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Manual acupuncture enhanced therapeutic efficacy in vascular dementia rat model: systematic review and network meta-analysis

Yuanyu Song[1], Yinghua Chen[2*], Junfeng Li[2], Wei Sun[1] and Fangfang Jin[1]

Abstract

Objective This study aimed to systematically evaluate the efficacy of electroacupuncture and manual acupuncture for treating vascular dementia and to determine the optimal acupuncture point combination scheme for efficacy.

Methods The PubMed, Embase, Web of Science, Cochrane, CNKI, VIP, and Wanfang electronic databases were searched up to July 2024 to identify relevant randomized controlled trials. RevMan 5.4 software and Addis software were used to assess the risk of bias for each study, determine subgroup classifications, and conduct meta-analyses.

Results A total of 29 RCTs involving 659 animals were ultimately included. The meta-analysis results revealed that acupuncture treatment had a significant effect compared with the vascular dementia model group [mean difference (MD) = −21.68, 95% confidence interval (CI) (−25.77, −17.59), $P < 0.00001$]. Manual acupuncture demonstrated better efficacy than electroacupuncture did [$MD = -0.42$, 95% CI (−12.72, 12.27)]. Among the different acupuncture point combinations, the Baihui (GV20) + Dazhui (GV14) combination yielded the best efficacy [$MD = -23.03$, 95% CI (−30.02, −16.04), $P < 0.00001$]. Compared with other acupuncture protocols, the experiment conducted by Caiyu Peng et al. exhibited superior efficacy [$MD = -24.96$, 95% CI (−92.68, −40.76)].

Conclusion Acupuncture significantly improves cognitive function in rats with vascular dementia. Manual acupuncture is more effective than electroacupuncture. Among the different acupuncture point combinations, manual acupuncture at GV20 and GV14 yields the best results. Compared with other acupuncture protocols, the best efficacy was observed when the two-vessel occlusion (2VO) model was used in 230 ± 10 g SD rats; when the Mingmen (GV4), Dazhui (GV14), Fengfu (GV16), Baihui (GV20), Shenting (GV24), Shuigou (GV26), Neiguan (PC6), Dalin (PC7), and Laogong (PC8) acupoints were selected; and when manual acupuncture with reinforcing and reducing methods was used for 30 min per day for 14 days.

Systematic review registration PROSPERO CRD42024551402

Keywords Manual acupuncture, Vascular dementia, Rats, Meta-analysis, Systematic review, Randomized controlled trial

Introduction

Vascular dementia (VD) is a cognitive disorder resulting from a reduction in cerebral blood flow (CBF) [1]. VD is the second leading cause of dementia after Alzheimer's disease, and it accounts for approximately 20% of all dementia cases. This proportion is projected to triple between 2022 and 2050 [2]. Therefore, VD has become a

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significant threat to public health. Surveys have indicated that the prevalence of VD is more pronounced among elderly individuals and males [3]. In addition to demographic characteristics such as age, sex, and education level, the onset and progression of VD are also linked to various conditions, such as hypertension [4] and metabolic syndrome. Smoking and alcohol consumption are also risk factors for VD [5].

Currently, the clinical treatment of vascular dementia (VD) primarily involves pharmacological interventions and rehabilitation training [6]. However, both approaches have limitations. In pharmacological treatment, antihypertensive drugs, NMDA receptor antagonists, and statins are commonly used for the prevention and management of VD [7]. However, these medications are associated with various side effects. For example, antihypertensive drugs such as beta-blockers can exacerbate depressive symptoms in patients [8]. NMDA receptor antagonists such as memantine may cause dizziness, headaches, and even psychiatric disorders [9]. Statins can cause insomnia and muscle pain [10]. On the other hand, rehabilitation training requires active patient participation and cooperation in a series of complex cognitive and physical tasks, which can be difficult to implement for patients with poor physical function, severe consciousness disorders, or emotional resistance. Therefore, there is an urgent need to explore safe and effective treatment approaches.

Acupuncture, a traditional Chinese medical therapy originating in ancient China involves the insertion of needles or the application of heat to specific acupoints on the body to regulate the flow of qi and blood, thereby achieving therapeutic effects and promoting health. Its fundamental principles include meridian theory and acupoint stimulation, which suggest that the human body has a complex meridian system. By stimulating specific acupoints along these meridians, the flow of qi and blood can be regulated, and the balance of yin and yang can be restored. Compared with pharmacological treatment, acupuncture has relatively fewer side effects. When it is performed correctly, the likelihood of complications (such as infection and bleeding) is low, thus making it more acceptable to patients [11]. Additionally, compared with rehabilitation training, acupuncture is a highly manageable and relatively passive treatment method. The procedure is primarily conducted by the physician, with the patient only required to remain still to receive the acupuncture stimulation, thereby making it feasible even for patients with low compliance [12]. Acupuncture can also be used in combination with other treatment methods, such as pharmacological interventions and rehabilitation training [13]. For example, when combined with drugs that improve cerebral circulation, acupuncture can enhance the effects of improving the brain blood supply [14], and when used alongside cognitive rehabilitation training, acupuncture can help patients better recover their cognitive functions [15].

Although clinical studies [16] have demonstrated that acupuncture is an effective treatment for vascular dementia (VD) in China, and numerous randomized controlled trials (RCTs) have examined this topic [17], it is important to note that some studies have shown that acupuncture has limited efficacy for treating VD [18]. Therefore, it is necessary to conduct a systematic review of the use of acupuncture for treating VD. Additionally, animal experiments play crucial roles in clinical research. Validating the efficacy and safety of acupuncture in animal models can provide both theoretical and empirical support for subsequent clinical trials. However, individual animal studies often have small sample sizes and may be subject to biases in design and execution, thus leading to insufficient reliability and reproducibility of the results. For example, differences in animal models, acupuncture techniques, and stimulation parameters used by various researchers can complicate the direct comparison and verification of results. Meta-analyses can more comprehensively summarize the outcomes of animal experiments, thus offering a more reliable basis for the design and implementation of clinical studies and mitigating the risks and uncertainties associated with clinical trials. Although some reviews have analyzed the effectiveness of acupuncture in improving learning and memory [19], these reviews did not comprehensively include all relevant studies. Therefore, the primary aim of this review is to conduct a thorough and systematic analysis of the available data.

Data and methods

Retrieval method

This meta-analysis was conducted in accordance with the PRISMA 2020 statement (see Additional file 1). Two authors (Yuanyu Song and Junfeng Li) independently searched PubMed, Embase, Web of Science, the Cochrane English Database, and the Chinese Journal Full-text Database (CNKI), VIP Journal Database (VIP), and Wanfang Data Resource System (Wanfang). The search was limited to articles published until July 2024. The search terms included acupuncture, electroacupuncture, acupoint, vascular dementia, vascular cognitive impairment, rats, and animals. Each search term was used individually or in combination. Detailed search strategies are provided in Additional file 2.

Inclusion criteria

- Study subjects: Animals (rats)
- Intervention measures: Acupuncture (electroacupuncture, manual acupuncture)
- Study design: VD animal model group and treatment group
- Outcomes: Morris water maze, including primary outcomes: escape latency and number of platform crossings in the hidden platform test. Secondary outcomes: time spent in the target quadrant
- Study type: Randomized controlled trials

Exclusion criteria

- Duplicate publications
- Publication types: Conference abstracts, pathological reports, guidelines, reviews, and academic papers
- Studies on specific acupuncture methods: Ear acupuncture, eye acupuncture, laser acupuncture, embedding, and scalp acupuncture
- Studies on specific acupoint selection: Frontal head zones, brain disease treatment in the intestine, well points, and triple needle at olfactory points
- Studies comparing different acupuncture techniques
- Exclusion of all literature obtained through graphical data
- Studies on acupuncture combined with other Chinese or Western medicine treatments
- Different methods of modeling cerebral infarction: Multi-infarct dementia and hemorrhagic dementia
- Studies comparing different electroacupuncture frequencies

Literature screening and data extraction

Two authors (Yuanyu Song and Junfeng Li) independently extracted data from articles meeting the inclusion criteria. This included study characteristics (article title, first author's name, publication year), animal characteristics (species, age, weight, modeling method), acupuncture characteristics (type, frequency, waveform, acupoint combination, treatment duration, duration of experiment), and outcome data (sample size, mean, standard deviation of escape latency, and number of platform crossings in both the acupuncture and model groups). If different acupuncture frequencies were reported, data from the highest frequency were extracted.

Literature quality assessment

Two researchers (Yuanyu Song and Junfeng Li) independently assessed the risk of bias for each included study using the Cochrane Risk-of-Bias Assessment Tool (ROB 2.0). The assessment covered the following domains: selection bias (random sequence generation, baseline characteristics, and allocation concealment), performance bias (randomization and blinding), detection bias (random outcome assessment and blinding), attrition bias (completeness of outcome data), and reporting bias (selective reporting of study results). Discrepancies were resolved through discussion with a third author.

Statistical analysis

(1) Heterogeneity analysis: Statistical analysis was performed using Review Manager 5.4.1 software. Continuous data were expressed as mean differences (MD) with corresponding 95% confidence intervals (CI), and significance was set at $P<0.05$. When $P\geq 0.1$ and $I^2\leq 50\%$, indicating no heterogeneity, a fixed-effects model was used. When $P<0.1$ and $I^2>50\%$, indicating heterogeneity, a random-effects model was employed.
(2) Network meta-analysis: The consistency between indirect and direct comparisons was assessed using the node-splitting model in Addis 1.16.7 software. Consistency was considered significant when $P>0.05$, and significant inconsistency was indicated when $P<0.05$. Effect sizes between intervention measures were evaluated, ranking the intervention groups and conducting direct comparisons among multiple interventions.
(3) Subgroup analysis: Subgroup analysis of different acupuncture methods, acupoint combinations, and treatment durations in the acupuncture group was performed using Review Manager 5.4.1.

Results

Literature retrieval results

In the preliminary search, we identified 1120 potentially relevant studies. After removing duplicates, we screened the titles and abstracts of the remaining 784 records, excluding 646 studies. The remaining 138 articles were downloaded for further screening, and, ultimately, 29 studies met the inclusion criteria. The literature screening flowchart is shown in Fig. 1.

General characteristics of included studies

A total of 29 studies were included in this review, involving 659 animals with weights ranging from approximately 180 to 400 g. Of these, 310 animals were assigned to the control groups and 349 animals to the experimental groups. The animal strains used were as follows: 26 studies employed SD rats [20–45], and 3 studies used Wistar rats [46–48]. Regarding

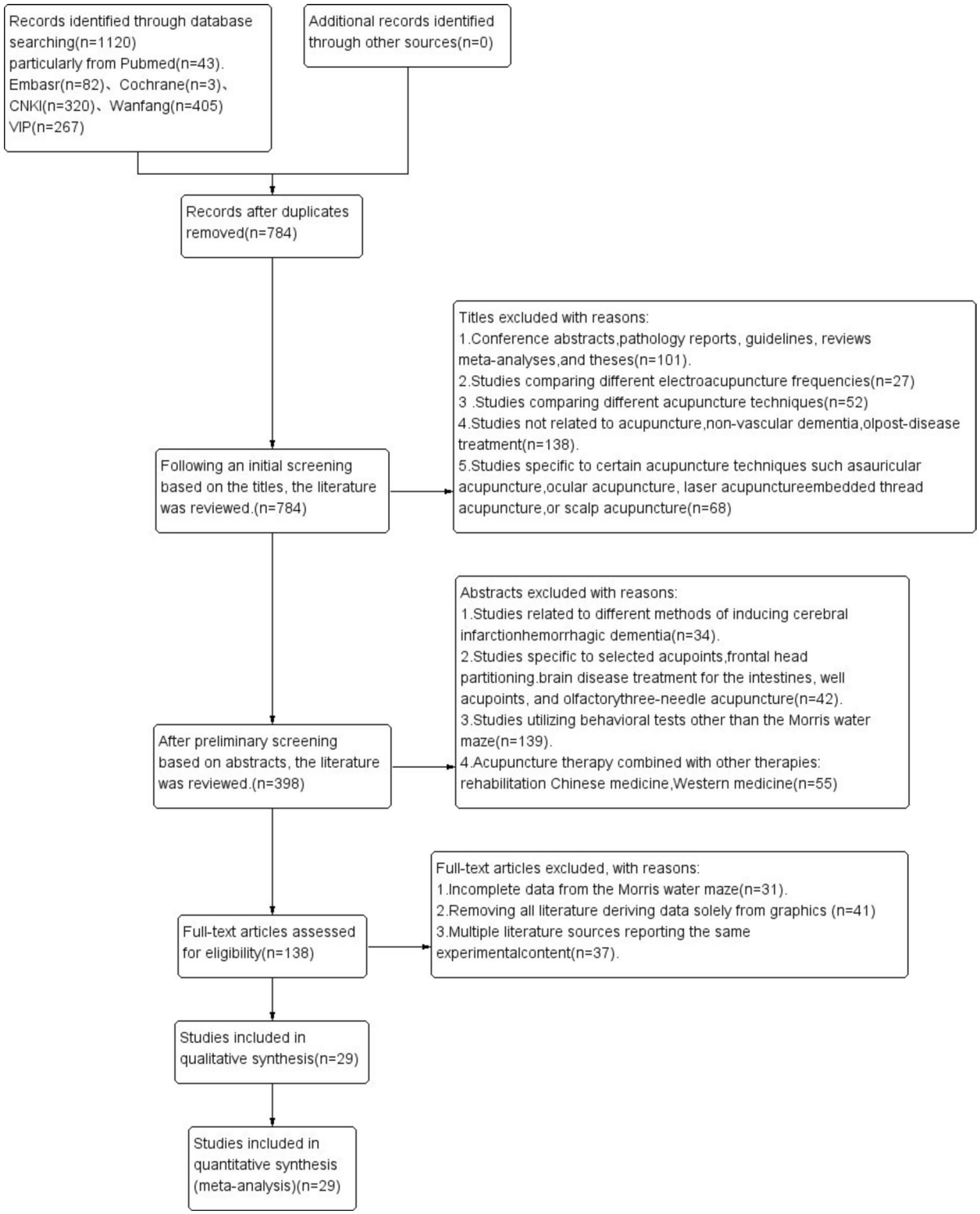


Fig. 1 Flow diagram of the study selection process

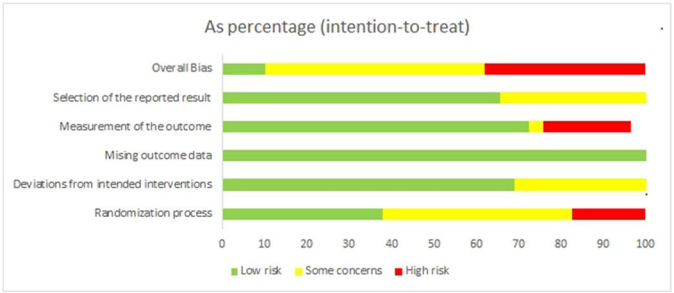
Table 1 Basic characteristics of the included literatures

Author & year	Species	Age	Weight	Sample size		Group		Intervention measures				Outcome measures
				Experimental group	Control group	Experimental group	Control group	Experimental group			Control group	
								Waveform frequency	Treatment duration	Acupoints	Model method	
Bu Yu, 2021 [20]	SD	Not provided	280–300 g	9	10	Electroacupuncture	Model	Continuous wave 20 Hz	20 min/day for 20 days	GV24, GB13	4VO	①, ②
Chen Yinghua, 2019 [21]	SD	2–3 months	220 ± 30 g	24	24	Electroacupuncture with hand needle	Model	Continuous wave 2 Hz	30 min/day for 21 days	Bilateral EX-HN1, bilateral GB20	4VO	①
Chen Lewen, 2021 [22]	SD	Not provided	280 ± 30 g	8	8	Electroacupuncture	Model	Sparse-dense waves 4/20 Hz	30 min/day for 24 days	Bilateral EX-HN1, bilateral GB20	2VO	①
Dong Juan, 2017 [23]	SD	2–3 months	200 ± 20 g	10	10	Manual acupuncture	Model	Not provided	20 min/day for 15 days	GV20, GV24	Modified 2VO nimodipine	①, ②
Feng Delin, 2015 [24]	SD	Not provided	180–220 g	8	8	Electroacupuncture	Model	Continuous wave 3 Hz	20 min/day for 5 days	GV16, GV20, GV26, CV12, CV4	4VO	①, ②
Jia Shiqi, 2009 [25]	SD	Not provided	250–300 g	10	10	Electroacupuncture	Model	Continuous wave 10 Hz	10 min/day for 20 days	GV20, GV14	Modified 2VO nimodipine	①, ②
Li Min, 2006 [26]	SD	2 months	200–300 g	14	13	Electroacupuncture	Model	Continuous wave 150 Hz	20 min/day for 20 days	LI15, SJ5, ST31, ST36	4VO	①, ②
Li Min, 2010 [27]	SD	2 months	180–220 g	12	12	Electroacupuncture	Model	Continuous wave 150 Hz	30 min/day for 15 days	GV20, GV14	4VO	①, ②
Li Xinhua, 2018 [28]	SD	Not provided	400 g ± 10 g	10	10	Manual acupuncture	Model	Not provided	30 min/day for 15 days	GV20, GV14, BL23	Modified 2VO nimodipine	①
Li Hua, 2019 [29]	SD	Not provided	280–300 g	15	15	Electroacupuncture	Model	Continuous wave 20 Hz	20 min/day for 20 days	GV16, GV20, GV26, CV4	4VO	①, ②
Shao Ying, 2008 [30]	SD	Not provided	180–220 g	9	8	Electroacupuncture	Model	Continuous wave 150 Hz	20 min/day for 15 days	GV24, GB13	4VO	①, ②
Tang Zhongsheng, 2011 [31]	SD	Not provided	280–300 g	10	11	Electroacupuncture	Model	Continuous wave 150 Hz	20 min/day for 20 days	GV24, GB13	4VO	①, ②
Wang Li, 2002 [32]	SD	2 months	200–250 g	14	13	Electroacupuncture	Model	Continuous wave 150 Hz	20 min/day for 15 days	GV20, GV14	4VO	①, ②
Wang Li, 2007 [33]	SD	2–3 months	200–250 g	12	11	Electroacupuncture	Model	Continuous wave 50 Hz	20 min/day for 15 days	GV20, GV14	4VO	①, ②
Wei Dengming, 2011 [34]	SD	Not provided	200–250 g	10	10	Electroacupuncture	Model	Continuous wave 50 Hz	20 min/day for 10 days	GV20, GV14	Modified 2VO nimodipine	①, ②

Table 1 (continued)

Author & year	Species	Age	Weight	Sample size		Group		Intervention measures				Outcome measures
				Experimental group	Control group	Experimental group	Control group	Experimental group			Control group	
								Waveform frequency	Treatment duration	Acupoints	Model method	
Wei Yuwei, 2021 [35]	SD	Not provided	300–350 g	13	13	Electroacupuncture	Model	Continuous wave 20 Hz	20 min/day for 20 days	GV24, GB13	4VO	①, ②
Xu Pan, 2022 [46]	Wistar	8 weeks	280 ± 20 g	12	13	Manual acupuncture	Model	Not provided	30 s/day for 15 days	CV17, CV12, CV6, SP10, ST36	2VO	①, ②
Yan Bing, 2006 [36]	SD	Not provided	280–300 g	9	7	Electroacupuncture	Model	Continuous wave 150 Hz	20 min/day for 15 days	GV20, GV14, BL23, BL20	4VO	①, ②
Zhang Guannan, 2011 [47]	Wistar	Not provided	170–230 g	12	12	Electroacupuncture with hand needle	Model	Sparse-dense waves 2 Hz	10 min/day for 15 days	GV20, GV14	Modified 2VO nimodipine	①
Zheng Jie, 2009 [48]	Wistar	2 months	212 ± 15 g	7	8	Electroacupuncture	Model	Sparse-dense waves 2 Hz	20 min/day for 30 days	GV20, GV14	2VO	①
Yz Zhu, 2012 [37]	SD	12 months	400 ± 30 g	12	10	Electroacupuncture	Model	Continuous wave 4 Hz	20 min/day for 30 days	GV20, KI3	2VO	①
Cao Yajun, 2023 [39]	SD	Not provided	250 ± 10 g	6	6	Electroacupuncture	Model	Not provided	20 min/day for 12 days	GV20, GV24	2VO	①, ②
Chen Yang, 2024 [40]	SD	2 months	250 ± 20 g	12	12	Manual acupuncture	Model	Not provided	30 min/day for 15 days	GV20, BL23, ST40	2VO	①, ②
Li Xinhua, 2023 [41]	SD	2–3 months	210 ± 10 g	9	10	Manual acupuncture	Model	Sparse wave 1–20 Hz	30 min/day for 14 days	GV16, GV20, GV26, CV4, CV12	2VO	①, ②
Li Xiaoxiao, 2024 [42]	SD	6 weeks	260 ± 20 g	10	10	Electroacupuncture	Model	Sparse wave 200 Hz	30 min/day for 14 days	GV20, GV24, GB13, EX-HN1	2VO	①, ②
Ma Shuai, 2024 [43]	SD	8 weeks	160–200 g	6	6	Electroacupuncture	Model	Not provided	30 min/day for 14 days	GV20, GV16, GV14	2VO	①, ②
Peng Caiyu, 2024 [44]	SD	6 months	230 ± 10 g	12	12	Manual acupuncture	Model	Continuous wave 2 Hz	30 min/day for 21 days	GV4, GV14, GV16, GV20, GV24, GV26, PC6, PC7, PC8	2VO	①
Sun Wei, 2024 [45]	SD	8 weeks	260–280 g	12	12	Electroacupuncture	Model	Not provided	20 min/day for 12 days	Bilateral EX-HN1, bilateral GB20	4VO	①, ②

Appendix: Outcome measures: ① Escape latency. ② Number of platform crossings. *2VO*, bilateral occlusion of the common carotid arteries; *4VO*, four-vessel occlusion



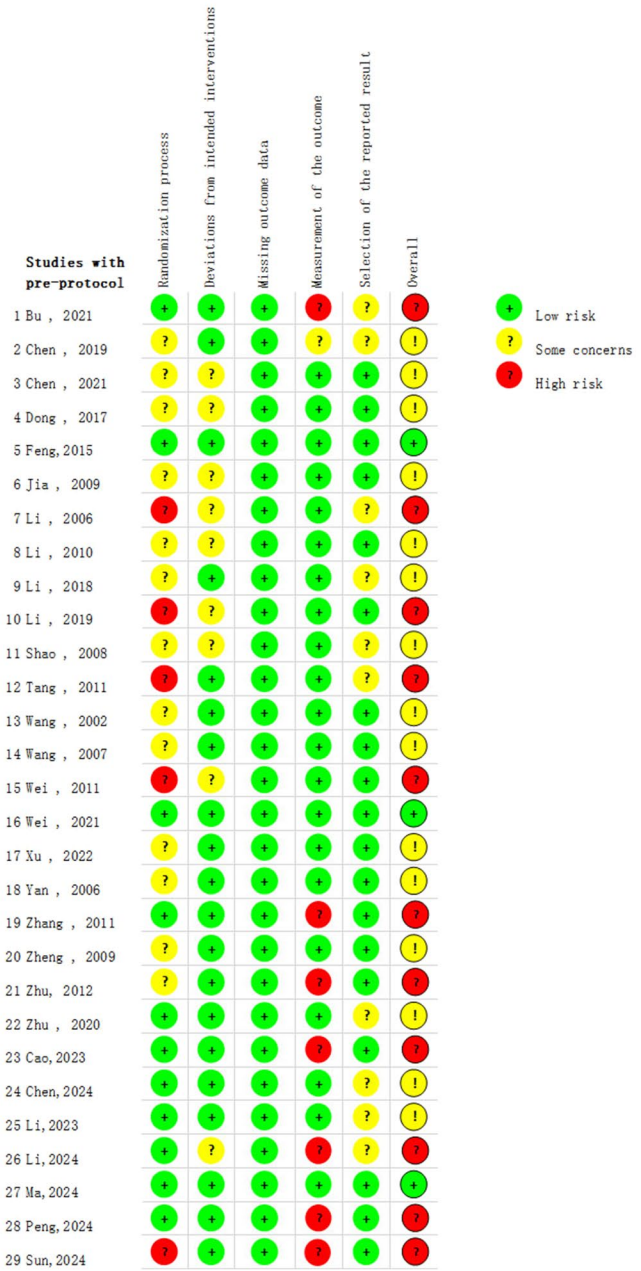


Fig. 2 1 and 2 Literature bias risk assessment

the modeling methods, 15 studies utilized the two-vessel occlusion method [22, 23, 25, 28, 34, 37–44, 46–48], and 14 studies used the four-vessel occlusion method [20, 21, 24, 26, 27, 29–33, 35, 36, 45]. As for the intervention methods, 7 studies applied manual acupuncture [23, 28, 38, 40, 41, 44, 46], 20 studies used electroacupuncture [20, 22, 24, 27, 29–37, 39, 42, 43, 45, 48], and 2 studies compared electroacupuncture with manual acupuncture [22, 48]. In terms of electroacupuncture treatment, 16 studies used continuous wave treatment [20, 21, 24–27, 29–37, 45], while 6 studies employed sparse-dense wave treatment [22, 39, 42, 43, 47, 48]. Regarding treatment duration, 1 study had a treatment duration of 30 s [46], 2 studies had a duration of 10 min [25, 47], 15 studies had a duration of 20 min [20, 23, 24, 26, 29–37, 40, 48], and 11 studies had a duration of 30 min [21, 22, 27, 28, 31, 32, 40–45]. The treatment course varied: 17 studies had a course of ≤ 15 days [22–24, 27, 28, 30, 32–34, 36, 38, 40–44, 46, 47], 7 studies had a course between 15 and 20 days [20, 25, 26, 29, 31, 35, 39], and 5 studies had a course between 20 and 30 days [21, 37, 45, 48]. The basic characteristics of the included studies are summarized in Table 1.

Literature bias risk assessment

As shown in Fig. 2 (1 and 2), all included trials were assessed using the risk-of-bias (RoB 2.0) tool. Seventeen studies were classified as having a high risk of bias [20, 22, 25–27, 29, 31–34, 37–39, 42, 44, 45, 47], while 9 studies were classified as having an unclear risk of bias [21, 23, 28, 30, 36, 40, 41, 46, 48], primarily due to the lack of randomization and blinding. The remaining three studies were classified as having a low risk of bias [24, 35, 43], with all assessed domains in these studies showing low risk.

Meta-analysis results

Escape latency

A total of 29 studies were included in this analysis. The results of the meta-analysis indicated that the escape latency in the acupuncture group was significantly shorter than that in the model group, with a statistically significant difference (*MD*: − 21.68; 95% *CI*: − 25.77, − 17.59; *P* < 0.00001) (see Fig. 3). A bias analysis of the 31 included outcome measures showed a symmetrical funnel plot for the latency to escape, suggesting an absence of publication bias (see Fig. 4).

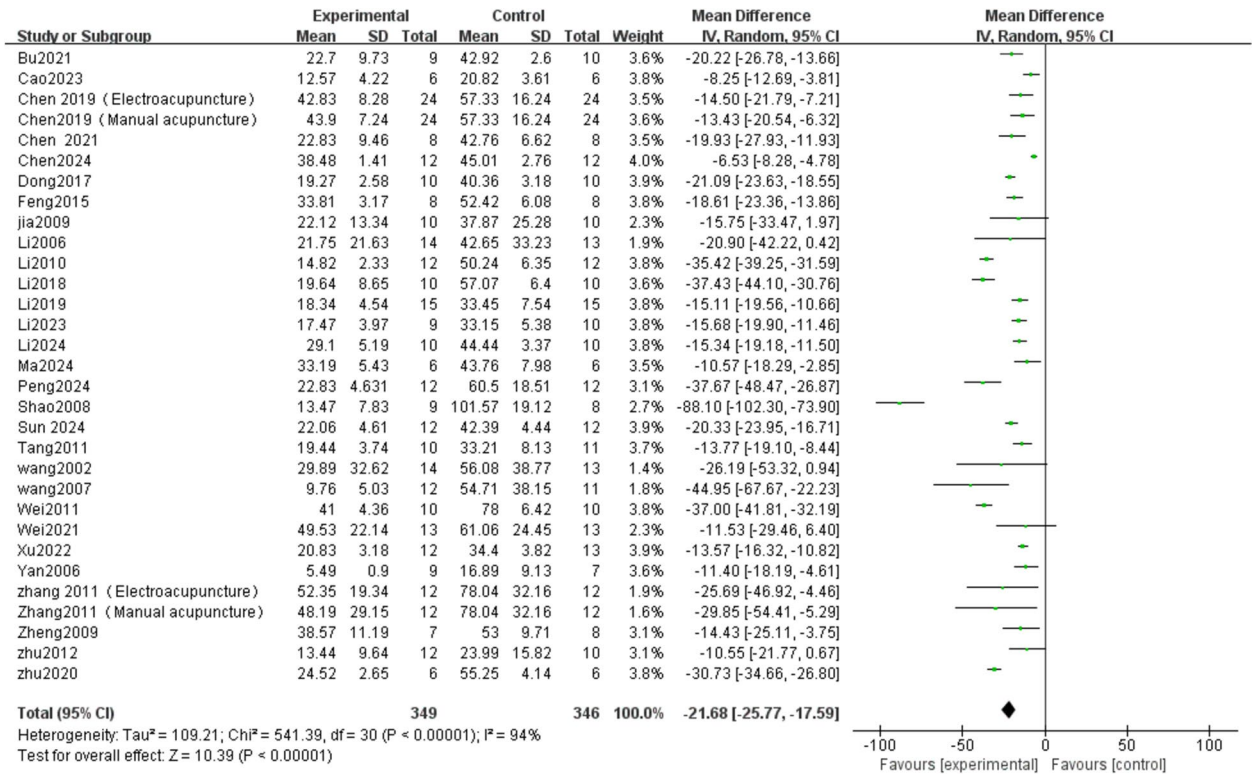


Fig. 3 Forest plot showed that escape latency decreases with acupuncture therapies in vascular models. Effect of acupuncture on outcomes of the water maze: effect on escape latency time versus the control group

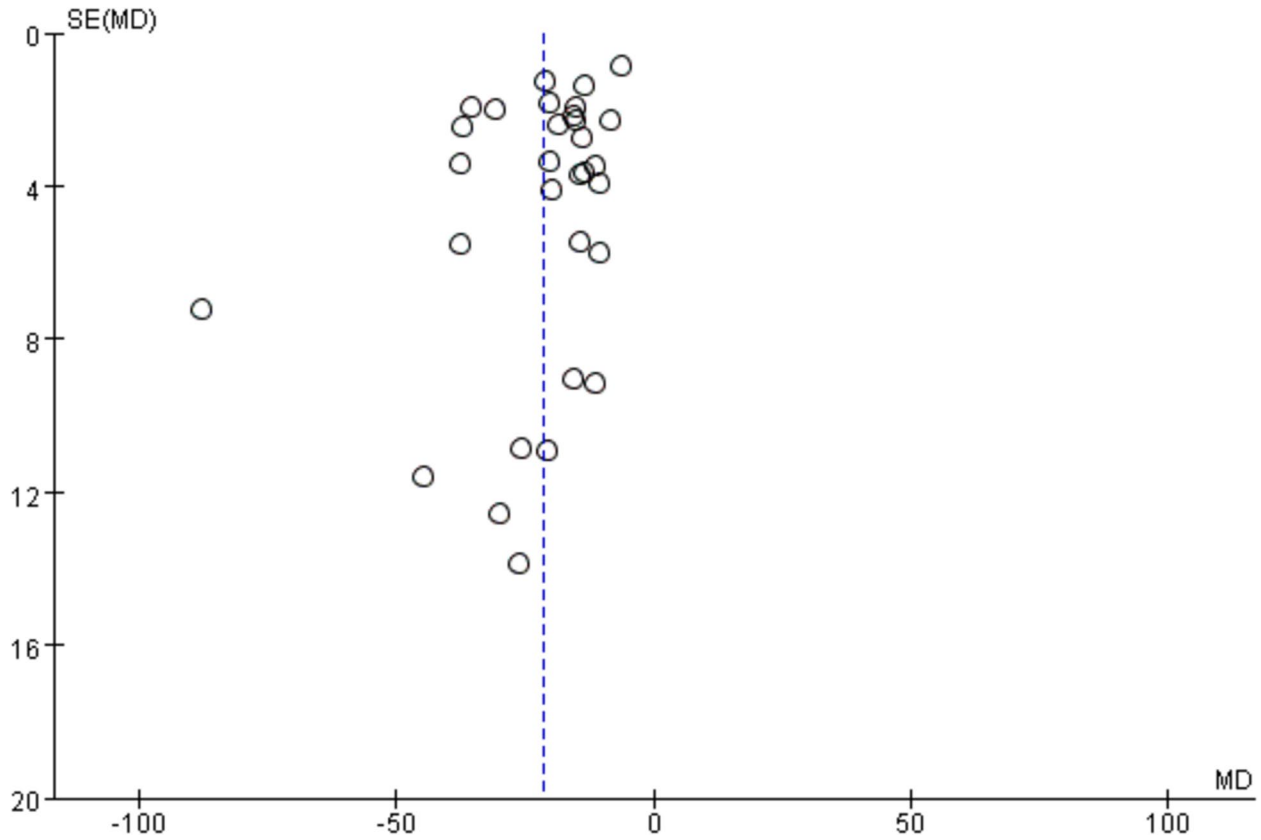


Fig. 4 Forest plot showed that escape latency decreases with acupuncture therapies in vascular models. Effect of acupuncture on outcomes of the water maze: effect on escape incubation funnel plot

Number of platform crossings

A total of 14 studies were included in this analysis. The results showed that the acupuncture group crossed the platform significantly more times than the model group, with a statistically significant difference (*MD*: 3.52; 95% *CI*: 2.71, 4.33; $P < 0.00001$) (see Fig. 5). A publication bias analysis conducted on the 20 outcome measures also indicated a symmetric funnel plot for the number of crossings, suggesting no publication bias (see Fig. 6).

Subgroup analysis and heterogeneity test

Escape latency is the most important indicator in the Morris water maze. Subgroup analysis of this result was performed based on different acupuncture methods, acupoint combinations, and treatment durations (see Figs. 7, 8, 9, and 10).

In the subgroup analysis of acupuncture methods, electroacupuncture (EA) (*MD*: − 21.63; 95% *CI*: − 26.80, − 16.45; $I^2 = 92\%$) and manual acupuncture (MA) (*MD*: − 21.84; 95% *CI*: − 28.81, − 14.87; $I^2 = 97\%$) both exhibited high heterogeneity ($I^2 > 50\%$). These results suggest that the subgroup analysis did not significantly alter the overall heterogeneity. Sensitivity analysis showed that removing any single study did not eliminate the heterogeneity. The between-group comparison ($P = 0.96$, $P > 0.05$) revealed no significant statistical difference between the EA and MA groups.

In the subgroup analysis of acupoint combinations, heterogeneity was reduced compared to the overall analysis. The combinations CV20 + CV14 (*MD*: − 23.03; 95% *CI*: − 30.02, − 16.04; $I^2 = 17\%$), GB20 + EX-HN1 (*MD*: − 16.97; 95% *CI*: − 21.77, − 12.18; $I^2 = 51\%$), and CV24 + GB13 (*MD*: − 14.84; 95% *CI*: − 17.36, − 12.31; $I^2 = 0\%$) showed statistically significant differences between combinations ($P = 0.03$, $P < 0.05$).

In the subgroup analysis of treatment duration, the group with a duration of ≤ 15 days (*MD*: − 17.52; 95% *CI*: − 18.50, − 16.54; $I^2 = 97\%$) exhibited high heterogeneity ($I^2 > 50\%$). Sensitivity analysis using stepwise exclusion did not significantly alter the results. For the 15 < duration ≤ 20 days group (*MD*: − 13.49; 95% *CI*: − 15.93, − 11.05; $I^2 = 43\%$) and the 20 < duration ≤ 30 days group (*MD*: − 17.74; 95% *CI*: − 20.34, − 15.13;

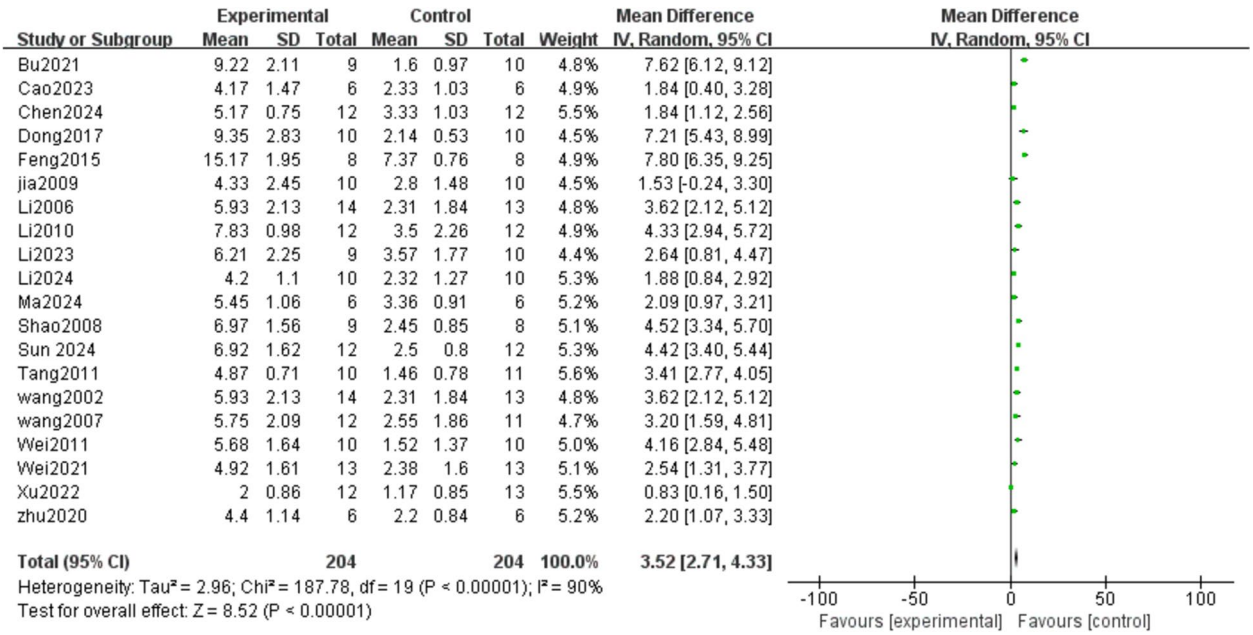


Fig. 5 Forest plot showed that platform crossing times increases with acupuncture therapies in vascular models. Effect of acupuncture on outcomes of the water maze: effect on frequency of crossing former platform

$I^2 = 21\%$), statistically significant differences were observed between different treatment durations ($P = 0.01$, $P < 0.05$).

In the subgroup analysis of modeling methods, the two-vessel occlusion (2VO) group ($MD: -15.41$; 95% $CI: -16.42, -14.40$; $I^2 = 95\%$) and four-vessel occlusion (4VO) group ($MD: -22.07$; 95% $CI: -23.77, -20.38$; $I^2 = 93\%$) showed significant differences between the two modeling methods ($P < 0.0001$).

The statistical results indicated that the combination of CV20 + CV14, the 20 < duration ≤ 30 days group, and

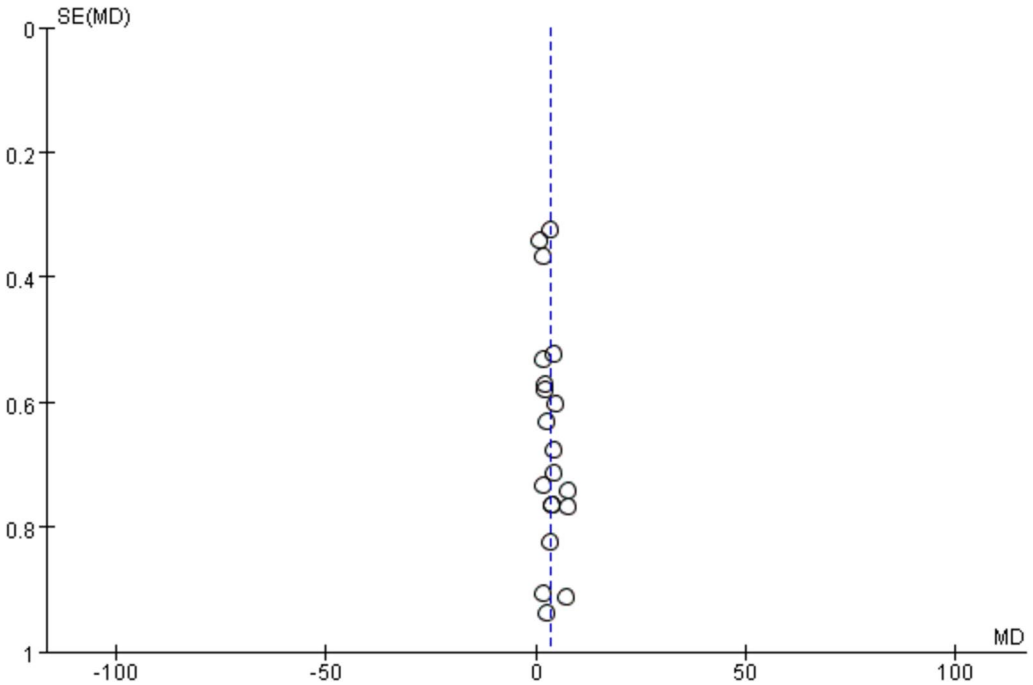


Fig. 6 Forest plot showed that platform crossing times increases with acupuncture therapies in vascular models. Effect of acupuncture on outcomes of the water maze: effect on platform crossing times funnel plot

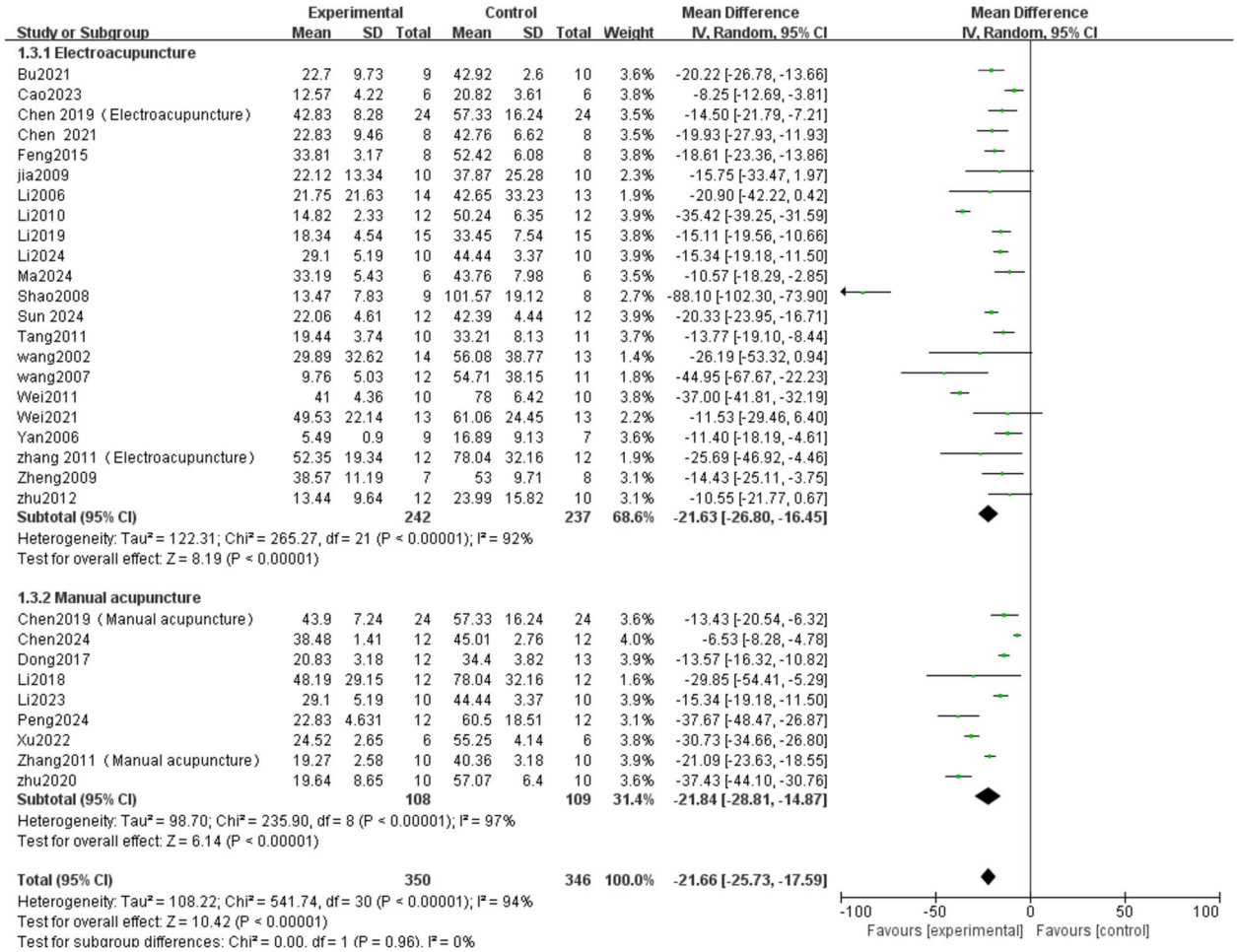


Fig. 7 Escape latency subgroup analysis: acupuncture methods

the 4VO group were superior in mean values compared to the other subgroups.

Network meta-analysis

Consistency test

A network meta-analysis was conducted on escape latency under different intervention measures. The node-splitting model was employed to assess the consistency between direct and indirect comparisons. The results showed $P > 0.05$ and $PSRF = 1.0$, indicating that a consistency model should be adopted for analysis.

Network meta-analysis results

Among the 29 included studies, two pairwise comparisons were made. A statistically significant difference was observed in the improvement of learning and memory abilities in VD rats between the electroacupuncture (EA) and manual acupuncture (MA) groups compared to the model group (see Figs. 11 and 12).

Ranking of network meta-analysis results

The network meta-analysis results indicated that compared to EA, MA more effectively improved the learning and memory levels in rats ($MD = -0.38$, 95% CI: -12.83, 11.80) (see Figs. 13 and 14, Table 2).

A network meta-analysis was also conducted on nine studies using MA. The results showed that compared to other studies, Caiyu Peng's study [44] in 2024 demonstrated the best efficacy (see Fig. 15).

Discussion

Clinical relevance and mechanism of acupuncture

This systematic review examined previous animal studies on the use of acupuncture treatment for vascular dementia (VD). The results suggested that acupuncture significantly reduces escape latency and increases the number of platform crossings in VD rats, thereby enhancing cognitive function. Additionally, acupuncture has mild

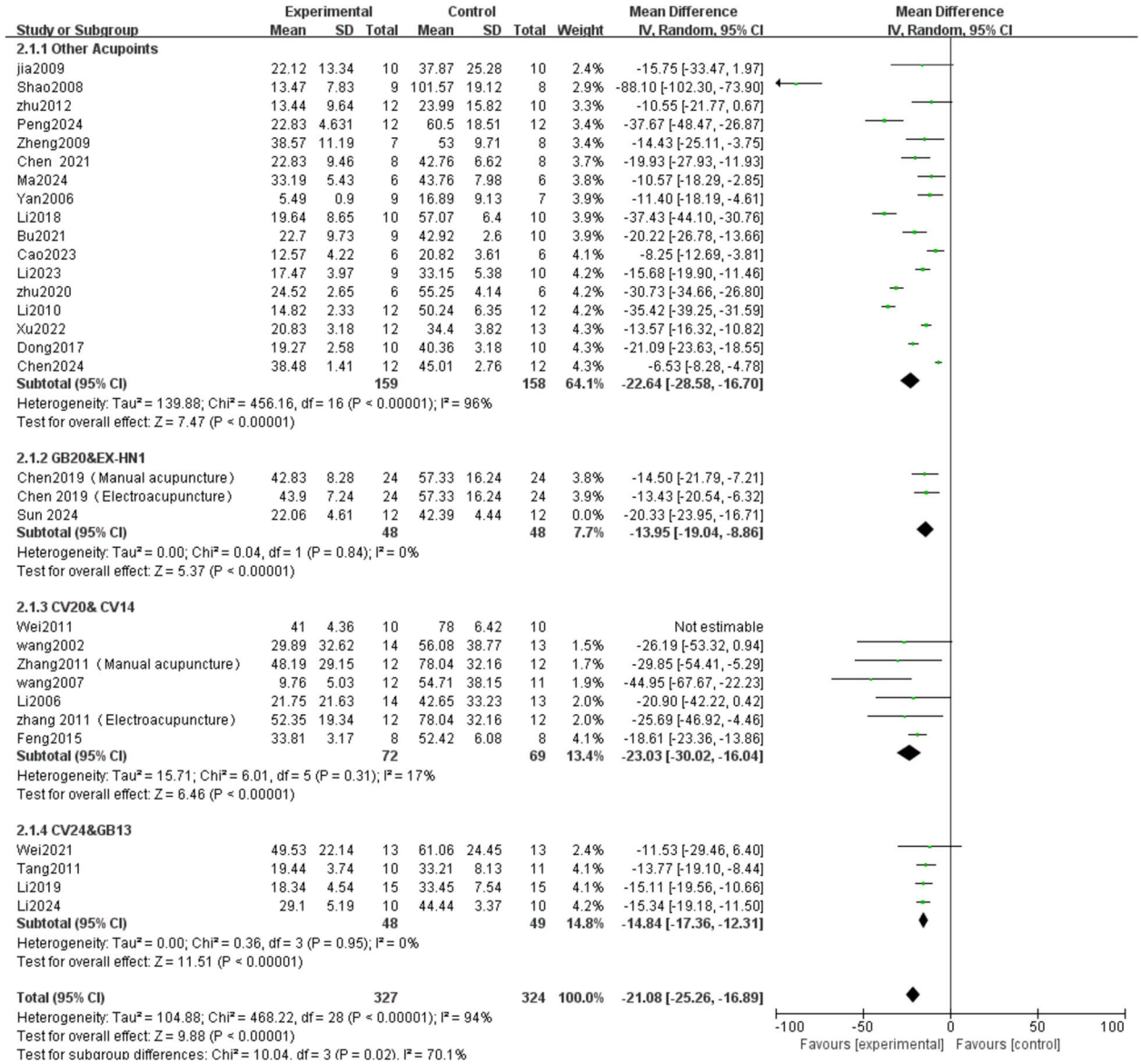


Fig. 8 Escape latency subgroup analysis: acupoint combinations

adverse effects and relatively high safety, thus making it a promising candidate for clinical application.

Acupuncture is widely utilized in treating disorders related to the nervous system, digestive system, and rehabilitation. Its clinical relevance for vascular dementia can be summarized in five key areas.

1. Inhibition of oxidative stress: Research has indicated that aging accelerates the degeneration of cerebral blood vessels, leading to cerebral ischemia and hypoxia [49]. Consequently, preventing cerebral ischemia has become a key focus in VD treatment. During ischemia, metabolic disruptions such as hypoxia, acidosis, increased malondialdehyde levels, and decreased glutathione levels occur in brain cells [50]. Studies have shown that acupuncture can improve brain tissue metabolism by increasing antioxidant enzyme activity (e.g., SOD) and reducing malondialdehyde levels, thereby mitigating brain damage [51].
2. Reduction in the inflammatory response: Acupuncture modulates inflammatory factor levels in VD patients by reducing the levels of proinflammatory cytokines (e.g., TNF-α and IL-1β) and increasing the levels of anti-inflammatory cytokines (e.g., IL-10), thereby alleviating central nervous system inflamma-

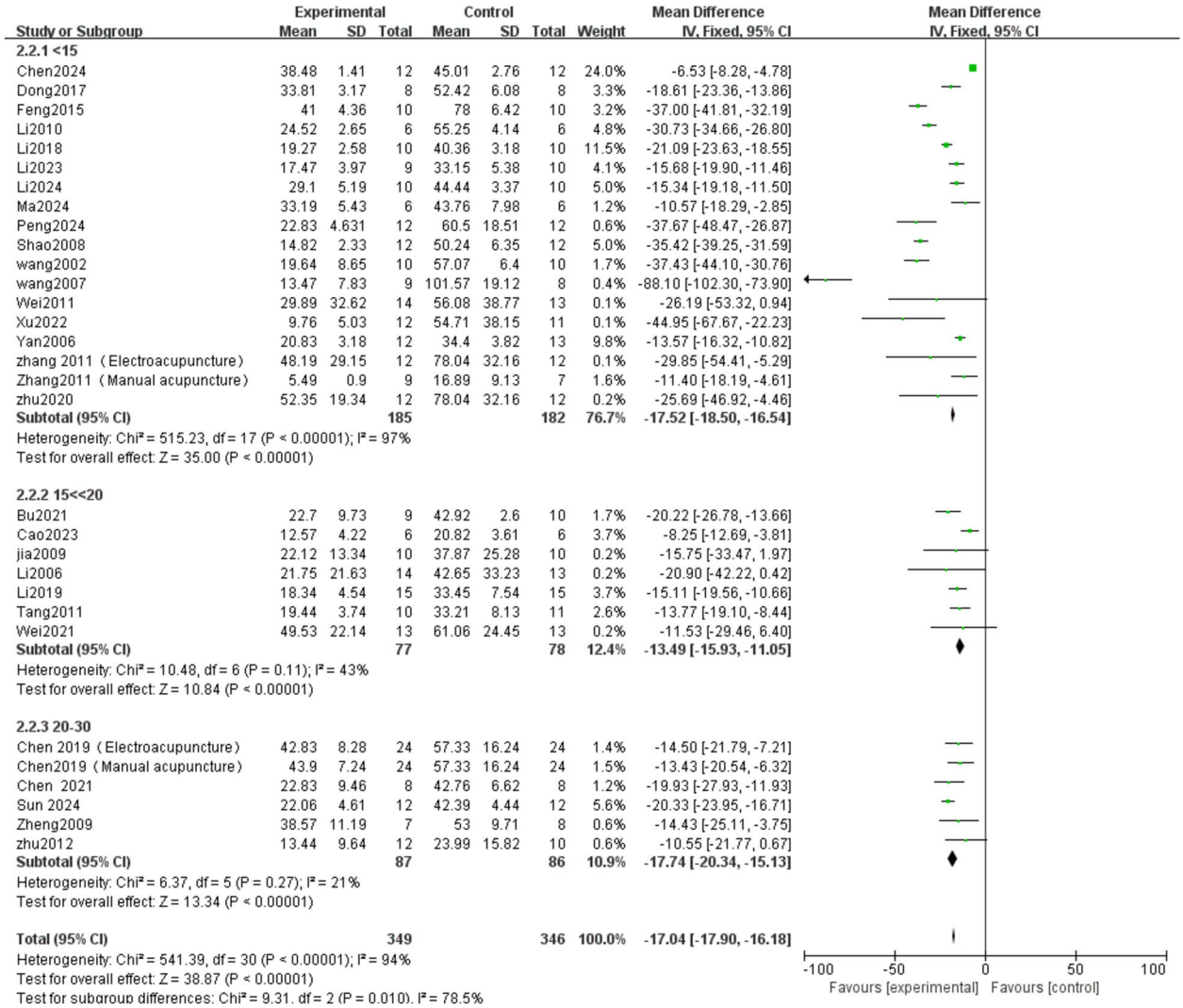


Fig. 9 Escape latency subgroup analysis: escape incubation funnel plot

tion and improving cognitive function [52]. Previous studies have demonstrated that acupuncture inhibits microglial activation and regulates the NF-κB signaling pathway to reduce the release of inflammatory factors. For example, Du S. Q. et al. [53] reported that electroacupuncture significantly reduced TNF-α and IL-1β levels in the hippocampus of VD rats while increasing IL-10 levels, thereby suppressing central inflammation and enhancing cognitive function. By modulating both pro- and anti-inflammatory factors, acupuncture effectively mitigates inflammation, protects neurons, promotes neural repair, and improves cognitive function in VD patients [54].

3. Enhancement of cognitive function: Acupuncture significantly improved scores on the mini-mental state examination (MMSE) [55] and Hasegawa Dementia Scale (HDS) [56], thus highlighting its role in enhancing cognitive function. Specifically, acupuncture stimulates certain acupoints, improves cerebral blood circulation, and regulates neurotransmitter levels, thereby enhancing memory, attention, and executive function. A previous systematic review and meta-analysis [57] revealed that the acupuncture group exhibited greater improvement in MMSE scores than did the control group, with a statistically significant pooled effect size of 2.18. These findings suggest that acupuncture not only enhances cognitive function but also slows the progression of VD.
4. Improvement of psychiatric and behavioral symptoms: Acupuncture treatment effectively improves psychiatric and behavioral symptoms in VD patients, as reflected by a reduction in activities of daily living (ADL) scale scores [58], thereby increasing self-care ability. Studies indicate that acupuncture regulates

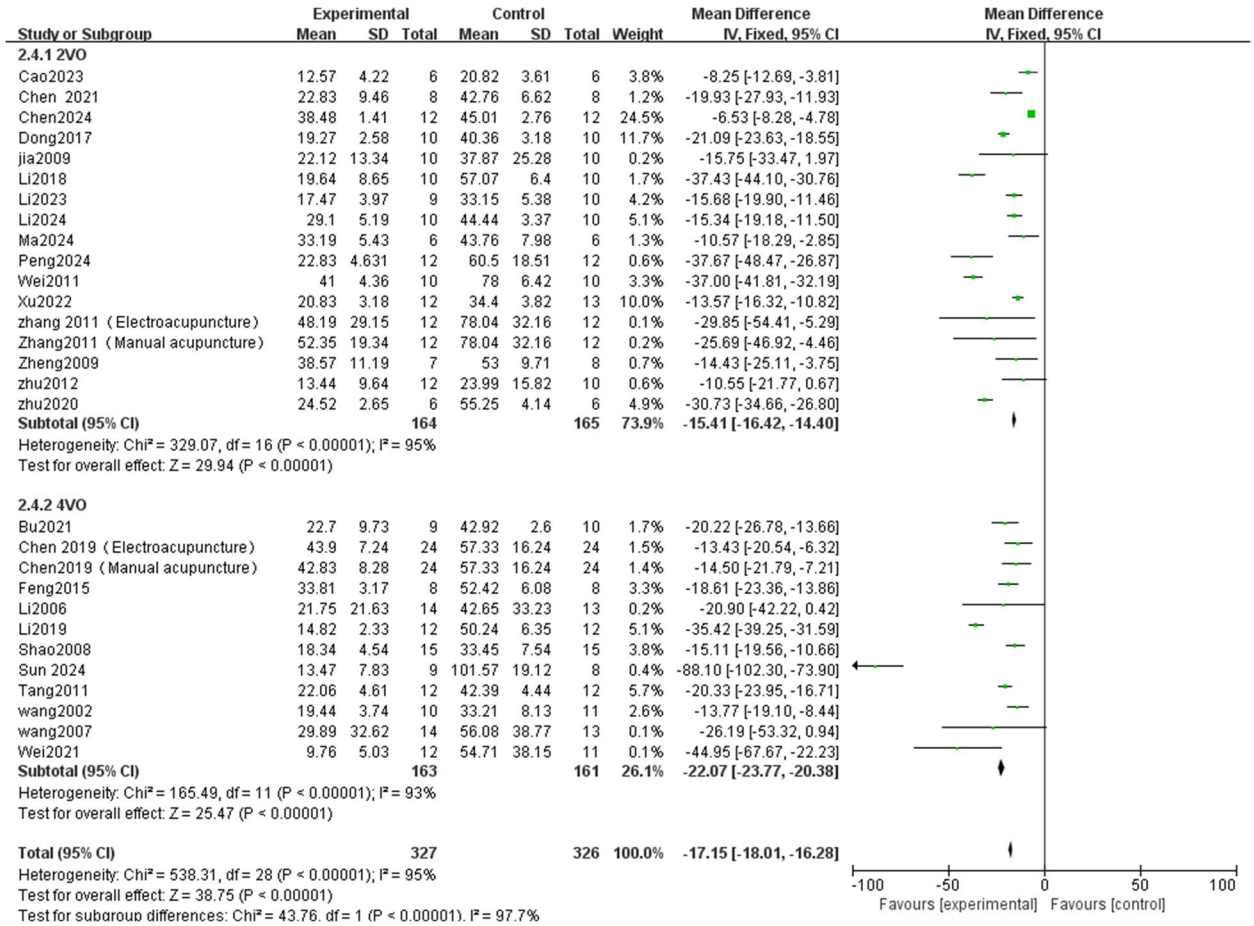


Fig. 10 Escape latency subgroup analysis: molding method

the nervous system and improves cerebral blood flow, thus alleviating depressive and anxious symptoms, which in turn improves self-care. For example, one study [57] reported that the ADL scores of patients in the acupuncture group significantly decreased after treatment, with a combined effect size of 5.99, indicating a notable improvement in self-care ability.

5. Enhancement of electroencephalographic physiological indicators: P300 is a unique bioelectrical response found in the human brain. As an electroencephalographic physiological indicator, P300 can be used to assess the degree of cognitive impairment. Studies have shown that after 3 weeks of scalp acupuncture treatment, patients' P300 levels significantly increase, and during the treatment period, patients' cognition, self-care abilities, and nervous system responses all improve [59]. These findings indicate that scalp acupuncture aids in the recovery of cognitive function in patients with vascular dementia and improves their quality of life. Acupuncture can improve the cognitive function of patients with cognitive impairment and dementia, playing an important role in the treatment of vascular dementia. The acupoints [60], methods [61], and duration of treatment [62] are considered important factors affecting the efficacy of acupuncture. This study conducted subgroup analyses on these three factors. The subgroup analysis of acupoint selection revealed that GV20+GV14 was more effective than other combinations in terms of therapeutic effects. GV20, which belongs to the governing vessel, is also known as "the meeting of three yangs and five meridians," meaning that all meridians converge here and are located at the center of the top of the head [63]. Research has shown that GV20 can regulate cerebral blood flow in ischemic areas and promote neuroregeneration of the central nervous system [64]. GV14 is the meeting point of the three yangs and the governing vessel, which is located in the depression below the seventh cervical vertebra on the midline of the back [65]. Studies have shown that GV14 can increase the proliferation of neural stem cells, improve perfusion in ischemic areas, and medi-

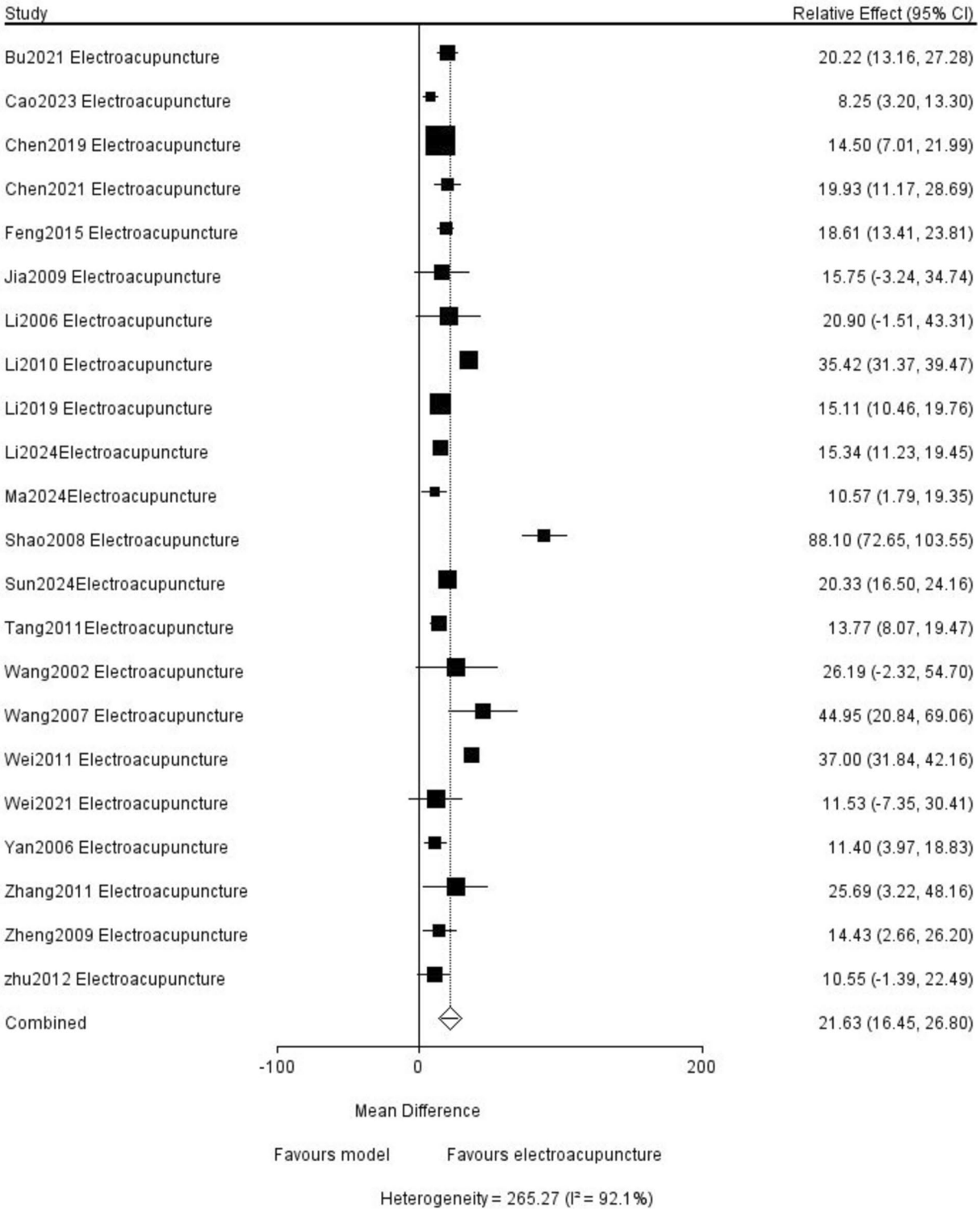


Fig. 11 Network meta-analysis showed that VD rats improved their learning and memory ability after acupuncture treatment: electroacupuncture

ate antiapoptotic pathways [66]. The combined use of GV20 and GV14 can increase the levels of neurotrophic factors, including BDNF and VEGF [67] and release vasodilatory mediators to increase the release of acetylcholine and endothelial nitric oxide synthase in the ischemic cerebral cortex [68]; these

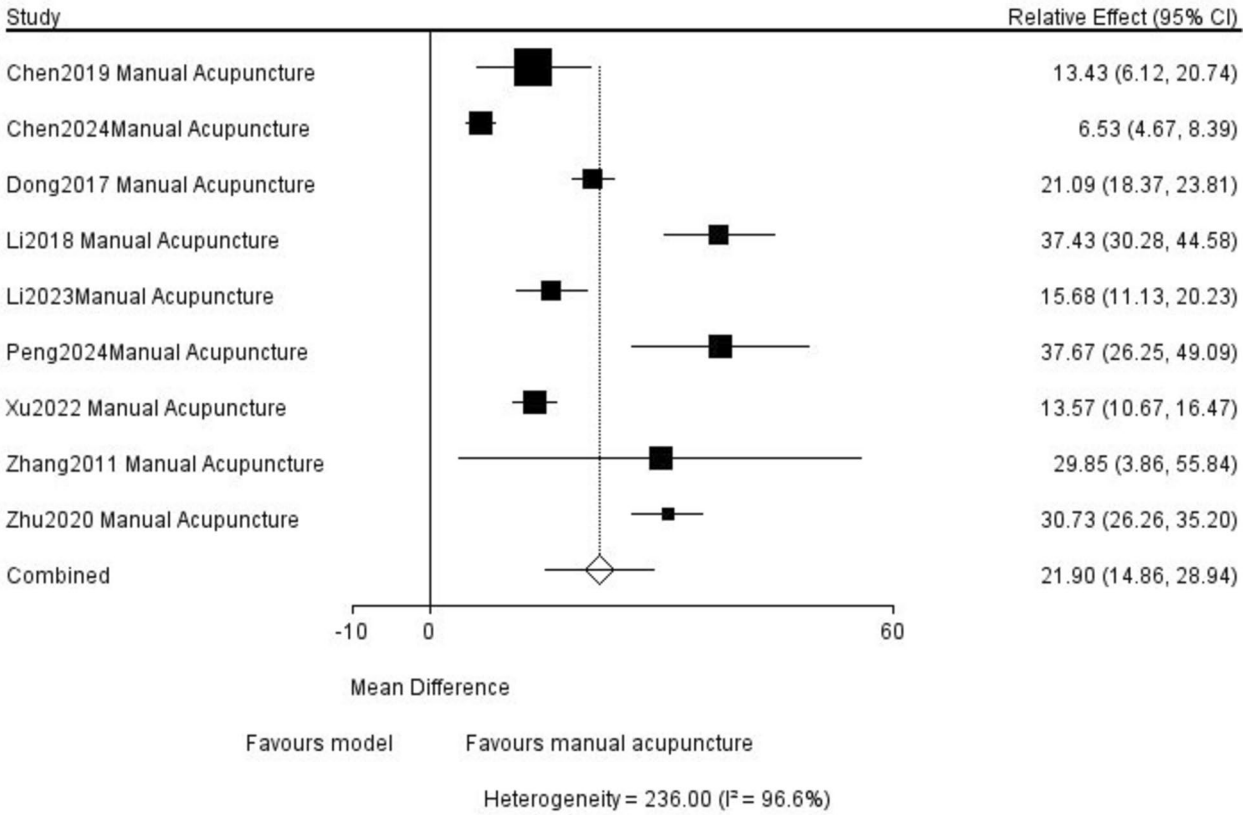


Fig. 12 Network meta-analysis showed that VD rats improved their learning and memory ability after acupuncture treatment: manual acupuncture

electroacupuncture	−0.38 (−12.83, 11.80)	21.91 (15.08, 28.80)
0.38 (−11.80, 12.83)	manual acupuncture	22.31 (12.06, 32.77)
−21.91 (−28.80, −15.08)	−22.31 (−32.77, −12.06)	model

Fig. 13 Network meta-analysis results: comparison of EA and MA ladder diagram

phenomena lead to enhanced transmission of signals back to the brain, increased cerebral blood flow, and improved cognition among rats.

Limitations

A comprehensive analysis of the factors influencing the efficacy of acupuncture, as presented in the literature, can provide an evidence-based foundation for future animal studies on acupuncture methods. The ultimate goal of these animal studies is to inform clinical practice. However, this meta-analysis has several limitations. First, most studies had a risk of bias, primarily due to randomization and blinding methods. Eleven studies clearly described randomization methods [20, 24, 35, 38–44, 47]. Thirteen studies only mentioned randomization without details and were evaluated as having an unclear risk of bias [21–23, 25, 27, 28, 30, 32, 33, 36, 46]. Five studies used randomization by surgical order and were rated as having a high risk of bias [26, 29, 31, 34, 45]. While all the papers were balanced at baseline, none mentioned allocation concealment. No study indicated whether the animals were randomly housed. Owing to the nature of acupuncture treatment, it is challenging to implement blinding. Only one study mentioned the blinding of data analysts [30], whereas the other 28 studies did not mention statistical blinding [20–29, 31–48]. The presence of high-risk studies necessitates caution when interpreting the analysis results. Second, this study retrieved data from seven Chinese and international databases. However, due to regional differences in acupuncture treatment, all of the

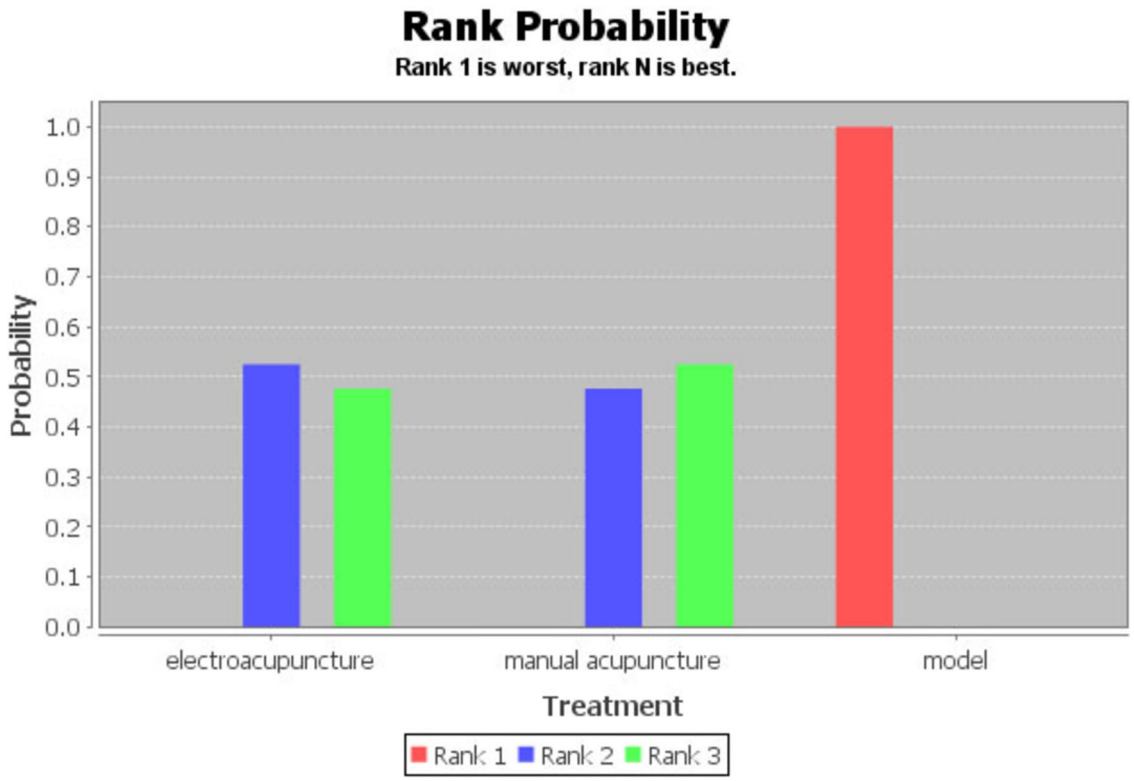


Fig. 14 Network meta-analysis results: comparison between EA and MA probability weight graph

included studies were conducted in China, thus limiting the generalizability of the findings. More international studies are needed to validate these results in the future. Third, this review had strict inclusion criteria and excluded studies obtained through graphical data and those combining acupuncture with other treatments. These exclusion criteria led to many studies not being included in this analysis. The outcome indicators in this study are continuous variables, and the accuracy of values converted from graphs is insufficient. Attempts to obtain original data from authors via email were unsuccessful. Studies combining acupuncture with other treatments focused on joint treatment outcomes, which did not align with the purpose of this study. Only 29 studies with small sample sizes were included. Additional high-quality studies are needed to verify these findings. Fourth, there was considerable heterogeneity in the combined analysis of outcome indicators, which may have affected the accuracy of the results. Subgroup analysis of four possible causes revealed that differences in acupuncture methods and modeling methods did not significantly reduce heterogeneity. Sensitivity analysis indicated that removing any single study did not eliminate heterogeneity. The high heterogeneity was due to varying acupoint selections and treatment durations across studies. Subgroup analysis of different acupoint combinations reduced heterogeneity. Among them, CV20 CV14 ($I^2=17\%$) and CV24 GB13 ($I^2=0\%$) both indicated low heterogeneity ($I^2<50\%$). However, GB20 EX-HN1 ($I^2=51\%$) exhibited increased heterogeneity. Sensitivity analysis revealed that the high degree of heterogeneity in the subgroup analysis was due to one study [45], which was included in the same research group but had different years, animal batches, and experimental equipment. After excluding this study, the heterogeneity of GB20 EX-HN1 (MD: −13.95; 95% CI: −19.04, −8.86; $I^2=0\%$) was reduced to $I^2<50\%$. In the subgroup analysis of treatment duration, the group with ≤ 15 days showed high heterogeneity ($I^2=97\%$, $I^2>50\%$). Sensitivity analysis via the leave-one-out method did not indicate any significant changes in the outcome measures. For the 15 < treatment duration ≤ 20 days group, the I^2 was 43%, and for the 20 < treatment duration ≤ 30 days group, the I^2 was 21%, both indicating low heterogeneity ($I^2<50\%$).

Reflections

While this meta-analysis suggested that the combination of GV20 and GV14 is most effective in VD rats, it is important to note that GV14 is located between the

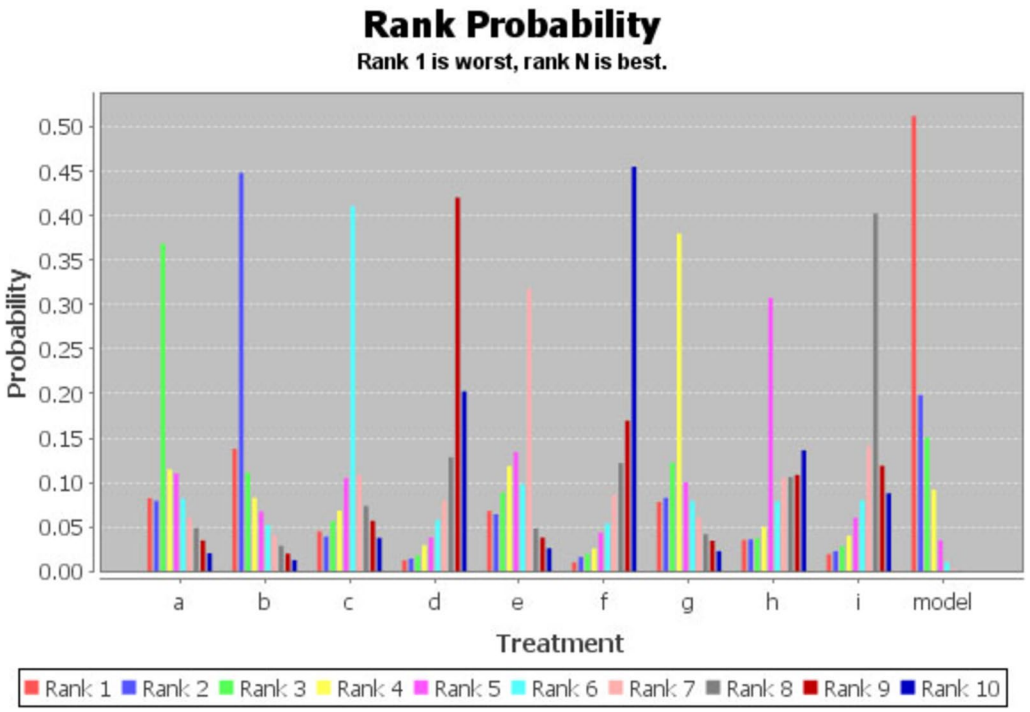


Fig. 15 Network meta-analysis results: total effective rate of MA probability ranking graph (a Chen [21], b Chen [40], c Dong [23], d Li [28], e Li [41], f Peng [44], g Xu [46] and H. Zhang [47], i Zhu [38]) (note: different colors represent rankings, with higher rankings indicating a greater likelihood of achieving that position. The intervention with the highest probability is ranked as the best. Since a lower latency to escape is preferable, Rank 10 is considered optimal, and the interventions with the highest probabilities from Rank 1 to Rank 10 are selected for sorting)

Table 2 Network meta-analysis results: comparison between EA and MA probability weight table

Drug	Rank 1	Rank 2	Rank 3
Electroacupuncture	0.00	0.52	0.48
Manual acupuncture	0.00	0.48	0.52
Model	1.00	0.00	0.00

Different colors represent rankings, with higher rankings indicating a greater likelihood of achieving that position. The intervention with the highest probability is ranked as the best. Since a lower latency to escape is preferable, Rank 3 is considered optimal, and the interventions with the highest probabilities from Rank 1 to Rank 3 are selected for sorting

seventh cervical vertebra and the first thoracic vertebra on the back of a rat [69], and 4VO surgery involves electrocoagulation of the bilateral foramina [70]. In animal experiments, the surgical incision for the 4VO operation coincides roughly with the location of GV14. This raises concerns about whether the surgical procedure might influence the experimental results, whether the wound will fully heal within 7 days postsurgery, and whether acupuncture could cause secondary damage to VD rats. These questions warrant further investigation. In clinical practice, Professor Chen Yinghua's observations indicate that acupuncture treatment for vascular dementia patients yields significant effects after 4 weeks, with longer treatment durations leading to better clinical outcomes. A review of the literature further suggests that clinical experts [71] recommend administering a 4-week course of traditional Chinese medicine compounds, such as Cuscutae Semen and *Cistanche tubulosa* capsules, with at least three courses recommended for optimal results. The "Clinical Application Guidelines for the Treatment of Vascular Dementia with Patent Chinese Medicine" [72] indicate that high-dose *Ginkgo biloba* (EGb761) treatment for 22 to 26 weeks is effective in alleviating cognitive and psychiatric symptoms in patients with mild to moderate vascular dementia, thus demonstrating good tolerability. Additionally, an animal study [21] revealed that 21 days of electroacupuncture treatment yielded better results than 14 days of treatment in successfully model rats, which contrasts with the findings of this meta-analysis. Future VD animal experimental designs may benefit from the inclusion of multiple treatment time points for comparative trials to determine the optimal treatment duration.

Future prospects

In the future, evidence-based medical research will continue to evolve. High-quality animal systematic reviews should be closely linked to clinical practice. Tian Jinzhou et al. [73] showed, through long-term clinical experience, that traditional Chinese medicine plays a significant role in treating VD. They developed the Scale for the Differentiation of Syndromes of Vascular Dementia (SDSVD), which identifies seven traditional Chinese medicine syndromes for VD: kidney essence deficiency, phlegm turbidity obstruction, blood stasis obstruction, liver yang hyperactivity, internal heat excess, fu stagnation turbidity retention, and qi and blood deficiency. In the future, disease research should continue to follow traditional Chinese medicine syndromes in VD animal models and integrate animal and clinical studies for mutual benefit. It is hoped that large-scale, rigorously designed randomized controlled trials will further validate the conclusions of this meta-analysis, thus providing more reliable references for clinical acupuncturists and ultimately alleviating the physical and mental burden of VD patients.

Conclusion

Acupuncture significantly improved cognitive function in rats with VD. MA yielded better efficacy than EA. In animal experiments in which VD was treated with acupuncture, the best results were observed when the 2VO model was used; when acupoints GV4, GV14, GV16, GV20, GV24, GV26, PC6, PC7, and PC8 were selected; when MA with reinforcing and reducing methods was used; and when needles were retained for 30 min once daily for 14 days. Further studies are needed to verify whether this treatment method can achieve similar efficacy in clinical settings.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13643-025-02821-3.

Additional file 1

Additional file 2

Additional file 3

Reporting statement

This study followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA).

Authors' contributions

YS, conceptualization, software, data curation, visualization, and writing — original draft. JL, data curation and visualization. WS, methodology and visualization. FJ, visualization and data curation. YC, conceptualization, writing — review editing, and supervision.

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Data availability

Data will be made available on request.

Declarations

Competing interests

The authors declare that they have no competing interests.

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