Acupuncture and Herbal Medicine

Research framework for scientific innovation and translational application of original acupuncture theories: a review based on Hand Twelve Jing-Well Points stimulation therapy

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Abstract

The field of acupuncture is currently facing paradigmatic issues, including the difficulty of turning theoretical strengths into technical discourse power, a gap between mechanistic research and clinical imperatives, and the fragmentation of research activities. Therefore, constructing a research paradigm grounded in traditional Chinese medicine theory and validated through contemporary scientific methods is essential. Hand Twelve Jing-Well Points (HTWP) acupuncture, an ancient therapy known for its rapid efficacy and practical application, offers an optimal solution for these challenges. In this study, the theoretical foundations, clinical effectiveness, biological explanations, and Translational applications of HTWP acupuncture were consolidated by integrating a four-step research framework. Initially, we developed the "Well point-Brain Connection" framework rooted in classical theories and informed by the "Root-Knot" concept. Subsequent clinical practice provided evidence of its effectiveness in modulating awareness and facilitating motor-cognitive rehabilitation for patients with central nervous system issues. Moreover, mechanistic research provides scientific verification of a "Sensation-Transmission-Effect" cascade that encompasses the activation of arousal circuits and the repair of the blood-brain barrier. Ultimately, the promotion of translation, standardization of systems, and the use of wearable technologies have aided the transition from passive therapy to proactive health management. This closed-loop concept offers compelling evidence for the "Well point-Brain Connection" and provides an applicable framework for scientific innovation and global distribution of innovative acupuncture hypotheses.

Keywords: Acupuncture, Central nervous system diseases, Hand Twelve Jing-Well Points, Research paradigm, Translational medicine, Well point-brain connection

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Introduction

Since the 1990s, global brain science initiatives have confirmed that the central nervous system (CNS) is the core regulator of human physiological functions and spurred innovative exploration into peripheral neural regulation[1], including median and vagus nerve stimulation. The U.S. Stimulating Peripheral Activity to Relieve Conditions (SPARC) program has shown through multiple studies that peripheral nerve stimulation can influence central functions by retrogradely engaging specific neuroendocrine and immune interactions, providing a novel "peripheral-to-central" therapeutic pathway for addressing visceral and CNS disorders. The concept of "peripheral nerve stimulation targets" aligns closely with the core theory of traditional Chinese medicine (TCM) regarding the acupuncture points on the body surface that regulate organ function. Together, these concepts reveal the biological basis for cross-level regulation

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between the periphery and CNS, showing an intrinsic resonance between traditional medicine and modern scientific research[2].

TCM has been extensively used in diagnosing and treating neurological disorders. Acupuncture, a peripheral stimulation therapy with unique advantages, is an effective tool for addressing complex neurological diseases because of its long history, simple operation, and clinical effectiveness[3]. Among its modalities, Hand Twelve Jing-Well Points acupuncture (HTWP Acu) is often used as an emergency intervention originating from traditional bloodletting therapy. Its theoretical roots can be traced back 2,500 years to the *Inner Canon of Huang Di (Huang Dì Nèi Jıng)*. Clinical studies have shown that stimulating specific acupoints, including *Shaoshang* (LU11) on the lung meridian of hand-taiyin, *Shang Yang* (LI1) on the large intestine meridian of hand-yangming, *Zhong Chong* (PC9) on the pericardium meridian of hand-jueyin, *Guan Chong* (TE1) on the triple energizer meridian of hand-shaoyang, *Shao Chong* (HT9) on the heart meridian of hand-shaoyin, and *Shao Ze* (SI1) on the small intestine meridian of hand-taiyang, can safely alleviate symptoms of CNS injury[4]. Consequently, their convenience, cost-effectiveness, and potential therapeutic value have attracted considerable attention. The aim of this review is to consolidate the theoretical origins, clinical efficacy, mechanistic elucidation, and translational progress of HTWP Acu. This review seeks to discover a pathway for scientific innovation and the translation of original acupuncture theories by exploring the mechanisms by which peripheral stimulation achieves cross-level central regulation. Ultimately, we also aim to bridge the gap between empirical tradition and scientific innovation by providing a therapeutic solution that integrates eastern wisdom with modern science to promote global health. In this study, English and Chinese databases, including Web of Science, PubMed, and China National Knowledge Infrastructure (CNKI), were searched for literature published between 1990 and 2025 using the keywords "Jing point" "Jing-Well point" "bloodletting" along with the pinyin designations and international standard codes of each Jing-Well point.

Theoretical origin of HTWP Acu

The theoretical foundation of HTWP Acu is based on TCM systems. Meridian pathways, which are the source of generating *qi* and blood in the 12 meridians, are systematically constructed through the root-branch theory, meridian circulation, and organ theory. Many physicians have accumulated extensive experience in regulating brain and mental functions *via* HTWP Acu through clinical practices, including emergency consciousness restoration and heat-clearing *qi* regulation. This provides a traditional basis for modern research into its central regulatory mechanisms.

Classical TCM theory on HTWP Acu for brain regulation

In traditional Chinese culture, brain functional activities (thinking, memory, and consciousness) are often associated with the "heart" which is used to represent the "brain" idioms like "skillful hands and a clever mind" and "ten fingers connect to the heart" actually refer to "brain" revealing the close, bidirectional connection between hands and brain. This means that brain consciousness activities can produce specific representations in the fingers, while finger stimulation can rapidly influence brain functions[5]. This indicates that ancient people intuitively recognized the special "finger–brain" connection[6], providing a cultural cognitive foundation for modern research on HTWP Acu. Ancient Chinese medical texts also contain numerous discussions on the relationship between the fingers and the brain. The theory of root-branch-leaf nodes explains that the 12 meridians take the four limbs well points as their "roots" serving as the source of meridian *qi*, and the head, chest, and abdomen as their "nodes". The *Lingshu,* an ancient Chinese medical treatise, explicitly states that HTWP Acu can treat visceral diseases, confirming the structural and functional pathways that link the fingers and the brain.

The development of HTWP Acu for brain regulation in ancient medicine

Ancient physicians primarily used HTWP in clinical practice using two main approaches: diagnosis and treatment. For diagnosis, they observed the HTWP and nail characteristics to aid in assessing the disease. As noted in the *Lingshu*, gallbladder function can be evaluated based on nail morphology and coloration, indicating correlations between changes in the HTWP sign and bodily functions. Japanese researchers employed the heat sensitivity method using lit incense sticks to detect bilateral symmetry in heat perception at the HTWP, which helped identify pathologies in the related meridians and viscera[7]. HTWP Acu primarily involves point pricking and bloodletting. Ancient practitioners used triangular needles, whereas modern clinical practice widely adopts disposable lancets owing to their cost-effectiveness, safety, and adjustable depth. Standard procedures include securing the patient's finger with the thumb and index finger while applying local massage or distal compression (1–10 times) to promote congestion. The needle depth was controlled at 1 to 3 mm based on individual variations, with bloodletting volumes ranging from 1 to 10 drops. Owing to the significant pain associated with HTWP pricking, clinicians typically conduct non-retained point pricking, which requires applying pressure on the needle hole after the procedure to stop the bleeding.

HTWP Acu is currently the most widely used in China and Japan; however, there are differences in clinical practice[7]. First, the standards for locating acupoints vary. In China, the PC9 acupoint is located at the tip of the distal phalanx of the middle finger, whereas in Japan, it is located on the radial side of the distal phalanx of the middle finger. Second, there is no standardization in the units of stimulation depth used. Third, there were significant differences in bloodletting volume, with Japanese clinical bloodletting typically ranging from 30 to 40 drops. These differences highlight the need to establish international standards for acupoint localization and operational procedures. Japanese scholars, based on Eastern medicine and the theory of well-conductive channels, have confirmed that HTWP Acu can enhance

immunity and regulate autonomic nervous system functions. Its clinical protocol primarily involves HTWP Acu combined with pricking points on the head, back, and chest to treat autonomic nervous system disorders and musculoskeletal diseases. In TCM, on the other hand, it focuses on acute conditions, diseases of the five Zang organs, and febrile diseases[8], including emergency interventions for restoring consciousness, relief of sore throat, pain, chest tightness, abdominal distension, depression, and menstrual disorders. Collectively, these applications create a multilevel therapeutic system for HTWP, ranging from acute interventions to functional regulation.

Clinical evidence of HTWP Acu

As a medical discipline rooted in clinical practice, acupuncture must be supported by solid and reproducible clinical evidence for its modern development. With lifestyle changes and evolving disease patterns, the clinical applications of HTWP Acu have surpassed conventional theoretical frameworks. The therapeutic philosophy has evolved from empirical practice to evidence-based medicine, showing broad prospects for treating multisystem diseases. The clinical evidence for HTWP Acu is consolidated in this article, with the aim of identifying universal clinical patterns and providing a core foundation for establishing an HTWP diagnosis and treatment system.

CNS diseases

Classical texts and modern clinical evidence indicate that HTWP Acu exerts significant regulatory effects on brain function. The spectrum of HTWP Acu-related disorders can be categorized into four types (Table 1), based on disease progression: acute brain injury, encephalopathy sequelae, cognitive impairment, and mental and emotional disorders. This classification highlights the differential therapeutic advantages at various pathological stages, thus informing clinical strategy selection (Figure 1).

Table 1

Clinical efficacies of HTWP acupuncture for CNS disease

Sort	Disease	Object (T/C)	Method	HTWP intervention	Clinical manifestation	Laboratory finding	Refs
1. Acute brain injury	Within 48 h of ischemic or hemorrhagic stroke	180/180	RCT	MA	Overall GCS↑, eye and language response of GCS score at 15, 30, 50, 80 min↑	No difference	[9]
	Within 6 h from ACOP	20/20	RCT	MA	GCS score difference↑	Unreported	[10]
	Within 24 h of severe TBI	14/13/13/16	RCT	MA	BP in 2 days, 7 days↑	Unreported	[11]
2. Encephalopathy sequelae	Within 24 h of severe TBI	30/30/30	RCT	MA	NDS↑, FMA↑	Unreported	[12]
	Acute ischemic stroke	50/50	RCT	MA	MBI↑, FMA↑, MAS↓, MMSE↑, NIHSS↓, NDF↓	FGF23↓, Apelin-13↓, HDL↑, LDL↓, TC↓, TG↓	[13]
	Cerebral infarction—caused hemidysesthesia	100/50	RCT	MA	Unreported	Cerebral hemodynamics improved in MCA, PCA, and BA.	[14]
	Ischemic or hemorrhagic stroke somatosensory disorder	31/30	RCT	MA	FMA↑, MBI↑, Lindmark↑	Unreported	[15]
3. Cognitive impairment	VD	140	RCT	MA	MMSE↑, ADL↑	mean cerebrovascular velocity↑	[16]
	VD	30/30	RCT	MA	MMSE↑, ADL↑	VEGF↑, AChE↓	[17]
	children with severe MR	30/30	RCT	MA	DQ↑, IQ↑	Unreported	[18]
4. Mental and emotional	Post-stroke depression	20/20/20	RCT	MA	HAMD↓, BI↑	Unreported	[19]
	Male participant	18/0	Before and after	HTWP exercise	PERCLOS↓, BF↓, SRR↓, PVT↓, KSS↓	Unreported	[20]
	Mental fatigue	35/35	RCT	HTWP exercise	VAS fatigue scale↓, Stroop test choice reaction time↓	Resting parietal, temporal, occipital lobe HbO_2 ↑	[21]

↑: Upregulated by intervention; ↓: Downregulated by intervention; AChE: Acetyl cholinesterase; ACOP: Acute carbon monoxide poisoning; ADL: Activity of daily living; Apelin-13: G protein-coupled receptor APJ endogenous ligand; BA: Basilar artery; BF: Blink frequency; BI: Barthel Index; BL-HTWP: Bloodletting Puncture at HTWP; BP: Blood pressure; CNS: Central nervous system; DQ: Development quotient; FGF23: Fibroblast growth factor 23; FMA: Fugl-meyer assessment; GCS: Glasgow coma scale score; HAMD: Hamilton rating scale for depression; HDL: High-density lipoprotein; HTWP: Hand Twelve Jing-Well Points; IQ: Intelligence quotient; KSS: Karolinska; LDL: Low-density lipoprotein; MA: Manual acupuncture; MAS: Modified Ashworth scale; MBI: Modified Barthel index; MCA: Middle cerebral artery; MMSE: Mini-mental state examination; MR: Mental retardation; NDF: Neurological deficit scale; NDS: neuropathy disability score; NIHSS: National Institutes of Health Stroke Scale; PCA: Posterior cerebral artery; PERCLOS, Percentage of eyelid closure; PVT: Psychomotor vigilance task; RCT: Randomized controlled trial; SRR: Steering reversal rate; TC: Total cholesterol; TG: Triglyceride; VD: Vascular dementia; VEGF: Vascular endothelial growth factor.

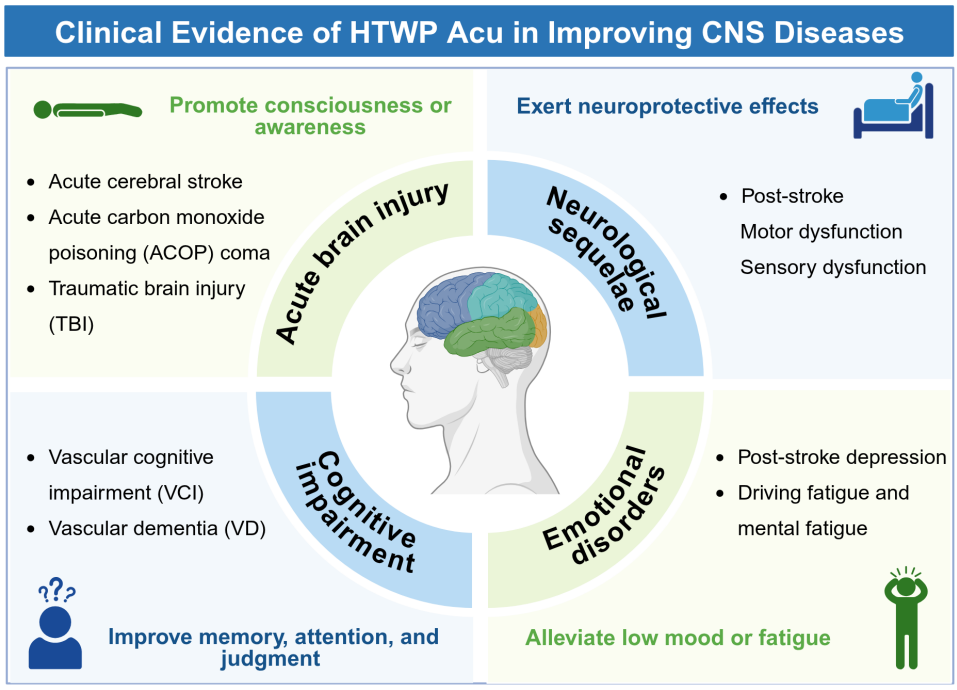

Figure 1. Schematic summary of clinical evidence for HTWP acupuncture (HTWP Acu) in improving CNS diseases. This schematic synthesizes the clinical evidence supporting HTWP acupuncture as a multi-modal intervention for CNS diseases, delineating its efficacy across four pathophysiological domains. CNS: Central nervous system; HTWP: Hand Twelve Jing-Well Points. Created with BioRender.com.

Acute brain injury diseases

Acute brain injury is characterized by high incidence, disability rates, and societal burden[22], and encompasses conditions, including acute stroke, traumatic brain injury (TBI), carbon monoxide (CO)-induced encephalopathy, and Intensive Care Unit (ICU)-acquired delirium. Brain ischemia and hypoxia can lead to neuronal death, clinically manifesting as acute impairment of consciousness with sensory and motor deficits. Current conventional treatments experience limitations, including strict time window constraints, prolonged consciousness recovery periods, and medication dependency risks. Conversely, HTWP Acu, through its immediate awakening effect and early neuroprotective action, shows a unique clinical value in this field.

(1) Acute Stroke: Approximately 1.9 million neurons and neural structures in patients with acute cerebral ischemia sustain irreversible damage by the minute due to delayed treatment[23]. A meta-analysis of 34 randomized controlled trials (RCTs) ($n = 2,757$) showed that acupuncture effectively improved Glasgow Coma Scale (GCS) and the National Institutes of Health Stroke Scale (NIHSS) scores in patients with stroke[24]. Our team's early case-control and single-center clinical studies revealed that combining conventional Western medicine with HTWP Acu showed significantly better efficacy than standard Western treatment in patients with moderate/small-area hemorrhage or infarction. Subsequent multicenter RCTs ($n = 360$) further confirmed that adding HTWP Acu to standard treatment improves GCS scores within 15 to 80 minutes in patients with stroke within 48 hours, specifically by enhancing ocular movement and speech response[9]. Beyond its wakefulness-promoting effects, HTWP Acu has been shown to effectively reduce acute neurological deficits. A systematic review of 18 RCTs showed a significant improvement in the modified neurological severity score (mNSS) with HTWP Acu compared to control groups[25]. (2) Acute Carbon Monoxide Poisoning (ACOP) Coma: Patients with ACOP consciousness impairment lasting <6 hours were divided into HTWP Acu and control groups. The results showed that adding HTWP Acu to the standard medical treatment immediately improved the GCS score difference[10]. (3) TBI: Wu et al.[26] found that administering right median nerve electrical stimulation (RMNS) for 2 weeks during the acute phase of TBI resulted in restored consciousness within 6 months to 72.5% of patients in the RMNS group. The improvements in Global Outcomes of Sleep-Related Events (GOSE), Four Outcomes of Sleep-Related Events (FOUR), Columbia Recovery Scale-R (CRS-R), and Denver Sleep Rating Scale (DRS) scores were superior to those of conventional treatment alone. Since the HTWP is innervated by the median, radial, and ulnar nerves, a study involving 56 patients with severe TBI[11] reported that combining HTWP Acu and coix seed nasogastric feeding, mild hypothermia therapy within the first 7 days of hospitalization, could enhance the GCS and increase systolic blood pressure. Additionally, Xiao[27] applied HTWP Acu to manage severe delirium and found that it significantly reduced delirium episodes, lowered severity scores (DRS-*R*-98), and mitigated sedative-related side effects, providing a novel safety strategy for patients who are ill. In summary, HTWP Acu promotes wakefulness and regulates consciousness in various acute brain injuries. Its early intervention during the acute phase shows significant efficacy and can be combined with multiple therapies to achieve synergistic effects.

Encephalopathy sequelae diseases

During the pathological progression of acute encephalopathy, cerebral ischemia and hypoxia can trigger

a cascade of neuronal cell death. The main sequelae include post-stroke shoulder-hand syndrome, limb numbness, finger spasms, and hemiplegia. The core rehabilitation goals focus on motor function reconstruction and relief of sensory symptoms. HTWP Acu, when combined with acupuncture, medication, and modern rehabilitation training, has shown significant clinical efficacy in post-encephalopathy rehabilitation[28]. (1) Motor dysfunction: Zhang et al.[12] showed that the HTWP Acu group performed significantly better than the coix seed-only group in upper and lower limb Fugl-Meyer function scores. Wang et al.[13] further confirmed that HTWP Acu combined with contralateral channel needling effectively alleviated upper limb spasticity during post-stroke recovery, improved cognitive function, and reduced blood lipid levels and neurological damage. (2) Sensory dysfunction: Zhou et al.[14] observed the 28-day effects of HTWP Acu on cerebral blood flow in 150 patients with hemiplegic sensory impairment, showing a significant improvement in cerebral hemodynamics and enhanced cerebral perfusion. Wang[15] also reported that HTWP Acu combined with other acupuncture treatments showed faster efficacy in improving sensory and motor functions. In conclusion, HTWP Acu, when combined with various rehabilitation methods, exerts neuroprotective effects by improving cerebrovascular function in patients with underlying diseases.

Cognitive impairment diseases

Cognitive impairment disorders are mainly characterized by multidimensional functional abnormalities in cognition, memory, language, and emotions. They are classified into vascular cognitive impairment (VCI) and vascular dementia (VD), based on severity, with pathological mechanisms closely associated with chronic cerebral ischemia due to cerebrovascular lesions[29]. Accumulating studies have suggested a critical role of HTWP Acu in the regulation of cognitive function. Han et al.[30] found through a controlled study of 140 patients with VD that the HTWP Acu group showed significantly better Mini-Mental State Examination (MMSE) scores, activity of daily living (ADL) scores, and improvements in cerebral blood flow velocity compared to the non-acupoint control group. Notably, the LU11 and PC9 acupoints showed greater enhancement of cerebral blood flow velocity than the rivastigmine drug group did, indicating the acupoint-specific effects of HTWP Acu. Han et al.[30] further conducted a study using a factorial design to compare eight stimulation methods: frequencies (1/day *vs*. 2/day), courses (1 *vs*. 2 courses), and intervention timing (within 1 month *vs*. after onset). The results indicated that the stimulation method was the primary influencing factor, followed by course duration, with frequency having the least impact. In the study, initiating interventions within 1 month of onset using an optimized protocol of 1 to 2 daily needling sessions at HTWP Acu for two consecutive courses was recommended, providing evidence-based guidelines for standardized HTWP Acu application. Building on these findings, the research team innovatively used HTWP Acu based on meridian differentiation[17], showing that this, combined with moxibustion, significantly outperformed the donepezil hydrochloride group in improving the MMSE, Montreal Cognitive Assessment, and ADL scores. This therapy also regulated the serum levels of acetylcholine, acetylcholinesterase, and vascular endothelial growth factor (VEGF), indicating mechanisms such as protection of cholinergic neuron activity. Additionally, Luo et al.[18] combined HTWP Acu with educational training to treat children with severe intellectual disabilities and confirmed improvements in social adaptability, fine motor skills, language abilities, and social interaction. In summary, HTWP Acu showed significant advantages in enhancing cognitive function with an individualized intervention protocol centered on meridian differentiation.

Mental and emotional disorders

Traditional medicine posits that the brain is the abode of the primordial spirit, explaining why HTWP Acu regulates the emotional regulation center, primarily manifested by alleviating depressive states and reducing mental fatigue. (1) Post-stroke depression: Patients recovering from brain injury often develop secondary emotional disorders, including depression and anxiety, due to neurological deficits and a declining quality of life. Liang et al.[19] demonstrated that combining oral paroxetine with HTWP Acu and conventional acupuncture showed significant improvement in the Hamilton Rating Scale for Depression scores compared to monotherapy or acupuncture alone, and Modified Barthel Index scores also surpassed those of the acupuncture group only. (2) Driving and mental fatigue: Our team conducted virtual driving simulation experiments to systematically evaluate the effects of HTWP exercises on driver fatigue[20]. The results showed that these exercises significantly reduced Karolinska scores, psychomotor vigilance task reaction time, and percentage of eyelid closure (PERCLOS) values and increased the steering wheel reversal frequency and head movement reaction rate. This indicates that they effectively alleviate driving fatigue and enhance neurobehavioral response speed, possibly by regulating vagal nerve tension to improve autonomic balance, and activating the prefrontal cortex to boost local cerebral oxygen utilization. Yan[21] further confirmed that HTWP exercises outperformed the eye-closed rest control group in alleviating mental fatigue, using functional near-infrared spectroscopy. The mechanism likely involves increasing resting-state hemoglobin oxygen concentrations in the parietal, temporal, and occipital lobes, thereby improving effective brain network connectivity. In summary, HTWP Acu showed synergistic advantages in mind-body integrated therapy for emotional disorders.

Briefly, HTWP Acu offers a safe and effective complementary strategy for acute-phase intervention and recovery rehabilitation in patients with CNS disorders. It shows significant clinical translational value owing to its ability to regulate consciousness levels, promote awakening, facilitate motor function recovery, and improve cognitive and emotional functions. Its clinical advantages are primarily reflected in: (1) Timeliness advantage: Acute-phase intervention can rapidly improve consciousness disorders and seize the therapeutic time window; (2) Broad-spectrum effects: It promotes

awakening and enhances sensory-motor functions, cognitive abilities, and emotional regulation, showing multidimensional and holistic modulation of neural networks; (3) Synergistic efficacy: HTWP Acu therapy generally shows superior clinical outcomes when combined with conventional modern medicine treatments, rehabilitation exercises, or other acupuncture therapies compared to single-modality approaches. This synergistic effect facilitates its integration into existing integrated Chinese-Western medicine treatment systems, making it an effective strategy for optimizing clinical protocols. (4) Simplicity and safety: As a non-pharmacological external treatment, it requires minimal operation, is not restricted by equipment limitations or contraindications of most medications, and has fewer side effects. It offers unique advantages in prehospital emergency care, acute care, and long-term rehabilitation management and provides distinctive complementary strategies for modern neurological disease prevention and treatment systems.

Generalized disorders

Based on the theory of *Lingshu*, HTWP is the root of the 12 meridians and the head, face, chest, and abdomen as their nodes; this concept emphasizes the specific connections between HTWP and the corresponding organs[31]. Therefore, beyond CNS disorders, HTWP has potential regulatory advantages in systemic diseases. HTWP Acu can rapidly alleviate symptoms for respiratory infections, including sore throat and fever, commonly seen in conditions such as post-pneumonia high fever, acute tonsillitis, acute pharyngitis, and herpangina[32]. A meta-analysis showed that needling therapy significantly outperformed conventional antibiotic treatment in clinical effectiveness, fever reduction time, sore throat relief duration, immune function enhancement, and adverse reaction control. LU11 and LI1 are preferred acupoints[33], potentially exerting immune regulation by downregulating peripheral blood inflammatory cell counts and cytokine levels (tumor necrosis factor [TNF]-α, C-reactive protein) while modulating T lymphocyte subpopulation ratios[34]. In musculoskeletal disorders[35], it alleviates pain, joint mobility limitations, and nerve conduction efficiency issues caused by cervical spondylosis, osteoarthritis, and Raynaud disease[36], showing synergistic effects of local symptom improvement and systemic functional regulation. Peripheral neuropathies are functional syndromes caused by infections, metabolic disorders, or poisoning that affect the peripheral motor, sensory, and autonomic nerves, clinically manifesting as sensory abnormalities and motor dysfunction. HTWP Acu showed neuroregenerative effects in peripheral facial paralysis, diabetic peripheral neuropathy, and chemotherapy-induced neurotoxicity, effectively alleviating sensory abnormalities. Furthermore, HTWP showed system-specific effects across different medical systems[35]. For instance, SI1 acupoint promotes postpartum lactation and improves milk quality; LI1 and PC9 acupoints help alleviate inflammation in the head, face, and sensory organs (acute pericoronitis of wisdom teeth and stones); and the LU11 acupoint shows therapeutic effects on acute pain from infectious diseases, including herpes zoster and mumps. In summary, HTWP Acu therapy showed rapid efficacy and broad applicability in treating systemic diseases. This may achieve multitarget regulation through the neuroendocrine-immune network, providing new therapeutic approaches for integrated Chinese-Western medicine.

The potential mechanisms of HTWP Acu

The therapeutic efficacy of HTWP Acu has been initially validated; however, translating traditional empirical knowledge into modern scientific evidence requires an integrated mechanistic framework. This study, grounded in a thorough evaluation of over 30 years of research, shows that the effect of HTWP Acu is essentially a multitiered biological information transmission process, categorized into three consecutive stages: the "sensation–transmission–effect" cascade[3]. HTWP Acu initially stimulates peripheral sensory nerves and associated molecular substrates at the acupoint (sensation), subsequently propagating signals through the dorsal horn of the spinal cord and designated neural pathways to the thalamocortical centers (transmission), ultimately inducing neurovascular remodeling and maintaining immunological microenvironment homeostasis in the brain (effect).

In detail, the "sensation" step involves localized acupuncture stimulation and initial signal transduction at acupoints, dependent on physical activation of local sensory receptors. Earlier studies[5] showed that bloodletting manipulation, nociceptive stimulation, and acupoint specificity energetically influence outcomes, eliminating factors that reduce rabbit cerebral blood flow (CBF) elevation. The "transmission" phase involves neural pathway reaction and signal conduction: based on hand innervation, LU11 is radial nerve-innervated, LI1/PC9 by median nerve, and TE1/HT9/SI1 by ulnar nerve. The CBF-enhancing effect of HTWP Acu was significantly reduced 30 minutes after bilateral transection of the radial, ulnar, and median nerves in rats, confirming that fingertip nociceptor activation and primary afferent fibers are key signal transmission components. The "effect" stage involves targeted processes and functional reorganization, shown by HTWP Acu's reparative effects on awareness disturbances, neurological impairments, and cardiac injuries from hypoxic-ischemic brain damage. The scientific implications of these mechanisms are detailed mechanistically and in the life sciences (Figure 2).

Mechanism of HTWP Acu in CNS diseases

In pathologies, including cerebral ischemia and trauma, the neuronal survival microenvironment deteriorates. HTWP exerts acute neuroprotection *via* multidimensional regulation, which activates wake pathways, inhibits neuronal apoptosis, protects the blood–brain barrier (BBB), and suppresses inflammation and oxidative stress (Table 2). These findings support the post-cerebrovascular consciousness disorders, neural recovery, and cognitive improvement.

Activation of arousal circuits

Ascending reticular activating system (ARAS) conduction pathway damage is the core mechanism of consciousness

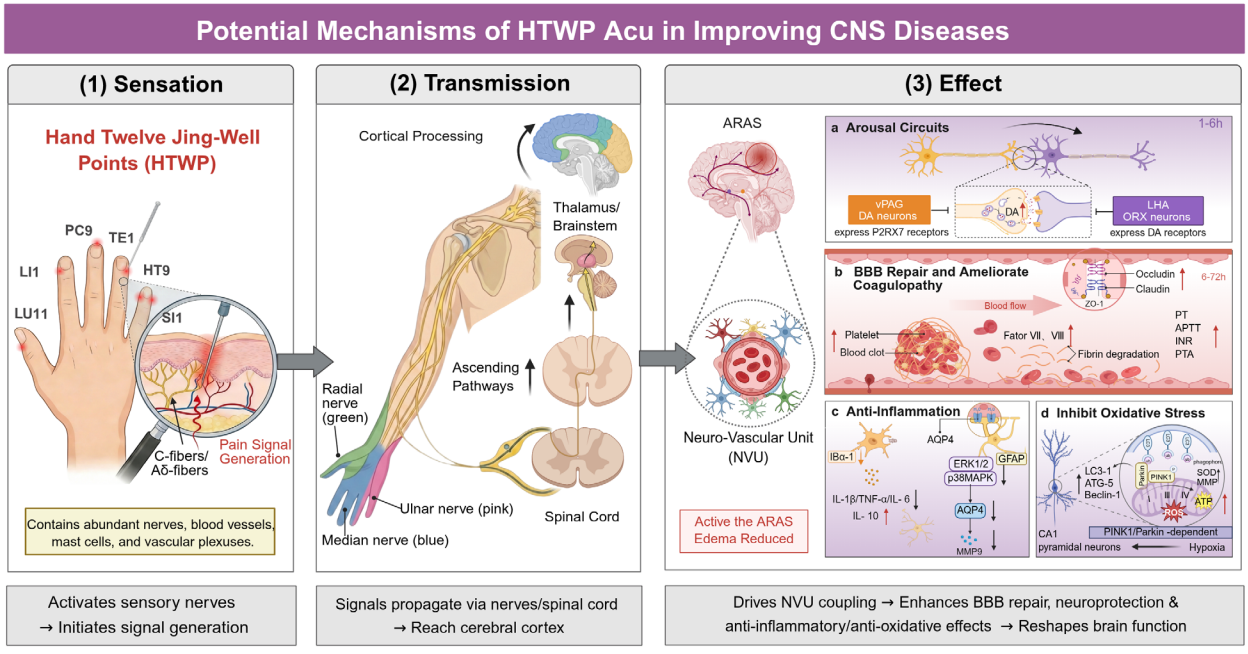

Figure 2. This schematic outlines the three-stage mechanism of HTWP acupuncture for CNS diseases: (1) Peripheral sensation: Acupuncture activates sensory nerves and molecular substrates at HTWP, which are rich in nerves, vessels, and mast cells and son on; (2) Central transmission: Signals travel *via* peripheral nerves, spinal cord, and brainstem to the cortex, engaging the ascending reticular activating system. (3) Central effects: Central signals drive neurovascular unit coupling, modulating vascular function (blood-brain barrier repair), neuronal protection (activation, anti-apoptosis), and immune microenvironment (anti-inflammation, antioxidative stress), ultimately reshaping brain function. aPTT: Activated partial thromboplastin time; ARAS: Ascending reticular activating system; BBB: Blood-brain barrier; CNS: Central nervous system; HTWP: Hand Twelve Jing-Well Points; INR: International normalized ratio; LHA: Lateral hypothalamic area; MMP: Mitochondrial membrane potential; ORX: Orexin; PT: Prothrombin time; PTA: Prothrombin time activity; SOD, Superoxide dismutase; TNF: Tumor necrosis factor; vPAG: Ventral periaqueductal gray. Created with BioRender.com.

impairment in CNS disorders, and activating/repairing brainstem ARAS neural transmission is critical to rapid arousal[44]. Our research confirmed HTWP Acu activates P2RX7 dopaminergic neurons in the ventral periaqueductal gray (vPAG), promoting awakening in TBI rats[37,45]. Based on the ARAS neuronal circuits, the lateral hypothalamic area (LHA) and tuberomammillary nucleus may receive projections from vPAG dopaminergic neurons. Zhao's studies have shown that HTWP Acu activates orexin (ORX) neurons expressing D2 receptors in the LHA, with the P2RX7 pathway as a critical mediator that regulates ORX neuron excitability[46]. Chemical genetic technology has confirmed that vPAG DA neurons, LHA ORX neurons, and their circuits collectively mediate the HTWP Acu arousal effect[47], revealing the central neuronal circuit for arousal modulation. Thus, HTWP Acu improves consciousness by regulating the activity of arousal nuclei. This provides a neural circuit basis for clinical arousal therapy in patients with consciousness disorders.

Repairing the BBB and improving cerebral microcirculation

BBB disruption causes vascular cerebral edema and reduces CBF, leading to neuronal hypoxia-ischemia. HTWP Acu exerts its neuroprotective effects by maintaining BBB integrity, regulating rCBF, and promoting consciousness and neurological recovery. Evans blue permeability was significantly reduced in MCAO and TBI rat models[38–39]. Using electron microscopy, Yu et al.[40] showed that HTWP Acu alleviates tight junction damage in MCAO models by upregulating occludin/claudin-5 messenger RNA (mRNA), while downregulating ICAM-1 and VEGF. Liu et al.[41] confirmed that it enhanced CBF in TBI rats 48 hours post-injury by inhibiting ERK/p38 mitogen-activated protein kinase pathway (MAPK) signaling, reducing MMP9/AQP4 expression, and decreasing brain water content. Li et al.[42] demonstrated that it reverses consumptive hypocoagulability in TBI mice 6 hours post-injury, improving hemodynamics/CBP and reducing tight junction gaps (occludin/ZO-1) and AQP4 to enhance BBB permeability. Thus, HTWP Acu offers acute neuroprotection by repairing the BBB, improving cerebral microcirculation, relieving edema, and restoring perfusion.

Inhibition of neuroinflammation and oxidative stress

After TBI, excessive pro-inflammatory factors and oxidative stress trigger damage cascades, exacerbating neuronal death and BBB disruption. Early studies have shown that HTWP Acu upregulates neuron-specific enolase-positive cells, indicating increased neuronal survival, and inhibits apoptosis by upregulating Bcl-2 and downregulating Bax[4]. Research on inflammation regulation has shown that it alleviates glial vascular unit damage in TBI rats by increasing NeuN-positive neurons while reducing GFAP (astrocytes) and Iba1 (microglia). It also improves repair by downregulating pro-inflammatory factors (TNF-α, interleukin [IL]-1β, IL-6) and upregulating IL-10, and inhibits excessive JNK/p38 MAPK pathway activation in the brainstem 48 hours after TBI, downregulating macrophage/microglia activation markers Nos2 and Cd86, and suppressing M1-type microglia overactivation in the caudate nucleus[48].

Table 2

Potential mechanisms of HTWP acupuncture ingredients for CNS disease

Refs	Model	Intervention	Parameters	Test sites	Efficacy indicators	Mechanism indicators
[37]	CCI	MA	Depth of 1 mm, applied for 5 min, immediately, for 2 days	Brainstem, vPAG	Coma duration↓, mNSS↓, I-VI Consciousness Scale improved	Neuronal projections (*P2rx7, P2rx3, Trpv1, Tacr1, Cacna1d*)↑, protein secretion (*Exoc1, Exoc3l1, Fgb, Fgr*)↑, *Drd3*↑, DA neurons expressing P2RX7↑
[38]	MCAO	MA	Depth of 1 mm, twice a day at 9:00 to 10:00 h and 16:00 to 17:00 h, for 3 days	Brain tissue	Extravasation of EB↓	Serum NOS↓
[39]	CCI	MA	20 μL at each acupoint, twice a day, for 2 days	Brain tissue	mNSS↓, brain water content↓, extravasation of EB↓, improved T2WI images, improved HE images	Degenerating neurons↓
[40]	pMCAO	MA	15–20 μL at each acupoint, once a day, for 3 days	Brain tissue	Brain water content↓, extravasation of EB↓, improved TTC images, slight shrinkage of astrocytes/neurons, continuous TJs, and BMs	Occludin↑, claudin-5↑, ICAM-1↓, VEGF↓
[41]	CCI	MA	Depth of 1 mm, 15–20 μL at each acupoint, twice a day, for 2 days	Brain tissue	mNSS↓, brain water content↓, extravasation of EB↓, improved T2WI images, improved HE images, CBF↑	AQP4↓, MMP9↓, ERK/p38 MAPK pathways↓
[42]	CCI	MA	Depth of 1 mm, 5 μL at each acupoint, once a day, for 3 days	Brain tissue, blood	mNSS↓, CBP↑, CPP↑, brain water content↓, extravasation of EB↓, improved HE images, bilateral hindlimb latency↓, left hindlimb amplitude↑	CCTs (PT↓, aPTT↓, INR↓, FIB↓, PTA↑, platelet count↑, Factor VII↑, Factor VIII↑), TEG (R time↓, K time↓, MA value↓, Angle↑) NeuN-immunoreactive cells↑, GFAP-immunoreactive cells↓, Iba1-immunoreactive cells↓, occludin↑, ZO-1↑, AQP4↑, IL-6↓, IL-1β↓, ICAM-1↓, BDNF↑, VEGF↑, HIF-1α↓
[43]	AHH-induced brain injury	MA	Once a day, for 7 days	Hippocampus	Necrotic pyramidal cells↓, alleviated mitochondrial swelling↓	Autophagosomes↑, S100B↓, GFAP↓, MDA↓, SOD↑, MMP↑, mitochondrial respiratory chain complex (I, II, IV)↑, mitochondrial ATPase activity↑, Beclin1↑, ATG5↑, LC3-I↑, PINK1/Parkin pathway↑

↑: Upregulated by intervention; ↓: Downregulated by intervention; AHH: Acute hypobaric hypoxia; aPTT: Activated partial thromboplastin time; AQP4: aquaporin 4; BM: Basement membrane; CBF: Cerebral blood flow; CBP: Cerebral blood perfusion; CCI: Controlled cortical impact injury; CCTs: Conventional coagulation tests; CPP: Cerebral perfusion pressure; DA: Dopamine; Drd3: Dopamine Rreceptor D3; EB: Evans blue; ERK: Extracellular signal-regulated kinase; FIB: Plasma fibrinogen; GFAP: Glial fibrillary acidic protein; HE: Hematoxylin-eosin staining; HTWP: Hand Twelve Jing-Well Points; INR: International normalized ratio; MA: Manual acupuncture; MAPK: Mitogen-activated protein kinase pathway; MCAO: Middle cerebral artery occlusion model; MDA: Malondialdehyde; MMP: Mitochondrial membrane potential; MMP9: Matrix metalloproteinases 9; mNSS: Modified neurological severity score; NOS: Nitric oxide synthase; T2WI: T2-weighted MRI; PT: Prothrombin time; PTA: Prothrombin time activity; SOD: Superoxide dismutase; TEG: Thromboelastography; TJ: Tight junction; TTC: 2,3,5-Triphenyltetrazolium chloride; vPAG: Ventral Periaqueductal Gray.

Hypoxia, a key feature of high-altitude environments, poses extreme physiological challenges for residents and travelers. The brain, which is highly hypoxia-intolerant, relies on mitochondrial autophagy for protection when mitochondrial function is impaired, because mitochondria are crucial to cellular respiration and energy metabolism. Studies have shown that HTWP Acu reduces pyramidal cell necrosis and apoptosis in the hippocampal CA1 region of hypoxic high-altitude brain injury models by lowering serum S100B, GFAP, and MDA while enhancing superoxide dismutase (SOD) activity (antioxidative stress), improving mitochondrial membrane potential (MMP), respiratory chain complex I/III/IV activity, and ATPase (enhanced mitochondrial function), activating the PINK1/Parkin autophagy pathway, and upregulating Beclin-1, ATG5, and LC3-I (promoting mitophagy)[43]. Additionally, HTWP Acu upregulates telomere biosynthesis genes (TERT, TRF1), increasing telomere copy numbers to alleviate mitochondrial dysfunction-induced apoptosis using the telomere-mitochondrial pathway[49–50]. Thus, HTWP Acu synergistically protects neurons by regulating inflammation, oxidative stress, and mitochondrial function.

Maintenance of ion and neurotransmitter balance

HTWP Acu regulates ion balance, neurotransmitters, and amino acid excitability, reducing K^+ elevation and Na^+ reduction in ischemic tissues to correct cytotoxic edema

from ion imbalance. It inhibits extracellular Ca^{2+}influx, mitigates neuronal calcium overload, and blocks calcium-mediated apoptosis. It also decreases NO_2 in ischemic brain tissue, thereby alleviating NO neurotoxicity[38]. It accelerates the clearance of excitatory amino acids (Glu and Asp) in neurotransmitter regulation and modulates Gamma-aminobutyric acid to restore the excitatory-inhibitory balance after CNS injury[51]. For energy metabolism, it enhances Na^+-K^+-ATPase, lactate dehydrogenase, and cytochrome oxidase activities under acute hypoxia, improving cellular energy efficiency.

Mechanisms of HTWP Acu in non-CNS diseases

HTWP protects the CNS; nevertheless, its role in systemic integration indicates that it is involved in physiological homeostasis. Japanese researcher Tetsuo Asami proposed that HTWP-generated neural impulses may reach the spinal center/hypothalamus through the spinal dorsal horn, sending inhibitory signals to target organs through motor/autonomic synapses[7]. However, peripheral regulatory mechanisms remain poorly understood owing to limited basic research. It also protects against acute high-altitude hypoxia-induced multiorgan damage, given its effects on cerebral ischemia/hypoxia/edema.

Protective effect of myocardial injury

At altitudes above 2,500 m, oxygen partial pressure and blood oxygen saturation drop, triggering autonomic nervous system dysregulation with symptoms, including tachycardia and dyspnea (acute altitude sickness). The myocardium, the primary supplier of energy, is highly sensitive to hypoxia. Hypoxia induces oxidative stress, reactive oxygen species (ROS) accumulation, and antioxidant enzyme imbalance, leading to oxidative damage. The mitochondria, which are central to respiration and energy metabolism, rely on autophagy for protection when impaired. In acute hypobaric hypoxia-induced myocardial injury in rats, HTWP Acu activates the hypoxia-inducible factor 1α (HIF-1α)/bcl-2 19-kDa interacting protein 3 (BNIP3) pathway to initiate mitophagy, evidenced by increased autophagosomes, improved mitochondrial membrane potential, enhanced respiratory chain complex activity, and elevated ATPase activity. The autophagy inhibitor 3-MA hinders this protection, confirming that autophagy is a key myocardial protective mechanism[52].

Protective effect on lung injury

Acute hypoxic lung injury involves hypoxia-induced lung cell damage, resulting in alveolar protein/edema, fluid exudation, and acute pulmonary edema. Concurrently, reduced alveolar surfactant levels and collapse impair the gas exchange, potentially leading to acute respiratory distress syndrome (ARDS). HTWP Acu bidirectionally regulates aquaporins in rats with hypoxic lung injury (downregulating AQP1 and upregulating AQP5 mRNA), ameliorating abnormal lung fluid transport and enhancing pulmonary barrier function[53]. Within 6 to 48 hours, it increases arterial partial pressure of oxygen in arterial blood (PaO_2) and oxygen saturation in arterial blood (SaO_2) while downregulating the HIF-1α/VEGF pathway, strengthening hypoxic adaptation[54].

Studies have shown that the targeted stimulation of specific acupoints has distinct therapeutic effects. In reproductive endocrine disorders, SI1 acupuncture increases serum prolactin (PRL), promotes mammary acinar development, and enhances uterine Cx-43 expression. Hormonal homeostasis is maintained during pregnancy by regulating estradiol (E_2) and progesterone (P) levels and the E/P ratio. These findings offer biological evidence for using acupoints in postpartum lactation deficiency, showing the unique mechanisms of reproductive endocrine management[55]. In summary, HTWP exerts synergistic multiorgan protection against non-CNS disorders.

Acupoint activation mechanism of HTWP Acu

Physiological basis of HTWP

Modern anatomy identifies the HTWP at specific body surface landmarks: 0.1 cun lateral to the nail root angle of the distal phalanx (except PC9). Wang et al.[56–57] confirmed that HT9 corresponds to the dorsal radial bone gate at the base of the distal phalanx of the little finger, with similar structures found at the base of the other fingers. Arterial branches create dorsal arches from the distal phalanx base, with osteogenic vessels along the dorsal concave bone surfaces, forming the anatomical basis for these bone gates, suggesting that all 10 hand acupoints are likely situated within this region.

The distal fingernail bed contains abundant nerves, blood vessels, mast cells, and vascular plexuses compared to common acupoints. With the highest sensory receptor density in the hand (2,000 tactile afferent nerves)[58], studies on rat acupoint show a gradient increase in vascular density and nerve fibers from *Quze* (PC3) to *Zhongchong* (PC9), with dermal nerves parallel to vessels forming branching relationships that confirm unique neurovascular architecture[59]. Mast cells, with a neurotropic/vasotropic distribution[60–61], release trypsin, histamine, and serotonin through degranulation, enhancing neural transmission to the CNS and promoting vasodilation, which aids in immune recruitment[62–63]. Notably, dermal vascular spheres, which help regulate temperature and neural reflexes similar to HTWP, may be targets for HTWP Acu therapy[64]. Overall, Well points' rich nerve endings, microvessels, mast cells, and vascular spheres provide an anatomical/physiological basis for acupuncture signal activation, which enhances signal transmission to target organs[65].

HTWP and brain close connection

Neuroscientific studies have confirmed that the hand occupies a larger area in the sensorimotor projection zone of the cerebral cortex than in other body regions. Research on primates[66] has shown that stimulating the fingers activates extensive cortical areas, with finger length positively correlated with brain volume, affirming hand-brain coevolution[67]. This connection may stem from embryonic tissue homology; the skin epidermis and cerebral cortex originate from neural crest ectodermal cells. The formation of dermatoglyphics (6–24 weeks

of gestation) overlaps with critical brain developmental phases, with certain morphological features correlated with sensorimotor cortex development[68]. At the sensory level, the parietal somatosensory cortex receives tactile information through receptors such as kinetocytes and annular ganglia. Yi's reconstruction[69] of mouse forelimb sensory neuron spinal projections revealed that fingertip afferent fibers project to the spinal cord, providing anatomical evidence for neural connections between the fingertips of the CNS. Motor studies[70] indicate hand motor regions are connected to various body parts, with finger stimulation activating the HandKnob area; rhesus monkey experiments show 22% of dorsal premotor cortex (PMd) neurons form "position fields" encoding hand spatial positioning[71]. Nailfold microcirculation hemodynamics indirectly reflect cerebral blood supply, indicating functional links between the finger and intracranial vascular networks. Zhao et al.[72] used resting-state functional MRI to confirm HTWP Acu regulates neural activity in the superior/middle temporal gyrus and thalamus in healthy individuals, enhancing functional connectivity between multiple brain regions and the thalamus, providing direct evidence of "Well point-Brain Connection."

Comparative analysis of HTWP Acu and acupoints with comparable efficacy

Based on its established clinical efficacy and mechanisms of action in multisystem disorders, we examined the therapeutic specificity of HTWP Acu by comparing it to acupoints of similar indications. Compared to the traditional emergency acupoint *Shuigou* (DU26)[73], HTWP Acu shows enhanced safety. DU26, located in the upper middle third of the superficial fascia of the philtrum, is innervated by the buccal and trigeminal maxillary branches. It regulates brain hemodynamics, provides neuroprotection, and suppresses neuroinflammation through the trigeminal pathway[74]. Our previous study showed reduced coma duration, improved consciousness, and activated LHA orexinergic neurons in TBI mice[75]; however, we discovered that DU26 was less effective in ameliorating neurological function at 6 h post-TBI than HTWP Acu. This difference may be attributed to HTWP's "cumulative effect" *via* synergistic stimulation, enhancing peripheral input to strengthen central arousal, improving neurological deficits and systemic conditions through visceral meridian connections, while also reducing risks associated with craniofacial manipulation.

Compared to *Shixuan* (EX-UE11), which is a fingertip stimulation acupoint, HTWP Acu has unique organ-regulatory properties, which are documented in the *Yellow Emperor's Inner Canon* and located at the distal extremities[31]. However, HTWP acts as the "Root," where the *qi* of the 12 meridians originates. This forms systematic connections with the viscera and cerebra lobes through the meridian system, embodying the holistic principle of "Root-Knot correspondence." In contrast, EX-UE11 is categorized as Extra Points, lacks specific visceral meridian affiliations, and is mostly utilized for potent local stimulation[76] or improving hand dysfunction[77]. Li et al.[78] observed similar glomus body distributions; however, HTWP showed enhanced modulation of the visceral function. For instance, LU11 reduces pulmonary inflammation, whereas HT9 regulates the scardiocerebral circulation. This makes HTWP Acu more suitable for complex clinical scenarios, such as acute brain injury complicated by multiple organ dysfunction. It provides a multilevel therapeutic system from emergency awakening to rehabilitation. Conversely, research on EX-UE11 frequently relies on small-sample and non-randomized designs that lack mechanistic elucidation. HTWP Acu is substantiated by comprehensive studies on the "Sensation–Transmission–Effect" cascade in activating arousal circuits and restoring the BBB. Future research should concentrate on comparative studies of HTWP specificity to further substantiate the distinct processes of the "Well point-Brain connection."

The scientific mechanism of HTWP Acu can be clearly described using a three-stage "Sensation–Transmission–Effect" regulatory cascade. The "Sensation" stage depends on the combined activation of bloodletting, pain stimulation, and acupoint specificity. The material foundation arises from the distinctive anatomical characteristics of the HTWP, where the nail beds of the distal phalanges are abundant in nerve endings, microvessels, mast cells, and glomus bodies, thus establishing an anatomical basis for enhancing local signal inputs. The "Transmission" stage facilitates central signal delivery through peripheral channels, namely the radial, median, and ulnar nerves, with the activation of primary afferent fibers acting as the key conduit. The "Effect" stage has multifaceted regulatory impacts: (1) Arousal Regulation: Activation of P2RX7 purinoceptor stimulates dopaminergic neurons in the vPAG and enhances vPAG dopaminergic projections to orexinergic neuronal circuits in the LHA, thereby forming a "peripheral-central" neuronal circuit; (2) BBB repair: mitigation of MMP9/AQP4-mediated tight junction disruption by inhibiting the ERK/p38 MAPK signaling pathway, upregulating barrier proteins (occludin, claudin-5), and enhancing cerebral microcirculation; (3) Inhibition of inflammation and oxidative stress: Inhibiting the JNK/p38 MAPK pathway to reduce microglial activation indicators (Nos2, Cd86), equilibrating pro-inflammatory (TNF-α, IL-1β) and anti-inflammatory (IL-10) cytokines, while enhancing the expression of anti-apoptotic genes (Bcl-2) and antioxidant enzyme activity. The similarity between the skin and the cerebral cortex in embryonic development, coupled with the functional relationship between nailfold microcirculation and intracranial circulation, substantiates the biological foundation of "Well point-Brain Connection" synergistic regulation. Moreover, protective mechanisms for non-CNS systems widen their therapeutic range, including cardiac protection, lung injury protection, and specialized targeted effects. This comprehensive evidence substantiates that HTWP Acu protects the CNS, cardiopulmonary system, and other systems *via* the synergistic effects of neuromodulation, vascular protection, and immune regulation, thereby establishing a scientific foundation for the contemporary use of acupuncture theory.

Translational applications of HTWP Acu

Building on literature reviews and modern research, Professor Guo Yi proposed the "Well point-Brain

Connection" theory to translate HTWP Acu from theory to clinical practice. He developed standardized stimulation protocols, simplified implementation methods, and intelligent devices, including manual techniques, finger-based exercises, and transcutaneous electrical stimulation gloves. This study enables a shift from hospital-based passive treatment to home-based proactive interventions by innovating the therapeutic approaches, effectively bridging medical research with societal applications[79].

Establishment of a standardized system for HTWP Acu

The foundation for translation is standardization. Specialized operative protocols are essential for broader applications to ensure the clinical efficacy and mechanisms of HTWP Acu. Owing to the lack of domestic/international standards, inconsistent historical texts, and a lack of consensus in modern literature on operational descriptions, creating a unified standard for HTWP Acu operation is essential.

Our team has conducted years of standardization research through various methods, including a literature review, surveys, and consensus validation. By integrating ancient texts, contemporary literature, and clinical experiences, we led the development of key standards, including "ISO international standards for three-edged bloodletting needles, national operating specifications for three-edged needles[80]; group standards for bloodletting therapy guidelines, and technical protocols for Jing point bloodletting[81]." These efforts have helped standardize the terminology, techniques, and operational methods for Jing-Well point needling[35].

Development and promotion of HTWP exercise

Based on the core requirements of strong Jing-Well stimulation in bloodletting protocols and considering challenges such as high operational complexity, difficulty for non-professionals, and poor long-term patient adherence, the service capacity and promotion of HTWP therapy are limited. Thus, it is crucial to expand application scenarios and convert effective clinical techniques into universal health behaviors[82]. Through expert discussions and surveys, our team identified optimal stimulation methods/intensities for general populations, developing finger-based HTWP exercises with fingertip pressure stimulation[83], simplifying interventions to be time/location/tool-independent. This approach facilitates the shift from passive treatment to active self-intervention.

During the development phase, our team collected near-infrared brain function data from healthy individuals pre-intervention, during, and post-intervention. We analyzed brain region activation and oxygenated hemoglobin changes in relevant pathways. The findings showed that the duration and intensity of the HTWP exercise significantly influenced the regulation of brain function. Observations in healthy individuals and patients with mild cognitive impairment (MCI) confirmed that these exercises activate the frontal, temporal, and parietal lobes while increasing oxygenated hemoglobin levels, indicating that cognitive improvement is linked to specific brain activation and elevated oxygenated hemoglobin[84]. This preliminary study clarified the effects of HTWP exercise on brain function in healthy individuals and patients with MCI, providing scientific evidence for optimization. HTWP exercises enhance CBF, showing efficacy against cognitive impairment, driving fatigue[20], mental fatigue[21], while promoting brain health protection. Additionally, our team developed exercise manuals/posters, which we promoted through on-line/off-line channels across 15 countries and over 300 institutions. This initiative has expanded our reach from hospitals to households and has shifted from treatment to prevention.

Development of HTWP transcutaneous electrical stimulation gloves

The HTWP exercise enabled active simulation of the contralateral Jing-Well points, which supported timely self-intervention. However, cognitive comprehension is required for a healthy exercise. During promotion, patients with cognitive impairment expressed a higher demand for Jing-Well point stimulation to enhance brain function as their disease progressed, yet they showed reduced technique mastery ability. New stimulation methods for long-term intervention in cognitively impaired individuals are required to address the clinical challenge of patients needing Jing-Well point stimulation who are unable to perform standardized operations. Based on the HTWP electroacupuncture research on vascular cognitive dysfunction, our team developed a transcutaneous electrical stimulation glove that targets these points. This portable, wearable glove enables precise acupoint localization using safe, noninvasive, variable-frequency electrical stimulation to deliver appropriate HTWP Acu and improve cognitive function.

A transcutaneous electrical stimulation glove was designed as a wearable medical device to enable convenient Jing-Well point stimulation anytime and anywhere. The core controller uses an STM32F030C8T6 microchip for its low cost, low power consumption, high integration, reliability, and easy production. The PCB design balances compactness and output performance with components arranged vertically along the signal flow for efficient transmission. Safety standards were adhered to according to YY 9706.210-2021 and YY 9706.102-2021 standards, ensuring that the module distances prevented electromagnetic interference. Bidirectional rectangular waves were used for pulse stimulation to ensure tissue transmissibility and low electrode corrosion. H-bridge circuits convert single-phase currents to bipolar pulses, reducing the size and electromagnetic radiation compared to transformer-based methods, enhancing durability and safety. Based on portable stimulator development experience[85–86], 10/20 Hz sparse-dense waves were selected for early clinical use owing to their strong patient acceptance.

The HTWP transcutaneous electrical stimulation glove maintains traditional distal acupuncture characteristics while enhancing precision through neuroelectrophysiological techniques. This enables stable HTWP stimulation in individuals with cognitive impairments. Research has connected the cognitive deficits in Alzheimer disease (AD) to medial temporal lobe

dysfunction, with patients showing reduced regional activity during tasks[87]. Our team's unpublished studies confirm that the glove significantly increases oxygenated hemoglobin levels in the bilateral prefrontal and superior temporal regions in the brains of patients with AD, thereby enhancing brain network connectivity. Preliminary clinical trials have validated brain function improvements, with RCTs showing that 12 weeks of glove intervention in early AD (including MCI) leads to overall cognitive function, particularly in memory and attention.

Conclusions and perspectives

Multidisciplinary integration has advanced the convergence of traditional acupuncture and modern biological research, leading to innovative achievements; however, paradigm-level challenges persist, such as the disconnection between theory, mechanism, and clinic, insufficient translation of achievements into technical discourse authority, and fragmented research. Thus, there is an urgent need to establish a TCM theory-based research framework that is validated by modern science. As a historically important foundational practice, HTWP acupuncture serves as an optimal model for reconciling traditional acupuncture theories with modern scientific validation *via* a systematic "Discovery-Driven Research Roadmap" involving four key aspects: distilling TCM classical theories (based on Miraculous Pivot) into testable hypotheses to build a "Well point-Brain Connection" framework; verifying its efficacy in CNS diseases through multicenter evidence-based studies; clarifying its "Sensation–Transmission–Effect" mechanism *via* modern neuroscience and molecular biology; and translating theoretical insights into standardized clinical technologies to shift from "passive treatment" to "active health" management. This trajectory offers a replicable framework for integrating TCM with modern science.

Nevertheless, significant scientific challenges remain regarding practice, evidence, and mechanisms. International standardization is hindered by unstandardized HTWP localization and manipulation techniques that lack consensus, necessitating consistent operating procedures to minimize heterogeneity and enable global promotion. Insufficient high-quality, multicenter, blinded randomized trials and overreliance on subjective behavioral assessments compromise the validity of the results. Future studies should develop a "behavior-biology" evaluation system that integrates fluid biomarkers and neuroimaging for real-time quantitative cortical excitability measurements. The connection between peripheral signaling and central effects remains unclear. Future research should consider integrating multiomics and advanced neuroscience to shift from "phenomenological description" to "mechanistic elucidation" while accelerating intelligent device development to extend applications to chronic disease management and community health. In summary, HTWP acupuncture represents the transformation of original TCM theories and offers a reference for TCM modernization. Future efforts should emphasize interdisciplinary integration and translational applications to integrate acupuncture into mainstream medical systems and contribute to global health.

Conflict of interest statement

Yi Guo is an editorial board ember of this journal, and other authors declare no conflict of interest.

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Author contributions

Zhifang Xu and Yi Guo conceived the project. Yu Luo and Zheng Zhu contributed to writing—original draft, writing—review and editing. Feifei Gao and Siru Qin contributed to writing—review and editing. Ningcen Li, Zhongxi Lyu, Liang Zhou, Yuanzhen Yang, and Baoming Dou contributed to formal analysis. Ning Ma contributed to funding acquisition and supervision.

Ethical approval of studies and informed consent

Not applicable.

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Data availability

All data generated or analyzed during this study are included in this published article.

Declaration of generative AI in scientific writing

The authors declare no generative artificial intelligence (AI) tools were used in compiling this review. All steps, including literature retrieval, original draft, writing, review and editing, were independently completed by the authors. All views and conclusions are the research team's original judgments.

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