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REVIEW

Acupuncture for Post-Stroke Cognitive Impairment: Mechanisms and Clinical Evidence (2020–2025)

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Abstract: Post-stroke cognitive impairment (PSCI), a prevalent and severe sequela following cerebrovascular accidents, impacts over a third of stroke survivors. This condition imposes a substantial socioeconomic burden on healthcare systems and informal caregivers. Acupuncture, a venerable therapeutic modality within traditional Chinese medicine with extensive clinical application, has been acknowledged by the World Health Organization as an adjunctive and complementary therapy for cerebrovascular rehabilitation. This comprehensive review synthesizes contemporary evidence from January 2020 through September 2025, demonstrating significant therapeutic efficacy of acupuncture in ameliorating PSCI. The therapeutic mechanisms underlying acupuncture's neuroprotective effects encompass modulating NVU (Nerve-vascular unit) functioning (including improving cerebral blood flow and cerebral perfusion, preserving BBB (Blood brain barrier) integrity, and attenuating neuroinflammatory processes), brain network remodeling (including modulating neural-plasticity, brain functional connectivity, excitability of local brain regions and node functions), and modulating cerebral energy metabolism (including enhancing mitochondrial function and glucose utilization). We conclude with critical analysis of translational barriers and prospective research trajectories for acupuncture-based interventions in post-stroke cognitive rehabilitation, establishing foundational frameworks for diversifying therapeutic algorithms and advancing precision medicine approaches in cerebrovascular cognitive recovery.

Keywords: PSCI, acupuncture, blood brain barrier, brain network, mitochondria

Introduction

Stroke remains a predominant global contributor to mortality and long-term disability among adults, resulting in profound impairments in motor and sensory functions. Furthermore, PSCI has emerged as a central obstacle impacting the efficacy of rehabilitation, patient autonomy, and reintegration into society. According to the most recent estimates from the 2021 Global Burden of Disease (GBD) study, stroke persists as the world's second leading cause of death (approaching 7 million cases) and represents the third leading cause for both mortality and cumulative disability attributable to non-communicable diseases (NCDs).[1,2] PSCI represents a spectrum of cognitive dysfunction following cerebrovascular events, extending from mild subjective cognitive symptoms to severe post-stroke dementia. Epidemiological data indicate that approximately one-third of stroke survivors develop dementia within three years post-onset, while more than half demonstrate varying degrees of cognitive dysfunction. These cognitive deficits predominantly affect executive functioning, attention, memory, and processing speed. Such impairments significantly compromise neurological recovery and overall clinical outcomes, imposing considerable economic and caregiving burdens on families and healthcare systems.[3,4] Figure 1 delineates the risk determinants frequently correlated with PSCI. Establishing efficacious prophylactic and therapeutic modalities for PSCI constitutes the foremost clinical imperative. Addressing this challenge represents a critical research priority, necessitating urgent multidisciplinary collaboration between neuroscientific and rehabilitation nursing disciplines.

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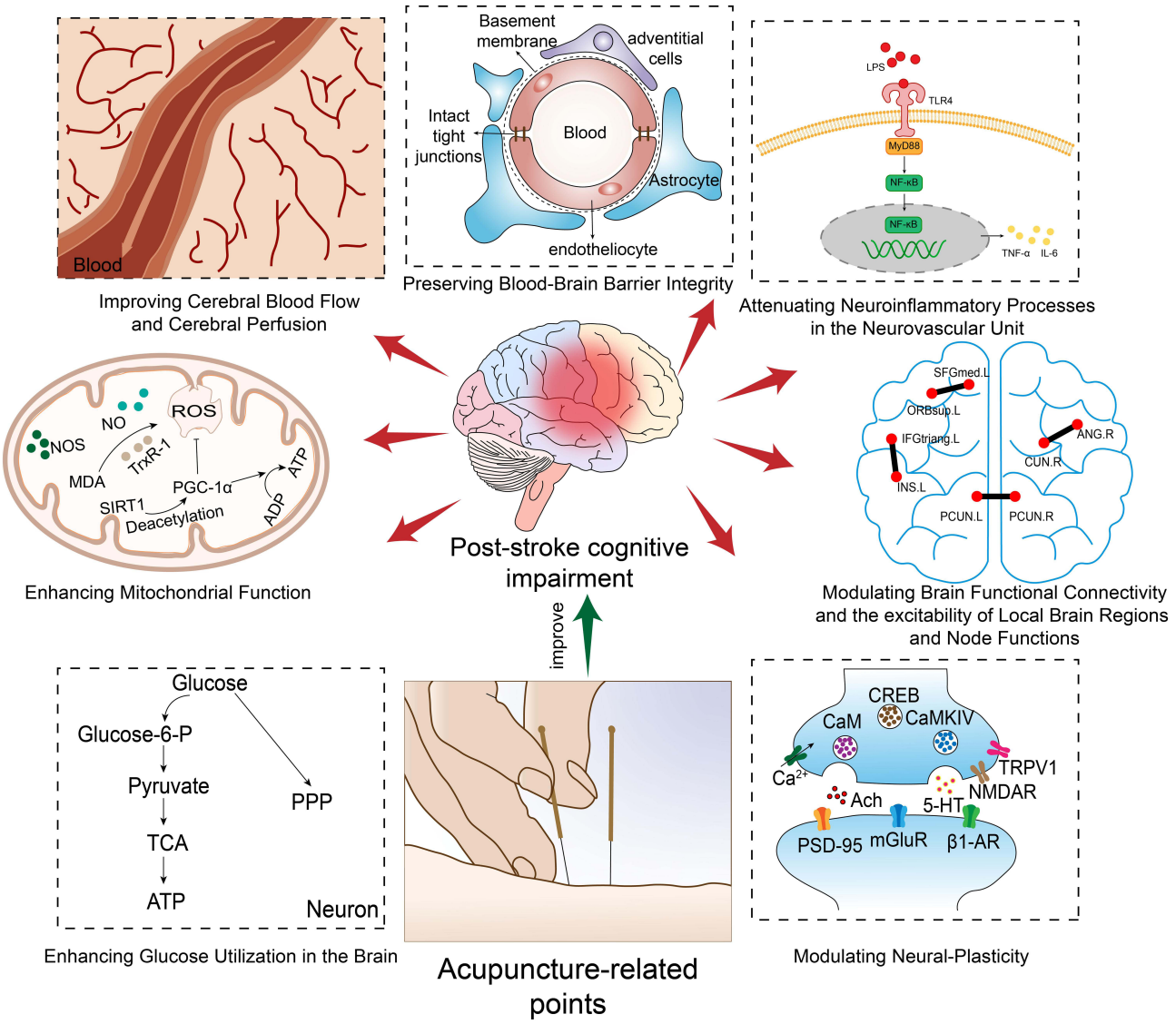
Graphical Abstract



Current standard clinical approaches for managing PSCI primarily encompass pharmacotherapeutic strategies (including cholinesterase inhibitors, memantine, and related compounds) alongside cognitive rehabilitation protocols.[5–7] However, pharmacological efficacy remains modest with substantial patient-to-patient variation, while adverse effects including gastrointestinal disturbances may compromise treatment tolerability.[5,6] The sustained adherence to and clinical utility of cognitive rehabilitation interventions require additional robust evidence validation. These limitations have directed scientific inquiry toward evidence-based complementary therapeutic modalities with established clinical precedent, notably acupuncture. This foundational component of traditional Chinese medicine represents millennia of empirical expertise in addressing post-stroke neurological sequelae. Accumulating clinical evidence and preliminary research demonstrate acupuncture's efficacy in enhancing cognitive performance and functional independence in stroke survivors.[8–10] Neuroimaging studies indicate that acupuncture can modulate functional connectivity and activity in key cognition-related brain networks-including the default mode network, central executive network, and salience network-suggesting central regulatory effects on neural circuitry underlying cognitive recovery after stroke.[11] Mechanistically, acupuncture is thought to exert coordinated

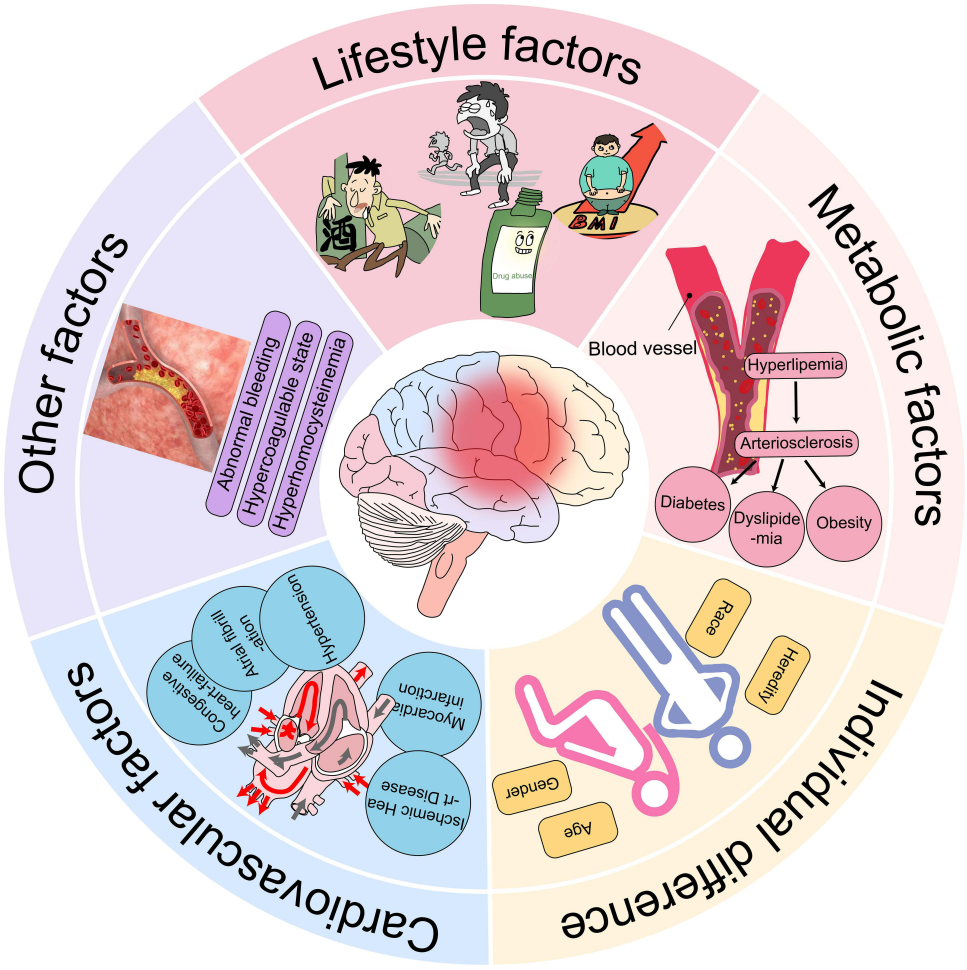


Figure 1 Common risk factors leading to PSCI.

neuroprotective actions by suppressing neuroinflammation and microglial activation, reducing oxidative stress and neuronal apoptosis, and regulating autophagy-mediated pathways such as the mTOR/NLRP3 axis, which collectively preserve neural integrity and promote synaptic plasticity.[12] Although acupuncture demonstrates established therapeutic benefits, its underlying biological mechanisms remain incompletely understood, limiting broader clinical adoption and professional acceptance. Recent advances in proteomics, metabolomics, neuroimaging, and network pharmacology reveal that acupuncture operates through multitarget mechanisms, simultaneously modulating neuroendocrine-immune networks, metabolic cascades, and neural circuits across multiple organizational levels. Given the increasing incidence of PSCI and the critical need for effective interventions, we systematically reviewed foundational and clinical research from the past five years to assess acupuncture's therapeutic potential in PSCI prevention and treatment, clarify mechanistic underpinnings, provide current clinical evidence, and identify future research directions. Despite promising research trajectories, current investigations remain constrained by limited sample sizes, heterogeneous stimulation protocols, and insufficient longitudinal follow-up data, necessitating further validation of precise regulatory mechanisms. This review will comprehensively examine acupuncture's impact on cerebral network architecture and operational dynamics through functional connectivity analysis.

Search Strategy

We retrieved English databases including PubMed, Web of Science, MEDLINE and Embase. Search terms include theme title and related words, such as "acupuncture" or "electroacupuncture (EA)" and "post-stroke cognitive impairment (PSCI)" or "Vascular cognitive impairment (VCI)""vascular dementia (VD)". Keywords are connected by the logical

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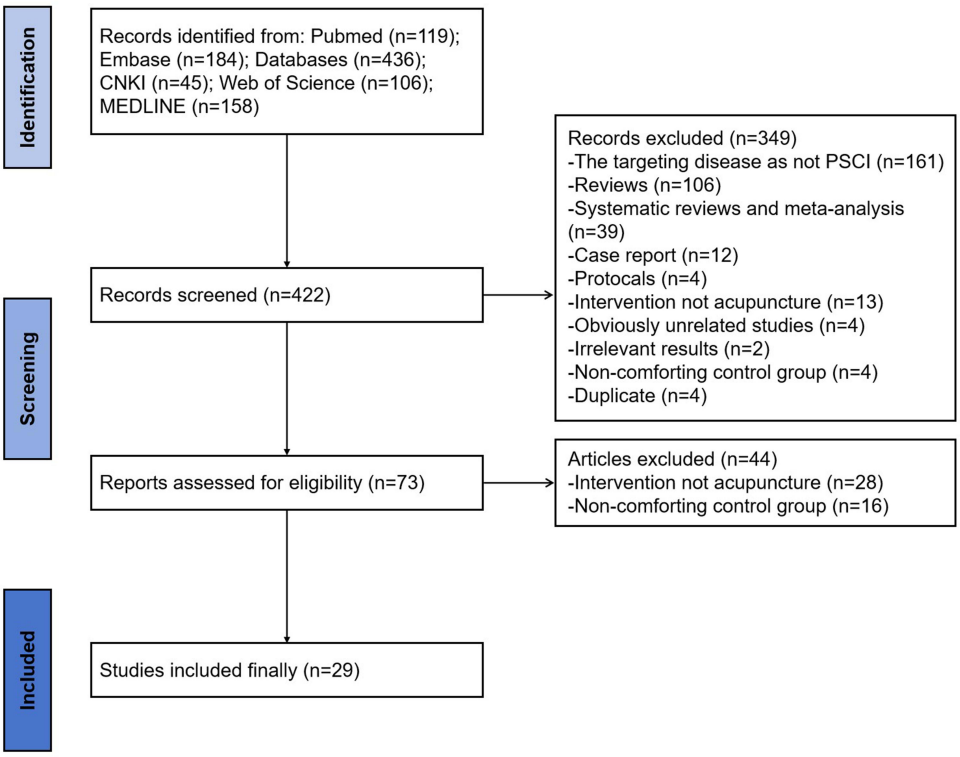

Figure 2 PRISMA diagram.

operator "AND". The search covers all publicly available journal publications from each database from January 2020 to September 1, 2025, The specific process of literature screening is shown in Figure 2.

Inclusion Criteria

The primary conditions under investigation are post-stroke cognitive impairment (PSCI), vascular cognitive impairment (VCI), and vascular dementia (VD). Diagnosis for these conditions is not restricted by factors such as gender, age, or disease progression. Research methodologies predominantly encompass clinical trials and preclinical investigations. The therapeutic interventions for the treatment arm include traditional acupuncture, electro-acupuncture, scalp acupuncture, or a combination of acupuncture with ancillary treatments. Conversely, the control arm is administered non-acupuncture interventions, which may consist of sham acupuncture, placebo, or conventional therapies.Exclusion criteria: irrelevant literature, duplicated papers, conference proceedings, speeches, letters to editors, non-English publications.

Exclusion Criteria

Studies will be excluded if they meet any of the following criteria: (a) ambiguity in diagnostic criteria for the clinical trial; (b) the primary intervention involves non-acupuncture therapies, with the control group receiving identical acupuncture treatment as the experimental group; (c) evidence of duplicate publication; or (d) inclusion in other study types, such as reviews, conference abstracts, and case reports.

Study Selection and Data Extraction

Following the established search protocol, two independent reviewers executed the literature retrieval and screening. A third reviewer resolved any discrepancies. The ROBIS tool was employed by the two reviewers to evaluate the risk of bias (RoB) in randomized controlled trials, with findings presented in the Figure 3. For animal studies, the SYRCLE bias risk tool was utilized. Upon identifying eligible studies, the following data points were extracted for human studies: references, authors, publication year, country, study design, sample size, stroke onset timing, PSCI diagnostic criteria,

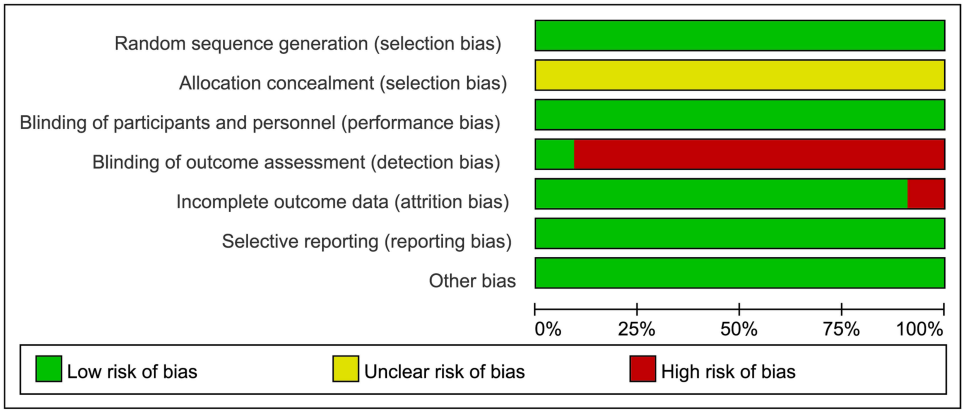

Figure 3 Risk assessment of bias.

interventions, control groups, outcome measures, primary results, and adverse events. For animal studies, the extracted variables included: references, model type, interventions, outcome measures, and key mechanistic markers. These results are comprehensively documented in the Tables S1 and S2.

Acupuncture Modulates Neurovascular Unit Functioning in PSCI

The onset and subsequent remission of PSCI fundamentally correlate with the dynamic interplay between regional cerebral perfusion, BBB integrity, and focal neuroinflammatory processes. Regardless of whether the precipitating event involves ischemic or hemorrhagic pathology, microvascular compromise results in profound dysregulation between metabolic demands and essential substrate delivery. This pathophysiological disruption precipitates cascading structural and functional impairments, constituting a critical impediment to neural network reorganization and optimal cognitive recovery.[13,14] Consequently, a multifaceted therapeutic approach targeting the restoration of regional cerebral perfusion, BBB stabilization, and modulation of neuroinflammatory cascades represents a pivotal strategy for enhancing post-stroke cognitive rehabilitation. Evidence demonstrates that compromised regional cerebral blood flow and hypoperfusion following cerebrovascular accidents result in inadequate neuronal energy metabolism and impaired synaptic function, thereby disrupting higher-order cognitive processes including learning and memory consolidation.[15] Following cerebrovascular accidents, BBB integrity becomes compromised, exhibiting increased permeability that permits infiltration of plasma proteins, neurotoxic compounds, and pro-inflammatory mediators into neural parenchyma.[16–18] This pathological process exacerbates regional cytotoxic edema and neuronal dysfunction, thereby impeding cognitive rehabilitation.[19] Preserving BBB structural and functional integrity remains critical for maintaining cerebral microenvironmental homeostasis and fostering neuroplastic mechanisms.[18] This investigation encompasses three interconnected therapeutic targets: first, restoration of regional cerebral blood flow to ameliorate metabolic dysfunction secondary to chronic hypoperfusion; second, neuroprotection of BBB architecture to sustain microenvironmental stability; and third, suppression of neuroinflammatory cascades to minimize secondary injury while promoting neural repair mechanisms. Elucidating these regulatory pathways provides fundamental insights into the molecular mechanisms underlying post-stroke cognitive recovery.

Improving Cerebral Blood Flow and Cerebral Perfusion

Extensive evidence demonstrates that chronic cerebral hypoperfusion constitutes a hallmark feature of PSCI.[20–24] This sustained reduction in cerebral blood flow originates not merely from macrovascular stenosis or occlusion at the stroke lesion, but fundamentally stems from NVU dysfunction and compromised neurovascular coupling mechanisms within the microcirculation.[25–27] When neurovascular coupling becomes dysregulated, the brain forfeits its capacity for activity-dependent regional blood flow modulation.[28–30] This pathophysiological disruption precipitates localized metabolic insufficiency, compromises synaptic plasticity, and disrupts the delicate equilibrium between functional integration and segregation across distributed neural networks, ultimately manifesting as measurable cognitive deterioration.[31–33]

Consequently, restoration of cerebral perfusion and NVU integrity represents the cornerstone of PSCI therapeutic intervention. Acupuncture exerts NVU protection through multi-target regulation, including preservation of BBB integrity, modulation of glial activation, suppression of neuroinflammation, and promotion of neurovascular remodeling via pathways such as PI3K/AKT, ERK1/2-Cx43, and NF-κB.[34–38] These convergent mechanisms synergistically enhance cerebrovascular circulation and facilitate cognitive recovery.[39,40]

Research demonstrates that acupuncture modulates autonomic nervous system function, thereby augmenting cerebral perfusion and facilitating neuronal regeneration in compromised regions including the hippocampus.[41] Acupuncture effectively enhances cerebral blood flow, which is essential for delivering oxygen and nutrients required for neuronal recovery and cognitive restoration.[42,43] This enhanced perfusion mitigates ischemic damage and promotes cognitive rehabilitation in stroke patients. Trigeminal nerve stimulation exerts significant effects on cerebrovascular dynamics, increasing cerebral blood flow (CBF) through retrograde-induced potentials, trigeminal parasympathetic reflexes, and other central mechanisms.[44] A randomized, double-blind, sham acupuncture-controlled clinical trial revealed that participants receiving true acupuncture exhibited a significant enhancement in MoCA scores after a six-week treatment period.[45] Furthermore, cerebral blood flow (CBF) values within various brain regions, notably deep nuclei like the amygdala and caudate nucleus, were markedly elevated compared to the sham acupuncture cohort. Conversely, the sham acupuncture group did not demonstrate a significant improvement. These findings indicate that true acupuncture effectively modulates cerebral perfusion in patients with vascular cognitive impairment (VCI), augmenting cognitive function through improved blood flow in specific cerebral areas, with effects that are both immediate and cumulative.

Chronic alterations in cerebral blood flow and perfusion constitute primary etiological factors in PSCI. Through a randomized single-blind trial,[46] 54 patients were stratified into scalp acupuncture, intermittent theta-burst stimulation (iTBS), and combination therapy groups. Four-week interventions were administered, with cognitive assessment via Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination (MMSE) scales. Functional near-infrared spectroscopy (fNIRS) monitored cerebral hemodynamic changes. Results demonstrated that combination therapy significantly outperformed monotherapies in activating multiple frontal and temporal cortical regions, particularly the right temporal cortex and lateral prefrontal cortex, substantially improving cognitive performance scores. The therapeutic efficacy stems from a tripartite mechanism: enhanced regional cerebral perfusion, activation of cognitive processing neural networks, and promotion of global neural plasticity and functional reorganization. Consequently, integrated scalp acupuncture and iTBS protocols represent an innovative neurological rehabilitation strategy. Researchers[47] confirmed that EA stimulation of Baihui (GV20) and Shenting (GV24) significantly ameliorated neurological deficits, spatial learning and memory impairments, and cerebral infarction following middle cerebral artery occlusion/reperfusion in rats. Triphenyltetrazolium chloride staining revealed substantial reduction in cerebral infarct volume, which, combined with neurological and cognitive improvements, confirmed that EA alleviates ischemic injury and enhances cerebral tissue perfusion, thereby promoting cerebral blood flow-mediated recovery. A randomized controlled trial involving 90 patients with mild cognitive impairment following cerebral infarction was conducted.[48] Participants were allocated to either a control group receiving oxiracetam monotherapy or an observation group treated with a combination of oxiracetam and acupuncture. Following a 4-week intervention period, the combination therapy group demonstrated significant increases in serum GDNF and SIRT1 levels, alongside reductions in S100β and NSE. Furthermore, improvements were noted in middle cerebral artery hemodynamic parameters, including mean flow velocity (Vs, Vd, Vm) and resistance index (RI). Cognitive assessments, reflected by MoCA and MMSE scores, and the Barthel index for daily living activities, were markedly superior in the observation group compared to the control group, achieving a total effective rate of 92.68%. These findings suggest that the combined administration of acupuncture and oxiracetam may enhance cognitive recovery by optimizing cerebral hemodynamics, augmenting neurotrophic factor expression, and mitigating neuroinjury markers.

Preserving Blood-Brain Barrier Integrity

The BBB, serving as a critical component and primary functional element of the NVU, maintains cerebrovascular integrity and homeostatic function essential for restricting blood-borne neurotoxic substances from accessing brain parenchyma while facilitating optimal neuronal activity. During acute ischemic stroke and ensuing pathophysiological cascades, multiple interconnected molecular mechanisms—including inflammatory cascade activation, enhanced oxidative stress burden, matrix

metalloproteinase upregulation, and dysregulated vascular endothelial growth factor signaling—converge to precipitate substantial BBB compromise. This disruption manifests through tight junction protein degradation and relocalization, basement membrane proteolysis, endothelial cell dysfunction, and impaired transcellular transport mechanisms, culminating in pathological BBB hyperpermeability.[49] The immediate sequelae involve vasogenic edema, extravasation of plasma proteins, and leukocyte infiltration into the parenchyma. Over time, these processes culminate in white matter tract degeneration, thereby impeding neural network restoration. This BBB-mediated tissue damage is increasingly recognized as a mechanistic nexus between acute cerebrovascular events and the subsequent development or exacerbation of PSCI.[50,51] Extensive preclinical research demonstrates that acupuncture intervention significantly attenuates cerebral edema and neurological dysfunction following ischemic stroke, with the underlying mechanisms potentially linked to BBB preservation.[37,52,53] Current evidence indicates that acupuncture may confer neuroprotective effects on BBB integrity through multiple pathways: suppression of neuroinflammatory cascades, mitigation of oxidative stress-induced cellular damage, modulation of matrix metalloproteinase/tissue inhibitor of metalloproteinase (MMP/TIMP) homeostasis, stabilization of tight junction protein expression, and regulation of neurovascular coupling signaling networks.[54,55]

In investigations of PSCI rehabilitation, researchers[56] examined the efficacy of specialized electroacupuncture stimulation (SMES) in facilitating neurotrophic factor delivery via middle cerebral artery occlusion/reperfusion (MCAO/R) rodent models of cerebral ischemia. Experimental findings demonstrate that SMES significantly enhances BBB permeability, thereby augmenting therapeutic compound penetration. Critically, this transient permeability enhancement maintains safety parameters—the intervention preserves structural and functional integrity of hippocampal cholinergic neurons, mitochondrial architecture, and autophagic processes without inducing deleterious cellular responses. Furthermore, results indicate SMES activates the p65-VEGFA-tight junction protein signaling cascade, substantially elevating exogenous NGF concentrations within hippocampal tissue of MCAO/R subjects. Intracerebral NGF administration enhances synaptic plasticity in hippocampal regions of MCAO/R animals (Figure 4). These findings establish

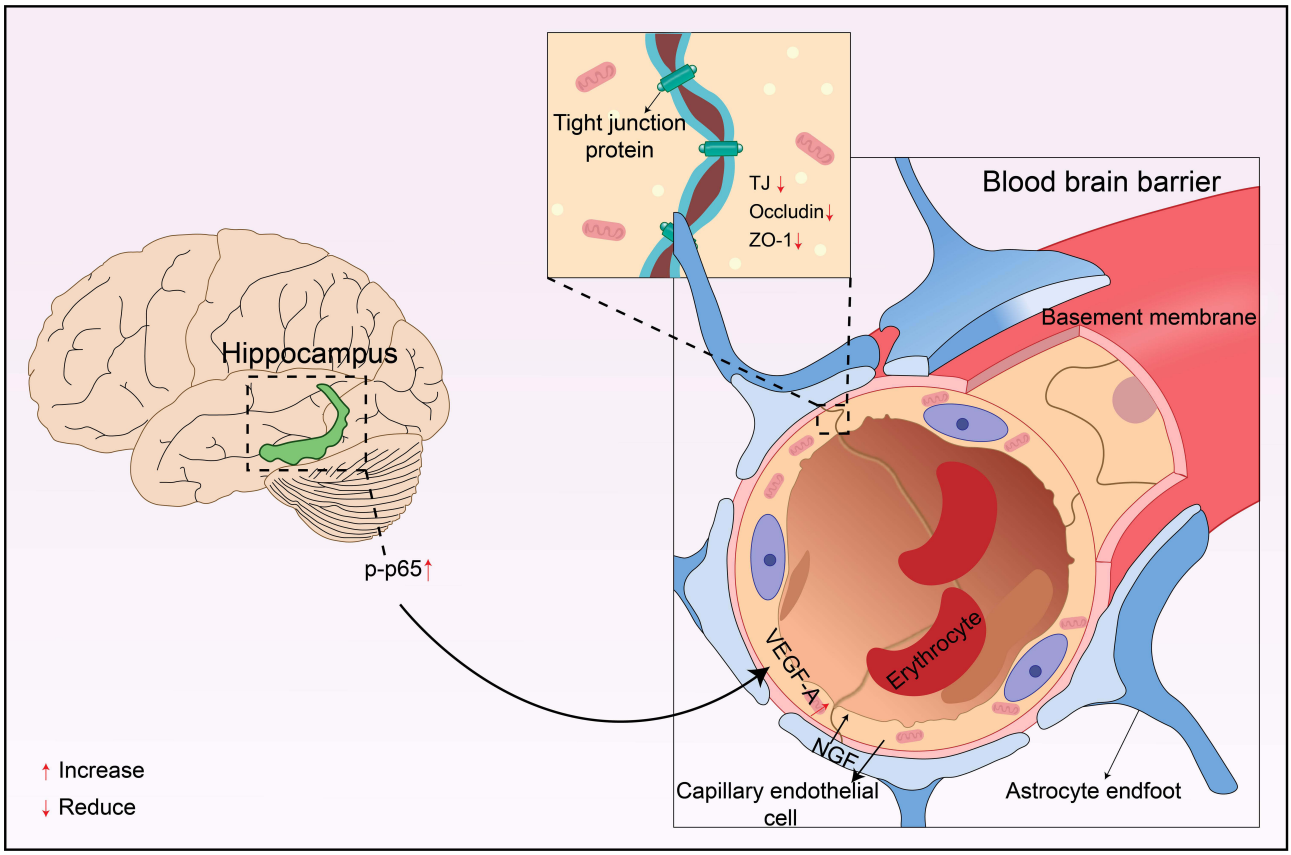

Figure 4 SMEs can promote the p65-VEGFA-TJs signaling pathway, which mediates the transmembrane transport of NGF across the hippocampal blood-brain barrier, thereby improving the cognitive function of rats in the recovery period of MCAO/R.

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novel evidence supporting combinatorial macromolecular therapeutics with acupuncture modalities for central nervous system pathologies, validating acupuncture's neuroprotective capacity in ameliorating PSCI. Zhao's research[57] cohort demonstrated that EA delivery at specific frequencies (2/100 Hz) induces controlled BBB permeability enhancement. This increased permeability facilitates neurotrophic factor translocation and subsequent internalization by prefrontal cortical neurons, particularly nerve growth factor (NGF), thereby ameliorating cognitive deficits and reducing hippocampal neuronal apoptosis in MCAO/R-induced ischemic models. Comprehensive validation through Evans blue extravasation analyses, immunofluorescence imaging, and standardized behavioral assessments, including Morris water maze protocols, confirmed that EA safely and reversibly modulates BBB permeability during post-stroke recovery phases, potentiating neuroprotective and cognitive-restorative effects of exogenously administered NGF.

Attenuating Neuroinflammatory Processes in the Neurovascular Unit

Accumulating evidence indicates that memory dysfunction may result from cerebral ischemic injury, glial activation, and consequent oxidative stress and neuroinflammation. Lin et al[58] investigated the cellular mechanisms underlying EA treatment for post-stroke memory impairment. Their findings demonstrate that EA intervention ameliorated ischemic stroke sequelae in MCAO/R rats and attenuated memory deficits. The pivotal discovery reveals that EA's therapeutic efficacy correlates with its capacity to modulate the neuroinflammatory microenvironment through promoting microglial phenotypic transition from the pro-inflammatory M1 state to the anti-inflammatory, neuroprotective M2 state. Expanding evidence supports that memory disorders may arise from cerebral ischemic damage, glial activation, and subsequent oxidative stress and neuroinflammation. Zhang et al[59] elucidated the mechanisms by which EA ameliorates PSCI. Through experimental investigation, the researchers determined that EA stimulation at the "Shenting" and "Baihui" acupoints significantly improved neurological deficits and reduced cerebral infarct volume. Behavioral assessments confirmed that EA effectively enhanced learning and memory performance in experimental animals. The underlying mechanism involves EA-mediated upregulation of cytokine IL-33 expression, thereby activating the IL-33/ST2 signaling cascade. This pathway activation facilitates microglial polarization toward the M2 phenotype with anti-inflammatory and reparative functions, while simultaneously enhancing cerebral white matter structural integrity and restoring inflammatory mediator homeostasis, ultimately conferring neuroprotection and cognitive enhancement. A randomized controlled clinical trial involving 102 patients diagnosed with PSCI was conducted.[60] Participants were allocated into three arms: acupuncture combined with transcranial direct current stimulation (tDCS), tDCS alone, and a control group receiving nimodipine (western medicine). The acupuncture plus tDCS group received tDCS treatment augmented by acupuncture aimed at invigorating the mind and promoting qi circulation. Acupoints utilized included Baihui, Shuiguang, bilateral Neiguan, Yintang, and Sanyinjiao on the affected side. Following a 4-week intervention period, the combined therapy demonstrated significant improvements in MoCA, LOTCA, and Barthel Index scores. Furthermore, serum levels of homocysteine (Hcy) and neuron-specific enolase (NSE) were notably reduced, concurrent with an upregulation of brain-derived neurotrophic factor (BDNF) expression. These findings suggest that the synergistic effect of combining acupuncture and tDCS may enhance cognitive function and activities of daily living in patients by modulating factors associated with neural injury and repair.

Luo and colleagues[61] investigated the therapeutic mechanisms underlying EA intervention in PSCI. Using a rat middle cerebral artery occlusion model, the researchers demonstrated that EA significantly ameliorated neurological deficits, reduced infarct volume, enhanced spatial learning and memory performance, and attenuated hippocampal tissue damage. The neuroprotective effects were mediated through upregulation of miR-135a-5p expression, which subsequently suppressed the mTOR/NLRP3 signaling cascade, thereby attenuating autophagy and neuroinflammatory responses while reducing pro-inflammatory cytokines (TNF-α, IL-6) and oxidative stress markers. Administration of the autophagy inducer rapamycin or miR-135a-5p inhibitor abrogated these beneficial outcomes, confirming the critical regulatory role of the miR-135a-5p/mTOR/NLRP3 axis in EA-mediated PSCI amelioration. Toll-like receptor 4 (TLR4), a key pattern recognition receptor, mediates post-ischemic neuroinflammation, making TLR4 pathway modulation a promising therapeutic target for PSCI management. Proteomic analysis[62] revealed that EA stimulation at acupoints GV24 and GV20 altered hippocampal protein expression profiles in cognitively impaired rats, with upregulation of damage-associated molecular patterns including heat shock protein β1 (Hspb1) potentially contributing to EA-mediated

cognitive enhancement. In four-vessel occlusion models, EA treatment at GV20, CV17, BL17, CV6, and SP6 suppressed hippocampal TLR4 and MyD88 protein and mRNA expression, decreased circulating IL-6 and TNF-α levels, and facilitated hippocampal neuronal repair, resulting in cognitive function restoration.[63] Furthermore, EA at GV20 and ST36 concurrently inhibited TLR4/NF-κB signaling while activating the Sirt1/STAT3 pathway, upregulating Sirt1, STAT3, and IL-17 expression, ultimately improving learning and memory capacities in vascular dementia models.[64]

Acupuncture Modulates Brain Network Remodeling in PSCI

The recovery of PSCI depends not only on the restoration of structural and functional integrity within the focally damaged brain region, but is also profoundly influenced by the dynamic modulation of global brain networks. Stroke-induced disruption of neural pathways results in diminished signal propagation efficiency and impaired inter-regional connectivity, consequently compromising higher-order cognitive domains including learning, memory, and attention. During disease progression, the brain undergoes reorganization through multi-tiered compensatory mechanisms to preserve information processing efficacy.[65,66] Thus, understanding how to facilitate optimal brain network remodeling at both structural and functional levels is critically important for enhancing post-stroke cognitive recovery.

Neuro-plasticity represents a fundamental mechanism underlying this process. Following cerebrovascular accident, neuronal dendritic architecture, synaptic connectivity, and neurotransmitter systems undergo adaptive reorganization to reconstruct compromised neural circuitry and restore cognitive capacity. Facilitating neuroplastic processes enhances the compensatory potential of surviving neurons and accelerates learning and memory recovery. Furthermore, post-stroke functional connectivity is frequently disrupted, characterized by impaired communication between critical networks or aberrant compensatory connections.[67] Modulating functional connectivity helps reestablish information flow equilibrium across brain regions and strengthen coordination within cognitive networks, thereby enhancing information integration and processing efficiency. Concurrently, regional excitability and nodal function in affected or compensatory areas substantially influence cognitive performance.[68,69] Optimizing excitatory/inhibitory balance within brain regions and enhancing core node functional states facilitates efficient information input and output reconstruction while supporting higher-order network collaborative activities. This section examines post-stroke cognitive recovery significance through three hierarchical levels: neuro-plasticity, functional connectivity modulation, and regional excitability with key nodal function, providing conceptual frameworks for understanding brain network reconstruction mechanisms.

Modulating Neural-Plasticity

Neuroplasticity denotes the central nervous system's capacity for structural and functional reorganization through the establishment of novel synaptic networks throughout the lifespan, constituting the fundamental mechanism underlying neurological recovery in conditions such as PSCI. This adaptive phenomenon encompasses a continuum ranging from acute, transient modifications in synaptic efficacy to enduring architectural remodeling within neural circuits. Acupuncture intervention has demonstrated efficacy in mitigating post-ischemic synaptic dysfunction through enhancement of synaptic density, restoration of synaptic morphological integrity and neurotransmission capabilities, and augmentation of synaptic plasticity mechanisms, consequently attenuating cognitive deficits. Specifically, EA stimulation at Baihui (GV20) and Shenting (GV24) acupoints significantly upregulates postsynaptic density protein-95 (PSD-95) expression, a critical scaffolding protein at excitatory synapses essential for synaptogenesis. Additionally, this intervention elevates miR-81 expression while suppressing frontal cortical IL-16 downregulation mediated by miR-81, collectively enhancing spatial cognition and memory consolidation in middle cerebral artery occlusion (MCAO) rodent models.[70] Moreover, EA at GV20 and GV24 demonstrates the capacity to attenuate protein expression and phosphorylation of NMDA receptor subunit 2B (NR2B), α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptors (AMPARs), and calcium/calmodulin-dependent protein kinase II (CaMKII) within hippocampal tissue, facilitating long-term potentiation (LTP) induction and optimizing synaptic transmission efficiency and plasticity within the CA3-CA1 hippocampal circuit, resulting in enhanced cognitive performance in two-vessel occlusion (2VO)-induced models.[71] Collectively, these investigations demonstrate that acupuncture stimulation of Zusanli (ST36), Baihui (GV20), Qianding (GV21), Xinhui (GV22), Shenting (GV24), Geshu (BL17), Pishu (BL20), and Shenshu (BL23) acupoints promotes PSD-

95 upregulation, facilitates LTP enhancement, modulates neurotransmitter and neuropeptide release, and augments synaptic plasticity, thereby providing therapeutic benefit for PSCI.

Modulating Brain Functional Connectivity

Among the therapeutic mechanisms underlying acupuncture's efficacy in treating PSCI, the reconstitution of cerebral functional connectivity networks has emerged as a focal area of intensive investigation. Stroke-induced focal neuronal damage and remote diaschisis disrupt pre-existing neural architectures, resulting in compromised interhemispheric communication, aberrant circuit dynamics, and deteriorated cognitive network functionality. Recent advances in neuroimaging modalities, including ffMRI, electroencephalography (EEG), and magnetoencephalography (MEG), have enabled researchers to examine acupuncture's influence on cerebral network integration and communication dynamics, thereby elucidating potential neuromodulatory pathways. Functional connectivity, serving as a cardinal metric of neural synchronization across brain regions, provides critical insights into structure-function relationships. PSCI patients characteristically exhibit diminished intra-network coherence within the default mode network (DMN), fronto-parietal network (FPN), and hippocampal circuitry.[72,73] Acupuncture interventions can reconstitute dysfunctional network coordination patterns and facilitate cognitive restoration through modulation of both resting-state and task-related functional architectures. Empirical evidence demonstrates that acupuncture stimulation modulates connectivity strength and topological patterns across multiple cognitive networks. Specifically, acupuncture enhances fronto-parietal information transfer efficiency, optimizing executive cognitive processes, while regulating limbic system dynamics and cortico-limbic coupling mechanisms underlying affective and mnemonic functions. Additionally, acupuncture may restructure thalamocortical pathways, modulating sensory integration and information processing capabilities. Graph-theoretical analyses examining nodal degree, global efficiency, and small-world properties indicate that acupuncture stimulation promotes network integrity and organizational optimization.[74–76] Collectively, these findings suggest that acupuncture's therapeutic efficacy derives from complex multi-level neuromodulation across hierarchical brain networks. Through systematic evaluation of network-level modifications, we seek to establish a robust theoretical framework for understanding acupuncture's neuromodulatory mechanisms.

In a randomized controlled trial, Guo et al[77] investigated the therapeutic efficacy of EA as an adjunctive intervention for cognitive rehabilitation in PSCI and elucidated its underlying neurobiological mechanisms. Thirty-four participants were randomized into two cohorts: an experimental group receiving combined EA and cognitive training, and a control group receiving cognitive rehabilitation monotherapy. Following a 12-week intervention period, researchers employed standardized neuropsychological assessments and diffusion tensor imaging (DTI) to quantify clinical outcomes and neural network connectivity alterations. Results demonstrated superior performance in the combined treatment group across multiple cognitive domains, particularly in MoCA total scores, memory subsystems, and attentional networks. Graph theoretical analysis revealed that clinical improvements corresponded with enhanced clustering coefficients and local efficiency metrics, both exhibiting positive correlations with MoCA performance. These findings indicate that EA facilitates more efficient local information processing. Through modulation of centrality measures and nodal efficiency within the default mode network and critical cognitive regions (encompassing frontal, temporal, and parietal cortices), EA appears to facilitate structural and functional neural network reorganization, ultimately promoting cognitive restoration. In a systematic review and meta-analysis, Li et al[78] demonstrated that comprehensive scalp acupuncture protocols for PSCI exhibit superior therapeutic efficacy compared to monotherapy approaches. Analysis revealed enhanced outcomes across multiple standardized assessments including MoCA, MMSE, and Loewenstein Occupational Therapy Cognitive Assessment (LOTCA), with P300 event-related potential biomarkers showing improvement trajectories. This enhanced therapeutic response derives from acupuncture's precision targeting of specific cortical regions—particularly areas encompassing frontal, parietal, and temporal cortices—thereby strengthening functional neural connectivity. The therapeutic stimulation enhances functional network integrity through augmentation of regional homogeneity (ReHo) and amplitude of low-frequency fluctuations (ALFF). Beyond these neuroimaging biomarkers, the intervention enhances white matter microstructural integrity, improves cerebral perfusion, and modulates key neurotransmitter release. At the molecular level, it restores neurobiological homeostasis by suppressing pro-inflammatory cytokines including tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β), while upregulating neurotrophic factors such as brain-derived

neurotrophic factor (BDNF). These convergent mechanisms collectively attenuate neuronal apoptosis, enhance synaptic plasticity, and establish synergistic activation of cognitive circuits. Ultimately, this multi-level regulatory framework facilitates recovery of memory consolidation, attentional control, and executive functioning, yielding significant improvements in patients' global cognitive capacity.

In a randomized neuroimaging trial, investigators at Dongzhimen Hospital[79] examined acupuncture's modulatory effects on dynamic functional network connectivity in ischemic stroke patients. Findings demonstrate that acupuncture significantly reconfigures aberrant temporal dynamics: specifically, reducing dwell time in hypoconnected states while augmenting inter-network coupling between the dorsal attention network and default mode network. These neurophysiological alterations correlate significantly with motor function improvements, suggesting that acupuncture facilitates neurorehabilitation through restoration of optimal network segregation-integration balance. The intervention represents a promising therapeutic approach for ameliorating post-stroke cognitive and motor impairments via correction of pathological dynamic connectivity patterns. A recent study[80] involving patients experiencing cognitive dysfunction post-ischemic stroke demonstrated that an 8-week regimen of acupuncture alongside cognitive training yielded a superior total effective rate (95.0%) in the observation group compared to the control group (77.5%). The observation group also exhibited significant improvements in NIHSS, MMSE, MoCA, FMA, and MBI scores. Furthermore, resting-state functional magnetic resonance imaging (rs-fMRI) data indicated a notable enhancement in functional connectivity between the left hippocampus and the right frontal lobe, the right hippocampus and the left frontal lobe, and the right parietal lobe within the observation group following treatment. These findings suggest that acupuncture at the Baihui and Shenting acupoints, when integrated with cognitive training, may bolster hippocampal connectivity with the frontal and parietal lobes, regions crucial for cognition. This, in turn, could improve neural network integration, thereby effectively mitigating post-stroke cognitive and motor impairments.

Modulating the Excitability of Local Brain Regions and Node Functions

The hallmark features of PSCI pathogenesis involve disrupted regional cortical excitability patterns and compromised functionality of critical neural hub structures. These localized pathophysiological alterations impair intra-regional computational processes and disrupt inter-network connectivity, culminating in global cognitive deterioration. Contemporary neuroimaging and electrophysiological investigations demonstrate acupuncture's therapeutic potential to ameliorate these deficits through recalibration of regional oscillatory dynamics and restoration of hub node functionality. Following cerebrovascular accidents, ischemic damage and cerebral infarction frequently induce pathological hypoexcitability or hyperexcitability states within affected brain regions, compromising mnemonic and executive cognitive domains. Acupuncture intervention modulates neuronal excitability thresholds, restores excitatory-inhibitory neurotransmission homeostasis, and promotes synaptic plasticity mechanisms.[81,82] Through enhancement of metabolic demands and regional cerebral perfusion, this therapeutic approach augments neuronal function and reinforces the computational influence of critical network nodes. This section therefore examines how acupuncture optimizes regional excitability profiles and nodal characteristics via neural, metabolic, and network-based mechanisms, establishing a comprehensive theoretical framework for its underlying neurobiological foundations.

Decreased cortical excitability correlates strongly with substantial enhancements in memory, linguistic function, attention, and executive control. For instance, low-frequency repetitive transcranial magnetic stimulation (rTMS) operates by diminishing postsynaptic calcium influx and downregulating AMPA receptor expression, thereby inducing long-term depression (LTD) to suppress hyperactivity in the contralesional hemisphere.[83] Likewise, Zhong and colleagues[84] employed resting-state functional magnetic resonance imaging combined with graph theoretical analysis to demonstrate that transcranial direct current stimulation (tDCS) significantly strengthened functional connectivity between critical brain regions. This neuromodulatory intervention enhances global network efficiency, with this metric showing positive correlation with MMSE cognitive score improvements. Collectively, these findings underscore the therapeutic potential of non-invasive brain stimulation as an efficacious adjunctive treatment for PSCI, through strategic modulation of regional node dynamics and whole-brain network integration. Li and colleagues[85] utilized a rat MCAO model to investigate neuroplasticity mechanisms following ischemic stroke via resting-state fMRI and graph theoretical approaches. Seven days post-EA treatment at acupoints GV20 and ST36, researchers documented significant

neurological recovery and selective modulation of regional nodal centrality. Specifically, EA enhanced betweenness centrality in the right ventral hippocampus, a pivotal cognitive integration hub, while simultaneously reducing centrality and degree metrics in the right ventral thalamic nucleus and left septal nucleus. These findings indicate that EA ameliorates PSCI through selective reinforcement of cognitive centers while suppressing maladaptive hyperactivation in limbic regions. Through recalibration of these regional nodal properties, EA provides robust neuroimaging evidence supporting its role in optimizing post-stroke brain network architecture. In a randomized controlled trial, Luan et al[86] enrolled 61 patients diagnosed with PSCI. Participants were allocated to either an experimental group, receiving acupuncture alongside a therapeutic regimen focused on regulating spirit, stabilizing mind, and nourishing the brain, complemented by standard care, or a control group that underwent standard care alone. The intervention spanned eight weeks, utilizing standardized acupoints including Shangxing, Wujia, Shenting, Meihong, and Quadan. Post-intervention assessments revealed statistically significant improvements in the experimental group compared to the control group, evidenced by enhanced MoCA and Activities of Daily Living (ADL) scores, alongside reductions in serum homocysteine (Hcy) and erythrocyte sedimentation rate (ESR) levels. Quantitative electroencephalogram (qEEG) analysis further demonstrated a notable increase in the relative power of alpha and beta brain waves across the cerebral cortex in the experimental group, concurrently with a significant decrease in the relative power of theta and delta waves and the delta-to-alpha+beta ratio (DTABR). These findings suggest that the integrated approach of regulating spirit, stabilizing mind, and nourishing the brain may serve as an effective strategy for mitigating PSCI through the modulation of cerebral wave slowing.

Acupuncture Modulates Cerebral Energy Metabolism

Brain energy metabolism dysfunction represents a core pathophysiological process in post-stroke cognitive decline. Maintaining neuronal energy balance is critical for preserving neural activity and synaptic plasticity. Disruptions in cerebral metabolic networks trigger secondary neuronal damage after ischemic stroke and lead to poor neurological recovery, including vascular dysfunction, mitochondrial energy failure, and glucose metabolism impairment.[87] Since cerebrovascular mechanisms have been previously reviewed, this analysis examines recent developments in acupuncture's regulation of brain metabolism and improvement of cognitive function following stroke.

Enhancing Mitochondrial Function

The pathophysiological mechanisms underlying PSCI remain incompletely characterized. Current research primarily focuses on cerebrovascular dysfunction, neurodegeneration, inflammatory responses, and oxidative stress-mediated cellular damage.[88–90] The dynamic balance between mitochondrial fission and fusion processes maintains mitochondrial homeostasis and meets neuronal energy demands. Mitochondrial dynamics are regulated through multiple pathways, with SIRT1/PGC-1α demonstrating the strongest association with cerebral ischemia-reperfusion injury.[91] Studies indicate that EA modulates mitochondrial dynamics via SIRT1/PGC-1α pathway activation, improving mitochondrial architecture and oxidative capacity, thereby reducing hippocampal neuronal damage. Transmission electron microscopy and immunoblot analyses confirmed that EA treatment decreases mitochondrial fragmentation, strengthens antioxidant systems, and improves cognitive function in MCAO/R models.[92] Cerebral ischemia/hypoxia typically involves altered adenosine triphosphate (ATP) and NADPH oxidase (NOX) levels, with energy stress-induced changes in ATP and reactive oxygen species (ROS) potently activating AMP-activated protein kinase (AMPK).[93] As a cellular energy sensor, AMPK serves as an upstream regulator of PGC-1α transcription. Following cerebral ischemic injury, AMPK promotes catabolism while inhibiting anabolism, reducing neuronal damage and facilitating motor recovery. Guo and Lu demonstrated that acupuncture increases cerebral ATP levels and mitochondrial function through AMPK/PGC-1α pathway activation, reducing oxidative stress and improving post-ischemic neurological outcomes.[94] Hu et al[95] showed that EA at Baihui (GV20) in murine stroke-induced depression models increased hippocampal cannabinoid receptor type 1 (CB1R) expression, promoting mitochondrial biogenesis-related proteins nuclear respiratory factor 1 (NRF1) and transcription factor A mitochondrial (TFAM), enhancing mitochondrial function, and reducing cognitive impairment. Acupuncture's therapeutic effects were eliminated following CB1R blockade with antagonist AM251 or genetic silencing, confirming

this pathway's critical role. NLRP3 inflammasome activation triggers pyroptosis, an inflammatory cell death process involving interleukin-1β and interleukin-18 maturation and release.[96]

Pharmacological inhibition or genetic deletion of NLRP3 inflammasome reduces mature IL-1β and IL-18 secretion, providing neuroprotection in experimental stroke models.[97,98] Evidence suggests the NLRP3 inflammasome critically mediates PSCI pathogenesis. Reactive oxygen species are primary upstream NLRP3 inflammasome activators, with damaged mitochondria being the major ROS source in cerebral lesions.[99] EA at Shenting (GV24) and Baihui (GV20) acupoints ameliorates cognitive dysfunction by modulating endogenous melatonin levels, enhancing PINK1/Parkin expression, promoting mitophagy, and suppressing ROS/NLRP3 inflammasome activation.[100]

Enhancing Glucose Utilization in the Brain

Glucose functions as the principal metabolic fuel essential for physiological equilibrium maintenance. It crosses the blood-brain barrier through glucose transporters (GLUTs), providing critical energy for neural operations.[87] The brain exhibits extraordinarily high metabolic requirements for oxygen and glucose to support cellular respiration and adenosine triphosphate generation. Following acute cerebral ischemia-reperfusion injury, glucose transporter expression and cerebral glucose metabolism become markedly impaired, compromising neuronal integrity and inducing cognitive deterioration.[101] Acupuncture intervention improves cerebral glucose utilization, offering a potentially effective neuroprotective approach for mitigating PSCI. EA stimulation at GV24 and GV20 meridian points triggers the insulin receptor substrate/phosphoinositide 3-kinase/protein kinase B signaling pathway. This therapeutic modality increases hippocampal GLUT1 and GLUT3 expression while promoting glucose uptake and cerebral metabolism, consequently restoring neuronal energy balance and reversing learning and memory impairments (Figure 5).[102] Supporting investigations employing positron emission tomography/computed tomography imaging revealed that EA at Baihui (DU20) and

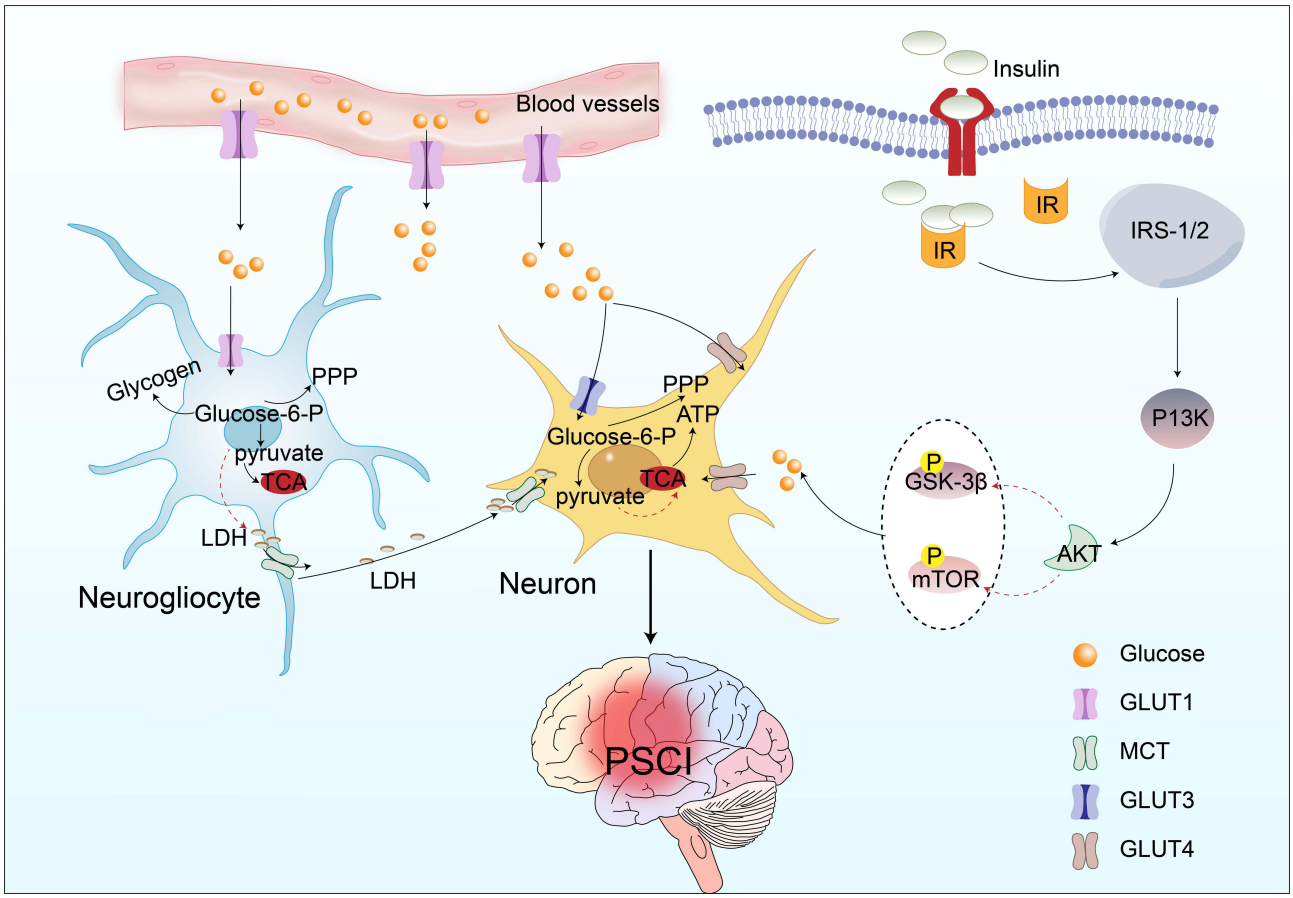

Figure 5 The mechanism by which IRS/PI3K/AKT regulate GLUT to participate in PSCI.

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Shenting (DU24) meridian points augmented glucose uptake in cerebral ischemia-reperfusion animal models, accompanied by increased hippocampal GLUT1 and GLUT3 protein levels, elevated ATP production, and diminished lactate formation. These results suggest that EA alleviates cerebral bioenergetic disturbances by enhancing glucose transport and metabolism, thus reducing post-ischemic cognitive deficits.[103]

Cerebral ischemia-mediated oxygen-glucose deprivation increases the AMP/ATP ratio, thereby activating autophagy pathways.[104] Autophagy plays a pivotal role in the pathogenesis and progression of cognitive impairment, while apoptosis inhibition mitigates ischemia-reperfusion injury.[105,106] Various signaling networks govern post-stroke autophagy, notably the phosphatidylinositol-3-kinase (PI3K)/protein kinase B (Akt) and nuclear factor kappa B (NF-κB) pathways.[107] Wang et al[108] demonstrated that EA at Baihui (GV20) and Shenting (GV24) acupoints ameliorated post-ischemic learning and memory impairments in rodent models. Their results showed that EA stimulates PI3K/Akt signaling, enhances autophagy-related proteins including Beclin-1 and mammalian target of rapamycin (mTOR), while simultaneously inhibiting p53 expression, thus regulating cellular autophagy, reducing neuronal apoptosis, and improving cognitive function. Additional studies confirmed through experimental paradigms that post-stroke stimulation of Baihui and Shenting acupoints enhances cognitive performance through increased hippocampal autophagic flux, evidenced by elevated expression of essential autophagy proteins Beclin-1 and LC3II and reduced p62 levels.[109]

Discussion

Extensive traditional Chinese medicine clinical data demonstrates that acupuncture enhances cognitive function in stroke patients. Treatment protocols are typically developed through expert consensus and prior research findings, employing single or multiple acupoint combinations with emphasis on synergistic point selection. Individualized acupoint prescriptions may be tailored to specific patient presentations. Neuropsychological assessments including the MoCA, MMSE, and Loewenstein Occupational Therapy Cognitive Assessment-Geriatric (LOTCA-G) serve as validated instruments for predicting onset, facilitating early detection, monitoring progression of PSCI, and evaluating therapeutic efficacy in clinical trials. Needling at Shenting (GV24), Baihui (GV20), Qianding (GV21), Dazhui (GV14), Mingmen (GV4), Shenshu (BL23), Shenmen (HT7), Xuanzhong (GB39), Sishencong (EX-HN1), Qihai (CV6), Zhongwan (CV12), Shanzhong (CV17), Neiguan (PC6), Sanyinjiao (SP6), Xuehai (SP10), Tianshu (ST25), Zusanli (ST36), Fenglong (ST40), Fengchi (GB20), and Taichong (LR3) demonstrates significant score improvements, indicating enhanced cognitive performance.[39] Nevertheless, current evidence remains heterogeneous, mechanistic pathways require further elucidation, and clinical translation encounters substantial methodological challenges.

Currently, most investigations utilize rudimentary cognitive screening instruments such as the MMSE or MoCA and related neuropsychological batteries as primary outcome measures. While these instruments offer clinical convenience, they demonstrate inadequate psychometric sensitivity and specificity, exhibiting vulnerability to confounding variables including educational attainment and sociocultural factors, thereby limiting their capacity to detect nuanced improvements in discrete cognitive domains (eg., executive function, processing speed) attributable to acupuncture interventions. Integration of objective, quantitative biomarkers including neuroimaging modalities (functional magnetic resonance imaging connectivity matrices), electrophysiological parameters (event-related potential P300 components), and cerebrospinal fluid/serum biomarkers (amyloid-beta 42, neurofilament light chain) into outcome assessment frameworks represents a critical research imperative for establishing multidimensional, psychometrically robust efficacy metrics. Insufficient interdisciplinary collaboration significantly constrains research innovation and translational applicability. Substantive PSCI acupuncture research necessitates comprehensive integration of expertise spanning traditional Chinese medicine theory, neuroscience, bioinformatics, and clinical epidemiology. Current collaborative efforts remain superficial, with disciplinary experts operating within isolated theoretical frameworks and methodological paradigms. A fundamental bottleneck involves translating traditional Chinese medicine theoretical constructs—including "governor vessel regulation" and "heart-kidney interaction"—into operationalizable, testable neuroscientific hypotheses amenable to contemporary investigational approaches. The absence of unified conceptual frameworks and experimental platforms impedes translation of mechanistic findings into clinical practice optimization and limits effective reverse-translation of clinical observations into mechanistic elucidation. The most distinctive methodological challenge in acupuncture research involves developing appropriate placebo controls and sham interventions. Rigorous randomized controlled trial

methodology requires establishing placebo controls sufficient for participant blinding. However, designing completely inert yet credible sham acupuncture protocols presents significant methodological challenges. Standard approaches include non-penetrating superficial stimulation at non-acupoints or blunt-tip placebo needles applied to peri-acupoint regions without tissue penetration. These approaches remain problematic, as minimal cutaneous stimulation may elicit physiological responses, and experienced participants may distinguish authentic acupuncture sensation from sham intervention, compromising blinding integrity. This methodological limitation generates substantial bias risk across trials, creating interpretive ambiguity and scientific controversy. Future investigations must optimize sham acupuncture protocols while incorporating diverse methodological approaches including independent outcome assessment, waitlist controls, or active comparisons with established cognitive rehabilitation interventions to comprehensively validate acupuncture-specific therapeutic efficacy.

This review synthesizes the therapeutic impacts of acupuncture on PSCI, detailing its mechanistic underpinnings. These mechanisms encompass modulating NVU functioning (including improving cerebral blood flow and cerebral perfusion, preserving BBB integrity, and attenuating neuroinflammatory processes), brain network remodeling (including modulating neural-plasticity, brain functional connectivity, excitability of local brain regions and node functions), and modulating cerebral energy metabolism (including enhancing mitochondrial function and glucose utilization). Collectively, this provides robust scientific evidence substantiating the clinical utility of acupuncture in PSCI management.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors confirm no conflicts of interest associated with this review.

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