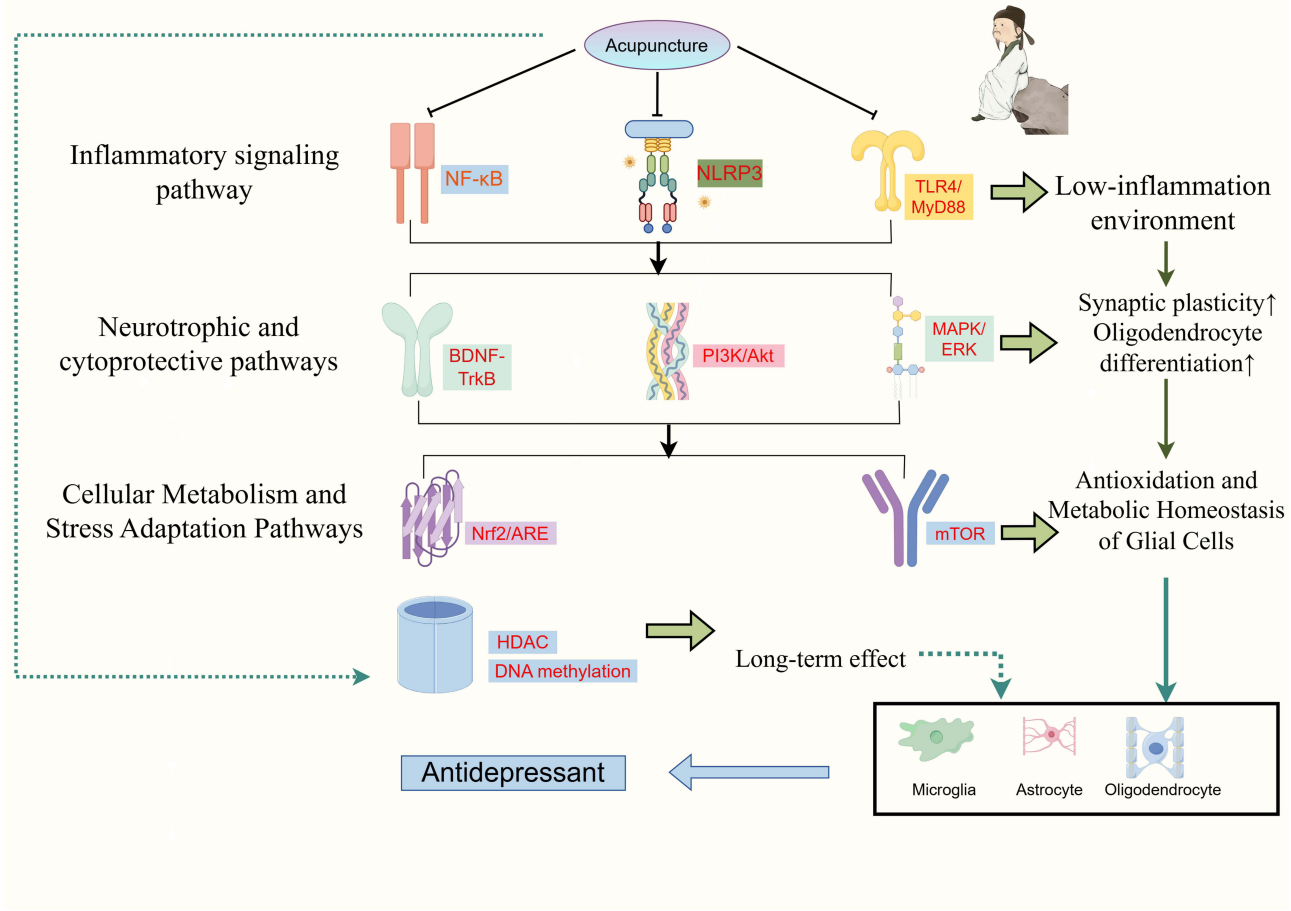

Figure 8 Acupuncture synergistically regulates shared pathways for antidepressant effects. Acupuncture modulates inflammatory responses (TLR4/NF-κB, NLRP3), neuroprotective functions (BDNF/TrkB, PI3K/Akt), metabolic processes (mTOR), and oxidative stress (Nrf2/ARE).

Summary and Outlook

Depression involves complex interactions between different types of glial cells and neurons. Acupuncture, an important part of traditional Chinese medicine, follows the principle of "holistic care and personalized treatment". This approach is consistent with the modern medical view that depression should be treated by targeting multiple biological processes at once. Acupuncture can affect various glial cells at the same time. The way these cells interact with each other helps explain how acupuncture relieves depression. This paper has reviewed the key roles of microglia, astrocytes, and oligodendrocytes in depression. It has also described how acupuncture influences these cells and their interactions to produce antidepressant effects. These findings provide scientific support for the traditional Chinese medicine concept of "selecting acupoints along meridians", and suggest that these mechanisms can support personalized acupuncture protocols tailored to glial cell phenotypes.

However, many questions remain. For example, we need more research on how different acupoint combinations, different levels of acupuncture stimulation, and specific brain regions affect particular types of glial cells. Studying these areas in the future could help us better understand how acupuncture works and improve its use in treating depression. Concurrently, clinical trials have demonstrated that acupuncture alleviates depressive symptoms; however, the causal link between its efficacy and glial cell regulation primarily stems from animal models. Direct evidence establishing glial functional recovery as the specific cause of clinical improvement in humans remains insufficient. Future research should employ neuroimaging techniques such as TSPO-PET and peripheral biomarkers to validate glial changes in humans; investigate the differential effects of acupuncture parameters on distinct glial phenotypes; and optimise intervention

https://doi.org/10.2147/JMDH.S581593

timing to promote myelin repair. These approaches will advance the evidence base from correlation to causation, ultimately refining clinical acupuncture treatment protocols.

To translate these broad goals into actionable science, two specific and interconnected dimensions warrant prioritized investigation. First, the role of sex differences demands greater emphasis. Beyond the noted structural variances in white matter, future studies must systematically evaluate whether acupuncture's modulation of microglial polarization, astrocytic support, and oligodendrocyte maturation exhibits sexual dimorphism. Clarifying these potential differences is essential for developing sex-informed, personalized treatment protocols. Second, the imperative for parameter standardization requires concerted effort. While our review highlights that stimulation frequency, intensity, and waveform influence outcomes, the field lacks a consensus on optimal parameters for targeting specific glial phenotypes. Establishing robust, reproducible parameter-effect relationships through controlled preclinical studies is a fundamental prerequisite for optimizing and standardizing clinical acupuncture protocols for depression.

Funding

This work was supported by the National Natural Science Foundation of China (No. 82430126); the Huang Zhendong Research Fund for Traditional Chinese Medicine of Jinan University (No. 201911); the Guiding Scientific Research Program of Hubei Provincial Department of Education (No.B2022120); the Joint supported by Hubei Provincial Natural Science Foundation and Innovation and Development of traditional Chinese medicine of China (No.2023AFD134); the Natural Science Foundation of Hunan Province, China [Grant Number 2025JJ60545]; and the Health Research Project of Hunan Provincial Health Commission [Grant Number 2025JJ60545].

Disclosure

The authors report no conflict of Interest in this work.

References

1. Wang DL, Fang FF, Liu CS, et al. Expert consensus on integrated traditional Chinese and Western medicine diagnosis and treatment of depression. *Chin J Integr Trad Western Med*. 2023;29:237–245. doi:10.13422/j.cnki.syfjx.20221806
2. Wan XM, Zhang R, Huang XT, et al. Effect of Xiaoyao Powder on IL-6 and TNF-α in hippocampus of depression rats with liver depression and spleen deficiency pattern induced by chronic unpredictable mild stress. *J Liaoning Univ Trad Chin Med*. 2020;22:47–51. doi:10.13194/j.issn.1673-842x.2020.02.014
3. Huang YT, Ma N, Qin QY, et al. Research progress of Xiaoyao Powder in treatment of depression. *Chinese Archives Traditional Chin Med*. 2025;1–22.
4. Troubat R, Barone P, Leman S, et al. Neuroinflammation and depression: a review. *Eur J Neurosci*. 2021;53(1):151–171. doi:10.1111/ejn.14720
5. Drevets WC, Wittenberg GM, Bullmore ET, Manji HK. Immune targets for therapeutic development in depression: towards precision medicine. *Nat Rev Drug Discov*. 2022;21(3):224–244. doi:10.1038/s41573-021-00368-1
6. Yao L, Jiang R, Wang CC, et al. Research progress on pathogenesis and treatment of treatment-resistant depression. *Progress Physiol Sci*. 2025;56:112–121. doi:10.20059/j.cnki.pps.2025.02.1016
7. Xu K, Xiao Y, Zhao WT, et al. A randomized controlled clinical trial of "regulating governor vessel and relieving depression" electroacupuncture for mild to moderate depression. *Modernization Trad Chin Med Materia Med-World Sci Technol*. 2024;26:2755–2762.
8. Hao MJ, Tang S, Yang KL, et al. Acupuncture for depressive disorders: a systematic review and meta-analysis of 52 randomized controlled trials. *Modernization Trad Chin Med Materia Med-World Sci Technol*. 2025;27:2298–2322.
9. Yang NN. Potential mechanisms and clinical effectiveness of acupuncture in depression. *Curr Neuropharmacol*. 2022;20:738–750. doi:10.2174/1570159x19666210609162809
10. Shen J, Hao C, Yuan S, et al. Acupuncture alleviates CUMS-induced depression-like behaviors of rats by regulating oxidative stress, neuroinflammation and ferroptosis. *Brain Res*. 2024;1826:148715. doi:10.1016/j.brainres.2023.148715
11. Hu JF, Li G, Wang FX, et al. An important mechanism of acupuncture for depression: regulation of immune homeostasis. *World Chin Med*. 2024;19:2818–2824.
12. Study on the mechanism of electroacupuncture against depression based on clock gene regulation of neuroinflammation. Guangzhou University of Chinese Medicine; 2024.
13. Allen NJ, Lyons DA. Glia as architects of central nervous system formation and function. *Science*. 2018;362(6411):181–185. doi:10.1126/science.aat0473
14. Sun H, Zhao H, Ma C, et al. Effects of electroacupuncture on depression and the production of glial cell line-derived neurotrophic factor compared with fluoxetine: a randomized controlled pilot study. *J Altern Complement Med*. 2013;19(9):733–739. doi:10.1089/acm.2011.0637
15. Wang D, Wang X, Wang R, et al. Acupuncture and moxibustion combined with umbilical therapy for 30 cases of anxiety and depression in patients with neurogenic bladder after spinal cord injury. *Zhongguo Zhen Jiu*. 2025;45(7):923–926. doi:10.13703/j.0255-2930.20240930-0004
16. Gao YY, Yang X, Liu K, et al. Study on the efficacy and mechanism of acupuncture with the method of calming heart and relieving depression for post-stroke depression. *World Chin Med*. 2025;20:1349–1355.

17. Liu JJ, Yang Z, Zhang XJ, et al. Effect of Shugan Huayu Jieyu decoction combined with acupuncture on post-stroke depression and its influence on physical and mental health of patients. *Chinese Archives Traditional Chin Med*. 2025;1–11.
18. Li H, Wu H, Cui J. Acupuncture combined with bamboo-based medicinal moxibustion for chronic insomnia complicated with mild depressive state: a randomized controlled trial. *Zhongguo Zhen Jiu*. 2025;45(1):3–9. doi:10.13703/j.0255-2930.20240407-k0002
19. Li ZX, Peng Z, Ji QY, et al. Integrated acupuncture of regulating spirit and reinforcing foundation for 24 cases of comorbid depression and insomnia. *Chin Acupuncture Moxibustion*. 2025:1–7. doi:10.13703/j.0255-2930.20241118-k0001
20. Study on clinical efficacy and mechanism of regulating qi electroacupuncture for depression based on pivot movement theory. Guangxi University of Chinese Medicine; 2025.
21. Lu JJ, Jin X, Hou YC, et al. Clinical observational study on acupuncture for post-stroke depression. *Modernization Trad Chin Med Materia Med-World Sci Technol*. 2024;26:1059–1069.
22. Maes M, Leonard BE, Myint AM, Kubera M, Verkerk R. The new '5-HT' hypothesis of depression: cell-mediated immune activation induces indoleamine 2,3-dioxygenase, which leads to lower plasma tryptophan and an increased synthesis of detrimental tryptophan catabolites (TRYCATs), both of which contribute to the onset of depression. *Prog Neuropsychopharmacol Biol Psychiatry*. 2011;35(3):702–721. doi:10.1016/j.pnpbp.2010.12.017
23. Sălcudean A, Popovici R-A, Pitic DE, et al. Unraveling the complex interplay between neuroinflammation and depression: a comprehensive review. *Int J Mol Sci*. 2025;26(4):1645. doi:10.3390/ijms26041645
24. Xia X, Li K, Zou W, Wang L. The central role of microglia in major depressive disorder and its potential as a therapeutic target. *Front Behav Neurosci*. 2025;19:1598178. doi:10.3389/fnbeh.2025.1598178
25. Zhang ZX, Guo Q, Chen XY. Research progress in the anti-inflammatory effect of exercise in ameliorating neuroinflammation-related depression. *Zhongguo Yi Xue Ke Xue Yuan Xue Bao*. 2025;47(2):191–197. doi:10.3881/j.issn.1000-503X.15991
26. Kwon HS, Koh SH. Neuroinflammation in neurodegenerative disorders: the roles of microglia and astrocytes. *Transl Neurodegener*. 2020;9(1):42. doi:10.1186/s40035-020-00221-2
27. Wang B, He T, Qiu G, et al. Altered synaptic homeostasis: a key factor in the pathophysiology of depression. *Cell Biosci*. 2025;15(1):29. doi:10.1186/s13578-025-01369-y
28. Li S, Gao M, Mou Z, et al. Advances in neurotransmitter-mediated prefrontal circuitry in depression. *Prog Neuropsychopharmacol Biol Psychiatry*. 2025;141:111475. doi:10.1016/j.pnpbp.2025.111475
29. Chen S, Zhang J, Wu G, et al. Norepinephrine system dysconnectivity in major depressive disorder: the effect of short term SSRI treatment. *Eur Neuropsychopharmacol*. 2025;97:40–50. doi:10.1016/j.euroneuro.2025.05.010
30. Wan M, Wang W, He M, et al. Cubebin alleviates chronic stress-induced depression-like behavior in mice by regulating the gut microbiome. *Eur J Pharmacol*. 2025;994:177384. doi:10.1016/j.ejphar.2025.177384
31. Zhou M, Zheng M, Liang S, et al. Inherent potential of mitochondria-targeted interventions for chronic neurodegenerative diseases. *Neural Regen Res*. 2026;21(4):1409–1427. doi:10.4103/nrr.Nrr-d-24-01507
32. Otto LR, Clemens V, Üsekes B, et al. Retinoid homeostasis in major depressive disorder. *Transl Psychiatry*. 2023;13(1):67. doi:10.1038/s41398-023-02362-0
33. Hu P, van Dam AM, Wang Y, Lucassen PJ, Zhou JN. Retinoic acid and depressive disorders: evidence and possible neurobiological mechanisms. *Neurosci Biobehav Rev*. 2020;112:376–391. doi:10.1016/j.neubiorev.2020.02.013
34. Schain M, Kreisl WC. Neuroinflammation in neurodegenerative Disorders-A review. *Curr Neurol Neurosci Rep*. 2017;17(3):25. doi:10.1007/s11910-017-0733-2
35. Jiang S, Zhang QA, Guo Q, Di Z. The glutamatergic system and astrocytic impairment in rat hippocampus: a comparative study of underlying etiology and pathophysiology of depression. *J Integr Neurosci*. 2019;18(4):387–392. doi:10.31083/j.jin.2019.04.1164
36. Albini M, Krawczun-Rygmaczewska A, Cesca F. Astrocytes and brain-derived neurotrophic factor (BDNF). *Neurosci Res*. 2023;197:42–51. doi:10.1016/j.neures.2023.02.001
37. Wang H, Chen C, Lin Y, et al. Connexin43 and its regulation of astrocyte gap junction function: influencing depression progression by mediating electrical and chemical signals. *CNS Neurosci Ther*. 2025;31(9):e70600. doi:10.1111/cns.70600
38. Verkhratsky A, Ho MS, Vardjan N, Zorec R, Parpura V. General pathophysiology of astroglia. *Adv Exp Med Biol*. 2019;1175:149–179. doi:10.1007/978-981-13-9913-8_7
39. Asano H, Aonuma M, Sanosaka T, et al. Astrocyte differentiation of neural precursor cells is enhanced by retinoic acid through a change in epigenetic modification. *Stem Cells*. 2009;27(11):2744–2752. doi:10.1002/stem.176
40. Pan S, Mayoral SR, Choi HS, Chan JR, Kheirbek MA. Preservation of a remote fear memory requires new myelin formation. *Nat Neurosci*. 2020;23(4):487–499. doi:10.1038/s41593-019-0582-1
41. Liu L, Qin L, Feng X, et al. White matter injury in major depressive disorder and current status of traditional Chinese medicine treatment. *Chin J Exp Traditional Med Formulae*. 2023;29:237–245. doi:10.13422/j.cnki.syfjx.20221806
42. Park MTM, Jeon P, French L, et al. Microstructural imaging and transcriptomics of the basal forebrain in first-episode psychosis. *Transl Psychiatry*. 2022;12(1):358. doi:10.1038/s41398-022-02136-0
43. Yang WY, He Z, Hu XH. Preliminary study of DTI in evaluating white matter microstructure changes in patients with depression. *Chin J CT MRI*. 2020;18:1–3+6.
44. Lin BB, Xie W, Liu WL, et al. Effect of electroacupuncture on motor cortex-striatum neural conduction tract in ischemic stroke rats observed by diffusion tensor imaging. *Chin J Rehabil Theory Pract*. 2017;23:756–761.
45. Hoogenboom WS, Perlis RH, Smoller JW, et al. Limbic system white matter microstructure and long-term treatment outcome in major depressive disorder: a diffusion tensor imaging study using legacy data. *World J Biol Psychiatry*. 2014;15(2):122–134. doi:10.3109/15622975.2012.669499
46. Hang WX, Yang Y-C, Hu Y-H, et al. General anesthetic agents induce neurotoxicity through oligodendrocytes in the developing brain. *Zool Res*. 2024;45(3):691–703. doi:10.24272/j.issn.2095-8137.2023.413
47. Niciu MJ, Henter ID, Sanacora G, Zarate CA. Glial abnormalities in substance use disorders and depression: does shared glutamatergic dysfunction contribute to comorbidity? *World J Biol Psychiatry*. 2014;15(1):2–16. doi:10.3109/15622975.2013.829585

48. Mu Y, Wei Z, Sun M, et al. SRSF10 regulates oligodendrocyte differentiation during mouse central nervous system development by modulating pre-mRNA splicing. *Nucleic Acids Res*. 2025;53(10). doi:10.1093/nar/gkaf455
49. Song SJ, Jiang L, Wu WC, et al. Function of oligodendrocytes and demyelinating diseases. *Chin J Tissue Eng Res*. 2022;26:3108–3116.
50. Tan H, Yu L, Meng JY, et al. Ameliorative effects of tetrahydrocurcumin and its nano-preparation on lipopolysaccharide-induced depression in mice. *J Anhui Med Univers*. 2025;60:79–86. doi:10.19405/j.cnki.issn1000-1492.2025.01.011
51. Adili A, Dilihumaer A, Zhu H, Tang H. Research progress on phosphodiesterase 4 inhibitors in central nervous system diseases. *Zhejiang Da Xue Xue Bao Yi Xue Ban*. 2024;53(3):390–398. doi:10.3724/zdxbyxb-2024-0023
52. Miguel-Hidalgo JJ. Neuroprotective astroglial response to neural damage and its relevance to affective disorders. *Explor Neuroprotective Ther*. 2023;3:328–345. doi:10.37349/ent.2023.00054
53. Xu N, Tan H, Wang L. Research progress on mechanism of acupuncture against depression by regulating astrocytes. *Acupuncture Res*. 2025;1–8. doi:10.13702/j.1000-0607.20250552
54. Li Z, Xu P, Deng Y, et al. M1 microglia-derived exosomes promote A1 astrocyte activation and aggravate ischemic injury via circSTRN3/miR-331-5p/MAVS/NF-κB pathway. *J Inflamm Res*. 2024;17:9285–9305. doi:10.2147/jir.S485252
55. Shen SY, Liang L-F, Shi T-L, et al. Microglia-derived interleukin-6 triggers astrocyte apoptosis in the hippocampus and mediates depression-like behavior. *Adv Sci*. 2025;12(11):e2412556. doi:10.1002/advs.202412556
56. Sompub K, Bizen N, Baldwin AS, Takebayashi H. NF-κB RelA regulates temporal oligodendrocyte differentiation in the postnatal brains. *Front Cell Neurosci*. 2025;19:1622874. doi:10.3389/fncel.2025.1622874
57. Zheng Y, Huang R, Pan J. Dynamic intercellular networks in the CNS: mechanisms of crosstalk from homeostasis to neurodegeneration. *Int J Mol Sci*. 2025;26(17):8155. doi:10.3390/ijms26178155
58. Zhang N, Zhang S, Liu X, et al. Oligodendrocyte-specific knockout of FPN1 affects CNS myelination defects and depression-like behavior in mice. *Free Radic Biol Med*. 2025;238:370–386. doi:10.1016/j.freeradbiomed.2025.06.055
59. Shi LQ, Ren L, Lv Q, et al. Effects of acupuncture combined with moxibustion on polarization of microglia in rats with PDD by regulating "Kidney-Brain-Tiangui" system. *J Trad Chin Med Liaoning*. 2024;51:170–175+223–225. doi:10.13192/j.issn.1000-1719.2024.10.044
60. Yao Z, Cai L, Zhao A, et al. Electroacupuncture alleviates neuroinflammation by regulating microglia polarization via STAT6/PPARγ in ischemic stroke rats. *Neuroscience*. 2023;532:23–36. doi:10.1016/j.neuroscience.2023.09.007
61. Liu W, Wang X, Yang S, et al. Electroacupunctre improves motor impairment via inhibition of microglia-mediated neuroinflammation in the sensorimotor cortex after ischemic stroke. *Life Sci*. 2016;151:313–322. doi:10.1016/j.lfs.2016.01.045
62. Wang Y, Yang X, Cao Y, et al. Electroacupuncture alleviates early brain injury via modulating microglia polarization and suppressing neuroinflammation in a rat model of subarachnoid hemorrhage. *Heliyon*. 2023;9(3):e14475. doi:10.1016/j.heliyon.2023.e14475
63. Tong T, Hao C, Shen J, et al. Electroacupuncture ameliorates chronic unpredictable mild stress-induced depression-like behavior and cognitive impairment through suppressing oxidative stress and neuroinflammation in rats. *Brain Res Bull*. 2024;206:110838. doi:10.1016/j.brainresbull.2023.110838
64. Li XY, Wang H-M, Zhao Y, et al. Effect of acupuncture on microglia activation in prefrontal cortex of chronic stress-induced depression rats. *Zhen Ci Yan Jiu*. 2021;46(1):52–57. doi:10.13702/j.1000-0607.200886
65. Yue N, Li B, Yang L, et al. Electro-acupuncture alleviates chronic unpredictable stress-induced depressive- and anxiety-like behavior and hippocampal neuroinflammation in rat model of depression. *Front Mol Neurosci*. 2018;11:149. doi:10.3389/fnmol.2018.00149
66. Chen L, Jiang H, Bao T, et al. Acupuncture ameliorates depressive behaviors by modulating the expression of hippocampal Iba-1 and HMGB1 in rats exposed to chronic restraint stress. *Front Psychiatry*. 2022;13:903004. doi:10.3389/fpsyt.2022.903004
67. Li W, Chang W, Cui K, et al. Electroacupuncture reduces microglial hyperactivity and synaptic phagocytosis in the medial prefrontal cortex to treat chronic pain comorbid with anxiety and depression. *Brain Res Bull*. 2025;230:111521. doi:10.1016/j.brainresbull.2025.111521
68. Shen ZQ, Chang W-Q, Liang L-F, et al. Electroacupuncture effects on trigeminal neuralgia with comorbid anxiety and depression: the role of frequency and acupoint specificity. *FASEB j*. 2025;39(2):e70337. doi:10.1096/fj.202402461RR
69. Chen S, Li J, Yan L, et al. Electroacupuncture alleviates the symptom of depression in mice by regulating the cGAS-STING-NLRP3 signaling. *Aging*. 2024;16(8):6731–6744. doi:10.18632/aging.205596
70. Jiang H, Long X, Wang Y, et al. Acupuncture ameliorates depression-like behaviors through modulating the neuroinflammation mediated by TLR4 signaling pathway in rats exposed to chronic restraint stress. *Mol Neurobiol*. 2024;61(5):2606–2619. doi:10.1007/s12035-023-03737-6
71. Huang WT, Deng L, Li B, et al. Effect of electroacupuncture on microglial activation and learning-memory ability in hippocampal dentate gyrus subgranular zone of depression rats. *Acta Laboratorium Animalis Scientia Sinica*. 2022;30:513–519.
72. Cao S, Yang J, Chen L, et al. IL-4- JAK1- STAT6 pathway mediates Electroacupuncture's effect on Microglial M2 polarization to treat inflammatory bowel disease with comorbid depression. *CNS Neurosci Ther*. 2025;31(8):e70572. doi:10.1111/cns.70572
73. Liang E, Wang C, Wei XQ, et al. Exploring the effect of acupuncture on hippocampal neuroinflammation in depression model mice based on TLR4/NF-κB signaling pathway. *J Liaoning Univ Trad Chin Med*. 2025;1–12.
74. Zou L, Song X, Zhao Y, et al. Effects of Tongdu Tiaoshen acupuncture on depression-like behavior and Endophilin A1/ROS pathway in hippocampal tissue of CUMS model rats. *Zhongguo Zhen Jiu*. 2025;45(9):1281–1289. doi:10.13703/j.0255-2930.20240922-k0001
75. Yao Z, Zhang Z, Zhang J, et al. Electroacupuncture alleviated the depression-like behavior by regulating FGF2 and astrocytes in the hippocampus of rats with chronic unpredictable mild stress. *Brain Res Bull*. 2021;169:43–50. doi:10.1016/j.brainresbull.2021.01.005
76. Xu MM, Zhang DM, Shi RX, et al. Effect of electroacupuncture intervention on behavior changes and levels of hippocampal transforming growth factor beta 3 and basic fibroblast growth factor proteins in depression rats. *Acupuncture Res*. 2016;41(2):138–143. doi:10.13702/j.1000-0607.2016.02.008
77. Li P, Huang W, Yan Y-N, et al. Acupuncture can play an antidepressant role by regulating the intestinal microbes and neurotransmitters in a rat model of depression. *Med Sci Monit*. 2021;27:e929027. doi:10.12659/msm.929027
78. Lian JL, Wu XM, Sun X, Wang YJ, Li YH. Effect of Tiaodu Jieyu acupuncture on cancer-related depression: a randomized controlled trial. *Zhongguo Zhen Jiu*. 2021;41(4):381–385. doi:10.13703/j.0255-2930.20200330-0004
79. Zhang Y, Hu W. Effect of Rab27b on brain-derived neurotrophic factor secretion in mouse astrocytes. *J Neurosci Mental Health*. 2024;24:235–242.

80. Luo D, Xu Z, Xiao Y, et al. Effect of electroacupuncture on GS, GLT1, GLAST of astrocytes in prefrontal cortex of CUMS rats. *Chin J Gerontol*. 2016;36:4143–4146.
81. Cai M, Park HR, Yang EJ. Electroacupuncture modulates glutamate neurotransmission to alleviate PTSD-like behaviors in a PTSD animal model. *Transl Psychiatry*. 2023;13(1):357. doi:10.1038/s41398-023-02663-4
82. Lai LF, Li X, Li H-Z, et al. Electroacupuncture improves synaptic plasticity and cognitive dysfunction via down-regulating HDAC3 in mice of Alzheimer's disease. *Zhen Ci Yan Jiu*. 2025;50(4):375–383. doi:10.13702/j.1000-0607.20240214
83. Xu XJ, Tan L, Tian JH, et al. Effect of acupuncture on behavior and serum metabolomics in CUMS depression rats. *Acta Chin Med Pharmacol*. 2020;48:58–62. doi:10.19664/j.cnki.1002-2392.200128
84. Zhang ZH, Gu Y, Huang Z, et al. Acupuncture regulates astrocyte neurotoxic polarization to protect blood-brain barrier integrity in delayed thrombolysis through mediating ERK1/2/Cx43 axis. *IBRO Neurosci Rep*. 2025;18:604–618. PMID: PMID: 40292080; PMCID: PMC12022658. doi:10.1016/j.ibneur.2025.04.005
85. Wu ZL, Xu -Y-Y, Chen Y-R, et al. Electroacupuncture alleviates neuropathic pain hyperalgesia and anxiety-like behaviors via the dorsal raphe nucleus-basolateral amygdala circuit. *Zhen Ci Yan Jiu*. 2025;50(8):851–861. doi:10.13702/j.1000-0607.20250181
86. Zhang C, Zhu G-Q, Wang -J-J, et al. Study on the mechanism of acupuncture underlying improvement of functional dyspepsia with depression-like behavior in rats. *Zhen Ci Yan Jiu*. 2025;50(1):76–83. doi:10.13702/j.1000-0607.20230948
87. Jiang S, Bao H, Fan L, et al. Effect of electroacupuncture at Siguan points on morphology of hippocampal astrocytes in depression rats. *China J Tradition Chinese Med Pharm*. 2015;30:216–218.
88. Choi DC, Lee JY, Moon YJ, et al. Acupuncture-mediated inhibition of inflammation facilitates significant functional recovery after spinal cord injury. *Neurobiol Dis*. 2010;39:272–282. PMID: 20382225. doi:10.1016/j.nbd.2010.04.003
89. Effect of electroacupuncture on expression of myelin-related proteins in hippocampus of SAMP8 mice. Fujian University of Traditional Chinese Medicine; 2024.
90. Huang S, Tang C, Sun S, et al. Protective effect of electroacupuncture on neural myelin sheaths is mediated via promotion of oligodendrocyte proliferation and inhibition of oligodendrocyte death after compressed spinal cord injury. *Mol Neurobiol*. 2015;52:1870–1881. PMID: 25465241. doi:10.1007/s12035-014-9022-0
91. Zhou B, Zhu Z, Ransom BR, Tong X. Oligodendrocyte lineage cells and depression. *Mol Psychiatry*. 2021;26:103–117. doi:10.1038/s41380-020-00930-0
92. Liu C, Yin H, Chen X, et al. Electroacupuncture promotes oligodendrocyte differentiation and myelin repair in a rat model of vascular dementia: investigation of the mechanism from NF-κB-mediated inflammation. *Neuroscience*. 2025;572:21–34. PMID: 40057224. doi:10.1016/j.neuroscience.2025.03.002
93. Liddelow SA, Guttenplan KA, Clarke LE, et al. Neurotoxic reactive astrocytes are induced by activated microglia. *Nature*. 2017;541(7638):481–487. doi:10.1038/nature21029
94. Vainchtein ID, Chin G, Cho FS, et al. Astrocyte-derived interleukin-33 promotes microglial synapse engulfment and neural circuit development. *Science*. 2018;359(6381):1269–1273. doi:10.1126/science.aal3589
95. Sun MS, Ma Z, Liu Y, et al. Exploring the central inflammatory mechanism of acupuncture in regulating chronic migraine based on astrocyte-microglia crosstalk. *World Chin Med*. 2022;17:2394–2399.
96. Rusin D, Vahl Becirovic L, Lyszczarz G, et al. Microglia-derived insulin-like growth factor 1 is critical for neurodevelopment. *Cells*. 2024;13(2):184. doi:10.3390/cells13020184
97. Wang JY, Zhang JL, Chen SP, et al. Electroacupuncture relieves hyperalgesia by regulating neuronal-glial interaction and glutamate transporters of spinal dorsal horns in rats with acute incisional neck pain. *Front Neurosci*. 2022;16:885107. PMID: 36389227; PMCID: PMC9643735. doi:10.3389/fnins.2022.885107
98. Su Z, Yuan Y, Chen J, et al. Reactive astrocytes inhibit the survival and differentiation of oligodendrocyte precursor cells by secreted TNF-α. *J Neurotrauma*. 2011;28:1089–1100. PMID: 21309692. doi:10.1089/neu.2010.1597
99. He JY, Ji X-Y, Huang B, et al. Microglia-derived exosomes modulate myelin regeneration via activating Nrf2 signaling pathway in oligodendrocyte precursor cells in MS. *Brain Behav Immun*. 2025;130:106092. doi:10.1016/j.bbi.2025.106092
100. Shi AN, Q M, Liu XL, et al. Research progress on mechanism of acupuncture intervention on neuroinflammation in depression. *J Clin Acupuncture Moxibustion*. 2025;41:108–113. doi:10.19917/j.cnki.1005-0779.025081
101. Li M, Yang F, Zhang X, et al. Electroacupuncture attenuates depressive-like behaviors in poststroke depression mice through promoting hippocampal neurogenesis and inhibiting TLR4/NF-κB/NLRP3 signaling pathway. *Neuroreport*. 2024;35(14):947–960. doi:10.1097/wnr.0000000000002088
102. Wang Q, Bi H, Huang H, et al. Electroacupuncture prevents the depression-like behavior by inhibiting the NF-κB/NLRP3 inflammatory pathway in hippocampus of mice subjected to chronic mild stress. *Neuropsychobiology*. 2022;81(3):237–245. doi:10.1159/000521185
103. Chen Y, Hao C, Chen W, et al. Anti-depressant effects of acupuncture: the insights from NLRP3 mediated pyroptosis and inflammation. *Neurosci Lett*. 2022;785:136787. doi:10.1016/j.neulet.2022.136787
104. Yang P, Chen H, Wang T, et al. Electroacupuncture promotes synaptic plasticity in rats with chronic inflammatory pain-related depression by upregulating BDNF/TrkB/CREB signaling pathway. *Brain Behav*. 2023;13:e3310. PMID: 37948105; PMCID: PMC10726860. doi:10.1002/brb3.3310
105. Wang L, Yang J-W, Lin L-T, et al. Acupuncture attenuates inflammation in microglia of vascular dementia rats by inhibiting miR-93-mediated TLR4/MyD88/NF-κB signaling pathway. *Oxid Med Cell Longev*. 2020;2020:8253904. doi:10.1155/2020/8253904
106. Sun PY, H C, Li N, et al. Effect of "regulating governor vessel and regulating spirit" acupuncture on CREB/BDNF/TrkB signaling pathway in hippocampus of post-stroke depression rats. *Chin Acupuncture Moxibustion*. 2022;42:907–913. doi:10.13703/j.0255-2930.20220206-k0003
107. Zhang K, Zhai W, Ge X, et al. Targeting BDNF with acupuncture: a novel integrated strategy for diabetes and depression comorbidity. *Heliyon*. 2023;9(12):e22798. doi:10.1016/j.heliyon.2023.e22798
108. Tong T, Chen Y, Hao C, et al. The effects of acupuncture on depression by regulating BDNF-related balance via lateral habenular nucleus BDNF/TrkB/CREB signaling pathway in rats. *Behav Brain Res*. 2023;451:114509. doi:10.1016/j.bbr.2023.114509
109. Liu Q, Zhang -M-M, Guo M-X, et al. Inhibition of microglial NLRP3 with MCC950 attenuates microglial morphology and NLRP3/Caspase-1/IL-1β signaling in stress-induced mice. *J Neuroimmune Pharmacol*. 2022;17(3–4):503–514. doi:10.1007/s11481-021-10037-0

110. Huang TI, Hsieh CL. Effects of acupuncture on oxidative stress amelioration via Nrf2/ARE-related pathways in alzheimer and Parkinson diseases. *Evid Based Complement Alternat Med*. 2021;2021:6624976. doi:10.1155/2021/6624976
111. Wu LB, Zhang F, Yu Q, et al. Electroacupuncture of acupoints of heart Meridian ameliorates acute myocardial ischemia via Akt/mTOR pathway. *Zhen Ci Yan Jiu*. 2022;47(2):121–128. doi:10.13702/j.1000-0607.201266
112. Jiang H, Zhang X, Lu J, et al. Antidepressant-like effects of acupuncture-insights from DNA methylation and histone modifications of brain-derived neurotrophic factor. *Front Psychiatry*. 2018;9:102. doi:10.3389/fpsyt.2018.00102