

Uncovering the mechanisms by which acupuncture improves motor function after stroke through neuroplasticity revealed by magnetic resonance imaging techniques

Y. Wu^{1#}, J. Li^{2#}, L. Pei^{1*}

¹Department of Acupuncture and Rehabilitation, Jiangsu Province Hospital of Chinese Medicine Affiliated Hospital of Nanjing University of Chinese Medicine, Nanjing, 210029, China

²Department of Radiology, Jiangsu Province Hospital of Chinese Medicine Affiliated Hospital of Nanjing University of Chinese Medicine, 210029, China

► Original article

ABSTRACT

*Corresponding author:

Lixia Pei, M.D.,

E-mail: plx821016@163.com

Received: November 2023

Final revised: January 2024

Accepted: February 2024

Int. J. Radiat. Res., July 2024;
22(3): 647-655

DOI: 10.61186/ijrr.22.3.647

Keywords: Acupuncture, stroke, motor function impairment, hemiparesis, neuroplasticity, MRI.

Co-first authors, contributed equally to this work.

Background: The motor function defects in stroke patients are mainly caused by damage to brain neurons and network disconnection, as viewed through neuroimaging. Structural and functional magnetic resonance imaging (sMRI and fMRI) are the most commonly used techniques in studying central nervous system diseases. This article reviews recent technological research to provide evidence for acupuncture research and development. **Materials and Methods:** Relevant articles were obtained from PubMed and China national knowledge infrastructure (CNKI) databases, as well as from CNKI database from 2014 to 2023. The data were then reviewed and the citations were examined. **Results:** The non-invasive technique of magnetic resonance imaging (MRI) is highly effective in accurately identifying abnormal brain activities, making it a top choice. As MRI technology rapidly evolves, additional techniques such as diffusion kurtosis imaging (DKI), diffusion spectrum imaging (DSI), and neurite orientation dispersion and density imaging (NODDI) can be used to observe post-IS motor neural injuries and related neural reshaping. **Conclusions:** These techniques about MRI could help doctors better understand the biological mechanisms underlying neural pathways and motor deficits in IS, aiding in the development of targeted therapies.

INTRODUCTION

Stroke ranks as the second highest contributor to global mortality and is among the top three leading causes of both death and impairment ⁽¹⁾. Ischemic stroke (IS) is the commonest type, accounting for approximately 86% of all stroke cases globally ⁽²⁾. Approximately 70% of IS patients experience varying degrees of motor function impairment ⁽³⁾, which has negative impacts on the patients, their families, and society. Prolonged insufficient blood supply to the brain tissue leads to irreversible tissue damage and subsequent neuronal dysfunction. Motor function deficits in IS patients are believed to be a direct consequence of damage to the motor cortex and the corticospinal tract ⁽⁴⁾ and are associated with disruptions in neural structure and functional connectivity ⁽⁵⁾. Therefore, structural remodeling and functional reorganization of relevant neurons have become the main focus in effectively ameliorating motor function deficits.

Post-stroke neuroplasticity denotes the brain's remarkable capacity to modify its

architecture and operations after injury, compensating for damaged cells and neural pathways, including neurogenesis, axonal sprouting, axonal regeneration, and synaptic plasticity. Due to the brain's remarkable plasticity and reorganization capabilities, exploiting these characteristics can enhance the clinical efficacy of treating IS.

In recent years, acupuncture, as a traditional Chinese medical therapy, has shown potential benefits in alleviating post-stroke motor dysfunction. However, despite existing studies suggesting that acupuncture enhances motor function after stroke through neuroplasticity, its precise mechanisms of action remain unclear. Given this challenge, MRI technology, as a non-invasive and high spatial resolution imaging method, provides a unique opportunity for us to get a deeper understanding of the mechanisms by which acupuncture improves motor function after stroke. Acupuncture, as an ancient and widely used therapy, has been considered to have unique advantages in the treatment of many conditions through thousands of years of practice and experience. However, its recent

application in stroke rehabilitation has attracted more attention. After stroke, patients often face challenges in losing the ability to move certain parts of their bodies, severely impacting their quality of daily life. Therefore, investigating how acupuncture improves motor function after stroke by enhancing neuroplasticity is of great meaning for improving the rehabilitation outcomes of patients with stroke. Although acupuncture is a traditional Chinese medical method, its low cost and high safety have been recognized by the World Health Organization (6), making it a popular alternative therapy in Europe and many Asian countries (7). Numerous studies have demonstrated the safety and efficacy of acupuncture in promoting motor function recovery for IS patients and its potential effects on neuroplasticity (8-10). MRI technology, as a powerful tool, has been widely used in the field of neuroscience. By using MRI technology, we can observe and measure structural and functional changes in the brain. For exploring the effects of acupuncture on post-stroke neuroplasticity, we need an imaging method that could result in high spatial resolution and functional information. Fortunately, MRI technology can meet this need and help us comprehensively know the relationship between acupuncture and the improvement of motor function after stroke. MRI is a valuable tool for diagnosing and assessing stroke in patients. MRI uses strong magnetic fields and radio waves to produce detailed images of the brain, allowing for the identification of areas affected by stroke and the assessment of the extent of the damage (11). MRI can accurately detect ischemic stroke (caused by a blocked blood vessel) as well as hemorrhagic stroke (caused by a burst blood vessel) which is crucial for determining the appropriate treatment. Additionally, MRI can also provide information about the size, location, and severity of the stroke, which can guide the development of a treatment plan and prognosis (12). Furthermore, MRI is non-invasive and does not use ionizing radiation, making it a safe imaging modality for patients. It also allows for the visualization of the brain in multiple planes and can provide important information about the blood vessels and surrounding tissues, aiding in the comprehensive assessment of stroke patients (13,14). In summary, MRI technology is invaluable in the evaluation and management of stroke patients, providing vital information for accurate diagnosis, treatment planning, and monitoring of the condition. Meanwhile, with scientific advancements, various innovative neuroimaging techniques have been applied to central nervous system disease research. Among them, sMRI and fMRI are two major branches based on magnetic

resonance imaging technology, allowing for non-invasive quantification of changes in brain neural structure and functional connectivity, as well as visualization of the effects of acupuncture.

Currently, there is a lack of comprehensive review studies on the use of sMRI and fMRI to explore the mechanisms through which acupuncture enhances motor function in ischemic stroke (IS) by promoting neuroplasticity. Therefore, this paper aims to fill this gap by conducting a thorough review of recent studies and experiments in this area. The focus will be on discussing the effects of acupuncture on post-stroke neuroplasticity as revealed by MRI technology, and how these changes contribute to the improvement of motor function. By conducting a comprehensive analysis of these studies, this paper aims to present a novel and comprehensive understanding of the mechanisms through which acupuncture works in stroke rehabilitation. Furthermore, it is hoped that this review will offer valuable insights for future clinical applications and research in this field.

MATERIALS AND METHODS

Methods

A search of the PubMed database was conducted to identify relevant articles published between 2012 and 2023. Additionally, the China National Knowledge Infrastructure (CNKI) database was searched for relevant articles published during the same time frame. The search terms included "Acupuncture," "Stroke," "Motor Function Impairment," "Hemiparesis," "Neuroplasticity," and "magnetic resonance imaging (MRI)." Researchers then individually reviewed the retrieved data and examined the references at the end of each paper.

Source of Data

Monographs and reviews from the PubMed and CNKI databases were selected for inclusion in this review, using searches conducted in December 2023. In total, 37 papers were selected for inclusion.

Data Screening and Evaluation

Inclusion criteria for the selected articles included: (1) Articles describing the effects of acupuncture on post-stroke neuroplasticity as revealed by MRI technology; (2) Reviews with standardized methods and rigorous methodologies. Articles meeting the following exclusion criteria were not included: (1) Meta-analysis articles; (2) Literature that was published too long ago.

RESULTS

Based on the information we collect; we mainly compare 1. Research on the Mechanism of Structural Magnetic Resonance Imaging (sMRI) Combined with Acupuncture and Acupuncture Neurostructural Remodeling; 2. Functional Magnetic Resonance Imaging (fMRI) combined with acupuncture and neuroplasticity-related mechanism research.

The density or volume changes in gray and white matter can be quantitatively analyzed through Voxel-Based Morphometry (VBM). Studies have indicated that an increase in gray matter density (GMD) or volume (GMV) in brain areas related to motor control suggests neurostructural remodeling, which is significant for functional recovery after stroke, such as in the supplementary motor area (SMA) ⁽¹⁵⁻¹⁷⁾ (see table 1). Lang *et al.* ⁽¹⁸⁾ found that acupuncture stimulation from the Shenting acupoint to the Yintang acupoint along the right anterior temporal line (MS6) in patients with right basal ganglia infarction resulted in an increase in GMV in the left basal ganglia area and bilateral cerebellum, suggesting that the central effect point of acupuncture-induced gray matter remodeling might be located in the extrapyramidal loop primarily composed of bilateral cerebellum and basal ganglia, which directly participate in the brain repair process, reflecting the local therapeutic effect of acupoints. In addition, Wu *et al.* ⁽¹⁹⁾ found that acupuncture treatment in patients with residual motor dysfunction after stroke resulted in a remarkable increase in GMV in the ipsilateral frontal lobe, precentral gyrus, and parietal lobe, while the GMV in the contralateral frontal gyrus decreased significantly, and these improvements in motor function were observed to have a direct relationship with these alterations.

Table 1. Increase in gray matter volume.

ref	GMV level
⁽¹⁸⁾	Increased
⁽¹⁹⁾	Increased

Zhao *et al.* ⁽²⁰⁾ treated patients with stroke using scalp acupuncture along the anterior temporal line and found a relative increase in FA values predominantly in the forceps minor of the cingulum radiations. Shen *et al.* ⁽²¹⁾ studied patients with basal ganglia infarction with the infarct area and cerebral peduncle as nodes and found that FA values continuously decreased over time, while ADC values increased, indicating the presence of WD. After acupuncture treatment using the "Xingnao Kaqiao" method, FA and ADC values showed more significant improvement compared to patients receiving pure medication treatment. Jong *et al.* ⁽²²⁾ discovered that after 4 weeks of acupuncture treatment with adjunctive electroacupuncture in patients, the

increase in FA values observed using DTT technique was significantly higher compared to patients undergoing only rehabilitation treatment, while the increase in AD values, which represents axonal degeneration, was relatively low.

The effectiveness of a 1.5 T MRI (Magnetic Resonance Imaging) scanner is well-established and widely used in medical imaging. It is considered to be a standard strength for MRI scanners and is effective in capturing detailed images of the body's soft tissues, organs and skeletal system. It can provide high-quality images that are useful for diagnosing a wide range of medical conditions. On the other hand, MRI scanners with higher strength such as 3 T or 7 T, offer several advantages over the standard 1.5 T scanner. These higher-strength scanners can produce even more detailed images with higher resolution, which can be especially useful for imaging smaller anatomical structures and for capturing fine details in the body. They also have the potential to provide clearer images of certain tissues and pathologies that may be more challenging to visualize with a 1.5 T scanner. However, it's important to note that while higher-strength MRI scanners offer these advantages, they also come with some drawbacks. For example, they may be more sensitive to motion artifacts and have higher susceptibility to image distortion in certain areas of the body. Additionally, patients with certain medical devices or implants may not be able to undergo imaging with higher-strength scanners due to safety concerns. Overall, the effectiveness of 1.5 T MRI scanners is well-established and they are widely used in medical imaging. However, for specific cases where higher resolution and sensitivity are required, MRI scanners with higher strength such as 3 T or 7 T, can offer additional benefits in capturing more detailed and clearer images of the body.

DISCUSSION

Mechanism of sMRI Combined with Acupuncture and Neurostructural Remodeling

sMRI is a powerful technique that utilizes a strong magnetic field to capture high-resolution images of brain tissue and investigate changes in brain structure ⁽²³⁾. By assessing various parameters such as gray matter volume, cortical thickness, cortical complexity, and covariance networks, sMRI enables researchers to gain valuable insights into the structure and function of the brain ⁽²³⁾. One of the measurement methods commonly employed in sMRI is voxel-based morphometry (VBM). This approach involves comparing the amount of gray matter at each voxel across different brain images. By examining gray matter alterations, researchers can evaluate neural structural remodeling. For instance, in the context of stroke recovery, an increase in gray

matter volume as measured by VBM has been found to be significant for motor function improvement. For example, the patient was a 49-year-old woman who presented with weakness and stiffness in her right lower limb. Since the patient had early arterial enhancement and FLAIR showed only a slightly elevated signal, the stroke was presumed to have occurred within 6 hours. In fact, the patient came to the emergency department within three hours of becoming ill. sMRI can very well help doctors understand the basic situation of patients.

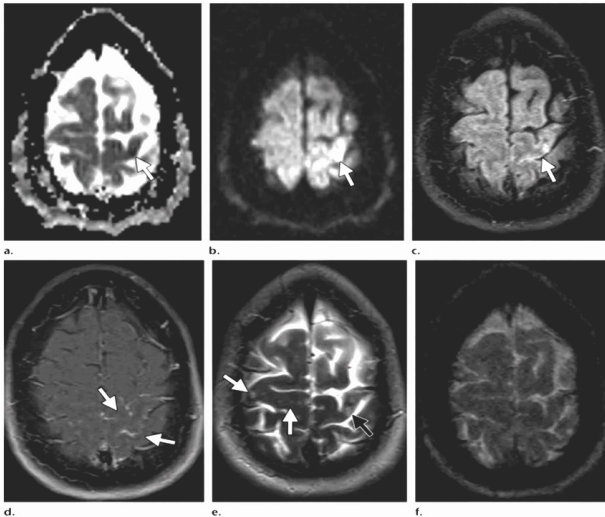


Figure 1. Example of early hyperacute ischemic stroke. **a, b:** ADC images and DWI show the diffusion-restricted area of the left motor cortex; **c:** FLAIR image of the corresponding region shows a slightly high signal of the local cortex; **d:** T1 enhanced scan showed local arterial enhancement, but no significant enhancement of cerebral cortex. **e:** The black arrow shows a slightly higher signal shadow in the left motor cortex. In addition, there are other scattered non-specific subcortical high signal shadows, but they are not related to this disease. **f:** No hemorrhagic transformation was observed in SWI sequence.

The combination of sMRI and acupuncture aims to provide a comprehensive understanding of the effects of acupuncture on the brain's structure and function. Research for this area investigates the following:

Neural plasticity: One of the mechanisms explored is how acupuncture promotes neuroplasticity. Studies using sMRI before and after acupuncture treatment can explore changes in grey and white matter volume, cortical thickness, and connectivity in relevant brain regions. This helps identify whether acupuncture induces structural changes in the brain.

Modulation of neural networks: Researchers also investigate the effect of acupuncture on functional connectivity networks in the brain. Functional MRI (fMRI) combined with acupuncture can assess changes in network connectivity and activity, shedding light on how acupuncture influences brain networks associated with pain perception, mood regulation, and other physiological processes.

Pain modulation: Acupuncture has been shown to be effective in managing pain, and sMRI studies aim to elucidate the neural mechanisms underlying this analgesic effect. By examining brain regions involved in pain modulation, for instance, the insula, anterior cingulate cortex, and periaqueductal gray, researchers can assess how acupuncture modulates pain-related brain activity and connectivity.

Brain-gut axis: Acupuncture is often used in the treatment of gastrointestinal disorders, and sMRI studies investigate the neurobiological mechanisms underlying its effects. By examining brain regions involved in the brain-gut axis, such as the amygdala and hypothalamus, researchers can explore how acupuncture modulates gut-brain communication and regulates digestive functions.

Overall, research on the mechanism of sMRI combined with acupuncture and neurostructural remodeling aims to provide a deeper understanding of how acupuncture affects brain structure and function. By elucidating the neural mechanisms involved, these studies contribute to the growing body of evidence supporting acupuncture as a therapeutic intervention for various health conditions.

According to the studies of Lang *et al.* ⁽¹⁸⁾ and We *et al.* ⁽¹⁹⁾, these suggests that acupuncture may indirectly induce neurostructural remodeling and functional reorganization through inter-hemispheric inhibition (IHI) ⁽²⁴⁾. IHI refers to the neurophysiological mechanism of reciprocal inhibition between the two cerebral hemispheres to maintain brain function equilibrium ⁽²⁵⁾. This competitive inhibitory cortical phenomenon is likely produced by inter-hemispheric excitatory pathways in the local inhibitory circuit within the corpus callosum and the primary motor cortex (M1) ^(26,27), and is commonly manifested as mutual inhibition between the bilateral frontal M1 areas. The corpus callosum acts as a bridge for the two halves of the brain and is composed of white matter and is closely connected to the gray matter involved in motor function, together forming the neural pathway for information transmission ⁽²⁸⁾. After acupuncture stimulation, sensory signals are conducted from the spinal cord to the thalamic neurons ⁽²⁹⁾, and IHI may be a neural mechanism for achieving motor function reorganization through the corpus callosum-gray matter pathway in the frontal lobe of patients with stroke.

The three-dimensional visualization of white matter and neural pathways in the central nervous system relies on analysis techniques such as Diffusion Tensor Imaging (DTI) and Diffusion Tensor Tractography (DTT). Various scalar values, such as Fractional Anisotropy (FA), Apparent Diffusion Coefficient (ADC), and Axial Diffusion Coefficient (AD), can be non-invasively obtained through these techniques. Among them, FA, which exhibits the

highest sensitivity to white matter integrity, is commonly used. White matter integrity is associated with the initial motor impairment and long-term recovery outcome of movements⁽³⁰⁾. In clinical practice, this technique can be used to monitor white matter reorganization related to acupuncture treatment in patients with stroke. A report observed brain changes in upper limb motor function impairment patients after "Tiaoren Tongdu" acupuncture treatment using DTI and found that the improvement in upper limb motor function after treatment was associated with an increase in FA values for the posterior limb of the internal capsule⁽³¹⁾, suggesting that acupuncture can reshape motor function by changing white matter integrity. The anterior temporal line projects to the primary motor cortex of the precentral gyrus, and scalp acupuncture directly affects the motor cortex, promoting white matter reconstruction in patients with ischemic stroke and improving motor functions controlled by the precentral gyrus and daily activities.

Wallerian degeneration (WD) refers to the gradual degeneration of distal axons and myelin sheaths after stroke, which indicates severe damage to the corticospinal tract (CST) primarily composed of the pyramidal tracts and is closely related to upper limb motor function⁽³²⁾. Schwann cells (SCs) are the main markers involved in WD and primarily assist in the clearance of myelin debris. These cells and the factors they secrete create a microenvironment suitable for the remodeling of damaged neurons and axons. Acupuncture at the Zusanli and Huantiao acupoints combined with electroacupuncture has been presented to upregulate the expression of S100 protein, a marker of SCs, which promotes the regeneration of SCs and the proliferation of neurotrophic factors to assist in nerve regeneration⁽³³⁾. SC reprogramming involves the upregulation of multiple genes, including c-Jun and Sox2, as well as the activation of transcription mechanisms such as the MAPK/ERK and NRG1/ErbB pathways⁽³⁴⁾. These^(21,22) confirms that acupuncture can delay the process of white matter degeneration, participate in the reprogramming process of SCs, secretion of relevant neurotrophic factors, remodeling of axons and myelin sheaths in white matter, protect motor neurons from damage caused by stroke, and further the recovery of motor function.

fMRI combined with acupuncture and neuroplasticity-related mechanism research

fMRI relies on the magnetic properties of deoxyhemoglobin and oxyhemoglobin to detect the blood oxygenation level dependent (BOLD) response caused by neuronal activity. When neurons are active, there is an increase in blood circulation to this area in order to fulfill the increased oxygen requirements as a result of neurovascular coupling. According to the state of the patients during

examination, fMRI can be classified into resting-state (rs - fMRI) and task-based (task-based fMRI), reflecting the brain damage caused by ischemic stroke (IS) and the functional connections between different brain regions. The analysis methods can be mainly classified into two categories: functional segregation and integration. The former focuses on connectivity analysis of local brain areas, including amplitude of low frequency fluctuations (ALFF) and regional homogeneity (ReHo), while the latter treats the brain as a whole internal network, relying on functional connectivity (FC), voxel-mirrored homotopic connectivity (VMHC), independent component analysis (ICA), and graph theory.

For instance, the patient was a 67-year-old man with a history of head and neck tumors. Abnormalities in the right occipital lobe were found on the PET/CT scan and further fMRI was performed (see figure 2). fMRI imaging revealed that the lesion in the right occipital lobe of the patient was a chronic stroke of about 3 weeks to 2 months.

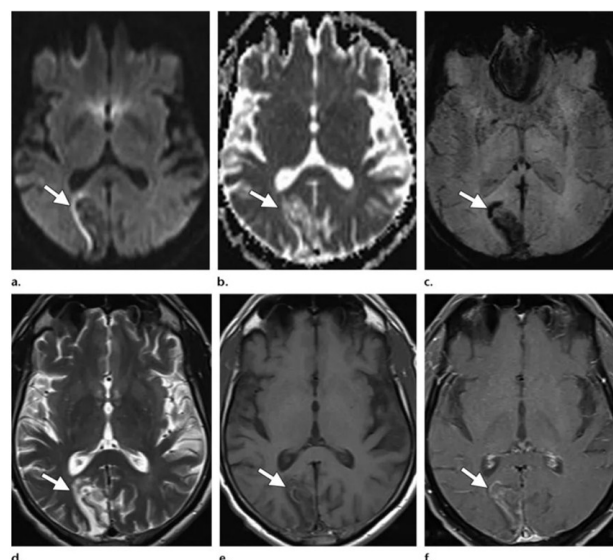


Figure 2. Examples of chronic ischemic stroke. **a:** DWI shows a low-signal area of the right occipital lobe with a high-signal edge visible around it, which may be due to the T2 penetration effect; **b:** ADC diagram shows the high signal in the corresponding area; **c:** SWI showed hemorrhage in the right occipital lobe. **d:** T2WI showed high signal in the corresponding region of the right occipital lobe; **e:** T1WI shows low signal in the right occipital lobe; **f:** The enhanced scan showed parenchymal enhancement in the corresponding areas.

The combination of fMRI with acupuncture and neuroplasticity-related mechanism research is an area of study that aims to understand the effects of acupuncture on the brain and how it may possibly facilitate neuroplastic changes. By using fMRI, researchers can observe changes in brain activity and connectivity before, during, and after acupuncture, which aims to stimulate specific points on the body. This technique helps in better understanding the neural correlates of acupuncture and its potential

effects.

The integration of acupuncture, fMRI, and neuroplasticity-related mechanisms provides a more comprehensive approach to studying acupuncture's impact on the brain. It may shed light on how acupuncture can potentially influence the central nervous system and promote neuroplastic changes that could be useful in applications such as pain management, mental health, and neurological disorders.

However, it's important to note that research in this field is still ongoing, and while there have been promising findings, more studies are required to fully cotton on the underlying mechanisms and implications of this combination.

The combined application of ALFF and ReHo methods in clinical practice provides more information about the mechanism of acupuncture's effect on motor function recovery. The ReHo value of brain regions indicates the consistency and centrality of neurons between brain areas and is more sensitive to detecting cortical activity at frequencies of 0.01 - 0.04 Hz. The ALFF value reflects the intensity of neuronal activity and mainly measures the low-frequency BOLD signal within the frequency band of 0.01 - 0.08 Hz in gray matter, but it is easily influenced by physiological noise such as respiration and heartbeat. To eliminate these error factors, the power spectrum within the low-frequency range (0.01 - 0.08 Hz) can be analyzed in ratio to the entire frequency range (fALFF).

After scalp acupuncture treatment, the ALFF value of the left BA39, adjacent superior temporal gyrus, and middle temporal gyrus increased in IS patients. The ReHo value in brain areas extending from the left middle temporal gyrus (including BA21) to BA37, the left BA40, and angular gyrus to BA7 also increased⁽³⁵⁾, indicating that acupuncture can assist in the recovery of motor neurons by enhancing the connectivity of brain areas related to sensory integration. In addition, Chen *et al.*⁽³⁶⁾ used the "paralysis acupuncture method" and found that needling the Zusanli and Quchi points on the healthy limb resulted in increased ReHo signals in the right precentral gyrus and superior frontal gyrus, while the ReHo values in the right superior parietal lobule, left angular gyrus, and left supplementary motor area decreased. This recovery mechanism is related to the increased blood flow in the motor neurons by needling the contralateral side. ReHo and ALFF are closely related to cerebral blood flow (CBF), and upregulation of CBF can promote neuroplasticity^(37,38). Previous studies have demonstrated that acupuncture can mediate molecular-induced blood supply in the renin-angiotensin system (RAS), such as inhibiting the expression of angiotensin II and angiotensin II type 1 receptor (AT1R) in tissues⁽³⁹⁾, as well as downstream Gq and CaM expression⁽⁴⁰⁾, leading to vasodilation. Acupuncture also increases

the expression of angiotensin II type 2 receptor (AT2R), which enhances CBF by mediating the angiogenic effects of angiotensin II, thereby enhancing the connectivity between damaged neurons and adjacent brain regions.

The implementation of motor function relies on the coordinated cooperation of multiple brain neuron clusters, including frontal lobe execution and voluntary movement planning, parietal lobe sensorimotor integration, and basal ganglia regulation of motor command intensity. Therefore, it is more suitable to study them using integrated network observation rather than isolated clusters. Based on whole-brain seed-based functional connectivity analysis, the primary motor cortex area (M1), premotor cortex area (PMA), and supplementary motor area (SMA), which are highly correlated with motor function, are often identified as regions of interest (ROI). By analyzing the linear correlation between ROIs and all other voxels in the entire brain, functional connectivity (FC) reveals the dynamic changes in synchronous brain networks under acupuncture intervention. Data analysis results show that the Yanglingquan and Zusanli acupoints are the most commonly used acupoints for treating IS with motor dysfunction^(41,42). Acupuncture can modulate FC in the somatosensory motor cortex^(43,44), indicating the plasticity of the brain's motor-related neural networks. Based on this theoretical basis, after acupuncture at the Yanglingquan acupoint, the rs - FC (resting-state functional connectivity) between the adjacent PMA, SMA, and superior marginal gyrus (SMG) in IS patients significantly increased⁽⁴⁵⁾. Liu *et al.*⁽³⁵⁾ also found an increase in the rs - VMHC value of PMA (BA6 and BA8) after scalp acupuncture treatment. The PMA and SMA are connected to the entire brain through the superior longitudinal fasciculus-frontoparietal (SLF-FP) tract, so the reshaping of the SLF-FP network may be one of the underlying mechanisms of acupuncture intervention in motor disorders caused by IS⁽⁴⁶⁾. Moreover, studies have set the affected and unaffected M1 as ROIs and found that the rs - FC between them significantly increased after acupuncture at the Yanglingquan or Zusanli acupoints in patients with unilateral IS^(47,48), suggesting that acupuncture can induce functional brain response asymmetry in the unaffected hemisphere, promoting functional reorganization in areas that have lost neuroplasticity.

Clinical data analysis suggests that patients with post-stroke hemiparesis not only have damage to the primary motor pathways, but also a complex array of integrated sequelae, containing changes in cognitive, visual, and auditory functions. Therefore, improvement in cognitive function and spatial attention is considered a possible mechanism for the recovery of motor-related brain networks. After 14 days of scalp acupuncture treatment on the anterior

temporal slope (MS6), the resting-state functional connectivity (rs - FC) between the left caudate nucleus and the left middle frontal gyrus, and between the right pallidum and the left frontal gyrus, was found to increase in patients with prior circulatory infarction⁽⁴⁹⁾, suggesting that acupuncture can improve the functioning of subcortical motor pathways outside the primary motor cortex. In a clinical study of patients with left middle cerebral artery acute ischemic stroke and residual hemiparesis, acupuncture stimulation at acupoints on the midline of the vertex (MS5) and the left anterior and posterior temporal slopes (MS6, MS7) was found to increase the functional connectivity (FC) of the sensory-related brain cortex, such as the precentral gyrus, BA7, and BA19, with the left supplementary motor area and the left parahippocampal gyrus⁽⁵⁰⁾, indicating that acupuncture can reshape the brain networks associated with perception, sensation, and cognition, thereby stimulating the recovery of motor-related neural function. Fu *et al.*⁽⁵¹⁾, using Granger causality analysis, analyzed the effective connectivity (EC) of the brain networks in patients with post-stroke hemiparesis and found a decrease in EC between the left frontal lobe network and the sensory motor network and between the anterior and posterior default mode networks, and an increase in EC between the bilateral frontal lobe network and the visual network, between the anterior default mode network and the sensory motor network, and between the sensory motor network and the salience network. In this causal flow of information in the aforementioned brain networks, the default mode network acts as a hub, receiving signals from the frontal lobe network and transmitting signals to the sensory motor network. This indicates that acupuncture can further the recovery of motor function by regulating the resting-state network associated with perception, thereby integrating effective connectivity in the brain network.

Strengthening and limitation

MRI, being a non-invasive technique, is highly effective in accurately identifying abnormal brain activities, making it one of the top choices. The use of these techniques can assist physicians in gaining a more accurate understanding of the potential neural pathways and biological mechanisms underlying motor deficits in IS, which contributes to the development of targeted treatments. The effects of acupuncture on promoting neural regeneration through biological mechanisms such as regulating cerebral blood flow, antioxidative stress, and reducing blood-brain barrier permeability have long been verified. In summary, acupuncture plays an indispensable role in restructuring the structure and function of the nervous system, which is crucial for the recovery of motor behavior and improvement in other bodily functions after stroke. Acupuncture can

increase the volume and integrity of white matter or gray matter, delay neurodegenerative processes, and facilitate the reshaping of relevant motor neural structures. Furthermore, the enhanced connectivity and activation of various motor cortices can assist in the recovery of patients' limb movements by contributing to the reorganization of neural functional connections, enabling early engagement in daily activities. MRI technology is rapidly evolving, and in addition to the aforementioned techniques, other techniques such as diffusion kurtosis imaging (DKI), diffusion spectrum imaging (DSI), and neurite orientation dispersion and density imaging (NODDI) can be used to observe post-IS motor neural injuries and related neural reshaping. Limitation: However, research combining acupuncture treatment with these novel techniques is currently lacking. Moreover, while there is a sufficient amount of fMRI research on gray matter BOLD signals that confirms the functional reorganization effects of acupuncture on gray matter, there are few reports on related results in white matter. In addition, seed-based analysis relies on prior knowledge or experience, thereby to a certain extent overlooking changes in brain regions beyond the seeded areas. In order to gain insights into the specific mechanisms and potential therapeutic strategies underlying brain reorganization, further exploration of white matter and whole-brain-related magnetic resonance techniques is needed.

CONCLUSION

This review of recent studies using sMRI and fMRI reveals the mechanism by which acupuncture improves IS motor dysfunction by promoting neuroplasticity. The use of these techniques could help doctors more accurately understand the biological mechanisms underlying neural pathways and motor deficits in IS, which could aid in the development of targeted therapies.

ACKNOWLEDGEMENTS

This study was supported by Peak Talent Project of Jiangsu Provincial Hospital of Traditional Chinese Medicine, Medical Research Project of Jiangsu Provincial Health Commission, and Provincial TCM Science and Technology Development Plan Project.

Funding: Peak Talent Project of Jiangsu Provincial Hospital of Traditional Chinese Medicine (No.: y2021rc50); 2021 Medical Research Project of Jiangsu Provincial Health Commission (No.: Z2021002); 2021 Provincial TCM Science and Technology Development Plan Project (No.: MS2021012).

Declarations: Ethics approval and consent to participate not applicable.

Conflicts of Interest: The authors declare that they

have no conflicts of interest.

Authors' contributions: Y-E W is the creator, directing the whole paper design and wrote the manuscript, J L directing the whole paper design and wrote the manuscript. L P participated in data analysis and manuscript revision. All authors read and approved the final manuscript.

REFERENCES

- GBD 2019 Stroke Collaborators. Global, regional, and national burden of stroke and its risk factors (2011-2019): a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Neurol*, **20(10)**: 795-820.
- Tu WJ, Zhao Z, Yin P, et al. (2023) Estimated Burden of Stroke in China in 2020. *JAMA Netw Open*, **6(3)**: e231455.
- Xuefang L, Guihua W, Fengru M (2021) The effect of early cognitive training and rehabilitation for patients with cognitive dysfunction in stroke. *Int J Methods Psychiatr Res*, **30(3)**: e1882.
- Frenkel-Toledo S, Levin MF, Berman S, et al. (2022) Shared and distinct voxel-based lesion-symptom mappings for spasticity and impaired movement in the hemiparetic upper limb. *Sci Rep*, **12(1)**: 10169.
- Olafson ER, Jamison KW, Sweeney EM, et al. (2021) Functional connectome reorganization relates to post-stroke motor recovery and structural and functional disconnection. *Neuroimage. Neuroimage*, **245**: 118642.
- Zheng WR, Li EC, Peng S, et al. (2020) Tu Youyou winning the Nobel Prize: Ethical research on the value and safety of traditional Chinese medicine. *Bioethics*, **34(2)**: 166-171.
- Mortara L, Coco G, Pozzi C (2022) Biomedicine and traditional Chinese medicine: a fruitful scientific and cultural interaction. *Acta Biomed*, **93(1)**: e2022070.
- Guo X and Cheng B (2022) Clinical Effects of Acupuncture for Stroke Patients Recovery. *J Healthc Eng*, **2022**: 9962421.
- Xu J, Pei J, Fu QH, et al. (2020) Earlier Acupuncture Enhancing Long-Term Effects on Motor Dysfunction in Acute Ischemic Stroke: Retrospective Cohort Study. *Am J Chin Med*, **48(8)**: 1787-1802.
- Mu JD, Ma LX, Zhang Z, et al. (2023) The factors affecting neurogenesis after stroke and the role of acupuncture. *Front Neurol*, **14**: 1082625.
- Liao Y, Liu F, Yang J, et al. (2022) Analysis of the Efficacy of Acupuncture Combined with Rehabilitation Training in the Treatment of Upper Limb Spasm after Stroke: A Systematic Review and Meta-Analysis. *Biomed Res Int*, **2022**: 8663356.
- Jia H, He J, Zhao L, et al. (2022) Combination of stem cell therapy and acupuncture to treat ischemic stroke: a prospective review. *Stem Cell Res Ther*, **13(1)**: 87.
- Zhan Y, Pei J, Wang J, et al. (2023) Motor function and fALFF modulation in convalescent-period ischemic stroke patients after scalp acupuncture therapy: a multi-centre randomized controlled trial. *Acupunct Med*, **41(2)**: 86-95.
- Qin S, Zhang Z, Zhao Y, et al. (2022) The impact of acupuncture on neuroplasticity after ischemic stroke: a literature review and perspectives. *Front Cell Neurosci*, **16**: 817732.
- Diao Q, Liu J, Wang C, et al. (2017) Gray matter volume changes in chronic subcortical stroke: A cross-sectional study. *Neuroimage Clin*, **14**: 679-684.
- Miao P, Wang C, Li P, et al. (2018) Altered gray matter volume, cerebral blood flow and functional connectivity in chronic stroke patients. *Neurosci Lett*, **662**: 331-338.
- Gauthier LV, Taub E, Mark VW, et al. (2012) Atrophy of spared gray matter tissue predicts poorer motor recovery and rehabilitation response in chronic stroke. *Stroke*, **43(2)**: 453-7.
- Lang Y, Li KS, Yang JY, et al. (2020) [Effect of acupuncture at the anterior oblique parietotemporal line on gray matter remodeling in patients with hemiplegia of cerebral infarction]. *Zhen Ci Yan Jiu*, **45(2)**: 141-7.
- Wu P, Zhou YM, Liao CX, et al. (2018) Structural Changes Induced by Acupuncture in the Recovering Brain after Ischemic Stroke. *Evid Based Complement Alternat Med*, **2018**: 5179689.
- Zhao N, Zhang J, Qiu M, et al. (2018) Scalp acupuncture plus low-frequency rTMS promotes repair of brain white matter tracts in stroke patients: A DTI study. *J Integr Neurosci*, **17(1)**: 61-69.
- Shen Y, Li M, Wei R, et al. (2012) Effect of acupuncture therapy for postponing Wallerian degeneration of cerebral infarction as shown by diffusion tensor imaging. *J Altern Complement Med*, **18(12)**: 1154-60.
- Kim MS, Moon BS, Ahn JY, et al. (2022) Elucidating the mechanisms of post-stroke motor recovery mediated by electroacupuncture using diffusion tensor tractography. *Front Neurol*, **13**: 888165.
- Tae WS, Ham BJ, Pyun SB, et al. (2018) Current Clinical Applications of Diffusion-Tensor Imaging in Neurological Disorders. *J Clin Neurol*, **14(2)**: 129-140.
- Di Pino G, Pellegrino G, Assenza G, et al. (2014) Modulation of brain plasticity in stroke: a novel model for neurorehabilitation. *Nat Rev Neurol*, **10(10)**: 597-608.
- Salehi Dehno N, Kamali F, Shariat A, et al. (2022) Comparison of Transcallosal Inhibition Between Hemispheres and Its Relationship with Motor Behavior in Patients with Severe Upper Extremity Impairment After Subacute Stroke. *J Stroke Cerebrovasc Dis*, **31(6)**: 106469.
- Rossini PM, Burke D, Chen R, et al. (2015) Non-invasive electrical and magnetic stimulation of the brain, spinal cord, roots and peripheral nerves: Basic principles and procedures for routine clinical and research application. An updated report from an I.F.C.N. Committee. *Clin Neurophysiol*, **126(6)**: 1071-1107.
- Belyk M, Banks R, Tendera A, et al. (2021) Paradoxical facilitation alongside interhemispheric inhibition. *Exp Brain Res*, **239(11)**: 3303-3313.
- Wang P, Meng C, Yuan R, et al. (2020) The Organization of the Human Corpus Callosum Estimated by Intrinsic Functional Connectivity with White-Matter Functional Networks. *Cereb Cortex*, **30(5)**: 3313-3324.
- Quiroz-González S, Torres-Castillo S, López-Gómez RE, et al. (2017) Acupuncture Points and Their Relationship with Multireceptive Fields of Neurons. *J Acupunct Meridian Stud*, **10(2)**: 81-89.
- Soulard J, Huber C, Baillieux S, et al. (2020) ISIS-HERMES Group. Motor tract integrity predicts walking recovery: A diffusion MRI study in subacute stroke. *Neurology*, **94(6)**: e583-e593.
- Yang FX, Gao JY, Liu G, et al. (2021) [Effect of tiaoren tongdu acupuncture method on fractional anisotropy of diffusion tensor imaging and upper extremity motor function after cerebral infarction]. *Zhen Ci Yan Jiu*, **46(7)**: 610-5.
- Darwish HS, ElShafey R, Kamel H (2021) Prediction of Motor Recovery after Stroke by Assessment of Corticospinal Tract Wallerian Degeneration Using Diffusion Tensor Imaging. *Indian J Radiol Imaging*, **31(1)**: 131-137.
- Hu LN, Tian JX, Gao W, et al. (2018) Electroacupuncture and moxibustion promote regeneration of injured sciatic nerve through Schwann cell proliferation and nerve growth factor secretion. *Neural Regen Res*, **13(3)**: 477-483.
- Nocera G and Jacob C (2020) Mechanisms of Schwann cell plasticity involved in peripheral nerve repair after injury. *Cell Mol Life Sci*, **77(20)**: 3977-3989.
- Liu H, Jiang Y, Wang N, et al. (2021) Scalp acupuncture enhances local brain regions functional activities and functional connections between cerebral hemispheres in acute ischemic stroke patients. *Anat Rec (Hoboken)*, **304(11)**: 2538-2551.
- Chen SQ, Cai DC, Chen JX, et al. (2020) Altered Brain Regional Homogeneity Following Contralateral Acupuncture at Quchi (LI 11) and Zusanli (ST 36) in Ischemic Stroke Patients with Left Hemiplegia: An fMRI Study. *Chin J Integr Med*, **26(1)**: 20-25.
- Adhikari BM, Hong LE, Zhao Z, et al. (2022) Cerebral blood flow and cardiovascular risk effects on resting brain regional homogeneity. *Neuroimage*, **262**: 119555.
- Li Z, Zhu Y, Childress AR, et al. (2012) Relations between BOLD fMRI-derived resting brain activity and cerebral blood flow. *PLoS One*, **7(9)**: e44556.
- Xin JJ, Gao JH, Wang YY, et al. (2017) Antihypertensive and Antihypertrophic Effects of Acupuncture at PC6 Acupoints in Spontaneously Hypertensive Rats and the Underlying Mechanisms. *Evid Based Complement Alternat Med*, **2017**: 9708094.
- Li J, He J, Du Y, et al. (2014) Electroacupuncture improves cerebral blood flow and attenuates moderate ischemic injury via Angiotensin II its receptors-mediated mechanism in rats. *BMC Complement Altern Med*, **14**: 441.
- Zhang J, Li Z, Li Z, et al. (2021) Progress of Acupuncture Therapy in Diseases Based on Magnetic Resonance Image Studies: A Literature Review. *Front Hum Neurosci*, **15**: 694919.

42. Sun ZG, Pi YL, Zhang J, et al. (2019) Effect of acupuncture at ST36 on motor cortical excitation and inhibition. *Brain Behav*, **9(9)**: e01370.
43. Zhang J, Lu C, Wu X, et al. (2021) Neuroplasticity of Acupuncture for Stroke: An Evidence-Based Review of MRI. *Neural Plast*, **2021**: 2662585.
44. Lu M, Du Z, Zhao J, et al. (2023) Neuroimaging mechanisms of acupuncture on functional reorganization for post-stroke motor improvement: a machine learning-based functional magnetic resonance imaging study, **17**: 1143239.
45. Han X, Bai L, Sun C, et al. (2019) Acupuncture Enhances Communication between Cortices with Damaged White Matters in Post-stroke Motor Impairment. *Evid Based Complement Alternat Med*, **2019**: 4245753.
46. Vergani F, Ghimire P, Rajashekhar D, et al. (2021) Superior longitudinal fasciculus (SLF) I and II: an anatomical and functional review. *J Neurosurg Sci*, **65(6)**: 560-565.
47. Ning Y, Li K, Fu C, et al. (2017) Enhanced Functional Connectivity between the Bilateral Primary Motor Cortices after Acupuncture at Yanglingquan (GB34) in Right-Hemispheric Subcortical Stroke Patients: A Resting-State fMRI Study. *Front Hum Neurosci*, **11**: 178.
48. Li Y, Wang Y, Liao C, et al. (2017) Longitudinal Brain Functional Connectivity Changes of the Cortical Motor-Related Network in Subcortical Stroke Patients with Acupuncture Treatment. *Neural Plast*, **2017**: 5816263.
49. Lin D, Gao J, Lu M, et al. (2023) Scalp acupuncture regulates functional connectivity of cerebral hemispheres in patients with hemiplegia after stroke. *Front Neurol*, **14**: 1083066.
50. Liu H, Chen L, Zhang G, et al. (2020) Scalp Acupuncture Enhances the Functional Connectivity of Visual and Cognitive-Motor Function Network of Patients with Acute Ischemic Stroke. *Evid Based Complement Alternat Med*, **2020**: 8836794.
51. Fu CH, Li KS, Ning YZ, et al. (2017) Altered effective connectivity of resting state networks by acupuncture stimulation in stroke patients with left hemiplegia: A multivariate granger analysis. *Medicine (Baltimore)*, **96(47)**: e8897.

