Heliyon 10 (2024) e39059

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Magnetic resonance imaging studies on acupuncture therapy in cerebral ischemic stroke: A systematic review

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ARTICLE INFO

Keywords:
Acupuncture
Magnetic resonance imaging
Ischaemic stroke
Treatment
Systematic review

ABSTRACT

Research has started using Magnetic Resonance Imaging (MRI) to elucidate the action of acupuncture on neuroplasticity following ischemic stroke (IS). Acupuncture is thought to be a potentially beneficial treatment for IS. However, the results remain inconsistent because of MRI processing techniques and study design variations. Therefore, this coordinate-based meta-analysis and systematic review aimed to assess the current state of knowledge about the regional brain fMRI imaging characteristics in acupuncture-treated IS patients. Twenty studies—including 392 IS patients and 256 health controls—met the inclusion criteria after searches via Chinese and English databases. The design techniques utilized in this research were mainly owned before-and-after controlled and randomized controlled trials. Only one study used independent component analysis (ICA), while the majority of MRI analytical techniques focus on functional connectivity (FC) and fractional amplitude of low-frequency fluctuation (fALFF/ALFF). The findings demonstrated a significant rise in the ALFF value of the left supplementary motor region after treatment with acupuncture. The left cerebellum, right inferior frontal gyrus, and hemisphere lobule VIII all showed substantial activation of Reho values. The triangular portion, BA 48, the left inferior network and inferior longitudinal fasciculus, as well as other brain areas decreased in the left inferior frontal gyrus; most research has used FC analysis employing motor areas as seed regions. We found that acupuncture regulated the motor-related network and reorganized the language-related network. Furthermore, acupuncture appears therapeutic for several IS effects, which may be connected to how acupuncture regulates the brain's plasticity.

1. Introduction

Stroke is a major cause of permanent impairment [1]. The World Health Organisation (WHO) estimates that one stroke happens every 5 s worldwide [3]. About 15 million people experience a stroke every year; one-third of them lose their lives, and one-third are

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https://doi.org/10.1016/j.heliyon.2024.e39059
Received 22 November 2023; Received in revised form 20 September 2024; Accepted 7 October 2024
Available online 16 October 2024

permanently turned off [4]. Ischemic stroke (IS), the primary type, accounts for over 80 % [2]. IS is a group of neurological deficiency syndromes brought on by brain tissue hypoxia and ischemia, as well as necrosis and softening brought on by a variety of factors. Patients' quality of life is significantly impacted by the varied degrees of motor impairment that afflict 60%–70 % of patients [5].

After IS occurs, neuronal cells undergo morphological changes and activate programmed cell death pathways [6]. Microglia and astrocytes rapidly migrate to the injury site, regulate the neurotransmitter microenvironment, and produce proinflammatory effects [7,8]. Currently, the clinical treatment of IS is mainly to restore brain tissue perfusion through drug thrombolysis or vascular intervention [9]. However, due to many contraindications such as age, genetic and environmental factors, the mortality of IS patients is still increasing year by year [10]. Due to the limitations of traditional treatments, there IS an urgent need to find alternative therapies for IS patients. Current studies have shown that acupuncture's multifaceted, all-encompassing mode of action is effective in treating IS. Acupuncture can regulate cerebral blood flow, hemorheology, immunity and intestinal flora, significantly promote angiogenesis and inhibit brain cell apoptosis. Some systematic reviews have shown that acupuncture can substantially improve IS [11,12]. Furthermore, according to a comprehensive assessment of preclinical research, acupuncture might decrease infarct size, improve nerve damage, and have neuroprotective functions in acute ischemia animal models [13]. However, additional investigation is needed on the effects of acupuncture on IS.

Studies have focused on the primary mechanism acupuncture aids in restoring neuronal function compromised by IS. The application of non-invasive functional magnetic resonance imaging (fMRI) in neuroscience has afforded researchers a novel perspective for investigating the mechanisms by which acupuncture modulates brain plasticity on a macroscopic scale. The utilization of brain imaging technologies to examine alterations in specific brain functional regions induced by acupuncture has emerged as a critical domain of medical research. Therefore, exploring the brain's structural, functional, and metabolic changes in treating IS with acupuncture is possible. Importantly, as research in this area gained attention, the mechanisms responsible for the central regulation of acupuncture on IS became apparent. However, there are few reviews of the use of brain imaging in IS treatment. Understanding the current research status is essential for enhanced future exploration.

Hence, we systematically reviewed brain imaging in IS treated with acupuncture. We summarised the research methods, characteristics and conclusions and systematically evaluated the evidence for CNS effects, such as brain structure and function of IS treated with acupuncture.

Table 1
Search terms and search strategy.

No.	Mesh
#1	Magnetic resonance imaging
#2	Functional magnetic resonance imaging
#3	neuroimaging
#4	Functional MRI
#5	Resting-state functional magnetic resonance
#6	rs-fMRI
#7	#1 OR #2 OR #3 OR #4 OR #5 OR #6
#8	ALFF
#9	fALFF
#10	Amplitude of Low-Frequency Fluctuations
#11	ReHo
#12	Regional homogeneity
#13	local connectivity
#14	coherence
#15	Independent Component Correlation Algorithm
#16	ICA
#17	Functional connectivity
#18	FC
#19	Region of interest
#20	ROI
#21	#8 OR #9 OR #10 #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20
#22	Acupuncture
#23	Needle
#24	Electroacupuncture
#25	Acupoint
#26	Scalp acupuncture
#27	taVNS
#28	#22 OR #23 OR #24 OR #25 OR #26 OR #27
#29	Ischemic Stroke
#30	clinical trials
#31	#7 AND #21 AND #28 AND #29 AND #30

2. Study methodology

2.1. Search strategies and study selection

We systematically evaluated the preferred reporting items according to the PRISMA criteria, as detailed in Supplementary Materials Table S1. The current investigation examined six databases for studies using MRI to examine the use of acupuncture for IS: PubMed, Web of Science, Cochrane Library, Chinese National Knowledge Infrastructure (CNKI), Chongqing VIP database (VIP), and Wanfang database (WF) from their inception until December 31, 2022, utilizing the primary keywords: neuroimaging and acupuncture; studies about ischaemic stroke were included. The terms and methods used for searches are presented in Table 1. Searches were restricted to articles published in Chinese and English, with searches of databases performed according to their specific features.

2.2. Eligibility criteria

Study inclusion was based on the PICOS principles. Studies meeting the criteria below were enrolled in the analysis:

Participants: Participants met established diagnostic criteria for IS, confirmed by computed tomography (CT) or magnetic resonance imaging (MRI) brain scans. The patient is stable and conscious, without cognitive deficit.

Intervention: Using manual acupuncture (MA) and electroacupuncture (EA).

Comparison: The control group can use non-acupuncture treatments, but the baseline information should remain the same as the intervention group.

Outcomes: Analytical techniques and fMRI or structural MRI can be used to assess brain responses in various approaches.

Type of studies: Randomized and non-randomized controlled clinical studies of acupuncture's efficacy in treating IS.

Studies with the following characteristics were excluded: studies with nonclinical patients as a research subject; Other interventions that did not belong to acupuncture; Repetitive published articles; Articles with unclear diagnostic criteria or unclear relevant outcome indicators; protocol, case reports, or case series; Patients complicated with other serious diseases.

2.3. Study selection

First, EndNote filtered all study titles and abstracts that the search strategy had returned, eliminating duplicates. Perusal of the title and abstract eliminated studies not conforming to the inclusion criteria. Two reviewers independently reviewed the full text versions to confirm eligibility. Any disputes arising during the screening process would be settled by conversation or consulting another peer.

2.4. Data extraction

Data were obtained by one investigator, with confirmation by a second investigator. The subsequent data were derived from the qualifying studies: Publishing data (primary author, year of publication); (2) Trial design (research design, sample size, comparison group, clinical outcome measures, neuroimaging procedures, scanning instruments, imaging modalities and circumstances, analytical methods); (3) acupuncture manipulation (primary acupoints, acupuncture modalities, retention).

Time, length of treatment); (4) participant characteristics (gender, age, diagnosis criteria, length of sickness); and (5) results as stated. Studies using comparable MRI analytic designs and procedures yielded peak coordinates and statistical significance levels. A conversation between the authors settled any differences of opinion.

2.5. SDM-PSI meta-analysis

The Signed Differential Mapping with Permutation of Subject Images version 6.22 (SDM-PSI) coordinate-based meta-analysis (CBMA) (https://www.sdmproject.com/). The data-driven method, CBMA, can reconstruct the brain activation map that is consistently active in several studies, combine and analyze primary imaging data of the entire brain, and provide insights into neurological disease mechanisms and brain function. SDM-PSI is a meta-analysis method for neuroimaging that utilizes coordinate values. It employs a random effects model to combine statistics, resulting in coordinate points that exhibit statistical differences. The following are the primary procedures involved: the t-values and peak coordinates of the differential brain regions (z-value converted to t-value) were extracted; (2) upper and lower bounds for the effect size of the included studies were estimated; (3) most probable effect size mappings and their standard errors were calculated using the MetaNSUE algorithm [14]; (4) effect sizes for individual studies were extrapolated multiple times; (5) the various meta-analyses produced by multiple inferences were brought together using Rubin rules and a standard random effects model [15]; and (6) inter-group heterogeneity tests were carried out on included studies. Our primary source of information has been the SDM-PSI instruction manual (https://www.sdmproject.com/manual/), which contains the precise operating protocols.

We present the outcomes of threshold-free clustering enhancement (TFCE) family-wise error (FWE) correction ($p < 0.05$, voxel extent$\geq$10). The conventional heterogeneity statistic, I^2, was obtained by extracting the peak MNI coordinates. A value of $I^2<50$ % indicates little heterogeneity. Publication bias was examined using funnel plots and Egger's test.

2.6. Meta-regressions analysis

We employed meta-regression analysis to ascertain the correlation between variations in ReHo/ALFF and the potential impacts of clinical factors by linear regression. The meta-regression analysis used a strict $p < 0.05$ threshold and cluster extent ≥10 voxels to determine significance.

2.7. Quality assessment

The quality evaluation was conducted using the Cochrane Bias Risk Tool. The risk of bias was evaluated across multiple domains, including an examination of selection bias by random sequence generation and concealment of allocation, performance bias by participant and personnel blinding, detection bias by blinding of outcome assessments, attrition bias indicated by incomplete information on outcomes, reporting bias indicated by selective reporting, and others. Each domain comprises multiple elements that must be assessed as 'low risk,' 'unclear,' or 'high risk.' Two independent evaluators reviewed the included studies, while a senior reviewer adjudicated any discrepancies. This study employed R software version 4.3.1 and R Studio version 4.3.1 for quality evaluation and visualization.

3. Results

3.1. Study characteristics

This review comprised 20 publications overall, detailed in Table 2. The database search turned up 176 articles. However, 45 of them were removed for being duplicates, following the search strategy. Following the screening of the title and abstract, 52 articles were eliminated. Out of 79 pertinent studies, 59 were excluded following the full-text review. As a result, our review encompassed a total of 20 articles. Fig. 1 depicts a PRISMA flowchart of the search process.

All research published between 2010 and 2022 and meeting the inclusion criteria originated from China. Three studies utilized a parallel-group design, eleven employed three parallel-arm group designs, while two used parallel-arm group designs. All clinical investigations included six hundred forty-eight patients, comprising 392 individuals with IS and 256 healthy controls (HC). All individuals with ischaemic stroke who fulfilled the diagnostic criteria for IS were examined. Age, gender, and symptom severity (FMA, NIHSS, MMSE) were the only demographic baseline factors that showed no marked differences between the two groups. A novel design paradigm for non-repetitive event-related (NRER) FMRI was applied in seven studies [27–31,34,35] for assessing the long-term effect of acupuncture on IS. The remaining research used the Rs-fMRI technique. Eight investigations [16,17,19,22,23,26,29,33] documented patients with malfunction of the right side of the limb; most lesions were found in the left hemisphere, namely in the basal ganglia. Conventional therapy was administered to each patient. The participants in the acupuncture-treated groups received 4–8 weeks of treatment, which included manual acupuncture (MA), electroacupuncture (EA), and scalp acupuncture (SA). The Main acupoints included Yanglingquan (GB34), Baihui (DU20) and Shenting (DU24). The specific methods of acupuncture intervention and the needle retention time have been reported in all 20 studies, but there are differences between studies. The trials conducted did not monitor alterations in brain function in patients with IS following acupuncture therapy.

3.2. Quality assessment

Quality evaluation was conducted using the Cochrane Bias Risk Assessment Tool which showed that six studies detailed the mechanism of random sequence generation. In contrast, one study addressed group masking and blinding, resulting in an uncertain risk of bias. The assessment of incomplete outcomes relies on the clarity of the baseline data presented in the survey. Despite the absence of a formal study protocol in any of the investigations, all anticipated outcome measures were reported, including those that were prespecified. We selected to regard trials with two or more reported secondary outcome measures as low-risk for selectively presented data.

Furthermore, we identified no alternative sources of bias. Overall, the study quality could have been improved, particularly in terms of concealment of allocation, blinding, and the blinding of outcome evaluations. The quality assessements are shown in Fig. 2.

3.3. Results of MRI studies

Among the fMRI studies, six utilized regional homogeneity (ReHo) analysis [16–21], four employed amplitude of low-frequency fluctuation (ALFF) analysis [22–25], one study applied both ReHo and ALFF [26], one utilized independent component analysis (ICA) [27], and eight studies calculated functional connectivity (FC) between brain regions using Pearson correlation coefficients [28–35]. All the information is detailed in Table 3.

Moreover, the ReHo was used in six studies. These studies show that acupuncture can regulate the ReHo values in the frontal lobe, limbic system, cerebellum, and bilateral motor areas.

ALFF was used in five studies. Acupuncture can regulate the ALFF value in various brain regions, particularly, the limbic system, temporal lobe, frontal lobe, and cerebellum.

ICA was only utilized for analysis in one study. The primary focus of this investigation was how acupuncture at GB34 affected the sensorimotor network in IS patients. The findings demonstrated that acupuncture might boost the impact of sensory input on motor

Table 2
Clinical and demographic features of the studies that were included.

No.	Author	Cohort	Diagnostic criteria	Study design	Disease duration	Symptom severity (baseline)	usual treatment	Treatments	Age	Main acupoints	Treatment frequency (each session duration, total period)	Scanning instrument/ experimental design
1	Zhang Yong 2014	ischemic stroke (8); HC (10)	MRI showing unilateral limb impairment with right hemisphere corona radiate, internal capsule, or basal ganglia infarction	Observational studies	2–12 weeks	NIHSS: 3–14; MMSE ≥21	Not reported	MA (8); HC (10)	MA: 60.4 ± 6.6 HC: 59.1 ± 7.8	GB34	MA for 30min	Siemens 3.0T; NRER-fMRI
2	Chen Junqi 2014	ischemic stroke (24)	ICD-9434 ; ICD-8433 the left basal ganglia with right hemiplegia	RCT	5.30 ± 3.71m; 3.38 ± 3.29m	CSS: 18.20 ± 4.02; 17.13 ± 4.76	aspirin, clopidogrel, statins	MA (12); SA (12)	MA: 56.10 ± 5.53 SA: 58.50 ± 7.05	TE5	MA, needing two times, 3–9, 16–22min.	GE Signa 3.0T; NRER-fMRI
3	Xie Zijing 2014	ischemic stroke (9); HC (8)	unilateral right-sided striatocapsular lesions	Observational studies	53.6 ± 41.6 days	NIHSS: 3–14; MMSE ≥22	Not reported	MA (9); HC (8)	MA: 57.8 ± 9.9 HC: 51.6 ± 4.8	GB34	Not reported	Siemens 3.0T; NRER-fMRI
4	Fu Caihong 2016	ischemic stroke (19); HC (17)	left hemiplegia, the lesion restricted to the internal capsule and neighboring regions in the right hemisphere	Observational studies	2 weeks-6 months	None	Not reported	MA (19); HC (17)	MA: 61.53 ± 8.92 HC: 53.94 ± 4.83	GB34	Not reported	Siemens 3.0T; NRER-fMRI
5	Ning Yanzhe 2017	ischemic stroke (20); HC (20)	ischaemic infarction of the corticospinal tract on the right hemisphere, resulting in left motor hemiparesis	Observational studies	first-ever ischemic stroke	None	Not reported	MA (20); HC (20)	MA: 61.32 ± 8.53 HC: 58.86 ± 8.53	GB34	MA: needing one time, 0–1min, 9–10min	Siemens 3.0T; NRER-fMRI
6	Li Yongxin 2017	ischemic stroke (17); HC (14)	unilateral ischaemic lesions resulting in motor impairments	Observational studies	3 weeks	NDS: 13-31	anti-platelet aggregation drugs	MA (8) IS (9) HC (14)	MA: 63.29 ± 12.27 HC: 62.21 ± 10.48	GV20, GB20, GB39, LI11, LI4, ST36, SP6	MA: Two hours every day, five days a week, for four therapy courses; one week per course	Siemens 3.0T; rs-fMRI
7	Yi Xiaoqi 2021	ischemic stroke (21); HC (18)	right limb motor deficits	Observational studies	≤2 weeks	FMA: 48.24 ± 14.35 (≤84)	usual medication	EA (21); HC (18)	EA: 66.2 ± 9.17 HC: 66.1 ± 7.42	Parietal region LI15 LI4 LI0 TE5 ST31 SP10 BL36 BL40 GB34 GB39	EA for 30min	Siemens 3.0T; rs-fMRI

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Table 2 (*continued*)

No.	Author	Cohort	Diagnostic criteria	Study design	Disease duration	Symptom severity (baseline)	usual treatment	Treatments	Age	Main acupoints	Treatment frequency (each session duration, total period)	Scanning instrument/ experimental design
8	Wang Yue 2022	ischemic stroke (63); HC (42)	the basal ganglia and/or the corona radiate region	Observational studies	≤3 months	NIHSS:3.81 ± 3.19 (0–15)	Not reported	MA (63); HC (42)	MA: 59.56 ± 9.82 HC: 56.64 ± 5.17	GB34	MA for 9min10s	Siemens 3.0T; Task-fMRI
9	Shi Xinyue 2022	ischemic stroke (40)	the Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke in China, 2014, located in the corona radiata or basal ganglia	Pre-post	≤2 months	FMA: 70.17 ± 29.45 NIHSS: 3.29 ± 2.88 MMSE: 26.63 ± 3.85	Not reported	MA (40)	L-MA: 60.38 ± 9.52 S-MA: 56.88 ± 11.29	GB34	MA for 9min	Siemens 3.0T; NRER-fMRI
10	Xie Ximei 2013	ischemic stroke (9); HC (10)	right limb motor deficits, located in the left basal ganglia	Observational Studies	≤1 month	Muscle strength of right upper and lower limbs ≥2, FMA: right limb motor deficits MMSE≥27	usual medication	MA (9); HC (10)	MA: 65.50 ± 2.32 HC: 66.20 ± 2.70	MA: DU20 GB20 LI11 LI4 ST36 GB34 GB39 SP6	30min, once a day, 5 d per course, 2 d off, for a total of 4 courses	Siemens 3.0T; rs-fMRI
11	Wang You 2022	ischemic stroke (10)	right limb motor deficits, located in the left basal ganglia	Pre-post	≤1 month	Muscle strength of right upper and lower limbs ≥2, FMA: right limb motor deficits MMSE≥27	Not reported	MA (10)	Not reported	MA: DU20 GB20 LI11 LI4 ST36 GB34 GB39 SP6	Not reported	Siemens 3.0T; rs-fMRI
12	Ding Caixia 2017	ischemic stroke (10); HC (10)	right limb motor deficits, located in the left basal ganglia	Observational Studies	≤1 month	Muscle strength of right upper and lower limbs ≥2, FMA: right limb motor deficits MMSE≥27	usual medication	MA (10); HC (10)	MA: 68.80 ± 2.70 HC: 66.20 ± 2.70	MA: LI15 LI11 LI10 TE5 LI4 ST36 ST40 GB34 SP6 LR3	30min, once a day, 5 d per course, 2 d off, for a total of 30 d	GE 1.5T; rs-fMRI
13	Wu Ping 2017	ischemic stroke (11)		RCT	≤6 month	NDS: 23.63 FMA: 83.73 MBI: 32.39 MMSE≥27	aspirin citicoline	MA (11)	MA: 69.36 HC: 52.81	MA: GV20, GB20, LI11, LI4, ST36, GB33, GB39, SP6	30min, once a day, 5 d per course, 2 d off between each course of treat ment, for a total of 4 courses	Siemens 3.0T; rs-fMRI
14	Xie ximei 2019	ischemic stroke (12)	right limb motor deficits, located in the basal ganglia	RCT	≤1 month	Muscle strength of right upper and lower limbs ≥2, FMA: right	usual medication	MA (12)	MA: 63.20 ± 1.34	MA: LI11 ST36 DU20 LI4 SP6 GB34 TE5	30min, once a day, 5 d per course, 2 d off, for a	Siemens 3.0T; rs-fMRI

(*continued on next page*)

Table 2 (*continued*)

No.	Author	Cohort	Diagnostic criteria	Study design	Disease duration	Symptom severity (baseline)	usual treatment	Treatments	Age	Main acupoints	Treatment frequency (each session duration, total period)	Scanning instrument/ experimental design
						limb motor deficits MMSE≥27					total of 6 courses	
15	Fu Caihong 2019	ischemic stroke (20); HC (20)	left limb motor deficits, located in the right basal ganglia and corona radiata	Observational Studies	2 week-3 month	Not reported	Not reported	MA (20); HC (20)	MA: 61.32 ± 8.53 HC: 58.86 ± 8.53	MA: GB34	Not reported	Siemens 3.0T; rs-fMRI
16	Zhou Yu 2020	ischemic stroke (10); HC (10)	right limb motor deficits, located in the unilateral basal ganglia and corona radiata	Observational Studies	2 week-3 month	Spastic paralysis of the right limb, Brunnstrom stage II-IV, Ashworth Scale score I-III	Not reported	MA (10); HC (10)	MA: 53.60 ± 7.67 HC: 54.20 ± 9.37	MA: LI15 LI11 LI4 TE5 BL40 SP9 SP6 BL57	30min	GE 3.0T; rs-fMRI
17	Chen Shuqi 2020	ischemic stroke (10)	left limb motor deficits, located in the right basal ganglia	Pre-post	1 month-3 year	Hemiplegia of left limb	Not reported	MA (10)	MA: 57.70 ± 7.69	MA: LI11, ST36	15min	GE 3.0T; rs-fMRI
18	Liu Huacong 2021	ischemic stroke (15); HC (15)	the left middle cerebral artery AIS with motor impairments in the right limb in the 2014 Guidelines for the Diagnosis and Treatment of Acute Ischaemic Stroke in China	RCT	≤3 day	NIHSS: 3.20 ± 2.46 SFMA:10.27 ± 1.96	anti-platelet, cholesterol-lowering, blood pressure stabilizers	SA (15); HC (15)	SA: 56.47 ± 8.25 HC: 61.73 ± 7.79	SA: MS5, MS6, MS7	Thirty minutes twice a day for one course over six days.	Siemens 3.0T; rs-fMRI
19	Wang Fei 2021	ischemic stroke (40); HC (40)	Guidelines for Prevention and Treatment of Cerebrovascular Disease in China	RCT	≤1 month	NIHSS: 13.35 ± 2.62 FMA: 35.32 ± 12.39 MBI: 20.68 ± 5.93	usual medication	MA (40); HC (40)	MA: 66.00 ± 8.00 HC: 67.00 ± 9.00	MA: DU20 DU24	30 min, every two days, for a total of 8 weeks	Siemens 3.0T; rs-fMRI
20	Zhan Yijun 2014	ischemic stroke (24); HC (22)	limb motor deficits	RCT	1 month–6 month	FMA: 42.88 ± 13.32 MBI: 53.12 ± 13.84 mRS: 2.73 ± 1.52	antihypertensives drugs to regulate blood sugar lipid-lowering agents drugs to inhibit platelet aggregation	MA (24); HC (22)	MA: 61.6 ± 6.64 HC: 62.2 ± 7.80	SA: MS6	30min, 5 times a week, 20 times per treatment course, for two course	GE 3.0T; rs-fMRI

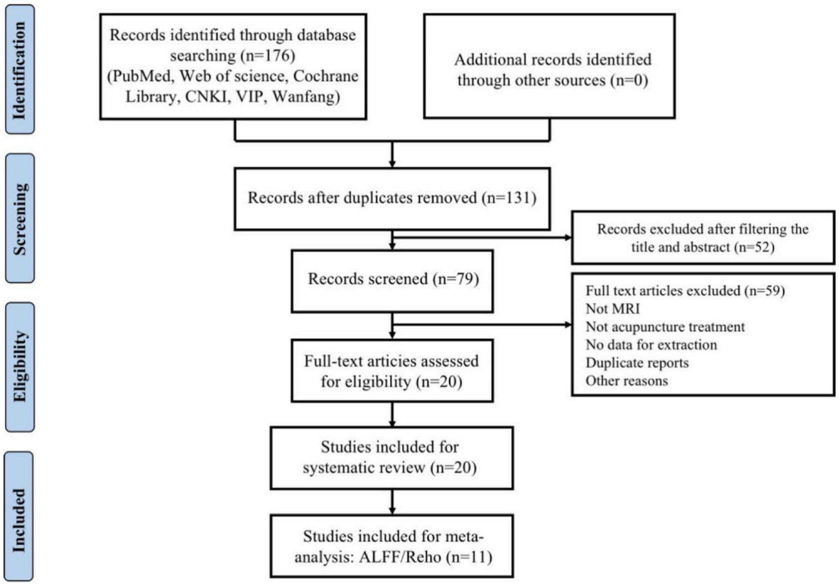

Fig. 1. A flowchart showing the selection of literature for the current study.

output, promote brain function remodeling in patients with IS, and regulate the activity of brain areas relevant to the sensorimotor network in both cerebral hemispheres.

Eight studies used a seed-based FC study, in which six studies used the bilateral M1 region of the brain as the seed point. Yi et al. demonstrated that acupuncture could augment FC between the bilateral primary motor cortex (M1) and the right anterior and posterior central gyrus, indicating a potential brain remodeling mechanism through which acupuncture facilitates functional recovery in individuals with IS. Ning et al. further corroborated that acupuncture enhances FC in the bilateral M1 regions among IS patients. Additionally, Li et al. revealed that acupuncture significantly elevated FC intensity between the M1 area and related motor networks bilaterally, suggesting its efficacy in restoring motor function in individuals with IS. Acupuncture treatment effectively restores motor function in people with IS and can cause widespread changes in functional brain activity.

Numerous comparison groups were included in these studies: pre-acupuncture vs post-acupuncture, acupuncture + medication vs drug, and acupuncture vs sham acupuncture. ① Acupuncture versus sham acupuncture (sham-A): Acupuncture can modulate the sensory-motor areas' functional connections within and between cerebral hemispheres as well as between the cerebellum and brain; ② Acupuncture + medication vs medication: the majority of the included studies compared the influence of acupuncture together with necessary medications and the straightforward administration of medications. Acupuncture is a successful treatment for IS, and when combined with medication, it not only restores the motor function network but also modifies the interactions between different brain areas. ③ Pre-versus post-acupuncture: self-control tests were carried out in three investigations before and after receiving acupuncture therapy. The outcomes demonstrated that acupuncture could regulate the activities of multiple brain regions, especially the motor-related brain regions.

3.4. Meta-analysis results

Eleven studies were included in the meta-analysis, involving an analysis of 186 patients about the alterations in ReHo (77) and ALFF (109) values pre- and post-acupuncture therapy. ① ALFF: The left supplementary motor area (SMA, $p < 0.05$, $Z = 4.629$) showed marked hyperactivation in ALFF values in participants receiving acupuncture. The right SMA, the left median network, the cingulum, the left SMA, and the right median cingulate/paracingulate gyri were all stretched by the left SMA; ② ReHo: The findings showed a marked reduction in activity in the left inferior frontal gyrus, triangular part, BA 48 ($p < 0.05$, $Z = -3.010$), and the left inferior network, inferior longitudinal fasciculus ($p < 0.05$, $Z = -2.860$), as well as a significantly increased number of ReHo signals in the left cerebellum, hemispheric lobule VIII ($p < 0.05$, $Z = 2.781$) and the right inferior frontal gyrus ($p < 0.05$, $Z = 3.037$). The hemispheric lobule VIII on the left cerebellum is connected to the hemispheric lobule VIIB on the left cerebellum and the crus II on the left cerebellum. In addition to the right inferior frontal gyrus, triangular portion (BA 48), and opercular part (BA 44), the right inferior frontal gyrus also extended to the right inferior frontal gyrus, opercular part, and right inferior frontal gyrus, triangular part. The triangular portion (BA 48) of the left inferior frontal gyrus extends to the following: the left median cingulate/paracingulate gyri (BA 24), the right median cingulate/paracingulate gyri (BA 24), the left median cingulate/paracingulate gyri, and the right SMA (BA 24). The left fusiform gyrus, BA 19, the left cerebellum, hemispheric lobule VI, BA 18, and the left fusiform gyrus, BA 18, were all reached via the left inferior network and inferior longitudinal fasciculus. Tables 4 and **5** display the cluster breakdowns and peak coordinates. Figs. 3 and **4** (BA 24) illustrate changes in brain regions before and after the use of acupuncture.

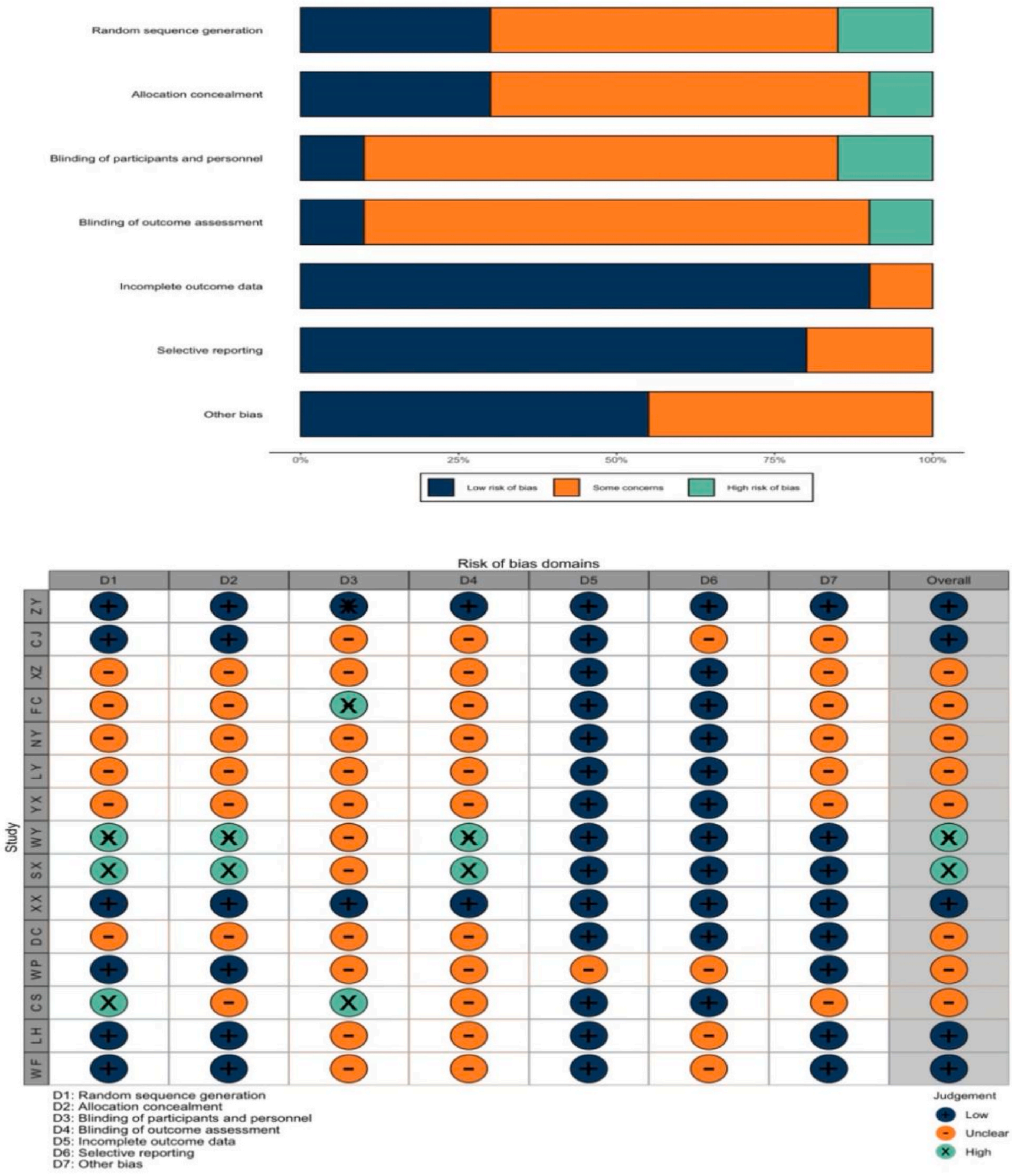

Fig. 2. Evaluation of the included study's quality.

3.5. Assessment of heterogeneity and publication bias

The assessment of heterogeneity demonstrated variability and diversity among the research considered. In the acupuncture therapy cohort, the left SMA, left cerebellum, right inferior frontal gyrus, and left inferior frontal gyrus exhibited minimal heterogeneity in the peak coordinate effect size differences ($I^2 = 1.80\%–13.15\ \%$). The results of heterogeneity are presented in Tables 4 and 5 The Egger test indicated no substantial publication bias in the acupuncture therapy group.

Table 3
Acupuncture-related fMRI studies on ischaemic stroke.

No.	Author(s)	Seed regions	Groups	Treatments	Findings
1	Zhang Yong 2014	bilateral PCC	ischemic stroke (8); HC (10)	MA (8); HC (10)	MA: the PCC and bilateral ACC ↑; the left postcentral gyrus and precentral gyrus ↓
2	Chen Junqi 2014	motor ability/sensations/basal ganglia	ischemic stroke (24)	MA (12); Sham-A (12)	MA vs. SA: the left thalamus and left cuneus; the right motor area/ right basal ganglia ↑
3	Xie Zijing 2014	motor-related network	ischemic stroke (9); HC (8)	MA (9); HC (8)	MA: the cerebellum and primary sensorimotor cortex ↑
4	Fu Caihong 2016	ICA (sensorimotor network)	ischemic stroke (19); HC (17)	MA (19); HC (17)	MA vs HC: Sensorimotor networks: cingulate gyrus, superior frontal gyrus, medial frontal gyrus, and lingual gyrus in the right hemisphere, cerebellum, and precuneus and left superior parietal lobule in the left hemisphere ↑; Left anterior cingulate gyrus, left superior frontal gyrus, right superior frontal gyrus, left middle frontal gyrus, left inferior frontal gyrus, left medial frontal gyrus, right medial frontal gyrus, left superior temporal gyrus, left cuneus, left precuneus ↓
5	Ning Yanzhe 2017	bilateral M1s	ischemic stroke (20); HC (20)	MA (20); HC (20)	MA: the suitable M1 and left M1 ↑
6	Li Yongxin 2017	bilateral PMd, PMv, bilateral PCG, bilateral SMA, and bilateral M1.	ischemic stroke (17); HC (14)	MA (8) IS (9) HC (14)	MA vs HC: bilateral M1 ↑; left SMA and right PMd and PCG ↑ Right SMA against right PMd and right SMA against right PCG ↓; bilateral M1, PMd, and PMv ↑
7	Yi Xiaoqi 2021	bilateral SMA	ischemic stroke (21); HC (18)	EA (21); HC (18)	EA vs. HC: Cerebelum_6_L, Left superior frontal gyrus, Cerebelum_Crus2_R ↑; right precentral gyrus, right superior frontal gyrus, right middle frontal gyrus, left postcentral gyrus, left inferior parietal border, angular gyrus, right insula, right insular inferior frontal gyrus, Cerebelum_7b_R ↓ EA: right precentral gyrus, right middle frontal gyrus, right precentral gyrus, right postcentral gyrus, right middle temporal gyrus ↑; left middle temporal gyrus, left anterior cingulate and paracingulate gyrus ↓
8	Wang Yue 2022	There are 22 motor, sensory, and movement-imaging cortices in each hemisphere.	ischemic stroke (63); HC (42)	MA 63); HC (42)	MA: Sensory tongue/larynx, lower limb, upper limb/hand/face, upper limb motor, and movement imagination areas ↑
9	Shi Xinyue 2022	bilateral SMA, PMd, PMv and PMA	ischemic stroke (40)	MA (40)	MA: Bilateral SMA, between contralateral SMA and ipsilateral PMV, between ipsilateral SMA and ipsilateral PMD, bilateral PMV ↑; SMA and PMv ↓
10	Xie Ximei 2013	Whole brain	ischemic stroke (9); HC (10)	MA (9)	EA: Anterior cingulate gyrus, caudate nucleus, putamen, globus pallidus, pons, anterior lobe of the cerebellum, cerebellar vermis ↑; Bilateral primary motor area (BA4), premotor cortex (BA4, 6), supplementary motor area (BA8), inferior parietal lobule (BA39), precuneus lobe (BA23) ↓
11	Wang You 2022	Whole brains	ischemic stroke (10)	MA (10)	EA: Anterior cingulate gyrus, caudate nucleus, putamen, globus pallidus, anterior cerebellar lobe, cerebellar vermis ↑
12	Ding Caixia 2017	Whole brain	ischemic stroke (10); HC (10)	MA (10); HC (10)	MA versus HC: Cuneiform lobe, caudate nucleus, putamen, globus pallidus, bilateral anterior and posterior central gyrus, left superior and middle frontal gyrus, ↑ MA: Cuneiform lobe, left superior frontal gyrus, middle frontal gyrus, and putamen ↑; caudate nucleus, putamen, and globus pallidus ↑
13	Wu Ping 2017	Whole brain	ischemic stroke (11)	MA (11)	The MA includes the frontal lobe (BA6, BA46), supramarginal gyrus (BA40), middle temporal gyrus (BA21), cerebellum, and insula ↑
14	Xie ximei 2019	Whole brain	ischemic stroke (12)	MA (12)	EA: Putamen, globus pallidus, caudate nucleus, superior parietal lobule, primary motor area, cingulate motor area, premotor area, bilateral supplementary motor area, and parietal lobule
15	Fu Caihong 2019	Whole brain	ischemic stroke (20); HC (20)	MA (20); HC (20)	EA: inferior parietal lobule, cingulate gyrus, insula, middle frontal gyrus, and precentral and postcentral gyrus ↑; bilateral medial frontal gyrus, right postcentral gyrus, and right precentral gyrus↓
16	Zhou Yu 2020	Whole brain	ischemic stroke (10); HC (10)	MA (10); HC (10)	MA: precuneus, thalamus, superior frontal gyrus, and middle occipital gyrus↑
17	Chen Shuqi 2020	Whole brain	ischemic stroke (10)	MA (10)	MA: left fusiform gyrus, left supplementary motor region, and right superior parietal lobule; right precentral gyrus and superior frontal gyrus↓
18	Liu Huacong 2021	Whole brain	ischemic stroke (15); HC (15)	SA (15); HC (15)	ALFF: the left BA39 that reaches the middle and superior temporal gyrus next to it ↑

(*continued on next page*)

Table 3 (*continued*)

No.	Author(s)	Seed regions	Groups	Treatments	Findings
					Reho: the left middle temporal gyrus (including BA21) reaching to the BA37↑; the left BA40 and angular gyrus extending to the BA7↑
19	Wang Fei 2021	Whole brain	ischemic stroke (40); HC (40)	MA (40); HC (40)	MA is made up of the following: left parietal lobe left middle frontal gyrus, left inferior frontal gyrus, right middle frontal gyrus, right hippocampus, and left inferior frontal gyrus↑
20	Zhan Yijun 2014	Whole brain	ischemic stroke (24); HC (22)	MA (24); HC (22)	SA: the cerebellum, praecuneus, precentral gyrus, superior frontal gyrus and parietal lobe ↑

Table 4
Coordinate-based meta-analysis of patient brain activity changes PRE and POST acupuncture treatment (ALFF).

Brain regions	MNI coordinates			SDM z-score	p-value	Voxels	Cluster breakdown (number of voxels)	I^2
	x	y	z					
L supplementary motor area	0	4	48	4.629	0.004999995	533	Left median cingulate/paracingulate gyri, BA 24 (86) Right supplementary motor area (45) Left median cingulate/paracingulate gyri (59) Left supplementary motor area (61) Right median cingulate/paracingulate gyri, BA 24 (81) Left median network, cingulum (22) Right median cingulate/paracingulate gyri, BA 23 (33) Left median cingulate/paracingulate gyri, BA 23 (38) Left anterior cingulate/paracingulate gyri (10) The right supplementary motor area, BA 24 (11) Left supplementary motor area, BA 32 (12) Left supplementary motor area, BA 6 (17) Right median cingulate/paracingulate gyri (20) The right supplementary motor area, BA 6 (21)	3.911843

Cluster extent cutoff: number ≥10 voxels; Voxel probability threshold: after correcting threshold (TFCE) of $p < 0.05$; Peak height threshold: $z > 1$; Abbreviations: MNI: Montreal Neurological Institute; BA: Brodmann area; I^2: heterogeneity I^2; L: left; R: right; ALFF: amplitude low-frequency fluctuations; SDM: signed differential mapping.

3.6. Meta-regression analysis

Meta-regression analysis was employed to examine for possible relationships between mean age and FMA score following acupuncture treatment. The right inferior occipital gyrus (BA 18, MNI coordinate: $x = 26$, $y = -98$, $z = -8$, SDM-Z value $= -1.736$, $p = 0.033333361$, and 161 voxels) and right precentral gyrus (BA 6, MNI coordinate: $x = 42$, $y = -10$, $z = 44$, SDM-Z value $= 2.603$, $p = 0.033333361$) are the brain regions where the analysis of mean age is significant (Table 6 and Fig. 5). The left median cingulate/paracingulate gyri (MNI coordinate: $x = 0$, $y = -2$, $z = 48$, SDM-Z value $= 3.045$, $p = 0.004999995$, and 696 voxels) is linked to the FMA scores in the meanwhile (Table 7 and Fig. 6).

4. Discussion

The efficacy of acupuncture in treating IS has been well recognized. Neuroimaging technology can objectively assess alterations to brain function, serving as an outcome measure to assess the clinical efficacy of acupuncture in the treatment of IS and elucidate its probable mechanisms. This systematic review aims to assess and summarise the processes underlying acupuncture's MRI neuroimaging effect in treating IS. 256 HCs and 392 patients from 20 eligible studies were included. We performed a meta-analysis of 11 trials using the SDM-PSI approach to investigate the changes in ALFF and ReHo following acupuncture for IS, respectively.

4.1. Features of MRI study on acupuncture treatment for IS

Since acupuncture originated in China and is frequently used in clinical practice to treat various disorders, including neurological diseases, the 20 publications in this study were likely all authored by Chinese researchers [36]. As a result, there may be some linguistic bias. Although the number of neuroimaging research utilizing acupuncture for IS has increased, the number of patients in each study remains modest, which may be a more prevalent occurrence in MRI investigations. Subject numbers are typically restricted by practical considerations, including scanning duration and expenses. The limited sample size will influence the accuracy of the results and may obscure clinically relevant effects [37]. To mitigate bias, ensure the dependability of findings, and comprehensively clarify the intricate neurological workings of acupuncture for IS, a more substantial sample size of RCTs is necessary.

This investigation included an RCT and a pre- and post-treatment comparison in the acupuncture for IS clinical trial design. With a high level of internal validity, the randomized controlled trial (RCT) with placebo as the control was regarded as a dependable

Table 5
Coordinate-based meta-analysis of patient brain activity changes PRE and POST acupuncture treatment (ReHo).

Brain regions	MNI coordinates			SDM z-score	p-value	Voxels	Cluster breakdown (number of voxels)	I^2
	x	y	z					
L cerebellum, hemispheric lobule VIII	−24	−72	−56	2.781	0.008000016	307	Left cerebellum, hemispheric lobule VIII (143) Left cerebellum, hemispheric lobule VIIB (56) Left cerebellum, crus II (24)	19.743328
R inferior frontal gyrus	52	14	14	3.037	0.026000023	55	Right inferior frontal gyrus, opercular part, BA 48 (20) Right inferior frontal gyrus, triangular part, BA 48 (18) Right inferior frontal gyrus, opercular part, BA 44 (15)	1.803715
L inferior frontal gyrus, triangular part, BA 48	0	0	60	−3.010	0.001999974	469	Left supplementary motor area, BA 6 (130) The right supplementary motor area, BA 6 (106) Left supplementary motor area (78) Right supplementary motor area (37) Left supplementary motor area, BA 32 (32) Left median cingulate/paracingulate gyri (130) Right median cingulate/paracingulate gyri, BA 24 (19) Left median cingulate/paracingulate gyri, BA 24 (25) The right supplementary motor area, BA 24 (11)	5.585011
L inferior network, inferior longitudinal fasciculus	−32	−68	−12	−2.860	0.012000024	125	Left cerebellum, hemispheric lobule VI, BA 19 (43) Left fusiform gyrus, BA 19 (24) Left inferior network, inferior longitudinal fasciculus (22) Left cerebellum, hemispheric lobule VI, BA 18 (16) Left fusiform gyrus, BA 18 (12)	13.154462

Cluster extent criterion: number ≥10 voxels; Peak height threshold: $z > 1$; Voxel probability threshold: after correcting threshold (TFCE) of $p < 0.05$; Abbreviations: MNI: Montreal Neurological Institute; BA: Brodmann area; I^2: heterogeneity I^2; L: left; R: right; ReHo: regional homogeneity; SDM: signed differential mapping.

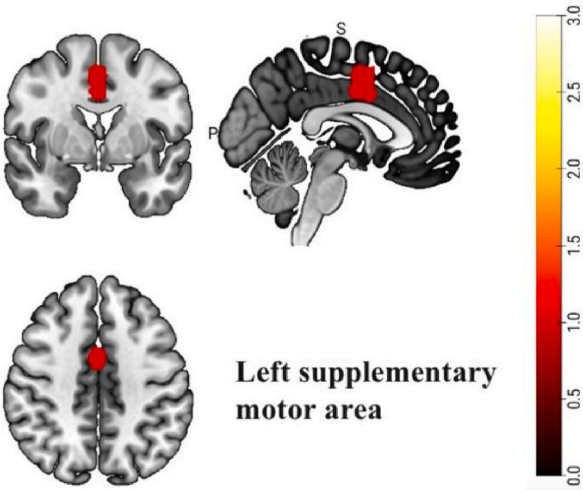

Fig. 3. Acupuncture treatment-related changes in grey matter areas in IS patients before and after (ALFF).

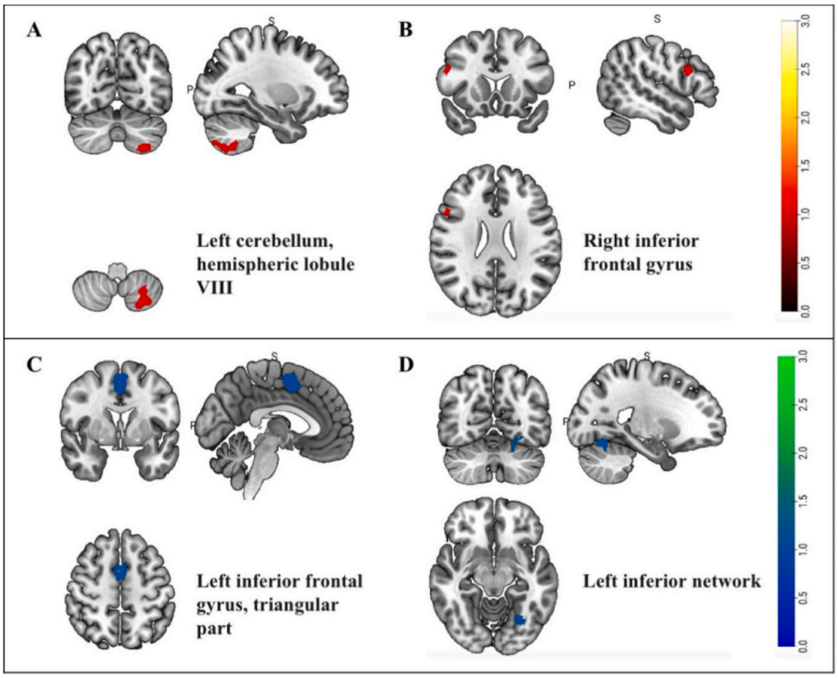

Fig. 4. Acupuncture-related changes in grey matter areas before and after treatment (ReHo).

Table 6
Age mean in the treatment group (ReHo) as determined by meta-regression analysis.

Region	MNI coordinate			SDM z-score	p-value	number of voxels
	x	y	z			
R precentral gyrus, BA 6	42	−10	44	2.603	0.033333361	21
R inferior occipital gyrus, BA 18	26	−98	−8	−1.736	0.033333361	161

Cluster extent threshold: number ≥10 voxels; Voxel probability threshold: $p < 0.05$; Peak height threshold: $z > 1$.

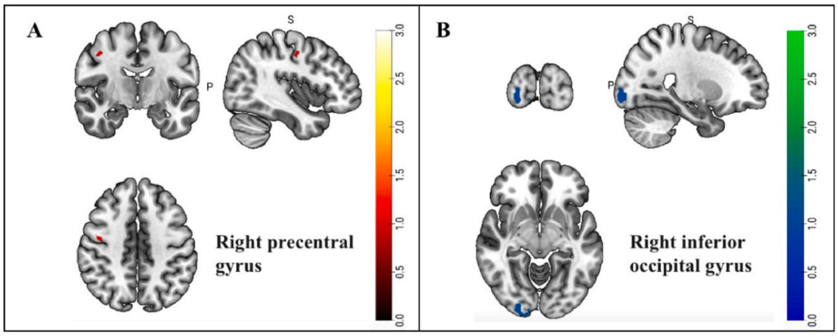

Fig. 5. Outcomes of meta-regression linear model analysis.

Table 7
FMA in the treatment group (ReHo) underwent meta-regression analysis.

Region	MNI coordinate			SDM z-score	p-value	number of voxels
	x	y	z			
L median cingulate/paracingulate gyri	0	−2	48	3.045	0.004999995	696

Cluster extent threshold: number ≥10 voxels; Voxel probability threshold: $p < 0.05$; Peak height threshold: $z > 1$.

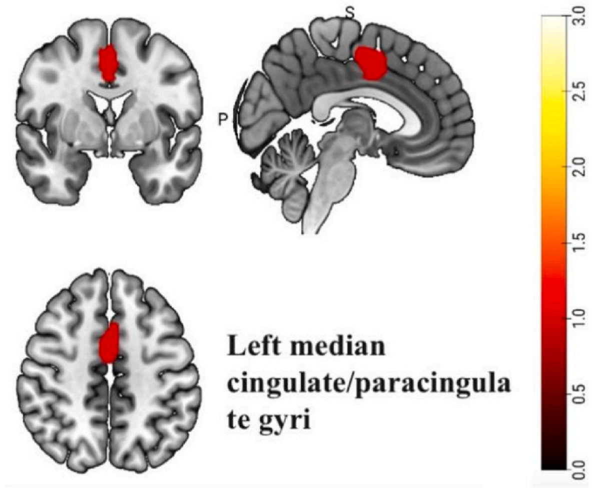

Fig. 6. Analyses of the Meta-regression linear model.

approach to evaluate the treatment's clinical efficacy. A placebo was employed as a control in a single study. Blinding is crucial in interventional trials, particularly regarding patient-reported outcomes. The blind approach is challenging to apply because of the unique nature of acupuncture, which could diminish the validity of the study's findings. Specifically, the efficacy of acupuncture or acupuncture together with medication contrasts with medication alone. Acupuncture has a cumulative impact, meaning that its effects are both immediate and long-lasting. The definition of the enduring effect of acupuncture is that the therapeutic benefits persist for a period following the conclusion of the treatment [38]. Therefore, to evaluate the potential neurological mechanisms that contribute to the long-term effectiveness of acupuncture for IS, further research should examine alterations in brain function in IS patients before and following acupuncture therapy, as well as during subsequent follow-ups. In a well-structured RCT, the intervention strategy should be the sole variable between research groups [39]. However, achieving this type of design for acupuncture studies is difficult due to various influencing factors, such as differences in acupuncturists, patients, needles, and techniques. Therefore, many more rigorous experimental design schemes are still needed to ensure the results' authenticity, accuracy and repeatability.

4.2. Analysis method of MRI studies

Diverse neuroimaging modalities and analytical approaches complicate the comparison of study outcomes; however, multimodal brain imaging techniques will mitigate these discrepancies and enhance our comprehension of the relationships among various results. Currently, the more commonly used indicators for fMRI analysis are ALFF, Reho, FC and ICA. ALFF is used to analyze the intensity of spontaneous neuronal activity in the resting state, reflecting the activity intensity of regional neurons and the physiological state of the brain [40]. It is frequently used for investigating the mechanisms associated with acupuncture. Zou et al. suggested fALFF, derived from ALFF, which represents the ratio of the power spectrum at low frequencies to the power spectrum across the full frequency range [41]. Integrating the abovementioned methodologies can provide a more comprehensive representation of the brain's spontaneous neural activity. Furthermore, both methods have been extensively employed in resting-state functional MRI investigations of neurocognitive diseases. Motor impairment frequently arises following a stroke.

Studies have shown that after a stroke, the motor-related brain region M1, which is remote from the area of the lesion, suffers varying degrees of structural and functional damage. The SMA is situated on the medial aspect of the mid-posterior cerebral hemisphere within the superior frontal gyrus, predominantly in the medial region of Brodmann area 6 of the cerebral cortex. It establishes fibre connections in the supplementary motor area primarily via the anterior limb of the internal capsule. It can partially compensate for the functionality of the corticospinal tracts in the impaired M1 region. In addition, the SMA area has a range of unique functions, such as motor execution and coordination and learning. When the body performs continuous repetitive movement, it needs to retrieve the motor memory, adjust the action type or inhibit the wrong action at the initial stage [42], and such tasks may increase in the recovery stage of stroke. The SMA region is essential for the implementation of complex and high-precision directives. The hyperactivity of the SMA region signifies that intracranial remodeling has transpired. The higher the activation intensity, the better the functional compensation, consistent with the findings of the present meta-analysis. Acupuncture enhances ALFF in the left SMA of individuals with IS, indicating a possible mechanism for its efficacy in treating IS.

ReHo is to expand the application of MRI in the clinic by processing the information acquired by BOLD-fMRI, local domain information and time series information for determination, which is essential for research on the clinical applications and actions of acupuncture. The abnormal ReHo value indicates that the activity of local neurons in the brain changes synchronously, indirectly reflecting the movement of functional brain areas. Acupuncture enhances ALFF in the left SMA of individuals with IS, indicating a possible mechanism for its efficacy in treating IS. The frontal lobe is at the centre of language processing. Research suggests that the left frontal-parietal network is responsible for language processing, primarily comprising the dorsal aspect of the left inferior frontal gyrus and the lower posterior temporal lobe. The brain network connectivity of aphasics is notably lower than that of healthy individuals. The left frontoparietal network's connection decreases with the severity of comprehension impairment [43], which may also help to explain why individuals with IS have language difficulty and even aphasia.

Furthermore, the cerebellum is crucial for maintaining balance and body-motor coordination. It is now thought that the degree of cerebellar activation in IS patients strongly correlates with their recovery of neurological function. The results of this investigation indicate that acupuncture can significantly lower the ReHo values of the left inferior frontal gyrus, triangular part, BA 48, and the left inferior network, inferior longitudinal fasciculus while raising the ReHo values of the right inferior frontal gyrus and the left cerebellum. Research indicates that electroacupuncture may help IS patients regain their ability to move and speak, enhance their neurological conditions, and better synchronize their local brain activity. The meta-regression analysis's findings also revealed a possible relationship between certain brain regions and the average age and FMA scale of IS patients, as well as the finding that acupuncture enhanced motor function in both the upper and lower limbs.

Various analytical techniques are employed to examine acupuncture's effectiveness from different angles. The most popular application of FC is the time-series correlation of functional activity signals between brain areas, allowing measurement of the functional integration of other brain regions [44]. Most current studies use seed point-based FC analysis methods, which are able to focus specifically on brain regions of interest. In recent years, fMRI studies on acupuncture in treating motor disorders after stroke have found that compared with IS patients, the functional brain networks of healthy people are typically activated and connected. The neurological function of IS patients is impaired. fMRI reveals a reduction in the FC of brain areas linked to movement, emotion, sensory, and cognition.

Furthermore, a six-month motor recovery is positively associated with the FC of the ipsilateral M1, contralateral thalamus, supplementary motor area, and middle frontal gyrus in the acute stage of IS [45], indicating that alterations in resting-state brain activity may be predictive of alterations in motor impairment. In this study, 6 studies selected the brain regions related to movement, including M1 and SMA. It was discovered that IS patients had a decreased FC in the motor cortex. Acupuncture effectively improved motor function in IS patients by modulation of the brain's motor-related network, strengthening the connection between the cerebellum and the primary sensorimotor cortex, and making up for the decreased connectivity between cortical and subcortical areas.

ICA is the earliest and most commonly used method in rs-fMRI analysis and can identify multiple resting-state networks simultaneously [46]. Recently, ICA has become commonly used for studying the functional brain network analysis of acupuncture treatment for cerebrovascular diseases, which provides a more intuitive neuroimaging analysis method for the degree of brain functional network damage in IS patients. Acupuncture can modulate multiple brain networks in IS patients and integrate effective network connections by transmitting information between higher-order cognitive networks and sensorimotor networks that act as relay stations. In this study, only one study adopted the analysis method of ICA and found that acupuncture could induce the response characteristics of the sensorimotor network of both the lesion side and the contralateral side and promote the reconstruction of motor function by bidirectional regulation of integrated sensorimotor connection.

4.3. MRI experimental designs

Task-based fMRI and rs-fMRI comprise the majority of fMRI experiments. Task-based fMRI induces corresponding neural activities in the cerebral cortex by performing specific tasks such as active or passive movements, analysing BOLD signal changes, and observing neuronal responses under particular tasks. Acupuncture tasks often include electroacupuncture or manual needle twisting. Research has shown that the human body's brain is highly active when it is at rest. In particular, specific brain networks, including the default mode network, are more active when the body is at rest than when performing a task. Therefore, researchers believe that rs-fMRI can provide a reflection of the spontaneous activity of the human brain. Task-based fMRI can predict an individual's ability to recover after a stroke, particularly in motor and learning. Studies have found that the partial paralysis of the hand movement in the early stages of IS is related to the extensive activation of the motor network in the bilateral brain, and the more pronounced the bilateral brain activation, the more serious the movement disorder [47]. In addition, the surviving brain region will affect the distant brain region during the movement. Most of the task-based fMRI studies of acupuncture for IS use block design and event-related design, compare the task state with the resting state, analyze the activation and negative activation effects of acupuncture in the healthy and affected brain areas of IS patients, and mainly observe the immediate impact of acupuncture [48]. This experimental design may be limited by using a single stimulus, which contrasts with clinical practice. The effect of acupuncture on rs-fMRI is garnering increasing attention [49]. Previous studies have shown that the human brain also has autonomic nervous activity in the resting state [50]. The signals during the resting state exhibit significant synchronization among various brain regions within the functional brain network, indicative of the spontaneous neural activity in the brain, thereby facilitating other data processing techniques to discern the characteristics or alterations in brain function before, during, and following acupuncture. Compared with the task-based state, the design of the resting state experiment is more straightforward. It imposes fewer requirements on patients, making it more appropriate for investigating the mechanisms of acupuncture. This also elucidates why the quantity of rs-fMRI utilized in the current study was markedly more than that employed in the task-based condition.

4.4. Selection of acupoints

Existing studies have reported that acupoints can cause specific responses in the brain, and acupuncture at different acupoints can cause activation patterns in various brain regions and may regulate relatively specific brain regions [51]. Most studies have used manual acupuncture as the primary treatment method in clinical practice. As well as the insertion of acupuncture needles into particular acupoints, physical manipulation of the needle can enhance its therapeutic efficacy. Acupuncture treatment for IS primarily targets acupoints on the Hand-yangming large intestine meridian, the Foot-yangming stomach meridian, and the governor meridian. The large intestine meridian of the Hand-yangming pathway corresponds with the modern anatomical understanding of contralateral control by the cerebral hemisphere over the body. Yangming Meridian is a meridian with more qi and blood, which can smooth joints, moisten tendons, and make limb movements powerful and flexible. In clinical treatment, acupuncture at the acupoints of the Hand and Foot Yangming meridians can improve the treatment efficiency, muscle strength and motor function of patients with IS. The governor meridian is closely related to the Yang meridian and is in charge of the person's spirituality and mental state. The brain governs the Shenqi activities of the whole body, and the brain's cognitive, consciousness and thinking actions are the concentrated expression of Yangqi functions. Acupuncture of the governor meridian allows the Shenqi to operate normally and the body to function correctly. From the perspective of acupoint selection, GB34, ST36, LI4, SP6 and LI11 are selected more frequently. GB34 is a he-sea point on the gallbladder meridian of Foot-Shaoyang, associated with the convergence of tendons, and serves as a principal acupuncture point for stroke treatment.

Research indicates that acupuncture at GB34 specifically improves FC between the anterior cingulate gyrus (ACC) and posterior cingulate gyrus (PCC) while also modulating autonomic activity, memory, and cognitive functions [52]. LI4 and LI11 are acupuncture points of the large intestine meridian of Hand-yangming. Acupuncture at these two points can provide prolonged and benign stimulation of speech and motor-related brain areas [53]. Acupuncture at ST36 exerts a comprehensive stimulatory effect on the cerebral cortex and limbic system, primarily evident through the observed activation of various regions, including the cingulate gyrus, postcentral gyrus, middle frontal gyrus, precentral gyrus, superior frontal gyrus, inferior frontal gyrus, middle temporal gyrus, and insula, significantly alleviating limbic disorders in IS patients. SP6 is a crossing point of the Foot Sanyin meridian, which can treat hemiplegia, limb disorders and other motor system disorders. It is a common point for acupuncture for treating IS. The activation of parietal motor brain areas by SP6 indicates that the acupuncture effect may pertain to the modulation of parietal sensorimotor centres, hence affecting limb disadvantage. We similarly found that although there was consistency in the acupoints selected in each of the above-included studies. However, as each study's objectives differed, acupoints with specific therapeutic effects were selected during treatment, which may have influenced the study results.

5. Limitations

Acupuncture has the functions of regulating zang-fu organs, dredging meridians, and harmonizing qi and blood. The medical community has widely recognized its clinical efficacy. Its Neuroplasticity mechanism has always been the focus of scholars at home and abroad. Recent fMRI studies investigating acupuncture's central mechanism of action in patients with ischaemic stroke motor dysfunction reveal that, despite extensive scholarly research and analysis, the conclusions remain inconsistent in clarifying acupuncture's central mechanism for treating motor dysfunction in stroke patients. The research paradigm has yet to form a unified standard. Mainly reflected in the following aspects: ① selection of systematic review: There may have been some heterogeneity because we only included 11 studies in the meta-analysis, which varied in terms of software, analytical techniques, and experimental design; ②Selection of study subjects: fMRI studies of acupuncture for IS need to be better established, and most fMRI studies have used healthy subjects as a comparison baseline. However, the complexity of functional brain networks, the bidirectional modulation of acupuncture effects, and the multidimensional nature of motor dysfunction in stroke make it challenging to conduct fMRI studies. ③Selection of study protocols: With the rapid development of brain imaging technology, fMRI data acquisition and analysis methods are more convenient and accurate than before, but in the process of clinical research, due to the lack of uniform standards, the results also vary greatly and can be biased, which is also a vital issue to be addressed in future research; ④Physiological factors: As an individual, human beings are influenced by a variety of factors. Patients' education level, lifestyle habits, occupation and psychological state affect brain function to varying degrees. Brain activity goes even when age and gender are similar, which may have implications for later studies of controlled brain function in patients with IS treated with different acupuncture. In addition, differences in MRI equipment, frequency, technique, the timing of needling and the acupuncturist may result in subtle alterations in the functional brain network. ⑤Selection of acupoints: The acupoints have structural and functional specificity. There were also significant differences in brain function changes between acupuncture at acupoints and non-acupoints or sham acupuncture. In the following study, we need to focus more on the effect of acupuncture on specific acupoints of brain function in IS patients. Therefore, in future studies, it is essential to control and refine the interfering factors that can be changed by developing various strategies to conduct multi-level, multi-system and multi-disciplinary combined fMRI studies, expand the clinical collection sample, set up multi-centre controlled trials and optimize the experimental design scheme as a whole, focusing on the disease and combining the characteristics of acupuncture treatment. Moreover, attention should be paid to multimodal research and statistics during the analysis, showcasing diverse results. These findings will better guide the clinical practice of acupuncture and elucidate its central mechanism of action.

6. Conclusions

As an advanced visualization method, MRI can help better understand acupuncture's mechanism. In the clinical literature included in this study, fMRI was applied as the primary test method, and the main analysis methods included ReHo, (f)ALFF, FC, and ICA. The meta-analysis's findings showed that acupuncture is a highly effective treatment for IS. Furthermore, it has been discovered that acupuncture alters ALFF and ReHo in particular brain regions, such as the left inferior network, left cerebellum, right inferior frontal gyrus, and left inferior frontal gyrus. These regions are closely associated with motor functions, sensory processing, language, and emotional information.

The findings above imply that acupuncture can potentially facilitate the reversible restoration of impaired neurological functions. This effect may be attributed to stimulating neural cell biological activity in specific brain areas, leading to alterations in neuronal activity, structural reorganization of the brain network, or changes in the strength of functional connectivity within those areas. These observations highlight acupuncture as a potential therapeutic target and mechanism of action for enhancing motor and cognitive functions in the human body. However, this study has several shortcomings, such as a lack of consistent, high-caliber original research and insufficient evidence. Consequently, carrying out well-planned multicenter, large-sample clinical, randomized controlled trials should be the primary goal of future research. These studies should aim to create uniform IS diagnostic standards and efficacy assessment indicators.

In conclusion, the specificity of acupuncture, along with limitations in blinded design and trial rigor, has led to certain constraints. Therefore, it is imperative to further standardize the methodology of acupuncture clinical studies to enhance the quality of literature and provide more robust evidence for elucidating the underlying brain imaging mechanisms of acupuncture for IS. It will make it possible to comprehend acupuncture's therapeutic benefits more thoroughly and promote the development of evidence-based medicine.

CRediT authorship contribution statement

Mengyuan Li: Writing – original draft, Methodology, Data curation. **Baohui Mu:** Writing – original draft, Methodology, Formal analysis. **Mengmeng Li:** Formal analysis, Data curation. **Xinyu Zhang:** Software, Resources. **Jing Zhang:** Validation, Supervision. **Haipeng Huang:** Writing – review & editing, Supervision, Resources. **Hongfeng Wang:** Writing – review & editing, Visualization, Software, Funding acquisition.

Data availability statement

Data are available from the authors upon reasonable request.

Funding

This work was supported by National Natural Science Foundation of China (Grant No. 82074548) and Project of Jilin Provincie Administration of Traditional Chinese Medicine (Grant No. 2023004). The study is the corresponding author of this article and participated in the writing of the manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

We are appreciative of all those who have participated in this study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e39059.

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