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Review Article

Effectiveness and Safety of Acupuncture and Related Therapies for Poststroke Insomnia: A Network Meta-Analysis

Xinwang Chen [1], Run Zhang [2], Yajing Guo [1], Jing Wen [1], Yuzhu Wu [1], Wenming Chu [1], *Yiming Wu [3]

1. *Henan University of Chinese Medicine, Zhengzhou, Henan Province, China*
2. *The Central Hospital of Enshi Tujia and Miao Autonomous Prefecture, Enshi, Hubei Province, China*
3. *The Third Affiliated Hospital of Henan University of Chinese Medicine, Zhengzhou, Henan Province, China*

***Corresponding Author:** Email: wuyimingsir@163.com

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Abstract

Background: Poststroke insomnia (PSI) is a frequent complication for stroke patients. Acupuncture and related therapies demonstrate efficacy in PSI management. Despite their many types, the optimal strategy remains unclear. This network meta-analysis (NMA) compared the effectiveness of various acupuncture and related therapies.

Methods: Seven databases were searched up to 1st February 2024. The primary outcome was a reduction in the Pittsburgh Sleep Quality Index (PSQI) score. The secondary outcomes were the response rate and adverse events. The treatment ranking probabilities were calculated using the surface under the cumulative ranking curve (SUCRA).

Results: In total, 59 randomized controlled trials (RCTs) involving 4415 participants were included. Electroacupuncture (EA) provided the best result for PSQI reduction (SUCRA = 0.79), followed by warm acupuncture combined with auricular acupoint stimulation (WA+AAS) (0.68) and manual acupuncture combined with auricular acupoint stimulation (MA+AAS) (0.63). For the response rate, manual acupuncture combined with acupoint catgut embedding (MA+ACE) ranked highest (0.86), followed by EA (0.850) and manual acupuncture combined with moxibustion (MA+MOX) (0.83). A total of 96 adverse events were reported: 7 related to acupuncture interventions and 89 to conventional medicine (CM).

Conclusion: Acupuncture and related therapies are effective and safe for PSI treatment. Among them, EA and MA+ACE are the most promising interventions for improving sleep quality poststroke.

Keywords: Acupuncture; Poststroke insomnia; Poststroke insomnia; Network meta-analysis

Introduction

Stroke is the second leading cause of death and disability worldwide (1), with over 2 million new stroke cases occurring annually in China and 11.9 million globally in 2021 (2). Poststroke sleep disturbances are common, with insomnia being the most prevalent (3). Poststroke insomnia (PSI) is defined as difficulty initiating or maintaining sleep or early-morning awakening occurring ≥ 3

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nights per week for ≥ 3 months, leading to daytime dysfunction following stroke. Approximately 33% of stroke patients experience PSI (4), which hinders physical and neurological recovery, induces stroke recurrence, increases mortality risk (5-7) and predisposes to depression and suicide, posing a serious public health burden (8). Improving sleep may therefore enhance stroke rehabilitation (9,10). Although pharmacotherapy (e.g., benzodiazepines) can improve sleep, it often causes hangover effects, tolerance, and withdrawal syndromes (11-13). Cognitive–behavioral therapy for insomnia (CBT-i) is recommended as first-line treatment, but it is costly and requires high patient compliance, limiting its applicability (14). Therefore, developing effective and feasible strategies for PSI is essential to support rehabilitation, prevent recurrence, and improve quality of life.

Acupuncture, an ancient therapy for disease prevention and management with minimal side effects, has been practiced in China for thousands of years and is now recommended in an increasing number of clinical guidelines (15). A literature review demonstrated that acupuncture and related therapies are widely applied in PSI management. Acupuncture administered by qualified acupuncturists may mitigate stroke-induced brain damage directly or indirectly and improve insomnia triggered by anxiety and depression (16). Acupuncture improves both subjective and objective sleep quality with long-term efficacy in PSI (17).

This study analyzed published randomized controlled trials (RCTs) and directly and indirectly compared the efficacy of various acupuncture and related therapies to determine the most effective choice for patients with PSI.

Methods

General guidelines of the study

We followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Network Meta-Analysis (PRISMA-NMA) checklist (Supplemental 1), which revises 11 items from the original PRISMA and adds five to enhance reporting quality (18). A MeaSurement Tool to Assess Systematic Reviews 2 (AMSTAR 2) can also be utilized to assess the methodological quality of systematic review guidelines (19). The protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42023401253).

Data Sources and Search Strategy

Eight databases, PubMed, Embase, the Cochrane Library, Web of Science, China National Knowledge Infrastructure, Wan Fang, China Biology Medicine disc (SinoMed), and the Chongqing VIP, were systematically searched up to 1 February 2024. The search was limited to RCT studies published in English or Chinese. Detailed search strategies are provided in the Supplementary Methods (Supplemental 2).

Study selection

The inclusion criteria were as follows: 1) Participants: Patients with PSI secondary to ischemic or hemorrhagic stroke. The diagnostic criteria for insomnia include the International Classification of Sleep Disorders (ICSD) (20) or the Chinese Classification of Mental Disorders (CCMD-3) (21) regardless of sex, race, or age. 2) Interventions: The treatment group was treated with manual acupuncture (MA), electroacupuncture (EA), MOX (moxibustion), or auricular acupoint stimulation (AAS) and other nonpharmacological therapies, including intradermal acupuncture (IA). 3) Comparison: The control group was treated with Western medicine, a placebo, or various acupuncture-related therapies described in the treatment group. 4) Outcomes: The PSQI score was the primary outcome; secondary outcomes were response rate and adverse events. For the PSQI, greater reductions indicated better outcomes. The response rate is the proportion of patients demonstrating satisfactory improvement in overall symptoms, derived from scales (e.g., PSQI reduction rate or insomnia severity index reduction rate) or traditional Chinese medicine symptom scores. Cases rated as "apparently effective," "effective," and "clinically cured" were consid-

ered improvements. 5) Studies: Published RCTs involving acupuncture for PSI were included.
The exclusion criteria were as follows: 1) duplicate publications or unavailable original data; 2) studies including three or more intervention groups; and 3) unclear acupuncture procedures per the Revised Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) (22).

Study selection and data extraction

Two reviewers (CXW and ZR) independently screened the literature following the same search strategy. Data from eligible RCTs were extracted after cross-checking between them. Data included the first author, study title, participants (age, duration, and sample sizes), study design (randomization and blinding), interventions, control interventions, outcome measures, results, and adverse events. Disagreements were reviewed by a third reviewer (WYM) and resolved through discussion.

Quality assessment

Risk of bias was assessed using Cochrane's risk of bias 2 (ROB2) tool (23). Each domain was rated as low risk, some concerns, or high risk of bias. Acupuncture procedures were appraised according to the STRICTA criteria.

Statistical analysis

Statistical analysis was performed with Review Manager 5.3 software (RevMan 5.3, The Cochrane Collaboration, Oxford, UK), RStudio 4.3.0, Graphical Models for Network Meta-Analysis (GeMTC 0.14.3), and Stata 15.0. Multi-arm (three- or four-arm) trials were divided into 2-arm trials. Missing data were calculated using the following formula:

$$SD_{change}=\frac{\bar{X}_{change}=\bar{X}_{post-treatment}-\bar{X}_{baseline}}{\sqrt{(SD_{baseline})^2+(SD_{post-treatment})^2-2\times r\times SD_{baseline}\times SD_{post-treatment}}}$$

Continuous outcomes (PSQI) were expressed as standardized mean differences (SMDs) with 95% confidence intervals (CIs), and categorical outcomes (response rate) as odds ratios (ORs) with 95% CIs. Heterogeneity was assessed using the I2 test (24). A random effects model was used when I2 > 50%; otherwise, a fixed effect model was used. Network plots in Stata 15.0 illustrated the relationships between all included interventions, with nodes representing treatments and edges representing available direct comparisons between treatment pairs. Node size and edge width were weighted by the number of studies in each direct comparison. When a closed loop existed, direct and indirect evidence were considered consistent if the 95% CI of the inconsistency factor (IF) was 0; otherwise, inconsistency was considered. To compare therapies' effects, NMA was performed in RStudio using Markov chain Monte Carlo simulation (four chains with overdispersed initial values, 500,000 iterations, and the first 20,000 were discarded because they may influence the arbitrary value) (25). Model convergence was assessed using Brooks-Gelman-Rubin diagnosis; a potential scale reduction factor close to 1 indicated better convergence (26). Treatment ranking probabilities were estimated using the surface under the cumulative ranking curve (SUCRA), and a treatment hierarchy was established (27). Funnel plots were generated in Stata to assess small study effects.

Results

Study search and description

A total of 1609 relevant studies were identified. After removing duplicates, 956 studies remained. Following title and abstract screening, 798 records were excluded. Finally, 59 trials with 4415 participants (28-86) were included in the NMA. Interventions in the treatment groups included MA, EA, MOX, AAS, MA+MOX, MA+IA, MA+AAS, MA + acupoint catgut embedding (ACE), and warm acupuncture (WA) + AAS (Fig. 1). The control group included conventional medicine (CM) and a placebo (PLA). Two RCTs (46,75) were three-armed trials, one RCT (62) was a four-armed trial, and the rest were two-armed trials. The baseline characteristics of the

included studies are summarized in the study dataset, and the patient characteristics are demonstrated in Supplementary 3.

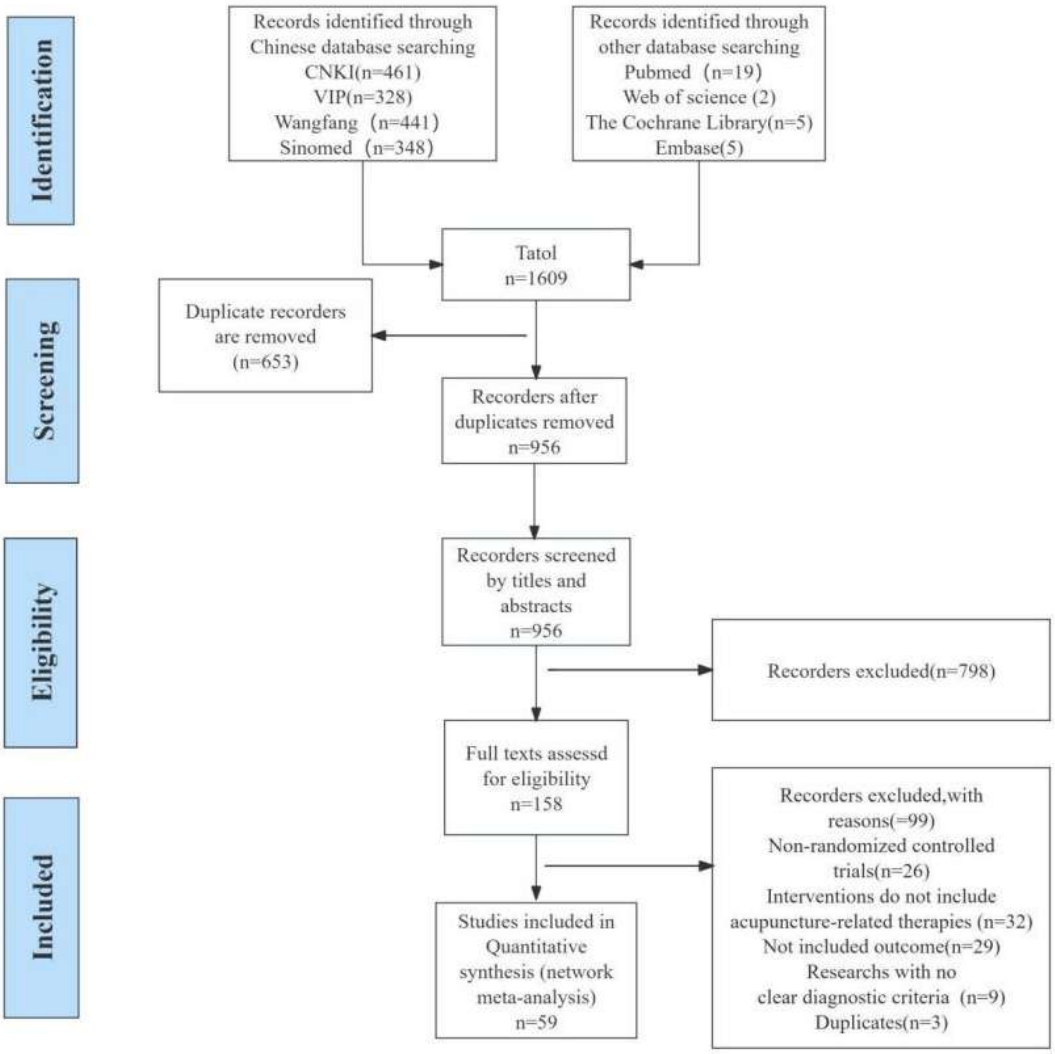


Fig. 1: The Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart of the selection process

Quality assessment of the included studies

Two researchers (ZR and GYJ) independently assessed the risk of bias. In the randomization process, four RCTs (33,44,45,72) (6%) reported random sequence generation and allocation concealment and were rated low risk; 54 RCTs lacking allocation concealment details were rated some concerns. One RCT (28) (1.6%) used a randomized method based on the order of admission, which is not rigorous method and therefore lacked allocation concealment, and was rated high risk. Regarding deviations from intended interventions, three RCTs (33,45,62) (5.5%) were rated low risk, and the remaining 56 RCTs were rated some concerns due to lack of blinding. Three RCTs (41,48,71) (5.5%) reported incomplete outcome data, but the reasons for dropout were clearly stated and did not affect the outcome; the other 54 RCTs were rated low risk. Regarding outcomes measurement, four RCTs (33,45,62,69,72,73) (6.7%) used blinding and were rated low risk; the remaining 55 RCTs were

rated some concerns. For selective reporting, one RCT (33) (1.6%) reported a protocol, which was rated low risk, whereas the remaining 58 were rated some concerns. Overall, one RCT (1.6%) was rated low risk, 57 RCTs (96.6%) some concerns, and one RCT (1.6%) high risk. Quality assessment results are demonstrated in Fig. 2.

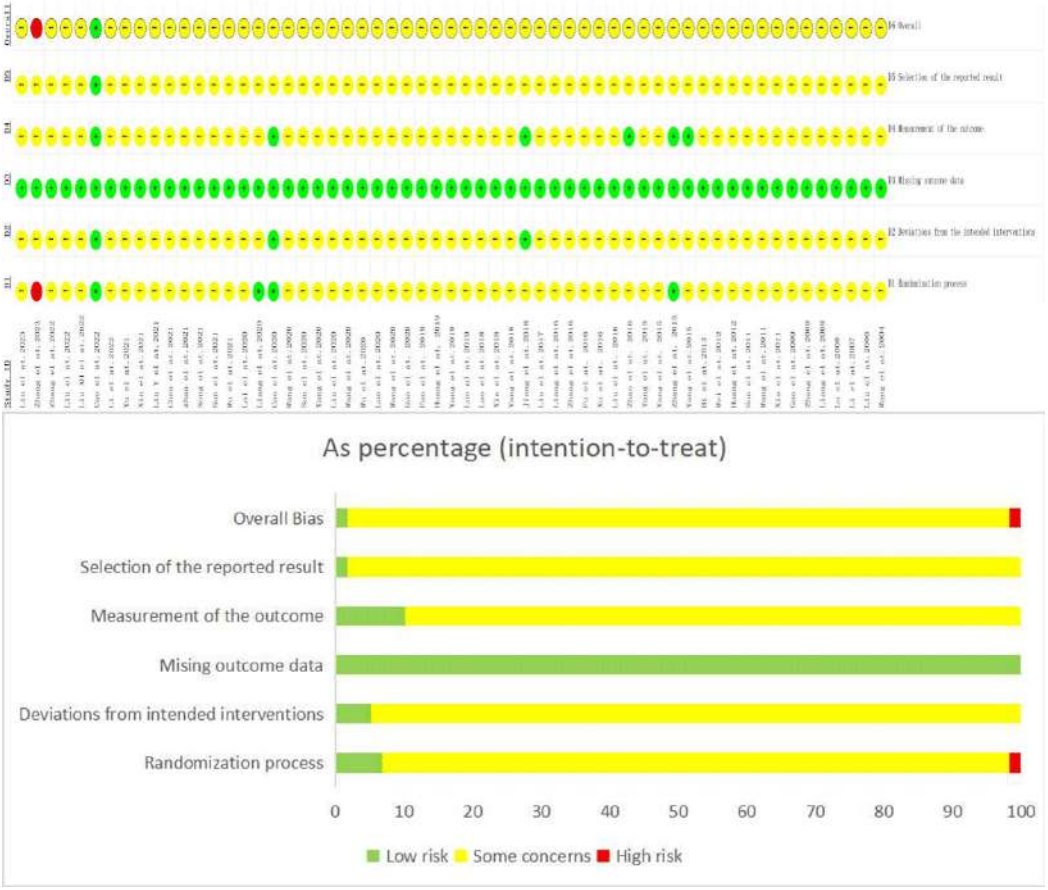


Fig. 2: Risk of bias

The reporting quality of the acupuncture procedures was assessed using the 17-item STRICTA checklist. Among 59 studies, 53 described acupunctures; all 53 (100%) reported the acupuncture style (Item 1a), needle type (Item 1b), and points used (Item 2b). Twenty-seven studies (52.94%) reported the "responses sought" (Item 2d); 42 (82.35%) described the needle retention time (2f); 33 (64.70%) reported insertion depth (2c); and 49 (96.07%) reported needle stimulation (2e). Forty-eight (94.11%) reported the number and frequency/duration of the sessions (Items 3a and 3b). Only four (7%) reported needling circumstances (4b) and acupuncturist information (5). None reported the "rationale for the control or comparator" (Item 2a) or "number of needle insertions per subject per session" (Item 6a) (Fig. 3).

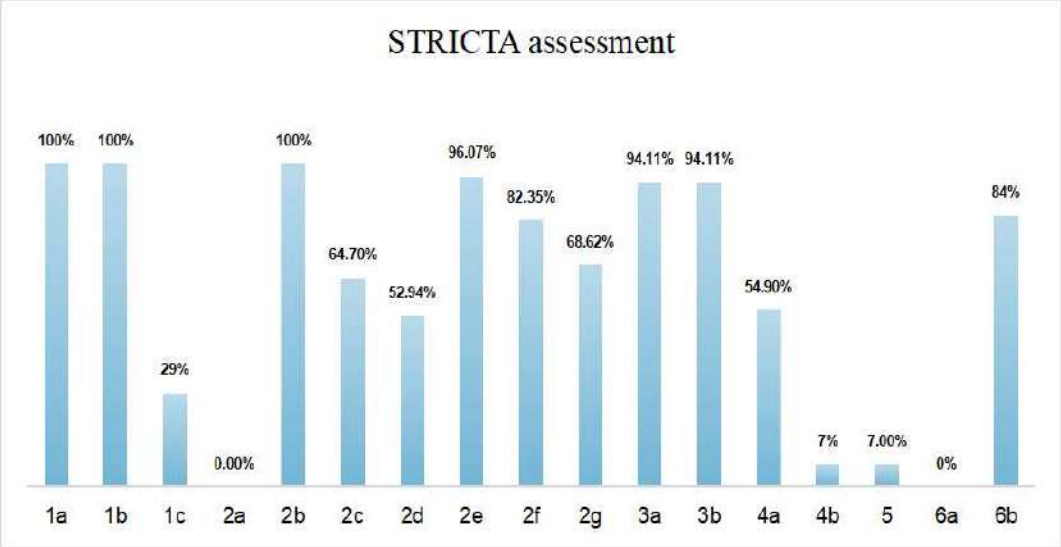


Fig. 3: Results of the Standards for Reporting Interventions in Clinical Trials of Acupuncture assessment for the included studies

Results of pairwise meta-analyses

PSQI score reduction

Nine pairwise meta-analyses compared PSQI score reductions (Supplementary 4-Table 1). CM was inferior to MA, EA, MOX, MA+MOX, and MA+AAS in terms of PSQI score reduction. Both EA and MA were significantly different from PLA. Other direct comparisons demonstrated no significant differences.

Response rate

Eight pairwise meta-analyses compared response rates (Supplementary 4-Table 2). MA, MOX, MA+MOX, and MA+AAS were more effective than CM. EA, MA+MOX, and MA+ACE were more effective than MA. The direct comparisons of AAS and CM demonstrated no significant differences.

Network meta-analysis

PSQI

Forty-nine RCTs involving 3932 participants with 10 therapies reported PSQI score reduction (Fig. 4a). The inconsistency test results demonstrated that the PSQI scores included seven closed loops, with IFs whose 95% CIs included 0, indicating no obvious inconsistencies (Fig. 4b). The NMA demonstrated that MA, EA, MOX, MA+MOX, and MA+AAS were superior to CM in PQSI reduction. EA and MA were significantly different from PLA. The meta-analysis details are demonstrated in Fig. 5. According to SUCRA, EA (0.79) ranked highest for PSQI improvement, followed by MA+ACE (0.68) and MA+AAS (0.63). The ranking probability plot is demonstrated in Fig. 4c. As demonstrated by the funnel plot (Fig. 4d), most included studies were distributed along the vertical line, indicating a low likelihood of a small sample effect.

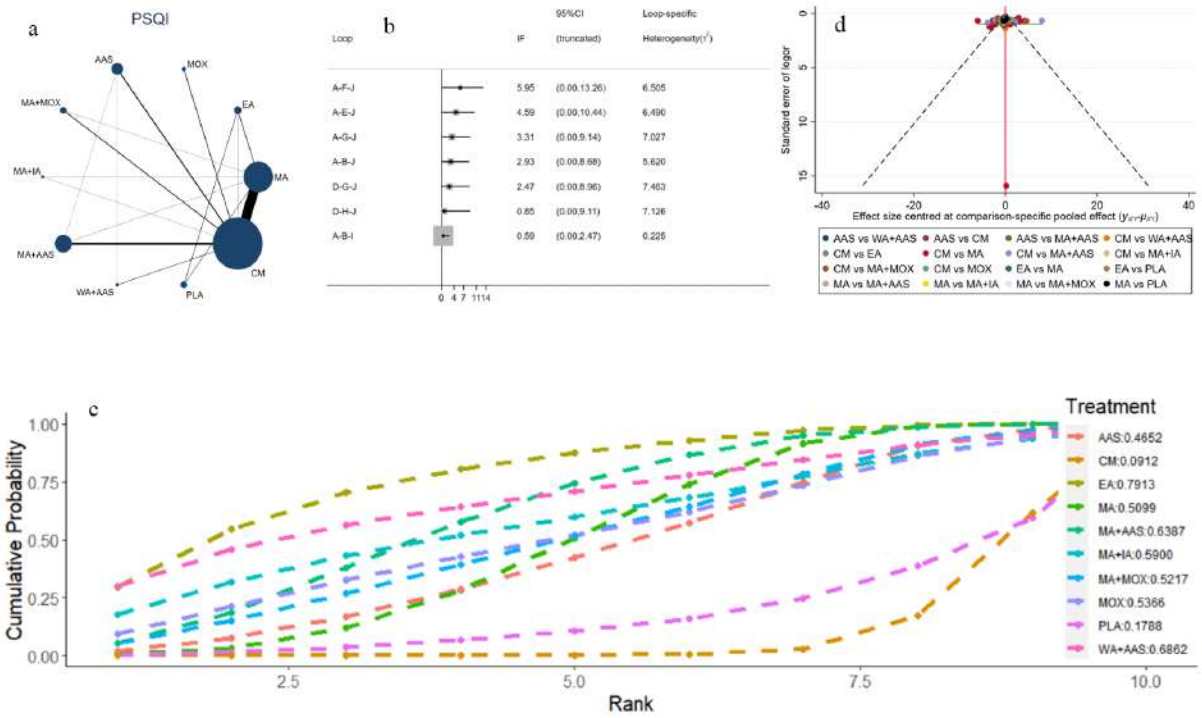
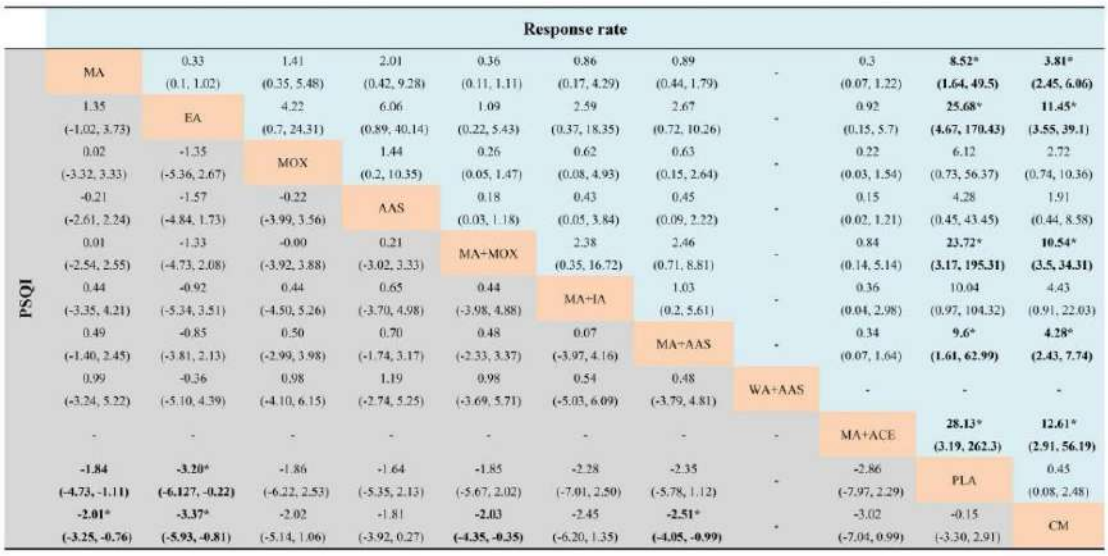


Fig. 4: Comparison of acupuncture and related therapies on the Pittsburgh Sleep Quality Index



	Response rate									
PSQI	MA	0.33 (0.1, 1.02)	1.41 (0.35, 5.48)	2.01 (0.42, 9.28)	0.36 (0.11, 1.11)	0.86 (0.17, 4.29)	0.89 (0.44, 1.79)	-	0.3 (0.07, 1.22)	**8.52*** **(1.64, 49.5)**	**3.81*** **(2.45, 6.06)**
	1.35 (-1.02, 3.73)	EA	4.22 (0.7, 24.31)	6.06 (0.89, 40.14)	1.09 (0.22, 5.43)	2.59 (0.37, 18.35)	2.67 (0.72, 10.26)	-	0.92 (0.15, 5.7)	**25.68*** **(4.67, 170.43)**	**11.45*** **(3.55, 39.1)**
	0.02 (-3.32, 3.33)	-1.35 (-5.36, 2.67)	MOX	1.44 (0.2, 10.35)	0.26 (0.05, 1.47)	0.62 (0.08, 4.93)	0.63 (0.15, 2.64)	-	0.22 (0.03, 1.54)	6.12 (0.73, 56.37)	2.72 (0.74, 10.36)
	-0.21 (-2.61, 2.24)	-1.57 (-4.84, 1.73)	-0.22 (-3.99, 3.56)	AAS	0.18 (0.03, 1.18)	0.43 (0.05, 3.84)	0.45 (0.09, 2.22)	-	0.15 (0.02, 1.21)	4.28 (0.45, 43.45)	1.91 (0.44, 8.58)
	0.01 (-2.54, 2.55)	-1.33 (-4.73, 2.08)	-0.00 (-3.92, 3.88)	0.21 (-3.02, 3.33)	MA+MOX	2.38 (0.35, 16.72)	2.46 (0.71, 8.81)	-	0.84 (0.14, 5.14)	**23.72*** **(3.17, 195.31)**	**10.54*** **(3.5, 34.31)**
	0.44 (-3.35, 4.21)	-0.92 (-5.34, 3.51)	0.44 (-4.50, 5.26)	0.65 (-3.70, 4.98)	0.44 (-3.98, 4.88)	MA+IA	1.03 (0.2, 5.61)	-	0.36 (0.04, 2.98)	10.04 (0.97, 104.32)	4.43 (0.91, 22.03)
	0.49 (-1.40, 2.45)	-0.85 (-3.81, 2.13)	0.50 (-2.99, 3.98)	0.70 (-1.74, 3.17)	0.48 (-2.33, 3.37)	0.07 (-3.97, 4.16)	MA+AAS	-	0.34 (0.07, 1.64)	**9.6*** **(1.61, 62.99)**	**4.28*** **(2.43, 7.74)**
	0.99 (-3.24, 5.22)	-0.36 (-5.10, 4.39)	0.98 (-4.10, 6.15)	1.19 (-2.74, 5.25)	0.98 (-3.69, 5.71)	0.54 (-5.03, 6.09)	0.48 (-3.79, 4.81)	WA+AAS	-	-	-
	-	-	-	-	-	-	-	-	MA+ACE	**28.13*** **(3.19, 262.3)**	**12.61*** **(2.91, 56.19)**
	-1.84 **(-4.73, -1.11)**	**-3.20*** **(-6.127, -0.22)**	-1.86 (-6.22, 2.53)	-1.64 (-5.35, 2.13)	-1.85 (-5.67, 2.02)	-2.28 (-7.01, 2.50)	-2.35 (-5.78, 1.12)	-	-2.86 (-7.97, 2.29)	PLA	0.45 (0.08, 2.48)
	-2.01* **(-3.25, -0.76)**	**-3.37*** **(-5.93, -0.81)**	-2.02 (-5.14, 1.06)	-1.81 (-3.92, 0.27)	**-2.03** **(-4.35, -0.35)**	-2.45 (-6.20, 1.35)	**-2.51*** **(-4.05, -0.99)**	*	-3.02 (-7.04, 0.99)	-0.15 (-3.30, 2.91)	CM

Fig. 5: Network meta-analysis of the Pittsburgh Sleep Quality Index score and the response rate

Response rate

Fifty RCTs involving 4020 participants with 10 therapies reported response rates (Fig. 6a). The inconsistency test demonstrated five closed loops. One closed loop had an IF whose 95% CI excluded 0, with a minimum IF value of 0.04 (Fig. 6b). The NMA demonstrated that MA, EA, MA+MOX, MA+AAS , and MA+ACE were more effective than CM. Five treatments, MA, EA, MA+MOX, MA+AAS, and MA+ACE were

significantly different from PLA (Fig. 5). The SUCRA results demonstrated the hierarchy of the response rates of the 10 treatments; MA+ACE (SUCRA = 0.857) had the highest probability, followed by EA (0.850) and MA+MOX (0.83). The ranking probability plot is presented in Fig. 6c. As shown by the funnel plot, most included studies were evenly distributed on either side of the vertical line X = 0, indicating a low likelihood of a small sample effect (Fig. 6d).

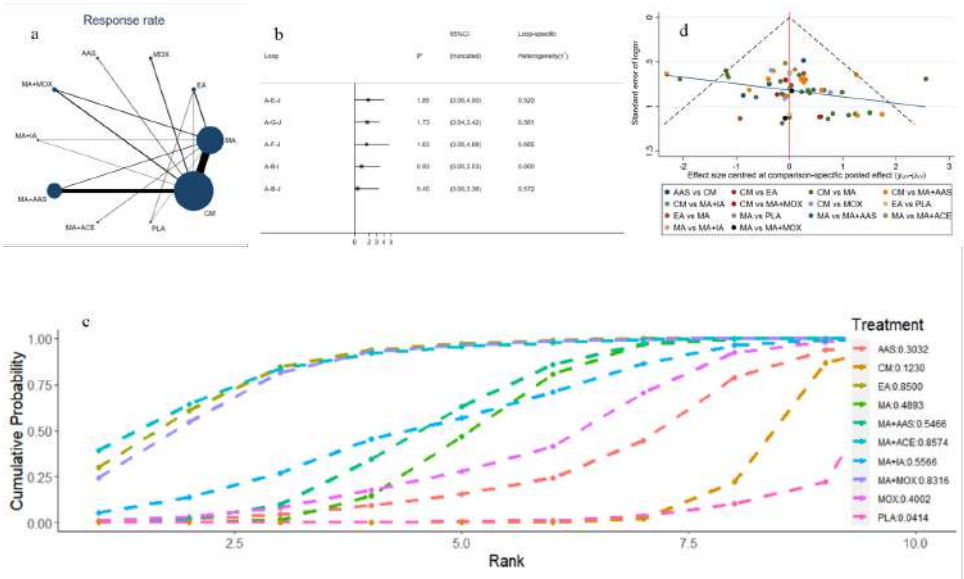


Fig. 6: Response rates associated with acupuncture and related therapies

Adverse events

Nine RCTs reported adverse events. Six studies reported seven types of adverse events related to MA+AAS and MA, including dizziness, fatigue, nausea, rash, short-term stress, fainting during acupuncture, and hematoma. Nine studies described 89 adverse events related to CM. Details are demonstrated in Supplementary 4c.

Discussion

This NMA included 59 RCTs comparing 11 acupuncture therapies. When PSQI scores decreased, pairwise meta-analysis demonstrated that MA, EA, MOX, MA+MOX, and MA+AAS were superior to CM. MA and EA were more effective than PLA. The NMA results were consistent with these findings. For the response rate, MA, MOX, MA+MOX, MA+ACE, and MA+AAS outperformed CM, with no direct comparisons with PLA in clinical efficacy. MA+ACE was more effective than MA, EA, and MA+MOX. The NMA demonstrated that MA, EA, MA+MOX, MA+AAS, and MA+ACE have greater efficacy than that of CA and PLA. However, no significant differences were observed among acupuncture types, possibly due to a publication bias favoring positive results. According to SUCRA rankings, EA, WA+AAS, and MA+AAS showed the highest probabilities for PSQI reduction, whereas MA+ACE, EA, and MA+MOX ranked highest for clinical efficacy.

The mechanisms of PSI remain unclear but may involve reduced neurotransmitter functionality, cerebral blood flow alterations, and abnormal brain functions poststroke (87,88). Acupuncture may modulate brain networks by regulating interactions between functional regions and neurotransmitters (89). In this NMA, EA and MA+ACE improved PSQI scores and clinical efficacy, respectively. EA, a modern acupuncture technique using mild electrical current through needles, stimulates specific meridians and improves biological parameters, including sleep (90). Stainless steel needle stimulation of bilateral Shenmen (HT7) in adult male Sprague–Dawley

(SD) rats for 20 minutes at 2 Hz increased rapid eye movement (REM) sleep and altered sleep/wake times, indicating that EA stimulates HT7 cells to improve sleep dysfunction by regulating the brain-derived neurotrophic factor (BDNF)-mediated endoplasmic reticulum stress response in the medial septum (91).

The therapeutic effects observed in this NMA likely stem from neurobiological processes involved in sleep regulation and neural repair post-stroke. PSI involves disrupted neurotransmitter homeostasis (particularly glutamate/gamma-aminobutyric acid [GABA] and monoamines), altered cerebral perfusion or microcirculation, and maladaptive plasticity or network dysfunction in hippocampal and limbic circuits. Acupuncture may alleviate these abnormalities by modulating neurotransmission, neurotrophic signaling, neuroinflammation, oxidative stress, and circuit-level connectivity (92, 93, 94).

This NMA analyzed only the effects of acupuncture and related therapies for PSI using PSQI scores and response rates. The Athens Insomnia Scale (AIS), 5-hydroxytryptamine (5-HT), dopamine (DA), and polysomnography (PSG) can be used as outcomes to monitor sleep quality. MA+AAS lowered AIS scores, prolonged total sleep time, and improved sleep efficiency. Acupuncture increased 5-HT and DA levels, but these outcomes were excluded due to limitations in the original literature data. This NMA will be updated if more RCTs incorporate additional indicators.

This study has some limitations. First, publication bias and regional restriction to Chinese studies may have limited international dissemination and reduced generalizability. Future research should follow international reporting standards and target high-impact journals. Second, most RCTs lacked follow-up and consistent parameter reporting; only a few studies specified key parameters (including EA frequency or stimulation duration). This inconsistency hinders the evaluation of sustained efficacy and dose–response relationships. Third, the methodological quality of many studies was suboptimal, characterized by small sample sizes, unclear blinding procedures, and insufficient compliance with the Consolidated Standards of Reporting Trials (CONSORT) and STRICTA guidelines. Future RCTs should strengthen randomization, allocation concealment, and standardized reporting of acupuncture procedures to improve reproducibility. Fourth, regarding outcome assessment, the current analysis focused primarily on PSQI and response rate, whereas other sleep-related biomarkers, including AIS, 5-HT, dopamine, and PSG-derived metrics, were underreported. Future trials should incorporate these parameters to comprehensively evaluate acupuncture's effects on neurophysiological sleep regulation.

Conclusion

This NMA supports the effectiveness of acupuncture and related therapies for PSI. EA demonstrated the greatest improvement in sleep quality (PSQI score), while MA+ACE achieved the highest clinical response rate, offering optimal benefits for PSI. Further high-quality, multicenter RCTs with standardized protocols and long-term assessments are required to validate and refine these results.

Supplementary materials

Supplementary 1: PRISMA-NMA statement reporting standard checklist; Supplementary 2: search strategies for each database; Supplementary 3: main characteristics of the included randomized controlled trials; Supplementary 4: pairwise comparisons and adverse events.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Data availability statement

All the data generated or analyzed during this study are included in this published article and its supplementary information files, and further inquiries can be directed to the corresponding author.

Conflict of interest

The authors declare that they have no competing interests.

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