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Review Article

Modulation of immune responses by acupuncture at Jing-Well points in neurological disorders: exploring mechanisms and clinical applications in the era of modern electrophysiology

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Abstract: Background: Neurological disorders are increasingly recognized as complex conditions involving extensive neuroimmune dysregulation, chronic inflammation, oxidative stress, autonomic imbalance, and progressive neuronal injury. Emerging evidence suggests that acupuncture, including stimulation at Jing-Well points, may exert immunomodulatory and neuromodulatory effects through interactions with peripheral sensory pathways, autonomic networks, inflammatory signaling cascades, and central nervous system electrophysiology. Recent advances in neuroimaging, electrophysiology, and molecular neuroscience have provided important mechanistic insights into the therapeutic potential of acupuncture in neurological diseases. Objective: This review aims to comprehensively explore the mechanisms by which acupuncture at Jing-Well points modulates immune responses in neurological disorders, with particular emphasis on neuroimmune interactions, electrophysiological mechanisms, and contemporary clinical applications. Methods: A narrative review of the current literature was conducted using evidence derived from experimental studies, clinical investigations, neuroimaging analyses, electrophysiological studies, and systematic reviews indexed in PubMed, Scopus, and Web of Science. Relevant studies evaluating acupuncture-mediated immune regulation, autonomic modulation, neuroinflammation, electrophysiological alterations, and neurological rehabilitation were critically analyzed and synthesized. Results: Available direct evidence regarding Jing-Well point stimulation remains limited. However, findings from broader acupuncture and electroacupuncture research suggest potentially relevant neuroimmune, autonomic, anti-inflammatory, and electrophysiological effects, including modulation of cytokine signaling, glial activation, oxidative stress, autonomic balance, cortical excitability, and neural connectivity. The extent to which these effects are specific to Jing-Well point stimulation remains to be established. Conclusion: Jing-Well point acupuncture may represent a potentially useful adjunctive neuromodulatory approach in neurological disorders. Current evidence, derived predominantly from broader acupuncture and electroacupuncture research, supports the biological plausibility of anti-inflammatory, autonomic, neuroprotective, and electrophysiological effects; however, Jing-Well-specific mechanisms and clinical benefits have not yet been firmly established. Standardized multicenter studies integrating molecular biomarkers, electrophysiological monitoring, neuroimaging, and clinically meaningful outcomes are required.

Keywords: Immune responses, acupuncture, Jing-Well points, neurological disorders, clinical applications, modern electrophysiology

Introduction

Neurological disorders encompass a broad spectrum of acute and chronic conditions, including ischemic stroke, traumatic brain injury, spinal cord injury, epilepsy, Parkinson's disease, Alzheimer's disease, multiple sclerosis, peripheral neuropathies, and other neuroinflammatory syndromes. Collectively, these disorders represent a major global health burden and are among the leading causes of disability and mortality worldwide [1]. Contemporary neuroscience has established that neurological disorders are not solely characterized by neuronal

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dysfunction but also involve complex interactions between the nervous and immune systems. Increasing evidence demonstrates that neuroinflammation, immune dysregulation, and impaired neuroimmune communication contribute significantly to disease initiation, progression, and recovery [2-4]. Microglia, astrocytes, peripheral immune cells, cytokines, chemokines, and autonomic neural circuits participate in bidirectional communication between the central nervous system (CNS) and immune system, influencing neuronal survival, synaptic plasticity, blood-brain barrier integrity, and tissue repair processes [5]. Consequently, modulation of neuroimmune responses has emerged as a promising therapeutic strategy for a variety of neurological disorders. Growing interest has therefore been directed toward complementary and integrative therapeutic approaches capable of influencing neuroimmune pathways while maintaining favorable safety profiles. Among these approaches, acupuncture has attracted considerable scientific attention due to its reported effects on autonomic regulation, inflammatory signaling, neuroendocrine activity, and neural network function [6-8]. Originating from Traditional Chinese Medicine (TCM), acupuncture involves stimulation of specific acupoints distributed along meridian pathways to restore physiological balance and homeostasis. Although traditionally developed through empirical clinical practice, acupuncture is the subject of growing investigation using modern biomedical approaches, including molecular immunology, systems neuroscience, neuroimaging, and electrophysiology [9]. Among the various categories of acupoints, the Jing-Well points occupy a unique position within traditional acupuncture theory. These twelve acupoints are located at the distal extremities of the fingers and toes and represent the initial or terminal points of the twelve primary meridians [10]. Traditionally, Jing-Well points have been associated with rapid regulation of consciousness, restoration of physiological function, and treatment of acute neurological and neurovascular conditions, including stroke, syncope, coma, convulsions, and altered mental states [11-13]. Their anatomical location at highly innervated distal regions, together with their historical clinical use in neurological disorders, has generated increasing interest regarding their potential neuromodulator and immunoregulatory properties. Despite centuries of clinical application, the biological mechanisms underlying Jing-Well point stimulation remain incompletely understood. Importantly, much of the current mechanistic evidence originates from broader acupuncture literature rather than studies specifically evaluating Jing-Well point stimulation. Nevertheless, emerging research suggests that acupuncture may influence multiple neuroimmune pathways through activation of peripheral sensory afferents, spinal and supraspinal neural circuits, autonomic nervous system regulation, and neuroendocrine signaling [14-17]. Experimental studies have reported modulation of inflammatory mediators, including reductions in tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and interleukin-6 (IL-6), together with increases in anti-inflammatory cytokines such as interleukin-10 (IL-10). However, the extent to which these mechanisms are specific to Jing-Well point stimulation remains to be determined. The potential neuroimmune effects of acupuncture are particularly relevant in neurological disorders characterized by chronic inflammation and immune-mediated neuronal injury. Neuroinflammatory processes contribute substantially to secondary tissue damage following ischemic stroke and traumatic brain injury, while persistent activation of microglia and astrocytes has been implicated in neurodegenerative disorders such as Parkinson's disease and Alzheimer's disease [18, 19]. Experimental and clinical studies involving acupuncture have reported beneficial effects on inflammatory signaling, oxidative stress, cerebral perfusion, neuroplasticity, and functional recovery. However, direct evidence specifically evaluating Jing-Well point acupuncture in these conditions remains comparatively limited, and the available literature often includes mixed-acupoint protocols or broader acupuncture interventions. Advances in electrophysiological and neuroimaging technologies have further expanded opportunities to investigate the biological basis of acupuncture. Techniques such as electroencephalography (EEG), functional magnetic resonance imaging (fMRI), transcranial magnetic stimulation (TMS), evoked potentials, nerve conduction studies, heart rate variability (HRV), and autonomic monitoring have provided objective measures of neural responses to acupuncture stimulation [20-22]. These studies suggest that acupuncture may modulate cortical excitability, sensorimotor

integration, autonomic balance, and functional connectivity within neural networks involved in pain processing, consciousness, cognition, emotional regulation, and immune control. Although several reports have examined distal acupoint stimulation, the electrophysiological characteristics and neuroimmune relevance of Jing-Well point stimulation remain insufficiently defined. Particular attention has also been directed toward the interaction between acupuncture and autonomic neuroimmune pathways. The vagus nerve plays a central role in the so-called cholinergic anti-inflammatory pathway, an important neural mechanism regulating systemic inflammatory responses [23-25]. Experimental studies have demonstrated that acupuncture can influence vagal activity and inflammatory cytokine production, thereby contributing to immune homeostasis. However, whether Jing-Well point stimulation exerts distinct or preferential effects on vagal-mediated inflammatory regulation compared with other acupoints remains unclear and warrants further investigation. Despite growing scientific interest, several challenges continue to limit translation of Jing-Well point acupuncture into mainstream neurological practice. Available studies vary substantially with respect to acupoint selection, stimulation parameters, methodological quality, outcome measures, and mechanistic endpoints. Moreover, direct comparisons between Jing-Well and non-Jing-Well acupoints are scarce, making it difficult to determine the specificity of observed biological effects. Additional translational research integrating molecular immunology, electrophysiological mapping, neuroimaging, and clinical outcomes is therefore required to establish robust mechanistic frameworks and evidence-based therapeutic applications.

Given these considerations, a focused evaluation of the available evidence regarding Jing-Well point acupuncture is timely. Therefore, this review aims to critically examine current knowledge concerning the neuroimmune and immunomodulatory mechanisms potentially associated with Jing-Well point stimulation in neurological disorders, with particular emphasis on modern electrophysiological findings and their clinical relevance. By integrating evidence from neuroimmunology, electrophysiology, molecular neuroscience, and clinical neurology, this review seeks to identify current knowledge gaps, highlight mechanistic insights, and outline future research directions for the development of evidence-based acupuncture interventions in neurological medicine.

Literature search

This article was conducted as a structured narrative review to synthesize contemporary mechanistic, preclinical, clinical, electrophysiological, neuroimaging, and review-level evidence concerning acupuncture at Jing-Well points in neurological disorders. The review was designed to clarify the extent to which reported neuroimmune and neuromodulatory effects were directly supported by Jing-Well point studies, rather than inferred from the broader acupuncture or electroacupuncture literature.

A comprehensive literature search was performed in PubMed/MEDLINE, Scopus, and Web of Science from database inception to Dec 2025. The search strategy combined controlled vocabulary, where applicable, with free-text terms related to Jing-Well points, acupuncture, neurological disorders, neuroimmune regulation, and electrophysiological assessment. The main search terms included: "Jing-Well point*", "well point*", "Shixuan", "bloodletting acupuncture", "acupuncture", "electroacupuncture", "neurological disorder*", "stroke", "traumatic brain injury", "spinal cord injury", "Parkinson* disease", "Alzheimer* disease", "multiple sclerosis", "epilepsy", "neuropathic pain", "neuroinflammation", "microglia", "astrocyte*", "cytokine*", "NF-kappa B", "NLRP3", "vagus nerve", "autonomic nervous system", "electroencephalography", "functional magnetic resonance imaging", "evoked potential*" and "heart rate variability". Boolean operators "AND" and "OR" were used, and database-specific strategies were adapted accordingly. The literature selection process is illustrated in **Figure 1**.

Studies were considered eligible when they evaluated acupuncture, electroacupuncture, bloodletting acupuncture, or Jing-Well point stimulation in relation to neurological disorders, neuroimmune mechanisms, autonomic regulation, inflammatory signaling, electrophysiological outcomes, neuroimaging findings, or neurological rehabilitation. Eligible evidence included mechanistic studies, animal and other

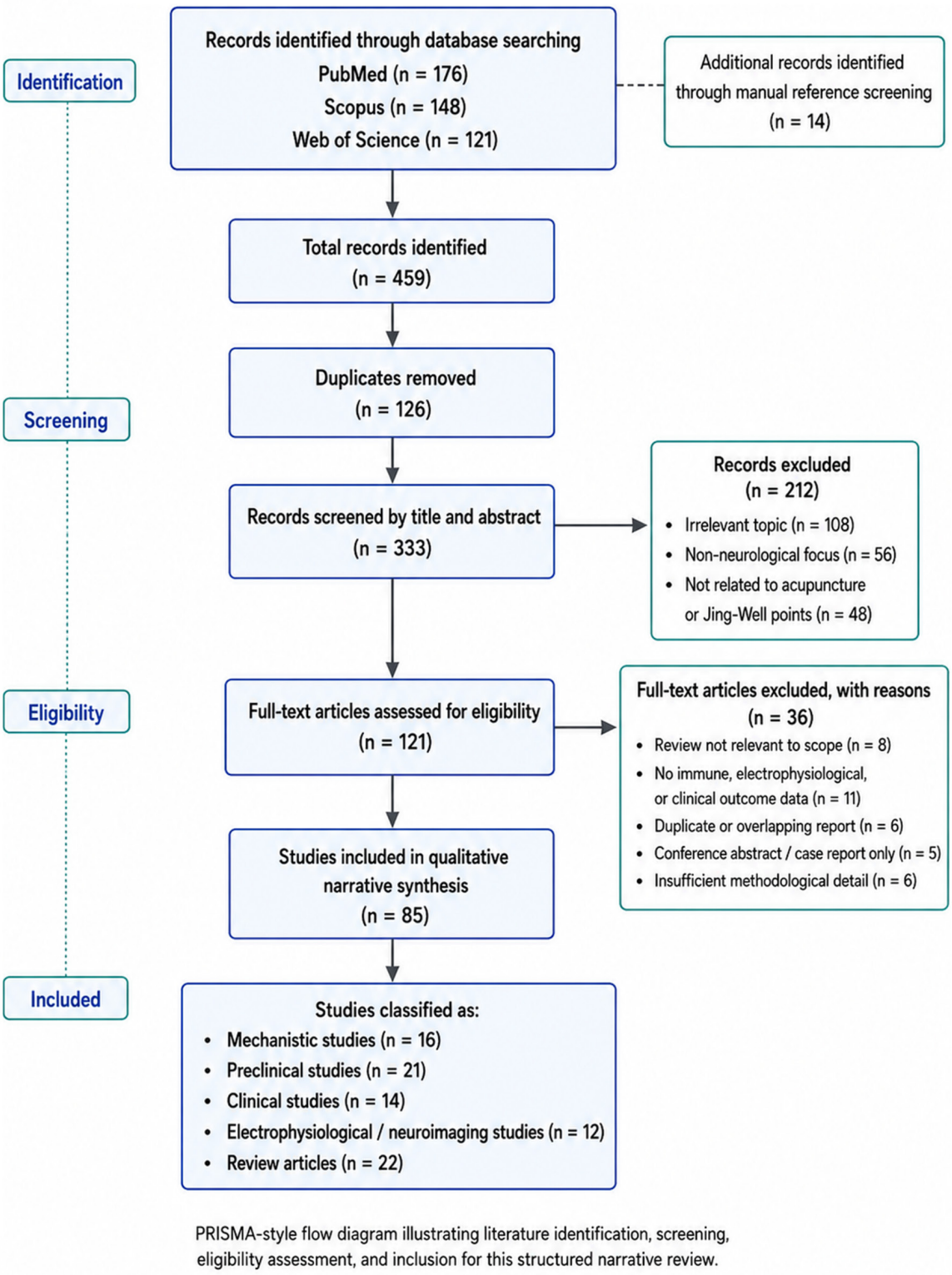

Figure 1. Literature selection flow diagram. Structured identification, duplicate removal, title and abstract screening, full-text eligibility assessment, and final inclusion of mechanistic, preclinical, clinical, electrophysiological, neuroimaging, and review studies evaluating acupuncture-related neuroimmune modulation in neurological disorders. The flow diagram is presented to enhance transparency of this structured narrative review and should not be interpreted as evidence of a formal systematic review or meta-analysis.

preclinical investigations, clinical trials, observational studies, electrophysiological and neuroimaging studies, systematic reviews, and high-quality narrative reviews. Reference lists of relevant reviews and landmark studies were also screened manually to identify additional eligible reports.

Studies were excluded when they were duplicate publications; conference abstracts without sufficient methodological information; case reports lacking mechanistic or clinical relevance; studies unrelated to acupuncture or neurological disorders; studies without relevant neuroimmune, autonomic, electrophysiological, neuroimaging, or clinical outcomes; and articles with inadequate information for meaningful interpretation. Studies evaluating multi-acupoint protocols were retained when relevant but were interpreted cautiously because the independent contribution of Jing-Well point stimulation could not be determined.

After removal of duplicates, titles and abstracts were screened for relevance, followed by full-text assessment of potentially eligible studies. Studies were categorized as: (1) Jing-Well-specific mechanistic studies; (2) broader acupuncture or electroacupuncture mechanistic studies; (3) preclinical neurological disease models; (4) clinical studies; (5) electrophysiological or neuroimaging investigations; and (6) systematic or narrative reviews. This classification was used to distinguish direct Jing-Well evidence from indirect evidence derived from broader acupuncture research.

Because of substantial heterogeneity in acupoint selection, stimulation modality, frequency and intensity, treatment duration, disease populations, study designs, biomarker panels, and clinical outcomes, quantitative pooling was not considered appropriate. Therefore, a narrative evidence-synthesis approach was applied. Findings were organized according to neuroimmune mechanisms, autonomic pathways, inflammatory mediators, electrophysiological and neuroimaging correlates, and clinical neurological applications. Particular emphasis was placed on identifying evidence gaps, especially the limited number of studies directly comparing Jing-Well and non-Jing-Well point stimulation.

The historical and theoretical background of Jing-Well points

Jing-Well points represent one of the fundamental concepts within the traditional framework of Traditional Chinese Medicine (TCM). These acupoints are located at the distal ends of the fingers and toes and correspond to the initial or terminal points of the twelve primary meridians. According to classical TCM theory, Jing-Well points are regarded as sites where meridian Qi emerges or enters the meridian system and therefore serve as important interfaces between the external environment and internal organ systems. Ancient medical texts, including the Huangdi Neijing (Yellow Emperor's Inner Canon), describe these points as having particular relevance for disorders characterized by sudden changes in consciousness, sensory function, or systemic physiological balance [22-26]. Within the Five Shu Point classification system, Jing-Well points represent the first category of acupoints along each meridian and are traditionally believed to exert rapid regulatory effects on physiological functions. Historically, these points have been used in the management of acute conditions such as syncope, coma, stroke, delirium, epilepsy, and severe pain syndromes. Their application in emergency acupuncture reflects the traditional view that stimulation of distal meridian points may facilitate restoration of physiological equilibrium and neurological function [27-30].

Traditional theories also attribute to Jing-Well points the ability to regulate yin-yang balance, clear pathogenic heat, and restore disrupted meridian flow. In TCM, neurological disorders are frequently interpreted as manifestations of imbalances involving Qi stagnation, internal wind, phlegm obstruction, heat accumulation, or deficiencies affecting the brain and meridian systems [31-33]. Although these concepts originate from a traditional medical framework, they have stimulated growing interest in identifying corresponding biological mechanisms using contemporary scientific approaches.

Importantly, modern investigations have attempted to explore whether the historical therapeutic significance of Jing-Well points may be associated with measurable neurophysiological, neurovascular, and immunological responses. However, while the traditional use

of Jing-Well points is well documented, direct scientific evidence demonstrating unique biological effects specific to Jing-Well points remains limited. Consequently, current interpretations should distinguish between established historical practice and emerging mechanistic hypotheses that require further experimental validation.

Anatomical localization and neurovascular characteristics

Interest in the biological basis of Jing-Well points has led to increasing investigation of their anatomical and physiological characteristics. These acupoints are located near the nail beds of the fingers and toes, regions that contain dense sensory innervation, rich microvascular networks, and specialized connective tissue structures. Histological studies have reported increased concentrations of free nerve endings, mechanoreceptors, mast cells, microvascular structures, and arteriovenous anastomoses in some acupoint regions compared with adjacent tissues [34-36]. The peripheral sensory afferents associated with these distal regions include both myelinated Aδ fibers and unmyelinated C fibers, which are involved in nociception, autonomic regulation, and neuroimmune communication. Stimulation of these fibers during acupuncture may activate ascending neural pathways projecting to the spinal cord, brainstem, hypothalamus, limbic system, and cerebral cortex [37, 38]. Neuroimaging studies investigating acupuncture more broadly have demonstrated activation of brain regions involved in pain processing, autonomic regulation, emotional responses, and immune modulation, including the hypothalamus, amygdala, insula, thalamus, anterior cingulate cortex, and periaqueductal gray matter [39]. However, it should be noted that much of this evidence derives from studies of acupuncture in general rather than investigations specifically focused on Jing-Well points.

Several studies have also reported distinctive bioelectrical properties in acupoint regions, including lower electrical resistance and higher electrical conductivity compared with surrounding tissues [40]. Proposed explanations include differences in connective tissue organization, vascular density, tissue hydration, and ionic composition. These observations have contributed to the development of electroacupuncture and bioelectrical mapping techniques, although the clinical significance of these properties remains incompletely understood. In addition to neural mechanisms, local vascular and connective tissue responses may contribute to acupuncture-induced biological effects. Experimental studies have demonstrated local release of signaling molecules such as substance P, calcitonin gene-related peptide (CGRP), nitric oxide, and adenosine following acupuncture stimulation, potentially influencing vasodilation, nociceptive processing, and immune cell activity [41]. Mechanical stimulation associated with needle manipulation may also activate connective tissue mechano-transduction pathways involving fibroblasts, extracellular matrix remodeling, and cytoskeletal signaling [42]. Collectively, these findings suggest that Jing-Well points are located within anatomically complex regions capable of participating in sensory, autonomic, vascular, and immune responses, although further research is needed to determine whether these characteristics are unique to Jing-Well points or shared by other acupoints.

Traditional and contemporary neurological applications of Jing-Well points

Classical Jing-Well points are the first or terminal points of the twelve primary meridians and comprise LU11, LI1, ST45, SP1, HT9, SI1, BL67, KI1, PC9, TE1, GB44, and LR1. The complete list of these twelve classical Jing-Well points, including their anatomical locations and historical neurological applications, is summarized in **Table 1**. Most are located at or near the nail corners of the fingers or toes; however, KI1 (Yongquan), the Jing-Well point of the Kidney meridian, is located on the plantar surface of the foot. These points should be distinguished from other acupoints frequently used in emergency and neurological acupuncture practice [42-46].

In particular, GV26 (Shuigou) is commonly used in traditional emergency acupuncture for syncope, impaired consciousness, and acute neurological presentations, but it is located on the Governing Vessel and is not classified as a Jing-Well point in the Five Shu Point system. Similarly, other neurological acupuncture protocols may include points such as GV20, LI4,

Table 1. Complete list of the twelve classical Jing-Well points and their historical neurological relevance

No.	Jing-Well Point	Meridian	Standard Anatomical Location	Traditional Function	Historical Neurological or Emergency-Related Application*
1	LU11 (Shaoshang)	Lung	Radial side of the thumb, approximately 0.1 cun from the nail corner	Clears heat; benefits the throat; restores consciousness	Syncope, fever-associated altered consciousness, acute throat-related symptoms
2	LI1 (Shangyang)	Large Intestine	Radial side of the index finger, approximately 0.1 cun from the nail corner	Clears heat; awakens consciousness	Syncope, acute facial symptoms, altered consciousness
3	ST45 (Lidui)	Stomach	Lateral side of the second toe, approximately 0.1 cun from the nail corner	Clears heat; calms the spirit	Disturbed consciousness, agitation, sleep-related symptoms
4	SP1 (Yinbai)	Spleen	Medial side of the great toe, approximately 0.1 cun from the nail corner	Regulates the Spleen; calms the spirit	Insomnia, anxiety-related symptoms, altered mental state
5	HT9 (Shaochong)	Heart	Radial side of the little finger, approximately 0.1 cun from the nail corner	Clears Heart heat; revives consciousness	Delirium, agitation, syncope, convulsive disorders
6	SI1 (Shaoze)	Small Intestine	Ulnar side of the little finger, approximately 0.1 cun from the nail corner	Clears heat; restores consciousness	Acute febrile conditions, altered consciousness
7	BL67 (Zhiyin)	Bladder	Lateral side of the little toe, approximately 0.1 cun from the nail corner	Regulates the Bladder meridian; clears heat	Headache, neck stiffness, traditional emergency applications
8	KI1 (Yongquan)	Kidney	Plantar surface of the foot, in the depression formed when the foot is plantar-flexed, approximately at the junction of the anterior one-third and posterior two-thirds of the sole	Descends excess; calms the spirit; restores consciousness	Syncope, agitation, seizure-like presentations, loss of consciousness
9	PC9 (Zhongchong)	Pericardium	Centre of the tip of the middle finger	Clears Pericardium heat; revives consciousness	Coma, delirium, heat-related altered consciousness, convulsions
10	TE1 (Guanchong)	Triple Energizer	Ulnar side of the ring finger, approximately 0.1 cun from the nail corner	Clears heat; benefits the sensory orifices	Acute febrile illness, headache, traditional emergency use
11	GB44 (Zuqiaoyin)	Gallbladder	Lateral side of the fourth toe, approximately 0.1 cun from the nail corner	Clears heat; calms the spirit	Headache, dizziness, sleep disturbance, agitation
12	LR1 (Dadun)	Liver	Lateral side of the great toe, approximately 0.1 cun from the nail corner	Regulates Liver Qi; clears heat; calms the spirit	Convulsive disorders, agitation, altered consciousness

*Traditional neurological or emergency-related applications are summarized based on classical acupuncture literature and historical clinical descriptions; these descriptions do not indicate confirmed clinical efficacy.

ST36, GB20, PC6, and EX-HN1; these are clinically relevant acupoints but are not Jing-Well points. Therefore, evidence derived from mixed-acupoint protocols should not be interpreted as evidence of a Jing-Well-specific effect.

Neuroimmune interactions in neurological disorders

Neuroinflammation and central nervous system immune regulation

The central nervous system (CNS) has historically been thought of as an immune-privileged structure removed from peripheral immune activity, but is now known as a very dynamic immunologic region that constantly communicates with immune system cells in the periphery. Neuroinflammation is one of the most common pathogenic mechanisms involved in many neurological diseases such as ischemic stroke, Alzheimer's disease, Parkinson's disease, multiple sclerosis, epilepsy, traumatic brain injury and peripheral neuropathies. Neuroinflammation can be beneficial for repair of tissue and neuroprotection but chronic or imbalanced neuroinflammation leads to neuronal damage, impairment of synapses, free radical production, and ongoing neurodegeneration [46].

The CNS resident immune cells (microglia) are key regulators of neural homeostasis and inflammatory responses. In normal conditions, microglia are constantly scanning the neural microenvironment by continuously conducting dynamic surveillance processes [47]. Microglia respond to injury, infection and ischemia, or neurodegenerative stimuli by becoming activated and secreting various cytokines, chemokines, reactive oxygen species (ROS) and nitric oxide. Too much microglial activation causes neuronal apoptosis, mitochondrial dysfunction, excitotoxicity and synaptic loss. Traditionally, activated microglia have been considered to have either pro-inflammatory M1 or anti-inflammatory M2 phenotypes, but recent studies have shown that microglial activation is a complex functional continuum [48]. Astrocytes are also key regulators of neuroimmune homeostasis. The astrocytes play an active role in regulating synapses, recycling neurotransmitters, maintaining blood-brain barrier, and in inflammatory signaling beyond their supportive roles. In neurological diseases, a common feature is reactive astrocytosis, which results in hypertrophy and increased expression of the glial fibrillary acidic protein (GFAP). The inflammatory mediators, including interleukin-1 beta (IL-1β), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α) and chemokines, are secreted by activated astrocytes and amplify local inflammatory responses and attract peripheral immune cells to CNS tissue [49].

Another important element of neuroimmune regulation is the blood-brain barrier (BBB). The BBB is formed by endothelial cells, astrocytic end-feet, pericytes and tight junction proteins that regulate the movement of molecules and cells across the BBB and maintain CNS homeostasis. Inflammatory conditions of the CNS lead to BBB disruption by endothelial dysfunction, caused by cytokines, oxidative stress and activation of matrix metalloproteinases. The BBB becomes more permeable allowing peripheral immune cells to infiltrate and further contribute to inflammatory injury and disease progression [50]. Emerging evidence suggests that neuroinflammation is not just a by-product of the consequences of neurological injury, but also a potent contributor to pathogenesis. Chronic inflammatory signaling is linked to neuronal network instability, alteration of neurogenesis, neural synapse dysfunction, and gradual cognitive/motor deterioration. As a result, effective methods that target modulation of neuroinflammatory pathways have been attracting considerable interest in contemporary neurological studies [30-37].

Peripheral immune system and CNS crosstalk

Contemporary neuroimmunology has increasingly focused on the relationship between the peripheral immune system and the CNS. Neurological disorders are now considered systemic diseases with complex communication among peripheral immune cells, lymphoid organs, autonomic pathways, and central neural structures. Peripheral immune activation may have a strong effect on CNS function, through cytokine signaling, immune cell trafficking and neurovascular interactions [51-53]. Pathological conditions may lead to disruption of the integrity of the BBB and allow infiltration of peripheral immune cells (macrophages, neutrophils, dendritic cells, natural killer cells, and T lymphocytes) into the CNS tissues. Such infiltrating immune cells produce pro-inflammatory mediators that contribute to further local increases in inflammatory changes involving

the nervous system. In ischemic stroke, for instance, early infiltration of neutrophils leads to oxidative damage and microvascular dysfunction, while activated macrophages and T cells are involved in secondary inflammatory damage and tissue remodeling [54].

T lymphocytes are especially involved in autoimmune and neurodegenerative diseases. In MS, autoreactive CD4+ T cells that target myelin break through the BBB and trigger inflammatory demyelination. Likewise, imbalances in the activity of T-cells have been associated with diseases such as Alzheimer's disease, Parkinson's disease and epilepsy. Chronic neuroinflammatory states often lead to dysfunction of regulatory T cells (Tregs) that suppress excessive immune activation, which can lead to chronic immune dysregulation [55-57]. The neurovascular unit (neuroglial unit) composed of endothelial cells, astrocytes, neurons, microglia and extracellular matrix components, forms an important interface between the immune system and CNS. Systemic inflammation causes generation of cytokines that directly affect endothelial permeability, neurotransmission and neuronal excitability. Afferent inflammatory mediators can also be released from the periphery and stimulate vagal afferent pathways and neuroendocrine circuits in the hypothalamus, connecting systemic immune activation and central autonomic control [58]. The gut-brain axis has recently been shown to be a source of neuroimmune communication. Microbial metabolites, immune modulation, vagal signaling, and inflammatory pathways are all pathways to how intestinal microbiota affect the functioning of the CNS. Dysbiosis and gut permeability changes have been linked to chronic pain syndromes, neuropsychiatric disorders and neurodegenerative diseases. The findings reiterate the systemic and multi-faceted aspects of neuroimmune interactions [30-35]. A bidirectional relationship between peripheral immunity and CNS function indicates a therapeutic potential for systemic inflammatory diseases. Acupuncture is of special interest in this regard for its reported balancing effect on peripheral immune activity, autonomic function and central neural signaling.

Major inflammatory signaling pathways in neurological disorders

In neurological diseases, a number of molecular signaling pathways are involved in the initiation and propagation of neuro-inflammatory responses (**Table 2**). Of these, the nuclear factor kappa B (NF-κB) pathway is one of the best studied inflammatory pathways. NF-κB is a transcription factor that activates the expression of pro-inflammatory cytokines, adhesion molecules, chemokines and enzymes that mediate oxidative stress. Activation of NF-κB has been implicated in stroke, Alzheimer's disease, Parkinson's disease, epilepsy, and spinal cord injury. Chronic inflammation is driven by persistent activation of NF-κB, which in turn leads to neuronal apoptosis and to synaptic dysfunction [54]. The NOD-like receptor pyrin domain-containing protein 3 (NLRP3) inflammasome is another important pathway. The NLRP3 inflammasome is an intracellular multiprotein complex that activates caspase-1 and promotes maturation of IL-1β and interleukin-18 (IL-18). Excessive activation of the inflammasome leads to pyroptosis, neurodegeneration and inflammatory amplification. Increased NLRP3 activity has been seen in Alzheimer's Disease, Traumatic Brain Injury, Parkinson's Disease and Ischemic Stroke [55-57] (**Table 2**).

Another pathway that is also relevant to neuroimmune regulation is the Janus kinase/signal transducer and activator of transcription (JAK/STAT) pathway. Activation of the JAK/STAT pathway by cytokines can affect the differentiation of immune cells and the activation of glial cells, as well as the expression of inflammatory genes. Chronic inflammation and autoimmune neurological diseases have been linked to dysregulated JAK/STAT signaling [58]. Another key pathway to neuroinflammatory toxicity is oxidative stress. Hyperproduction of ROS and RNS leads to damage of lipids, proteins, DNA and mitochondrial structures. Oxidative stress is closely associated with inflammatory signaling pathways, establishing a vicious cycle of neuronal damage and activation of immune responses. In addition, impaired ATP production and release of danger-associated molecular patterns (DAMPs) further contribute to inflammatory responses caused by mitochondrial dysfunction. These inflammatory pathways are interconnected and therapeutic interventions that target more than one neuroimmune mechanism concurrently might have more clinical value than those that target a single mechanism. The modulation of inflammatory signaling pathways via acupuncture has

Table 2. Neuroimmune pathways relevant to neurological disorders and their evidence in acupuncture research

Neuroimmune pathway or domain	Disease context	Principal biological targets or outcomes	Acupoint specificity	Evidence source and study type	Clinical versus experimental classification	Narrative strength of evidence*	Interpretation
Blood-brain barrier integrity and microcirculatory regulation	Ischemic stroke; traumatic brain injury	Blood-brain barrier permeability, cerebral edema, microvascular disturbance, endothelial integrity	Direct Jing-Well evidence available, primarily from bloodletting stimulation at the twelve hand Jing-Well points in rodent models; isolated human evidence is lacking	Jing-Well-specific preclinical studies; broader electroacupuncture animal studies	Predominantly experimental	Moderate for direct preclinical evidence; very low for clinical evidence	Supports a hypothesis of neurovascular protection; does not establish clinical efficacy of isolated Jing-Well stimulation
Cytokine and chemokine regulation	Stroke, traumatic brain injury, spinal cord injury, neuropathic pain, neurodegenerative disorders	TNF-α, IL-1β, IL-6, IFN-γ, IL-10, TGF-β, MCP-1, CXCL10	Mostly broader acupuncture or mixed-acupoint protocols; Jing-Well-specific cytokine evidence is limited	Animal electroacupuncture studies; limited clinical biomarker studies; reviews	Experimental predominant; limited clinical corroboration	Moderate for general acupuncture-related cytokine modulation; very low for Jing-Well specificity	Anti-inflammatory effects are biologically plausible but should not be attributed specifically to Jing-Well points without comparative studies
NF-κB and NLRP3 inflammasome signaling	Ischemic stroke, traumatic brain injury, Parkinson's disease, Alzheimer's disease, spinal cord injury	NF-κB activation, NLRP3, caspase-1, IL-1β, IL-18, pyroptosis	No convincing isolated Jing-Well point evidence identified; evidence is indirect	Broader electroacupuncture animal models and mechanistic studies	Experimental	Moderate experimental evidence for broader electroacupuncture; very low for Jing-Well specificity	Relevant mechanistic pathway, but current data cannot demonstrate a Jing-Well-specific anti-inflammasome effect
Microglial and astrocytic activation	Stroke, Parkinson's disease, Alzheimer's disease, spinal cord injury, neuropathic pain	Microglial activation state, GFAP-positive astrocytes, neuroinflammatory mediators, glial-associated neuronal injury	Predominantly non-Jing-Well or mixed-acupoint evidence	Animal studies and mechanistic reviews	Experimental	Moderate experimental evidence; very low direct Jing-Well evidence	Findings support a potential glial-modulatory role of acupuncture generally, not point-specific therapeutic effects
Oxidative stress and mitochondrial dysfunction	Stroke, traumatic brain injury, Parkinson's disease, Alzheimer's disease	Reactive oxygen species, nitric oxide, SOD, catalase, glutathione peroxidase, ATP production, mitochondrial membrane potential	Mostly indirect evidence from broader acupuncture literature	Preclinical electroacupuncture studies	Experimental	Moderate experimental evidence; very low Jing-Well-specific evidence	May contribute to neuroprotection; requires direct point-specific validation
Autonomic and vagal anti-inflammatory regulation	Systemic inflammation, stroke, chronic pain, neurodegenerative disorders	Vagal activity, sympathetic-parasympathetic balance, HRV, α7 nicotinic acetylcholine receptor signaling, inflammatory reflex	Evidence is mostly based on broader electroacupuncture paradigms; Jing-Well specificity remains uncertain	Experimental electroacupuncture studies; human physiological and HRV studies	Mixed, but predominantly experimental	Moderate for autonomic modulation by acupuncture broadly; very low for isolated Jing-Well stimulation	Autonomic regulation is a plausible pathway, but the relationship between Jing-Well stimulation, vagal activation, and clinical benefit remains unproven
Neurotrophic signaling and neuroplasticity	Stroke, traumatic brain injury, spinal cord injury, Parkinson's disease	BDNF, TrkB, NGF, GDNF, synaptic plasticity, neurogenesis	Mainly broader acupuncture and electroacupuncture evidence	Animal studies; limited rehabilitation studies	Experimental predominant	Moderate experimental evidence; very low Jing-Well-specific evidence	Potential mechanism for functional recovery, but no definitive evidence of point-specific superiority
Electrophysiological and neural network modulation	Stroke, epilepsy, Parkinson's disease, cognitive disorders, neuropathic pain	EEG rhythms, functional connectivity, fMRI activation, HRV, SSEP, MEP, cortical excitability	Few studies evaluate isolated Jing-Well stimulation; most use multi-acupoint protocols	Human neuroimaging, EEG, evoked-potential, and physiological studies	Mixed clinical and experimental evidence	Low-to-moderate for acupuncture generally; very low for Jing-Well specificity	Objective physiological effects are reported, but their Jing-Well-specific clinical relevance remains unclear

Note: *Evidence strength represents a narrative appraisal of available literature and does not constitute a formal GRADE assessment.

therefore become an exciting field of translational neuroscience research [59].

The pathways described below are not necessarily specific to Jing-Well point stimulation but represent neuroimmune mechanisms implicated in acupuncture research more broadly.

Autonomic nervous system and neuroimmune regulation

Acupuncture has increasingly been investigated as a potential modulator of autonomic nervous system activity. Studies involving general acupuncture and electroacupuncture protocols suggest that stimulation may enhance parasympathetic activity, reduce excessive sympathetic activation, and influence inflammatory reflex pathways [60-63]. Experimental evidence supporting vagal anti-inflammatory mechanisms - including vagotomy experiments, α7 nicotinic acetylcholine receptor signaling, splenic nerve involvement, and changes in catecholaminergic or cholinergic signaling - has predominantly been derived from non-Jing-Well or mixed-acupoint electroacupuncture models. Similarly, changes in heart rate variability and inflammatory mediators have been reported in broader acupuncture research, but direct correlations between autonomic indices and cytokine responses remain insufficiently characterized [62-64].

Therefore, it is biologically plausible that stimulation of Jing-Well points may engage peripheral sensory afferents and autonomic pathways relevant to neuroimmune regulation. However, current evidence is inadequate to conclude that Jing-Well point stimulation specifically increases parasympathetic activity, suppresses sympathetic activity, or activates the vagal anti-inflammatory reflex. Direct Jing-Well-specific studies incorporating standardized stimulation protocols, autonomic monitoring, cytokine assessments, vagal pathway experiments, and appropriate control acupoints are required to clarify these potential mechanisms.

Mechanisms of immune modulation by Jing-Well point acupuncture

The interaction between the nervous and immune systems has emerged as a major focus of contemporary acupuncture research. Increasing evidence suggests that acupuncture may influence neuroimmune communication through neural, endocrine, autonomic, and inflammatory pathways. However, it is important to note that much of the mechanistic evidence discussed in this section is derived from the broader acupuncture and electroacupuncture literature rather than studies specifically investigating Jing-Well point stimulation. Consequently, the mechanisms described below should be interpreted as plausible biological pathways that may contribute to the effects of Jing-Well point acupuncture but require further validation in Jing-Well-specific experimental and clinical studies.

Neural pathways potentially activated by Jing-Well point stimulation

One proposed mechanism underlying the therapeutic effects of acupuncture involves activation of peripheral sensory pathways and subsequent modulation of central neural networks [60]. Jing-Well points are located at distal regions of the fingers and toes that are richly supplied with sensory nerve endings and vascular structures. Mechanical or electrical stimulation at these sites may activate peripheral afferent fibers capable of transmitting sensory information to the spinal cord and higher central nervous system structures [61].

Current evidence from acupuncture research suggests that both myelinated Aδ fibers and unmyelinated C fibers contribute to signal transmission following acupuncture stimulation. Aδ fibers are primarily involved in rapid nociceptive and mechanosensory signaling, whereas C fibers participate in slower autonomic and neuroimmune responses. Activation of these afferent pathways may engage spinal reflex circuits as well as ascending projections involving the dorsal horn, spinothalamic pathways, reticular formation, hypothalamus, limbic structures, and cortical regulatory centers. Neuroimaging and electrophysiological studies of acupuncture have reported activation of several brain regions involved in autonomic regulation, pain processing, emotional responses, and immune modulation, including the periaqueductal gray matter, nucleus tractus solitarius, amygdala, hippocampus, anterior cingulate cortex, insula, and hypothalamus [62]. These neural structures participate in the integration

of sensory, autonomic, endocrine, and inflammatory signals and therefore represent plausible substrates for acupuncture-induced neuroimmune regulation. Nevertheless, direct evidence that stimulation of Jing-Well points preferentially activates these pathways compared with other acupoints remains limited. Attention has been directed toward the hypothalamus because of its central role in coordinating interactions among the nervous, endocrine, and immune systems. Experimental studies involving acupuncture have demonstrated alterations in hypothalamic activity that may influence autonomic regulation, neuroendocrine signaling, stress responses, and inflammatory processes [63]. Whether these responses are uniquely associated with Jing-Well point stimulation requires further investigation. Overall, current evidence supports the concept that acupuncture functions as a distributed neuromodulatory intervention capable of influencing multiple neural networks involved in neuroimmune communication. However, future studies directly comparing Jing-Well and non-Jing-Well acupoints are necessary to determine the specificity of these neural responses (**Table 3**).

Regulation of cytokine networks and inflammatory mediators

Regulation of inflammatory signaling pathways represents one of the most extensively investigated biological effects of acupuncture. Neuroinflammation is characterized by increased production of pro-inflammatory cytokines, activation of glial cells, disruption of blood-brain barrier integrity, and progressive neuronal injury, all of which contribute to the pathogenesis of numerous neurological disorders [65]. Experimental studies involving acupuncture and electroacupuncture have reported reductions in several pro-inflammatory mediators, including tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), interleukin-6 (IL-6), and interferon-gamma (IFN-γ) [66]. These cytokines play important roles in microglial activation, oxidative stress, neuronal apoptosis, and propagation of neuroinflammatory responses. Such observations have been reported in models of ischemic stroke, spinal cord injury, neurodegenerative disorders, and neuropathic pain. However, it should be emphasized that most of these findings originate from studies employing diverse acupuncture protocols rather than investigations specifically focused on Jing-Well point stimulation. In addition to suppressing pro-inflammatory signaling, acupuncture has been associated with increased expression of anti-inflammatory mediators such as interleukin-10 (IL-10) and transforming growth factor-beta (TGF-β) [67]. These cytokines contribute to immune homeostasis, regulation of glial activity, tissue repair, and resolution of inflammatory responses. Through modulation of both pro-inflammatory and anti-inflammatory pathways, acupuncture may help restore immune balance and reduce secondary inflammatory injury following neurological insults. Acupuncture has also been reported to influence chemokine signaling pathways involved in recruitment and migration of immune cells. Reductions in chemokines such as monocyte chemoattractant protein-1 (MCP-1) and CXCL10 have been observed in experimental studies, potentially limiting inflammatory cell infiltration and amplification of neuroinflammatory responses [68]. Similarly, modulation of inflammatory enzymes and mediators, including cyclooxygenase-2 (COX-2), inducible nitric oxide synthase (iNOS), prostaglandins, and nitric oxide, has been proposed as another mechanism through which acupuncture may exert anti-inflammatory effects [69]. Taken together, available evidence suggests that acupuncture may influence multiple cytokine and inflammatory signaling networks relevant to neurological disease. Nevertheless, direct evidence demonstrating that these immunomodulatory effects are specific to Jing-Well point stimulation remains limited, highlighting an important area for future mechanistic investigation.

Modulation of glial activation and blood-brain barrier integrity

Microglial and astrocytic activation are central components of neuroinflammatory responses in neurological disorders. Experimental studies involving acupuncture and electroacupuncture have reported reduced expression of pro-inflammatory mediators, attenuation of microglial activation, and modulation of reactive astrocytosis in models of cerebral ischemia, traumatic injury, neurodegeneration, and neuropathic pain. These effects may contribute to reduced cytokine release, oxidative injury, and secondary neuronal damage.

Table 3. Candidate neuroimmune and neuromodulatory mechanisms related to Jing-Well point stimulation and broader acupuncture research

Mechanistic domain	Principal biological targets or indicators	Findings reported in acupuncture research	Predominant evidence base	Jing-Well-specific evidence	Cautious interpretation
Peripheral sensory-afferent activation	Aδ fibers, C fibers, dorsal horn neurons, peripheral sensory endings	Acupuncture stimulation may initiate ascending neural signaling and engage spinal, brainstem, and autonomic circuits.	Anatomical, experimental, and general acupuncture studies	Limited direct evidence	Jing-Well points are located in highly innervated distal regions, but preferential activation of specific neural pathways has not been established.
Central neural-network modulation	Hypothalamus, insula, amygdala, anterior cingulate cortex, periaqueductal gray, nucleus tractus solitarius	Changes in cortical activity, functional connectivity, pain-processing networks, autonomic regulation, and neuroendocrine responses have been reported.	Mainly fMRI, EEG, and electrophysiological studies of broader acupuncture	Very limited	These neural effects are biologically relevant but cannot currently be considered Jing-Well-specific.
Cytokine and inflammatory-mediator regulation	TNF-α, IL-1β, IL-6, IFN-γ, IL-10, TGF-β, COX-2, iNOS	Reduced pro-inflammatory mediators and increased anti-inflammatory mediators have been reported in experimental and selected clinical acupuncture studies.	Mainly broader acupuncture and electroacupuncture studies	Limited	Cytokine modulation is a plausible acupuncture-related mechanism; direct confirmation for isolated Jing-Well stimulation is insufficient.
Chemokine regulation and immune-cell recruitment	MCP-1, CXCL10, leukocyte trafficking markers	Reduced inflammatory-cell recruitment and neuroinflammatory amplification have been reported in experimental models.	Preclinical broader acupuncture/electroacupuncture studies	Absent or very limited	Findings should be interpreted as indirect mechanistic support only.
Microglial and astrocytic regulation	Microglial activation markers, GFAP-positive astrocytes, inflammatory glial mediators	Reduced microglial activation, attenuation of reactive astrocytosis, and lower inflammatory signaling have been described in neurological disease models.	Primarily animal studies using broader acupuncture or mixed-acupoint electroacupuncture	Very limited	Glial modulation is plausible but remains unproven as a Jing-Well-specific mechanism.
Blood–brain barrier preservation	Tight-junction proteins, matrix metalloproteinases, endothelial and astrocytic markers	Experimental studies suggest reduced BBB disruption and inflammatory vascular injury after acupuncture interventions.	Predominantly preclinical broader acupuncture studies	Limited	No definitive evidence demonstrates that isolated Jing-Well stimulation independently preserves BBB integrity.
NF-κB and NLRP3 inflammasome-related pathways	NF-κB, NLRP3, caspase-1, IL-1β, IL-18	Suppression of inflammatory gene transcription, inflammasome activation, and neuroinflammatory signaling has been reported in animal models.	Experimental acupuncture/electroacupuncture literature	Very limited	These pathways are relevant to acupuncture research generally, but Jing-Well-specific causal evidence is lacking.
HPA-axis and stress-related neuroendocrine regulation	CRH, ACTH, cortisol, hypothalamic activity	Acupuncture may influence stress-related neuroendocrine responses and immune homeostasis.	Experimental and selected clinical studies of broader acupuncture	Indirect	HPA-axis modulation should be regarded as a possible, not established, Jing-Well-related pathway.
Autonomic regulation and vagal anti-inflammatory pathways	HRV, vagal activity, sympathetic activity, α7 nicotinic acetylcholine receptor, splenic nerve pathways	General acupuncture and electroacupuncture studies suggest possible effects on autonomic balance and inflammatory reflex pathways.	Mainly non-Jing-Well electroacupuncture studies, including vagotomy and receptor-blockade models	Insufficient	Vagal and autonomic mechanisms are biologically plausible but not demonstrated specifically for Jing-Well point stimulation.
Oxidative-stress reduction and mitochondrial protection	ROS, lipid peroxidation, SOD, catalase, glutathione peroxidase, ATP production, mitochondrial membrane potential	Reduced oxidative injury, apoptosis-related signaling, and mitochondrial dysfunction have been reported in preclinical models.	Mainly broader acupuncture and electroacupuncture studies	Indirect or very limited	These observations may support neuroprotection but do not prove a Jing-Well-specific effect.
Neurotrophic signaling, synaptic plasticity, and neural repair	BDNF, TrkB, GDNF, NGF, synaptic-plasticity and neurogenesis markers	Increased neurotrophic signaling and markers of neural repair have been reported after acupuncture interventions.	Predominantly animal and mixed-acupoint studies	Very limited	Potential relevance to recovery is suggested, but point-specific superiority has not been established.
Electrophysiological and neural-function modulation	EEG rhythms, fMRI connectivity, HRV, SSEP, MEP, cortical excitability	Changes in cortical oscillations, autonomic indices, neural connectivity, sensory conduction, and motor-pathway excitability have been reported.	Human electrophysiological, neuroimaging, and physiological studies; mostly multi-acupoint protocols	Very limited	Objective physiological changes are reported for acupuncture broadly; their specific relevance to isolated Jing-Well stimulation remains unclear.

Note: This table summarizes candidate mechanisms derived from direct Jing-Well-related observations where available and from broader acupuncture or electroacupuncture research. The strength of evidence is presented narratively and is not a formal GRADE assessment. For most pathways, especially vagal regulation, HPA-axis modulation, glial regulation, oxidative stress, mitochondrial protection, and neurotrophic signaling, Jing-Well-specific mechanistic evidence remains limited or indirect.

Acupuncture-related preservation of blood-brain barrier integrity has also been reported in several preclinical models, potentially through modulation of inflammatory signaling, matrix metalloproteinases, oxidative stress, and tight-junction-associated proteins. However, these findings are predominantly derived from broader acupuncture or mixed-acupoint electroacupuncture protocols. Direct evidence demonstrating that isolated Jing-Well point stimulation independently regulates glial activation or blood-brain barrier integrity remains limited.

Neuroendocrine, autonomic, and vagal-related pathways

The hypothalamic-pituitary-adrenal axis and autonomic nervous system provide important links between neural activity, endocrine signaling, and immune regulation. Broader acupuncture research suggests that acupuncture may influence stress-related neuroendocrine responses, autonomic balance, and inflammatory reflex pathways. Experimental electroacupuncture studies have also reported involvement of vagal, sympathetic, splenic, and cholinergic signaling pathways in the regulation of inflammatory mediators. Nevertheless, evidence involving vagotomy, α7 nicotinic acetylcholine receptor signaling, splenic nerve pathways, or neurotransmitter-mediated immune modulation has mainly been obtained from non-Jing-Well or mixed-acupoint models. Therefore, autonomic and vagal anti-inflammatory mechanisms should currently be regarded as biologically plausible pathways potentially relevant to Jing-Well point stimulation, rather than established Jing-Well-specific mechanisms.

Oxidative stress, mitochondrial function, and cellular survival

Oxidative stress and mitochondrial dysfunction contribute substantially to neuronal injury in stroke, traumatic brain injury, spinal cord injury, neurodegenerative disorders, epilepsy, and neuropathic pain. Studies of acupuncture and electroacupuncture have reported reductions in reactive oxygen species, lipid peroxidation, and apoptosis-related signaling, together with possible improvements in mitochondrial membrane stability, energy metabolism, and antioxidant enzyme activity. These changes may reduce secondary neuronal injury and support tissue recovery. However, the available evidence is heterogeneous and primarily derived from broader acupuncture literature. Further Jing-Well-specific studies are needed to determine whether stimulation at these distal points produces reproducible effects on oxidative stress, mitochondrial function, or cellular survival pathways.

Neurotrophic signaling, synaptic plasticity, and neural repair

Acupuncture-related modulation of neurotrophic factors and neuroplasticity pathways has been reported in experimental neurological models. Increased expression of brain-derived neurotrophic factor, glial cell-derived neurotrophic factor, and other molecular mediators associated with synaptic plasticity, neuronal survival, angiogenesis, and neural repair has been described following acupuncture or electroacupuncture interventions. These mechanisms may be relevant to functional recovery after stroke, traumatic injury, and neurodegenerative disease. However, most studies have used multi-acupoint protocols, and the independent contribution of Jing-Well point stimulation remains uncertain. Accordingly, neurotrophic and neuroplasticity-related findings should be interpreted as indirect mechanistic support rather than proof of a Jing-Well-specific therapeutic effect.

Electrophysiological mechanisms and modern technological insights

*Electroacupuncture and bioelectrical neuromodulation (**Table 4**)*

The incorporation of electrophysiological methods into acupuncture research has substantially advanced understanding of the potential biological mechanisms underlying acupuncture interventions. Among these developments, electroacupuncture (EA), which combines traditional needle insertion with controlled electrical stimulation, has emerged as one of the most widely investigated techniques. EA enables precise adjustment of stimulation parameters, including frequency, intensity, and waveform, thereby improving experimental reproducibility and facilitating mechanistic investigation [72]. Interest in electroacupuncture is particularly relevant to the study of Jing-Well points because these acupoints are located in distal anatomical regions characterized

Table 4. Electrophysiological techniques used in acupuncture research

Technique	Physiological Parameter	Findings After Acupuncture	Neurological Application
EEG	Cortical activity	Alpha/theta modulation	Epilepsy
fMRI	Brain connectivity	Limbic activation	Stroke
HRV	Autonomic balance	↑ Parasympathetic tone	Neuroinflammation
SSEP	Sensory conduction	Improved latency	SCI
MEP	Motor pathway integrity	↑ Corticospinal excitability	Stroke
PET	Metabolic activity	↑ Cerebral metabolism	AD

by dense sensory innervation and rich neurovascular structures. However, it should be emphasized that the majority of electrophysiological evidence discussed in this section is derived from studies of electroacupuncture applied to various acupoints rather than investigations specifically focused on Jing-Well points. Experimental studies have demonstrated that different stimulation frequencies may engage distinct neurophysiological pathways. Low-frequency stimulation (typically 2-10 Hz) has been associated with activation of endorphinergic mechanisms and parasympathetic regulation, whereas higher frequencies (50-100 Hz) may preferentially influence dynorphin-related pathways and sympathetic activity [73]. These frequency-dependent responses highlight the potential of electroacupuncture as a bioelectronic neuromodulatory intervention.

Several investigations have reported that electroacupuncture can activate peripheral sensory afferents and influence spinal, brainstem, hypothalamic, and cortical circuits involved in autonomic regulation, pain processing, and neuroimmune communication [66-69]. Experimental evidence also suggests potential effects on synaptic plasticity, neural network reorganization, and neurochemical signaling. Such observations have generated interest in the possibility that electroacupuncture may support functional recovery in neurological disorders through modulation of both neural and immune pathways. In neurological disease models, electroacupuncture has been associated with reduced excitotoxic injury, modulation of inflammatory signaling, stabilization of neural activity, and enhancement of neuroplasticity [72]. Nevertheless, additional studies directly comparing Jing-Well and non-Jing-Well stimulation protocols are required before these findings can be attributed specifically to Jing-Well point acupuncture.

Electroencephalographic changes following acupuncture stimulation

Electroencephalography (EEG) provides a non-invasive method for assessing real-time cortical electrical activity and has become an important tool for investigating neural responses associated with acupuncture interventions. EEG studies have reported alterations in oscillatory activity, neural synchronization, and functional connectivity following acupuncture stimulation, suggesting modulation of large-scale brain networks involved in sensory, cognitive, and autonomic processing [71]. Changes in alpha, beta, theta, and delta frequency bands have been reported following acupuncture interventions. Increased alpha activity has frequently been associated with relaxation and autonomic regulation, whereas alterations in theta activity have been linked to cognitive and limbic processing. Several studies have also reported normalization of abnormal EEG patterns in patients with chronic pain, epilepsy, and neuropsychiatric disorders following acupuncture treatment [73]. In epilepsy research, acupuncture has been associated with reductions in epileptiform activity and modulation of neural excitability, although findings remain heterogeneous and require further validation. Similarly, EEG-based studies in stroke rehabilitation have reported changes consistent with cortical reorganization and sensorimotor recovery. However, because many studies employ multiple-acupoint treatment protocols, the specific contribution of Jing-Well point stimulation remains difficult to determine. Advanced EEG methodologies, including quantitative EEG (qEEG), source localization techniques, and coherence analysis, have expanded opportunities for investigating acupuncture-related neural responses. These technologies may provide objective biomarkers for assessing cortical modulation, autonomic regulation, and

treatment responsiveness. Future integration of machine learning approaches with EEG data may further facilitate individualized neuromodulatory strategies and improve understanding of acupuncture-related brain dynamics [74].

Functional magnetic resonance imaging and neural network modulation

Functional magnetic resonance imaging (fMRI) has become a valuable tool for examining central nervous system responses to acupuncture. By measuring blood oxygen level-dependent (BOLD) signals, fMRI enables visualization of changes in regional brain activity and functional connectivity associated with acupuncture stimulation. Neuroimaging studies have reported modulation of multiple cortical and subcortical regions following acupuncture interventions, including the hypothalamus, thalamus, insula, anterior cingulate cortex, hippocampus, amygdala, prefrontal cortex, and brainstem nuclei [55]. These structures participate in pain modulation, autonomic regulation, emotional processing, cognition, and neuroendocrine control. Such findings have contributed to the growing concept that acupuncture may function as a systems-level neuromodulatory intervention rather than solely a localized sensory stimulus.

Particular attention has been directed toward the default mode network (DMN) and limbic system, both of which play important roles in self-referential cognition, emotional regulation, stress responses, and neuroendocrine function. Altered connectivity within these networks has been implicated in chronic pain, neurodegenerative diseases, depression, and cognitive dysfunction. Acupuncture-related modulation of these networks has therefore been proposed as a potential mechanism underlying therapeutic effects observed in some clinical studies [57]. In stroke rehabilitation, fMRI studies have reported changes in motor network connectivity and sensorimotor integration following acupuncture interventions. Similarly, studies involving Parkinson's disease and Alzheimer's disease have suggested possible modulation of neural circuits associated with motor control and cognition. However, most neuroimaging evidence derives from broader acupuncture literature, and direct evidence specifically examining Jing-Well point stimulation remains limited.

Evoked potentials and neural conductivity

Evoked potentials provide objective measures of neural pathway function and have been increasingly utilized to evaluate physiological responses associated with acupuncture. Somatosensory evoked potentials (SSEPs), motor evoked potentials (MEPs), auditory evoked potentials, and visual evoked potentials can assess neural conduction, cortical responsiveness, and functional integrity of sensory and motor pathways. Several studies have reported alterations in evoked-potential amplitudes and latencies following acupuncture interventions, suggesting possible effects on neural transmission and network excitability. Improvements in SSEP parameters have been interpreted as indicators of enhanced sensory pathway function, whereas increased MEP amplitudes and reduced conduction latency have been associated with improved corticospinal excitability and motor pathway recovery. In peripheral neuropathies, acupuncture has been reported to improve nerve conduction parameters and sensory function, although methodological heterogeneity limits definitive conclusions. Proposed mechanisms include modulation of inflammation, enhancement of microcirculation, neurotrophic support, and promotion of neural repair processes [66-70]. Event-related potentials (ERPs), particularly the P300 component, have also been investigated in cognitive and neuropsychiatric disorders. Changes in ERP parameters following acupuncture have been associated with improvements in attention, information processing, and cognitive performance. Nevertheless, dedicated studies examining the electrophysiological effects of isolated Jing-Well point stimulation remain scarce.

Artificial intelligence, digital acupuncture, and precision electrophysiology

Recent advances in artificial intelligence (AI), machine learning, and digital health technologies have created new opportunities for acupuncture research and personalized neuromodulation (**Table 4**). AI-based analytical methods can process complex electrophysiological and neuroimaging datasets, identify response patterns, and potentially predict treatment outcomes [43-47]. Machine-learning algorithms applied to EEG, heart-rate variability, neuroimaging, and physiological monitoring data may help identify biomarkers associated with treat-

ment responsiveness. Such approaches could facilitate individualized acupuncture strategies tailored to specific neurophysiological and immunological profiles [41].

Emerging technologies, including wearable biosensors, wireless electroacupuncture systems, and real-time physiological monitoring platforms, further expand opportunities for objective assessment of autonomic activity, neural oscillations, and treatment-related physiological changes [52-57]. These developments may support adaptive stimulation strategies in which treatment parameters are modified according to ongoing physiological feedback. Another promising area involves integration of acupuncture research with brain-computer interfaces (BCIs) and closed-loop neuromodulation systems. Although currently at an early stage of development, these approaches may eventually enable real-time monitoring and modulation of neural circuits involved in pain, motor control, cognition, and neuroimmune regulation [33].

Despite these technological advances, important challenges remain, including limited standardization of electrophysiological protocols, variability in stimulation parameters, small sample sizes, and insufficient multicenter validation studies. Addressing these limitations will be essential for establishing robust mechanistic evidence and clarifying the specific electrophysiological relevance of Jing-Well point acupuncture within modern neuroscience and bioelectronic medicine [34].

Clinical and preclinical evidence related to acupuncture and Jing-Well point stimulation in neurological disorders (Table 5)

Ischemic stroke and post-stroke neuroinflammation

Ischemic stroke remains one of the leading causes of mortality and long-term disability worldwide. In addition to the initial vascular occlusion, secondary injury mechanisms including neuroinflammation, oxidative stress, excitotoxicity, blood-brain barrier disruption, and immune-cell infiltration contribute substantially to neurological damage and functional impairment [22-25]. Consequently, modulation of post-stroke inflammatory responses has emerged as an important therapeutic target. Acupuncture has historically been used in stroke management and rehabilitation, including protocols incorporating Jing-Well points. Experimental studies involving acupuncture and electroacupuncture have reported reductions in inflammatory mediators, modulation of NLRP3 inflammasome activity, preservation of blood-brain barrier integrity, and improvements in neuroplasticity-related pathways [26]. However, most mechanistic evidence derives from broader acupuncture literature rather than studies specifically evaluating Jing-Well point stimulation.

Electrophysiological and neuroimaging investigations have suggested that acupuncture may influence cortical reorganization, sensorimotor network activity, and functional connectivity following stroke. Improvements in somatosensory evoked potentials (SSEPs) and motor evoked potentials (MEPs) have also been reported in some rehabilitation studies, potentially reflecting enhanced neural transmission and motor pathway recovery [27-30]. Clinical studies have described improvements in motor function, swallowing ability, activities of daily living, spasticity, and quality of life among stroke patients receiving acupuncture as part of multidisciplinary rehabilitation programs. Nevertheless, methodological heterogeneity, variability in acupuncture protocols, and limited Jing-Well-specific investigations preclude definitive conclusions regarding efficacy. Additional well-designed multicenter trials are needed to clarify the specific contribution of Jing-Well point stimulation in stroke rehabilitation.

Parkinson's disease

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by degeneration of dopaminergic neurons within the substantia nigra and dysfunction of basal ganglia circuitry. Increasing evidence indicates that neuroinflammation, oxidative stress, mitochondrial dysfunction, and immune dysregulation contribute to disease progression in addition to classical dopaminergic deficits. Experimental acupuncture studies have reported reductions in inflammatory signaling, modulation of microglial activity, attenuation of oxidative stress, and alterations in pathways involving NF-κB and NLRP3 inflammasome sig-

Table 5. Evidence summary for Jing-Well-specific and broader acupuncture studies in neurological disorders

Neurological disorder	Proposed biological context	Acupoint specificity	Evidence source and study type	Key biological targets or outcomes	Clinical versus experimental classification	Narrative strength of evidence*	Clinical interpretation
Ischemic stroke and post-stroke disorders of consciousness	Neuroinflammation, BBB disruption, oxidative stress, impaired neuroplasticity, cortical reorganization	Jing-Well points may be included in composite protocols; direct twelve Jing-Well evidence is mainly preclinical	Jing-Well-specific rodent studies; acupuncture rehabilitation trials; systematic reviews and meta-analyses of broader acupuncture	BBB permeability, inflammatory mediators, motor recovery, swallowing, consciousness, ADL, spasticity	Mixed; direct evidence is predominantly experimental	Low-to-moderate for adjunctive acupuncture rehabilitation; very low for isolated Jing-Well efficacy	May be considered as an adjunctive rehabilitation approach; isolated Jing-Well treatment cannot be recommended as an evidence-based stand-alone intervention
Parkinson's disease	Microglial activation, oxidative stress, mitochondrial dysfunction, basal-ganglia network dysfunction	No convincing isolated Jing-Well clinical evidence	Animal studies; small clinical studies of broader acupuncture; neuroimaging research	Motor symptoms, fatigue, sleep, autonomic symptoms, BDNF/GDNF-related pathways	Experimental predominant with limited clinical evidence	Low overall; very low Jing-Well-specific evidence	Potential symptomatic adjunct only; no evidence of disease modification or point-specific benefit
Alzheimer's disease and mild cognitive impairment	Neuroinflammation, amyloid- and tau-associated injury, oxidative stress, hippocampal and DMN dysfunction	No direct Jing-Well-specific evidence identified	Preclinical studies; small clinical acupuncture studies; EEG and fMRI investigations	Cognition, sleep, behavioral symptoms, microglial activation, neural connectivity	Mixed, with limited clinical evidence	Low overall; very low Jing-Well-specific evidence	Insufficient evidence for therapeutic recommendation; further controlled clinical research is required
Multiple sclerosis	Autoimmune inflammation, Th1/Th17 imbalance, Treg dysfunction, demyelination, fatigue and pain	No direct Jing-Well-specific clinical evidence	Small clinical studies of acupuncture; indirect mechanistic and symptom-management evidence	Fatigue, pain, spasticity, bladder symptoms, quality of life, immune regulation	Limited clinical and experimental evidence	Low	May support symptom management in selected patients but should not be considered disease-modifying therapy
Epilepsy and cortical hyperexcitability disorders	Cytokine signaling, glial activation, BBB dysfunction, altered cortical excitability	No established Jing-Well-specific evidence	Animal acupuncture studies; limited clinical adjunctive reports; EEG-based observations	Seizure frequency, cortical oscillations, IL-1β, TNF-α, NF-κB-related signaling	Experimental predominant	Very low to low	Insufficient evidence for clinical seizure control; acupuncture should not replace standard antiseizure therapy
Traumatic brain injury and spinal cord injury	Secondary neuroinflammation, oxidative stress, edema, mitochondrial dysfunction, impaired neural conduction	Direct twelve Jing-Well experimental evidence exists for selected TBI-related outcomes; clinical evidence is mostly broader acupuncture	Jing-Well-specific animal studies; broader rehabilitation studies; electrophysiological investigations	Microcirculation, BBB function, inflammatory mediators, motor recovery, spasticity, neuropathic pain, neural conduction	Mixed; direct evidence predominantly experimental	Moderate direct preclinical evidence; low clinical evidence	Promising adjunctive rehabilitation field, but direct clinical efficacy of Jing-Well stimulation remains unconfirmed
Neuropathic pain	Neuroimmune activation, spinal microglial activity, cytokine signaling, altered nociceptive processing	No clear isolated Jing-Well evidence	Broader acupuncture trials, individual-patient meta-analyses, mechanistic animal studies	Pain intensity, function, quality of life, microglial activation, inflammatory mediators	Mixed clinical and experimental evidence	Low-to-moderate for acupuncture-related symptom relief; very low Jing-Well-specific evidence	Acupuncture may be considered for selected patients as an adjunctive pain-management strategy; no Jing-Well-specific conclusion is justified
Cognitive, autonomic, and neuropsychiatric symptoms associated with neurological disease	Autonomic imbalance, stress signaling, sleep disturbance, altered cortical connectivity	Predominantly indirect; mixed-acupoint protocols are common	HRV, EEG, fMRI, physiological studies, and small clinical trials	HRV, alpha/theta rhythms, functional connectivity, sleep quality, anxiety, fatigue	Mixed	Low-to-moderate for physiological effects; very low Jing-Well-specific evidence	May inform future precision-neuromodulation studies but remains investigational in routine neurological care

Note: The table summarizes direct Jing-Well point studies together with broader acupuncture, mixed-acupoint, and electroacupuncture evidence. For several conditions, including Parkinson's disease, Alzheimer's disease, multiple sclerosis, epilepsy, and neuropathic pain, the available evidence is predominantly derived from non-Jing-Well-specific clinical or preclinical studies. Therefore, reported findings should not be interpreted as confirmation of Jing-Well-specific clinical efficacy.
*Traditional or historical descriptions should be interpreted as background information and do not represent confirmed clinical efficacy unless supported by controlled clinical evidence.

naling [50-52]. However, these findings largely originate from animal models and acupuncture protocols that are not specific to Jing-Well points. Neuroimaging studies have suggested that acupuncture may influence basal ganglia-thalamocortical circuits involved in motor control and functional connectivity. Additional studies have reported associations between acupuncture and increased expression of neurotrophic factors such as brain-derived neurotrophic factor (BDNF) and glial cell-derived neurotrophic factor (GDNF), which may support neuronal survival and synaptic plasticity [53]. Clinical trials have reported improvements in motor symptoms, sleep disturbances, fatigue, autonomic dysfunction, and quality of life in some patients with PD receiving acupuncture. However, existing studies vary considerably in methodological quality, sample size, and treatment protocols. Consequently, acupuncture should currently be regarded as a potential adjunctive therapy rather than a disease-modifying intervention, and further studies are required to determine whether Jing-Well point stimulation confers distinct benefits.

Alzheimer's disease and cognitive dysfunction

Alzheimer's disease (AD) is characterized by progressive cognitive decline associated with amyloid-beta accumulation, tau pathology, synaptic dysfunction, and neuronal loss. Neuroinflammation is increasingly recognized as a major contributor to disease progression, with activated microglia, reactive astrocytes, oxidative stress, and blood-brain barrier dysfunction playing important roles in neurodegenerative processes [38]. Experimental studies have suggested that acupuncture may influence inflammatory signaling pathways, oxidative stress, mitochondrial function, and neuroplasticity-related mechanisms. Reductions in microglial activation and inflammatory cytokine production have been reported in several preclinical investigations [39]. However, direct evidence linking these effects specifically to Jing-Well point stimulation remains limited.

Neuroimaging studies have reported changes in hippocampal activity, default mode network connectivity, and cortical activation patterns following acupuncture interventions. Similarly, EEG studies have identified alterations in theta and alpha oscillatory activity that may reflect changes in cognitive processing and neural synchronization [18-25]. Clinical investigations have suggested potential improvements in memory, attention, sleep quality, and behavioral symptoms among individuals with mild cognitive impairment or AD receiving acupuncture. Nevertheless, the available evidence remains heterogeneous, and larger randomized controlled trials are necessary before definitive clinical recommendations can be made.

Multiple sclerosis

Multiple sclerosis (MS) is a chronic autoimmune demyelinating disease characterized by inflammatory injury to myelin and axons within the central nervous system. The disease involves complex interactions among T cells, macrophages, cytokines, and blood-brain barrier dysfunction that contribute to neurological disability and progressive neurodegeneration. Experimental studies have suggested that acupuncture may influence immune regulation through modulation of T-cell differentiation, inflammatory cytokine production, and pathways involving Th1/Th17 responses and regulatory T-cell activity [22]. Additional studies have reported reductions in oxidative stress and microglial activation, together with increases in neurotrophic signaling and neural repair mechanisms. However, these observations are primarily derived from preclinical models and broader acupuncture literature. Clinical studies evaluating acupuncture in MS have reported improvements in fatigue, neuropathic pain, spasticity, bladder dysfunction, mood symptoms, and quality of life. While these findings suggest potential supportive benefits, evidence for disease-modifying effects remains insufficient. Future studies are needed to determine whether specific acupuncture approaches, including Jing-Well point stimulation, can meaningfully influence immune-mediated disease processes.

Epilepsy and cortical hyperexcitability disorders

Epilepsy is characterized by recurrent seizures resulting from abnormal neuronal excitability and hypersynchronous cortical activity. Increasing evidence suggests that neuroinflammation contributes to epileptogenesis through activation of microglia, cytokine production,

oxidative stress, and disruption of blood-brain barrier function. Experimental acupuncture studies have reported modulation of inflammatory signaling pathways, neurotransmitter systems, and neuronal excitability. Reductions in cytokines such as IL-1β and TNF-α, together with alterations in NF-κB signaling, have been observed in animal models. However, these findings should not be interpreted as specific to Jing-Well point stimulation because most studies have employed diverse acupuncture protocols.

EEG-based investigations have suggested that acupuncture may influence cortical oscillatory activity and neural network dynamics associated with seizure generation. Clinical studies evaluating acupuncture as an adjunctive treatment have reported variable effects on seizure frequency, sleep quality, anxiety, and quality of life [60-66]. Overall, while acupuncture demonstrates biological plausibility as a neuromodulatory intervention, current evidence remains insufficient to establish a definitive role in epilepsy management.

Traumatic brain injury and spinal cord injury

Traumatic brain injury (TBI) and spinal cord injury (SCI) involve both primary mechanical damage and secondary injury processes including neuroinflammation, oxidative stress, excitotoxicity, mitochondrial dysfunction, and apoptotic signaling. These secondary mechanisms contribute significantly to long-term neurological impairment and represent important therapeutic targets. Experimental studies have suggested that acupuncture may reduce inflammatory cytokine production, attenuate oxidative stress, preserve mitochondrial function, and promote neurotrophic signaling following traumatic injury [44]. Additional investigations have reported effects on edema formation, neural repair processes, and neuroplasticity-related pathways. However, as with other neurological conditions, most evidence derives from broader acupuncture literature rather than Jing-Well-specific studies. Electrophysiological studies have reported improvements in neural conduction parameters, motor evoked potentials, and autonomic regulation following acupuncture interventions [45]. Clinical studies have also described improvements in neuropathic pain, spasticity, bladder function, sleep quality, and rehabilitation outcomes in selected patient populations [46]. Although these findings support continued investigation of acupuncture as an adjunctive rehabilitation strategy, definitive conclusions regarding the efficacy and mechanistic specificity of Jing-Well point stimulation cannot currently be drawn. Future translational studies integrating clinical outcomes, neuroimaging, electrophysiology, and immunological biomarkers will be essential for clarifying its therapeutic role.

Discussion

This structured narrative review is formed by literature synthesis, which summarizes the existing literature on the possible neuroimmune and electrophysiological effect of acupuncture at Jing-Well points in neurological diseases. The key finding is that the point stimulation of the Jing-Well has biological plausibility as a neuro-modulatory intervention; especially in diseases associated with inflammation, autonomic dysregulation, oxidative injury, disruption of blood-brain barrier function and impaired neural plasticity. The evidence base is still not even, however. Although there are direct studies related to Jing-Well that are relatively few, they are limited to experimental models, and much of the mechanistic and clinical literature is about electroacupuncture or multi-point techniques. The benefits reported should be considered as those associated with the mechanisms of acupuncture, not necessarily as evidence of the efficacy of the Jing-Well points by itself.

The most direct and robust preclinical observations are associated with stimulation of the twelve hand Jing-Well points in models of cerebral ischemia and traumatic brain injury. These studies indicate that there is a lower permeability of the blood-brain barrier and a better amelioration of microcirculatory disturbance, thus giving the potential to protect the brain in early stages. More general acupuncture studies also suggest that inflammatory mediators like TNF-α, IL-1β and IL-6 can be dampened, while anti-inflammatory pathways like IL-10 and vagal signaling and autonomic balance can be strengthened. Experimental evidence also links modulation of microglial activation, oxidative stress, mitochondrial dysfunction, NF-κB signaling, and NLRP3 inflammasome activation

[30-36]. While these results provide a logical, biological model, the majority of these were determined by non-Jing-Well or mixed-acupoint protocols which cannot define mechanisms for each point.

EEG and Neuroimaging studies offer objective and complementary evidence that Acupuncture can modulate the excitability of the cortex, neural connectivity, sensorimotor integration, and autonomic regulation. These changes in EEG rhythms, HRV, evoked potentials, and functional magnetic resonance imaging connectivity have been observed in a variety of neurological and pain conditions [70-74]. These modalities are especially relevant as they can be considered as a link between mechanistic observation and patient-centered outcomes. However, methodological differences in stimulation frequency, needle manipulation, acupoint combinations, timing of measurements and analytic methods restrict the possibility of comparisons between studies. A major gap in knowledge is the absence of comparisons between Jing-Well and non-Jing-Well points.

Acupuncture could be of clinical benefit as a supplement to conventional neurological rehabilitation care or symptom management, particularly in post-stroke disability, pain, fatigue, sleep disturbance, spasticity and autonomic symptoms. At present, however, it is not justifiable to replace existing medical, surgical, pharmacological or rehabilitative treatments. The benefits of potential interventions should be evaluated as exploratory and/or supportive in Parkinson's disease, Alzheimer's disease, multiple sclerosis, epilepsy, and traumatic brain and spinal injury due to small sample sizes, a lack of uniformity in control procedures, and inconsistent clinical endpoints. Such statements are not yet supported at this time for any disease modification, seizure control, neuroprotection or point-specific superiority. In view of this, clinical recommendations need to differentiate specific claims from general acupuncture evidence, and to convey uncertainty to patients, clinicians, and policy makers when taking into consideration integrative interventions in the context of routine neurological care in various health-care settings.

More in-depth trials for Jing-Well should be done in the future. Isolated stimulation of the Jing-Well with standard treatment of mixed-acupoints, sham control, and conventional therapy should be compared in randomized studies, with the acupoints clearly localized, the stimulation modality, frequency, intensity, and duration of stimulation reported, and the skills of the practitioner reported, as well as the co-interventions. Mechanistic endpoints, including cytokine panels, HRV and EEG, evoked potentials and neuro-imaging measures, should be included in trials along with validated neurological outcomes. This multimodal design would help to understand whether any physiological changes associated with clinically meaningful recovery or not.

More large multicenter research is required for more generalizability and to minimize the risk of small study effects. Combined electroacupuncture protocols based on electrophysiology monitoring can also help precision treatments, but the latter is still in research. Transcriptomics, proteomics, metabolomics, and microbiome analyses could provide insights into molecular signatures of treatment response and biologically plausible responder subgroups. Last, but not least, there has to be a transparent preregistration, standardized reporting, sufficient blinding, a credible sham procedure, and a direct reporting of adverse events. This collaborative study could establish whether Jing-Well point acupuncture has a unique therapeutic role in the global evidence-based neurological care.

Limitations of current evidence

Despite growing interest in the potential neuroimmune and electrophysiological effects of Jing-Well point acupuncture in neurological disorders, several important limitations constrain interpretation of the available evidence. First, there is a relative scarcity of studies specifically investigating Jing-Well point stimulation. Much of the current mechanistic and clinical evidence is derived from broader acupuncture or electroacupuncture literature involving multiple acupoints, making it difficult to determine whether observed effects are attributable specifically to Jing-Well points or reflect more general acupuncture-related mechanisms. Second, many published studies are characterized by small sample sizes, which limit statistical power and reduce the generalizability of findings. Small-scale clinical trials may be particularly susceptible to random variation and

may overestimate treatment effects. Third, a substantial proportion of the available mechanistic evidence originates from animal models. Although these studies provide valuable insights into inflammatory signaling pathways, autonomic regulation, oxidative stress, and neuroprotective mechanisms, their translational relevance to human neurological disorders remains uncertain. Additional well-designed human studies are required to confirm these findings.

Fourth, considerable heterogeneity exists across acupuncture protocols, including differences in acupoint selection, stimulation techniques, treatment frequency, needle retention time, electroacupuncture parameters, outcome measures, and study populations. Such variability complicates comparisons among studies and limits the development of standardized therapeutic recommendations. Fifth, direct mechanistic validation remains limited. While numerous studies suggest potential involvement of inflammatory cytokines, autonomic pathways, neuroendocrine regulation, and electrophysiological changes, relatively few investigations have simultaneously assessed molecular biomarkers, neuroimaging findings, electrophysiological outcomes, and clinical responses. Consequently, causal relationships between Jing-Well point stimulation and specific neuroimmune mechanisms remain incompletely established.

Finally, publication bias cannot be excluded. Positive findings are more likely to be published than negative or inconclusive results, potentially leading to an overestimation of therapeutic efficacy and mechanistic certainty. Additionally, methodological limitations such as inadequate blinding, insufficient sham controls, and selective reporting may further influence the interpretation of available evidence. Taken together, these limitations highlight the need for larger multicenter clinical trials, standardized acupuncture protocols, rigorous mechanistic investigations, and direct comparisons between Jing-Well and non-Jing-Well acupoints. Such studies will be essential for clarifying the specificity, biological plausibility, and clinical relevance of Jing-Well point acupuncture in neurological disorders.

Future directions

Future research should focus on establishing a stronger mechanistic and clinical evidence base for Jing-Well point acupuncture in neurological disorders through the integration of advanced biomedical technologies and standardized study designs. One promising direction involves the application of multi-omics approaches, including genomics, transcriptomics, proteomics, metabolomics, and microbiome analyses. These technologies may help identify molecular pathways influenced by acupuncture, characterize patient-specific biological responses, and uncover novel biomarkers associated with treatment efficacy. Integrating multi-omics datasets with clinical outcomes could provide a more comprehensive understanding of the complex neuroimmune mechanisms potentially involved in acupuncture-mediated neuromodulation. Advanced neuroimaging techniques should also play a central role in future investigations. Functional magnetic resonance imaging (fMRI), positron emission tomography (PET), diffusion tensor imaging (DTI), and functional connectivity analyses may provide valuable insights into the neural networks and brain regions associated with acupuncture-induced immunomodulatory effects. Particular attention should be directed toward structures involved in neuroimmune regulation, including the hypothalamus, insula, anterior cingulate cortex, brainstem nuclei, and limbic system structures.

Future studies should further explore the relationship between electrophysiological changes and immune responses by integrating electroencephalography (EEG) with inflammatory biomarker assessments. Simultaneous evaluation of cortical activity patterns and cytokine profiles, including TNF-α, IL-1β, IL-6, and IL-10, may help clarify whether electrophysiological modulation is associated with measurable changes in systemic or central inflammatory processes.

Similarly, combining heart rate variability (HRV) analysis with inflammatory biomarker measurements may improve understanding of autonomic-immune interactions. Because HRV serves as a non-invasive indicator of autonomic nervous system activity, particularly parasympathetic function, integrated HRV-cytokine studies could provide important evidence regarding

the role of autonomic regulation in acupuncture-mediated immune modulation. Comparative clinical and mechanistic studies are also urgently needed. Direct comparisons between Jing-Well and non-Jing-Well acupoints would help determine whether observed neuroimmune and electrophysiological effects are point-specific or represent broader acupuncture-related phenomena. Such investigations could address one of the major knowledge gaps identified in the current literature.

Conclusion

Jing-Well points have longstanding traditional relevance in the management of acute neurological and consciousness-related conditions, and their distal anatomical location provides a plausible basis for sensory, autonomic, and neurovascular responses. Current research from the broader acupuncture and electroacupuncture literature suggests potentially relevant effects on inflammatory signaling, autonomic regulation, oxidative stress, glial activation, neural plasticity, and electrophysiological function. However, these observations should not be interpreted as proof that such mechanisms are specific to Jing-Well point stimulation. Direct Jing-Well-specific evidence remains limited, particularly for neuroimmune modulation, vagal anti-inflammatory mechanisms, electrophysiological changes, and clinical efficacy across neurological disorders. At present, Jing-Well point acupuncture may be considered a biologically plausible adjunctive approach rather than an established disease-modifying neurological intervention. It should not replace evidence-based medical, pharmacological, surgical, or rehabilitation treatment.

Future research should directly compare isolated Jing-Well stimulation with non-Jing-Well points, sham procedures, and conventional care. Well-designed multicenter clinical trials should employ standardized point localization and stimulation parameters, clinically meaningful outcomes, transparent adverse-event reporting, and integrated assessment of inflammatory biomarkers, autonomic indices such as heart-rate variability, EEG, evoked potentials, and neuroimaging measures. Such studies are necessary to determine whether Jing-Well point stimulation has distinct neuroimmune or electrophysiological effects and to define its appropriate role in evidence-based neurological care.

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Disclosure of conflict of interest

None.

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