Acupuncture Treatments for Post-stroke Depression: A Systematic Review and Network Meta-analysis

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Abstract

Background: Depression is one of the most common complications after stroke, with a prevalence of 30-33%. Patients with post-stroke depression (PSD) usually experience anxiety, hopelessness, and insomnia, which have a negative impact on their daily activities and post-stroke rehabilitation.

In this review, we aimed to explore the impact of acupuncture in alleviating symptoms of PSD and to evaluate the difference in effectiveness between acupuncture combined with pharmacotherapies and various non-pharmacotherapies in order to provide guides and advice for clinical personnel.

Methods: Six databases (Cochrane Library, PubMed, EMBASE, China National Knowledge Infrastructure, Wanfang Database, Chongqing VIP Database) and two clinical trials registration platforms were searched from inception to May 2021. Randomized clinical trials (RCTs) comparing needle-based acupuncture with pharmacotherapy, and other non-pharmacotherapy or invalid group were included. Two independent reviewers identified eligible studies. Two reviewers independently abstracted and recorded data into a pre-made form. A Bayesian network meta-analysis (NMA) was conducted to assess and compare different techniques using RStudio 3.6.0. The primary outcome was the change in scores of scales measuring depressive symptoms. The secondary outcomes were changes in serotonin levels and in quality of life.

Results: Fifty-nine RCTs were included. The results of this NMA showed that compared with western medicine (WM), acupuncture alone or with repetitive transcranial magnetic stimulation (RTMS), Traditional Chinese medicine (TCM) alone or with WM, were superior for alleviating depression symptoms. Compared to Usual Care, acupuncture alone or plus other therapies could significantly decrease scores of the Hamilton Depression Rating scale. However, there was no significant difference found among acupuncture, WM, TCM with AC plus any of other treatment.

Conclusions: The results of this study indicate that acupuncture alone or combined with other therapies appear to be effective in improving depression symptoms of stroke survivors. Moreover, in comparison with WM, acupuncture alone or plus RTMS, TCM, TCM with WM, or WM, were more effective in improving depression symptoms. Also, acupuncture with RTMS seems to be the most effective with the highest probability.

Background

Stroke is the second leading cause of death according to the World Health Organization (WHO) in 2019, responsible for approximately 11% of total deaths.¹ Moreover, it is also one of the leading causes of disability worldwide, and causes the loss of a great number of healthy life-years due to serious post-stroke sequelae (such as paralysis, aphasia, dysphagia, epilepsy, and cognitive difficulty).²⁻⁵ Facing severe symptoms and different physical disabilities, stroke survivors might face tremendous health challenges, and they are more likely to suffer from psychological disorders. Depression is one of the most common complications after stroke, with a prevalence of 30-33%.⁶⁻⁹ Patients with post-stroke depression (PSD) usually experience anxiety, hopelessness, unwillingness to communicate, and insomnia, which could have a negative impact on the daily activities and post-stroke rehabilitation.¹⁰ Moreover, it is suggested that PSD is associated with an increased risk of mortality in stroke survivors.⁶ Therefore, it is quite crucial to devise an effective and safe treatment for PSD. The selective serotonin reuptake inhibitors (SSRIs) are commonly recommended as the first-line pharmacological treatments.¹¹ However, there still exists a debate on whether SSRIs could increase the risk of intracerebral hemorrhage and subsequent stroke.^{12,13}

Acupuncture, as a minimal invasive technique, has been widely used for improving symptoms of a variety of health problems in China and worldwide.¹⁴⁻¹⁶ Many published studies investigated the effectiveness of acupuncture for PSD. One meta-analysis by Xin Yan Zhang etc. included seven studies comparing the effectiveness rate of acupuncture with control group in alleviating the symptoms of PSD. Their results supported that acupuncture was an effective and safe treatment for PSD¹⁷ (RR 1.16, 95% CI 1.08-1.24). Another study by Xue Wang etc. evaluated the effectiveness of acupuncture combined with western medicine for PSD based on 24 studies. The meta-analysis showed acupuncture combined with fluoxetine was superior to fluoxetine alone for relieving depressive symptoms.¹⁸ Moreover, more clinical trials evaluated whether there was a better effect when AC combined other non-pharmacotherapies for PSD. The study by Zhang LIN etc. investigated the efficacy of AC plus Tai Chi in recovering the neurological function and treating depression in PSD.¹⁹ Another study compared the difference of AC combined plus cognitive therapy with paroxetine.²⁰ The authors of Yaqun WANG etc. enrolled 103 participants to evaluate the effect of AC plus Jieyu Qingxin Decotion (a Traditional Chinese herbal medicine) combined compared with paroxetine.

In this review, we seek to explore the true effect of acupuncture in alleviating symptoms of PSD based on both direct and indirect evidence using the network meta-analysis (NMA) method.²¹ Moreover, we also aim to evaluate the difference in effectiveness between acupuncture with pharmacotherapies and other non-pharmacotherapies in order to provide optimized guidance and advice for clinical personnel.

Methods

This review was reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) for Network Meta-Analyses,²² and was registered in the International Prospective Register of Systematic Reviews (PROSPERO) database in November 2020 and updated in July 2021 (Registration no.: CRD42020218752)²³.

Literature search

The Cochrane Library, PubMed, EMBASE, China National Knowledge Infrastructure (CNKI), Wanfang Database, Chongqing VIP Database (CQVIP) were searched for systematic reviews of published articles from inception to May 2021. The clinical trials registration platform and websites were additionally searched, including the International Clinical Trials Registry Platform (ICTRP), ClinicalTrials.gov, ISRCTN registry, <https://scholar.google.com.tw/>, <https://xueshu.baidu.com/>. There was no restriction in language or publication year. Backward and forward reference searching was applied. The references of relevant reviews and systematic reviews were retrieved to search for potential eligible studies. The search strategy of this study is shown in Supplementary Appendix 1.

Inclusion Criteria

Studies comparing needle-based acupuncture (alone or combined with other treatments) with pharmacotherapy, other non-pharmacotherapy or invalid group (including placebo, waitlist and blank control) were included.

P - Participants who were clinically diagnosed with stroke, 18 years or older, and with any degree of stroke impairment severity and at any stage of the disease.

I - Acupuncture treatments were specified to needle-based acupuncture, including but not limited to manual, electro-acupuncture, fire acupuncture, warm acupuncture, ear (auricular) acupuncture, head acupuncture, and more.

C - Acupuncture treatments alone or combined with other treatments (pharmacotherapy and non-pharmacotherapy therapies) were compared with pharmacotherapy, other non-pharmacotherapy or invalid groups (including placebo, waitlist and blank control).

O - Outcomes reflecting changes in scores of PSD.

S - Only randomized controlled trial (RCT).

Studies comparing with different types of acupuncture were excluded.

Literature Selection and Data Extraction

Two independent reviewers extracted data from selected RCTs. The basic characteristics such as first author, study title, participants (gender, age, sample size), study design (randomization, blinding), details of interventions, outcome measures, results and adverse events were abstracted and recorded into a pre-made form. Any disagreements were reviewed by a third reviewer and resolved by discussion among all reviewers.

Risk of Bias Assessment

The risks of bias of included RCTs were assessed based on the Revised Cochrane Risk of Bias tool 2.²⁴ which five domains were evaluated. The appraisal of acupuncture procedures was assessed by Revised Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA).²⁵ The Grading of Recommendations Assessment, Development and Evaluation (GRADE) was used to assess the certainty of the evidence.^{26,27}

Statistical Analysis

Pairwise meta-analysis

Risk ratios with 95% credible intervals were used for dichotomous outcomes. Mean differences or standardized mean differences with 95% credible intervals were used for continuous outcomes. We assessed clinical and methodological heterogeneity through examination of the characteristics of the included trials. Heterogeneity across trials was assessed by X^2 and I^2 statistics. Publication bias was examined using Begg's and Egger's funnel plot method when applicable. The contour-enhanced funnel plot was obtained as an aid to distinguish asymmetry due to publication bias.

Network meta-analysis

A network plot was drawn to present the geometry of the network of comparisons across trials to ensure the network meta-analyses was feasible. Trials were excluded if they were not connected by interventions.

We performed Bayesian network meta-analyses to compare the effects of different prophylactic agents. Markov chains were used to generate samples. Model convergence was assessed using the Brooks-Gelman-Rubin plots method. Global heterogeneity was assessed on the bias of the magnitude of heterogeneity variance parameter estimated from the network meta-analyses models. A node-splitting method was used to examine the inconsistency between direct and indirect comparisons when a loop connecting three arms existed. The ranking probabilities for all treatments were estimated, and a treatment hierarchy using the probability of being the best treatment could be obtained. This process was performed using the Surface Under the Cumulative Ranking curve (SUCRA). We used the frequentist approach to compare stability if necessary. Statistical analysis was performed with STATA 15.0 and RStudio 3.6.0.

Results

Search Results

Initially, 7,472 records were identified. After screening titles and abstracts, 7,406 records were excluded and the remaining were considered potentially eligible for full-text screening. Finally, 59 studies^{20,28-86} involving 5308 participants published from 2003 to 2021 were included in this review. The flow chart of process of the study selection and studies considered for inclusion is shown in Supplementary Appendix 2.

Characteristics of Included Studies

The main characteristics of the included studies are shown in Table 1. Fifty-nine studies involving 5,308 participants were included. All of them were from China. Apart from Usual Care (UC) (defined as controlling blood pressure and blood sugar, physical exercises or pharmacotherapy for stroke rehabilitation, and no special treatment for depression), twelve various treatments were included. Among them, acupuncture (AC) with pharmacotherapy, which is divided into AC with Western Medicine (WM) and AC with Traditional Chinese Medicine (TCM), (in this case, traditional Chinese herbal remedies), and AC with both TCM and WM. There were also five therapies comprising AC plus non-pharmacotherapy, including repetitive transcranial magnetic stimulation (RTMS), Tai Chi, Cognitive Therapy (CT), psychotherapy, and moxibustion (AM). There was one RCT exploring the treatment difference between AC with RTMS and AC alone. One study investigated the efficacy of AC combined with Tai Chi in comparison with WM. Another study evaluated AC combined with psychotherapy. Eleven studies were divided into three groups, while others were based on two groups. Twenty-eight explored the effect of AC alone in comparison with WM or UC.

Assessment Results of Risk of Bias and Reporting Quality Based on STRICTA

The quality assessment results are given in Supplementary Appendix 3. Seven studies (7, 11.86%) had low risk of bias arising from the randomization process (Domain 1). Nine studies (9, 15.25%) were evaluated as “low” for the risk of bias due to deviations from the intended interventions (Domain 2). In terms of overall risk of bias, 26 studies were ranked as “high”, 27 as “some concern”, and 6 as “low”.

The assessment results of reporting quality showed that all of the studies (100%) reported the style of acupuncture (Item 1a), and 38 RCTs (64.4%) demonstrated the needle type (Item 2g). There were 39 (66.1%) studies that presented the “response sought” (Item 2d). Only 18 (30.5%) reported the “number of needle insertions per subject per session” (Item 1c). None illustrated the “setting and context of treatment, including instructions to practitioners, and information and explanations to patients” (Item 4b) and “rationale for the control or comparator” (Item 6a). The details of the STRICTA assessment for each study are listed in Supplementary Appendix 4.

Network meta-analysis

The network evidence plots were presented in Figure 1. The main results of the NMA for depression. Fifty studies involving 4,547 patients reported changes in depression scores in the HAMD scale, 21 for HAMD-17, 1 for HAMD-21, 28 for HAMD-24. The scores of different versions of HAMD were standardized. One study comparing the treatment of acupuncture combined with psychotherapy was excluded due to its failure to directly or indirectly connect with other interventions.⁷⁸ Six three-armed-based studies and 43 two-arm based studies were included. A total of 104 arms were included, 41 arms for WM, 28 for AC, 11 for AC with WM, 7 for UC, 4 for AC with TCM, 4 for AM with WM, 2 for AM with TCM with WM, 2 for TCM, 1 arm for AC with RTMS, 1 for AC with Tai Chi, 1 arm for AM with TCM, 1 for AC with CT, 1 for AM. Among these studies, the largest number of studies were those comparing AC with WM (n=20). The following comparison type of studies were AC with WM versus WM (11, 22%) and AC versus UC (7, 14%). The main results of the NMA for depression are displayed in Table 2.

On the whole, interventions administering combined therapies were more effective in comparison with those using single therapy. The results of NMA showed that compared with WM alone, the administration of AC with RTMS, AC with TCM and WM, AC with TCM, TCM alone, AC with WM, and AC alone were superior in alleviating depression symptoms (MD, -8.75 95% CI: -16.75, -0.76; MD, -5.83, 95% CI: -11.22, -0.42; MD, -6.68, 95% CI: -10.16, -3.18; MD, -5.43, 95% CI: -10.73, -0.13; MD, -4.34, 95% CI: -6.64, -2.05; MD, -3.49, 95% CI: -5.19, -1.79, respectively). Compared to UC, AC

alone or in combination with other interventions could lower HAMD scores (*AC with RTMS*: MD, -14.43, 95% CI: -22.81, -6.08; *AC with TCM with WM*: MD, -11.51, 95% CI: -17.85, -5.17; *AC with TCM*: MD, -12.35, 95% CI: -17.11, -7.62; *AC with Tai Chi*: MD, -10.19, 95% CI: -18.59, -1.83; *AC with CT*: MD, -9.64, 95% CI: -18.10, -1.21; *TCM*: MD, -11.11, 95% CI: -17.28, -4.99; *AM*: MD, -8.02, 95% CI: -15.73, -0.34; *AC with WM*: MD, -10.02, 95% CI: -14.04, -6.04; *AM with WM*: MD, -8.03, 95% CI: -13.17, -2.94; *AC*: MD, -9.17, 95% CI: -12.17, -6.22; *WM*: MD, -5.68, 95% CI: -9.04, -2.33). However, no significant difference was found among AC, WM, and TCM with AC plus any other treatment (AC with RTMS, AC with TCM, AC with TCM with WM, AC with Tai Chi, AC with WM, AC with CT, AM and AM with WM).

Examination of consistency with the node-splitting analysis approach indicated that there was no significant inconsistency ($P > 0.05$) (Supplementary Appendix 5). The analysis of heterogeneity showed the I^2 of direct comparison was 97.66%, and the global I^2 was 97.38%. The I^2 of each comparison group was seen in Supplementary Appendix 6.

Table 3 presented the values of SUCRA, the hierarchy of thirteen treatments. According to SUCRA, AC plus RTMS had the highest probability in improving depressive symptoms with probability of 49.43%. The next were AC with TCM with WM (10.99%), AC with TCM (10.62%), AC with Tai Chi (10.30%), which were very close. The probability of AC with CT and TCM were 8.10% and 7.48% respectively. The figure of SUCRA was attached in Supplementary Appendix 7.

Pairwise Meta-Analysis

Ten studies^{56,58,64 40,45,54,55,62 29,36} used the Modified Edinburgh-Scandinavian Stroke Scale (MESSS) to measure neurological impairment. The result of pairwise meta-analysis showed that AC was significantly associated with better neurological function improvement than UC or WM (MD, -8.45, 95% CI: -12.85, -4.05; MD, -5.11, 95% CI: -6.50, -3.73, respectively). Similarly, AC with WM and AC with TCM was superior to WM (MD, -5.07, 95% CI: -8.41, -1.73; MD, -5.32, 95% CI: -8.89, -1.66, respectively) (Supplementary Appendix 8).

The confidence assessment result of NMA

The CINeMA system (<https://cinema.ispm.unibe.ch/>) was used to classify the confidence in the results of NMA, which six domains was evaluated, including: (a) within- study bias, (b) reporting bias, (c) indirectness, (d) imprecision, (e) heterogeneity, and (f) incoherence. One comparison (AC versus AC with TCM) was ranked “high”; eight were “moderate”; eight were “low”. The details are presented in Table 4.

Discussion

This network meta-analysis found that compared with WM, AC alone or in combination with RTMS, TCM, WM, or TCM with WM seemed to be more effective in improving depression symptoms. When compared with UC, AC alone or combined with any other therapy (including AC with RTMS, AC with TCM, AC with TCM and WM, AC with Tai Chi, AC with WM, AC with CT, AM, and AM with WM) was superior. However, we did not find any significant difference between any comparisons of these interventions. Additionally, the pairwise meta-analysis showed that combined therapies of AC with WM, AC with TCM, and AC alone were significantly associated with better neurological function improvement in contrast to UC or WM.

The result of SUCRA showed that AC with RTMS had the highest probability of being the most effective therapy to alleviate depressive symptoms. It is reported that RTMS, as a non-invasive approach, could induce excitability changes in the motor cortex via a wire coil generating a magnetic field that passes through the scalp. However, the physiological mechanism of RTMS after-effects is yet to be clear.⁸⁹ The updated evidence-based guidelines by Lefaucheur et al. demonstrated that RTMS has a significant effect in several psychiatric diseases. It is also highly recommended (Level A) for major depression,⁹⁰ which was consistent with our findings. Nonetheless, it needs to be interpreted with caution because there was only one eligible study included which compared AC alone and AC with RTMS. More relevant research is needed to confirm the true function and safety of RTMS for patients with PSD.

In this study, various combined therapies were evaluated, including AC with RTMS, AM with TCM, AC with Tai Chi, AC with TCM with WM, AC with TCM, AC with CT, AC with WM, AM with WM. We first explored the difference in effectiveness for PSD between these therapies using the network meta-analysis approach, which synthesized the direct comparison evidence and indirect comparison evidence. However, some comparisons contained only a few eligible studies, such as those on AC with RTMS versus AC, AC with CT versus WM, and AC with Tai Chi versus WM. Therefore, it is suggested that future research could focus on the effectiveness of these different comparisons for patients with PSD. We will also conduct an update if further studies are published.

One published network meta-analysis by Hang et al. compared the effect of different acupuncture approaches for specific parts in treating patients with PSD.⁹¹ Twelve acupuncture therapies were included in their study, and they found that scalp acupuncture plus conventional acupuncture was the most effective method based on the ranking probability. For this study, we put more focus on the effectiveness of acupuncture combined with other therapies for PSD. Due to the complexity in the nature of acupuncture treatments and their procedure, we were not able to conduct a relevant subgroup analysis. Therefore, we could only differentiate the types of acupuncture by their main characteristics,

which induced huge heterogeneity among acupuncture treatments. The details were presented in Supplementary Appendix 9. The most frequently used acupoints included Bai-Hui, Shen-Ting, and Nei-Guan.

This is the first review to compare the effectiveness of acupuncture with other therapies for PSD using network meta-analysis, which may provide novel and useful guidance for clinicians and readers. However, there are still several limitations. Firstly, although we conducted a systematic search for eligible studies, only Chinese studies were eligible and subsequently included. Secondly, the newest assessment tool of ROB 2 was used to evaluate the quality of included RCTs, and the assessment result indicated that the overall quality of RCTs was not high. Therefore, more high-quality RCTs are needed.

Conclusion

In our review, we provide an overview of the current research evidence on the effectiveness of AC alone or in combination with other therapies for the treatment of PSD. Twelve various treatments are included. Among them, there are five therapies of AC plus non-pharmacotherapy (RTMS, Tai Chi, CT, psychotherapy, moxibustion), while AC plus pharmacotherapy treatments also include AC with WM and AC with TCM. The results of NMA indicate that combined therapies, including AC with RTMS, AC with TCM, AC with TCM with WM, AC with WM, and AC alone may be more effective in alleviating depression symptoms as compared with WM. With the highest probability, AC with RTMS seems to be the most effective with the highest probability in treating PSD. Nonetheless, more high-quality studies are needed to provide sufficient evidence.

Declarations

Acknowledgements

Not applicable.

Ethics approval and consent to participate

Findings from the study will be disseminated through a peer-reviewed article.

Consent for publication

Not applicable.

Conflict of interest

None

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No

Authors' contributions

Linda Zhong and ZB were responsible for the conception and design of this study. LWC and LY performed the search and evaluated studies for inclusion. LWC and JC extracted data from selected RCTs. JC and SL assessed the quality of selected RCTs. CSY and BFL Ng assessed the quality of certainty of the evidence. HJL and ECL Yu performed data analysis. ZB and AYL reviewed the work. WCL and HJL drafted the paper. All authors critically revised and approved the final paper.

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Tables

Table 1. Description of included studies.

Study	Age	Arm	Sample size	Interventions			Follow up
	(Treatment /Control)			(Treatment /Control)	Group 1	Group 2	Group 3
Xin TONG 2012 ⁵⁸	58.5±8.4	2	30/30	AC+WM	WM	-	8w
Yanxiang LIU 2010 ⁴⁸	male 63.8±10.0/female 59.8±8.7	2	40/40	AC	UC	-	4w
Siqi WU 2020 ⁶⁴	60.1±10.7/58.3±11.2	2	30/30	AC+WM	WM	-	8w
Xiaoling Wu 2009 ⁶⁵	56±9.63	2	38/36	AC+WM	WM	-	40d
Lijun YAO 2017 ²⁰	65±11/63±12	2	30/30	AC+CT	WM	-	4w
Lei JIANG 2011 ⁴²	58.93±3.58/59.67±3.43	2	30/30	AM+WM	WM	-	6w
Peiyang SUN 2013 ⁵⁶	58±8/59±9	2	30/30	AC	WM	-	4w
Peiyang SUN 2015 ⁵⁵	59±7/58±8	2	33/30	AC	WM	-	4w
Xiao CHANG 2012 ²⁸	56.8/55.9	2	32/30	AC+TCM	WM	-	6w
Zhongjin ZHANG 2011 ⁸²	56.7±12.1/55.8±9.7	2	40/38	AC	UC	-	3w
Guibo ZHANG 2010 ⁸¹	65±5/66±5	2	30/30	AC+WM	WM	-	4w
Ru ZHANG 2011 ⁷¹	50.1-71.2/49.9-68.7	2	39/39	AC+RTMS	AC	-	4w
Lin ZHANG 2017 ⁷⁰	59±9/58±8	2	30/30	AC	WM	-	8w
Gang XU 2014 ⁶⁷	59.4±7.6/60.8±6.9	2	20/18	AC+WM	WM	-	6w
Shuqing DAI 2010 ³³	64.36±5.46/65.32±5.09	2	24/24	AC+TCM	WM	-	4w
Jian ZHU 2012 ⁸⁵	NR	2	20/20	AM+WM	WM	-	6w
Yonggang ZHU 2012 ⁷⁴	67.3±4.5/68.9±6.1	2	21/21	AC	WM	-	8w
Li LI 2011 ⁴⁵	65±13/63±12	2	20/19	AC	WM	-	4w
Hongjie LI 2011 ⁷⁹	29-60/32-63	2	23/20	AC	WM	-	6w
Ziling LIN 2010 ⁴⁶	52-84	2	20/20	AC	UC	-	4w
Yun WU 2011 ⁶²	62±11/64±11	2	36/36	AC	WM	-	8w
Haifeng JIAO 2012 ⁴⁴	43-78,63.3/45-76	2	17/16	AC+WM	WM	-	4w

Laiqun WANG 2010 ⁵⁹	40-70/40-68	2	30/30	AC+TCM	WM	-	8w
Changchang YAN 2018 ⁸⁸	62.1±13.5/62.3±13.6	2	45/45	AM+WM	WM	-	4w
Yuan CHENG 2007 ³¹	72±8/69±7/69±6	3	19/20/21	special AC	AC	UC	6w
Yuan CHENG 2008 ³²	61.7±8.1/63.2±7.9/62.9±7.3	3	20/20/20	special AC	AC	UC	6w
Rongrong NIE 2011 ⁵⁰	64.2±9.85/63.1±9.55	2	33/30	AC	WM	-	4w
Zhiwei SU 2010 ⁵³	55.8±6.1/54.2±6.5	2	30/30	AC	WM	-	30d
Guomin JIANG 2007 ⁷⁸	60.5	2	25/25	AC+Psych	Psych	-	4w
Zhenya JIANG 2011 ⁴³	60.32±3.26/61.18±2.94	2	33/33	AC+WM	WM	-	4w
Xiaobing ZHAO 2012 ⁸⁷	56±13.9/57±12.8	2	45/45	AC+WM	WM	-	20d
Aisong GUO 2011 ³⁶	40-65	3	32/31/32	AC	WM	AC+WM	6w
Aiwen CHEN 2017 ²⁹	57±11/58±11	2	30/30	AC	UC	-	4w
Lujie CHEN 2018 ³⁰	62.37±6.28/60.21±5.78	2	30/30	AC	WM	-	4w
Ruhua SUI 2009 ⁵⁴	62.93±7.25	2	36/36	AC	UC	-	4w
Wa GAO 2017 ³⁵	58.12±3.27	2	33/33	AC	AC+Cupping+Psych	-	10d
Shile HUANG 2014 ⁴¹	61.43±9.91/62.10±8.11/62.77±9.32	3	30/30/30	AC	WM	AC+WM	6w
Long HUANG 2011 ⁴⁰	65.22±8.69/65.39±11.26/63.25±10.28	3	30/30/30	AC+TCM	TCM	WM	60d
Aibing ZHANG 2009 ⁸⁰	63±11total	2	40/35	AM+TCM	WM	-	30d
Xiaojing DUAN 2012 ⁷⁷	58.80±9.60/60.22±8.12	2	30/30	AC	WM	-	8w
Fengkui ZHU 2010 ⁷⁵	NR	2	30/30	AC+WM	WM	-	4w
Yahui WANG 2016 ⁶⁰	66±6/65±7/66±8	3	30/30/30	AC	UC	-	4w
Wenge SUN 2012 ⁵⁷	54.7±2.9/54.2±3.1	2	50/40	AC+TCM	UC	-	3w
Ruiyou GUO	65.8±9.61/67.6±12.43/64.5±12.07	3	40/40/40	AC	WM	UC	6w

2009 ³⁷								
Sukun LIU 2006 ⁴⁷	60.0±9.8/59.6±8.9	2	101/145	AC	WM	-	6w	
Yafen ZHOU 2014 ⁸⁴	64±15/65±11	2	75/72	AC+WM	WM	-	8w	
Huiyuan PENG 2011 ⁵¹	64.6±11.3/73.7±11.8	2	58/59	AC	WM	-	4w	
Wei ZHANG 2011 ⁷²	28-80/30-83/44-85	3	52/49/49	AC+TCM	AC	TCM	45d	
Yaqun WANG 2020 ⁶¹	70.44±5.62/70.53±6.44	2	52/51	AC+TCM+WM	WM	-	60d	
Rongrong NIE 2013 ⁴⁹	64±10/63±10/64±10	3	42/41/40	AM+WM	AM	WM	4w	
Hong ZHAO 2003 ⁸⁶	NR	2	50/50	AC	WM	-	8w	
Wei XIAO 2009 ⁶⁶	53±6/51±8	2	40/40	AC+WM	WM	-	30d	
Huiqin DING 2020 ³⁴	54.63±3.51/54.27±3.43	2	61/61	AC+WM	WM	-	4w	
Jiaping WU 2010 ⁶³	56.2±9.2/55.7±9.4	2	150/150	AC	WM	-	60d	
Shuchang SONG 2014 ⁵²	57.25±11.32/57.46±11.57	2	100/100	AC	WM	-	8w	
L. ZHANG 2018 ⁷⁶	63.7±6.8/62.4±7.6	2	45/45	AC+ Tai Chi	WM	-	30d	
Zhien ZHOU 2020 ⁷³	64.52±1.10/65.16±12.60	2	140/85	AC+TCM+WM	WM	-	12d	
Jun HE 2007 ³⁹	53.16±11.20/53.86±12.34	2	180/76	AC	WM	-	30d	
Xijun HE 2005 ³⁸	41-72/39-71	2	86/86	AC	WM	-	8w	

NOTE: AC, Acupuncture; AM, Acupuncture and moxibustion; TCM, Traditional Chinese medicine; WM, Western medicine; UC, Usual care; RTMS, Repetitive transcranial magnetic stimulation; CT, Cognitive therapy.

Table 2. The result of NMA for depression.

AC+RTMS											
-2.93 (-12.58, 6.7)	AC+TCM+WM										
-2.08 (-10.73, 6.59)	0.85 (-5.55, 7.28)	AC+TCM									
-4.25 (-15.38, 6.84)	-1.33 (-10.71, 8.09)	-2.17 (-10.66, 6.31)	AC+Tai Chi								
-4.79 (-15.94, 6.36)	-1.86 (-11.3, 7.59)	-2.72 (-11.22, 5.77)	-0.54 (-11.51, 10.38)	AC+CT							
-3.31 (-12.82, 6.17)	-0.39 (-7.94, 7.17)	-1.25 (-6.49, 3.99)	0.93 (-8.42, 10.33)	1.49 (-7.92, 10.81)	TCM						
-6.4 (-16.96, 4.19)	-3.48 (-12.24, 5.34)	-4.33 (-12.07, 3.47)	-2.15 (-8.26, 8.26)	-1.62 (-8.77, 8.77)	-3.07 (-11.78, 5.67)	AM					
-4.4 (-12.71, 3.86)	-1.48 (-7.32, 4.39)	-2.34 (-6.48, 1.84)	-0.16 (-8.19, 7.9)	0.38 (-7.68, 8.46)	-1.08 (-6.85, 4.67)	1.99 (-5.33, 9.28)	AC+WM				
-6.41 (-15.29, 2.49)	-3.47 (-10.09, 3.19)	-4.33 (-9.52, 0.89)	-2.16 (-10.77, 6.47)	-1.61 (-10.26, 7.01)	-3.07 (-9.66, 3.49)	0 (-6.93, 6.92)	-1.99 (-6.48, 2.5)	AM+WM			
-5.26 (-13.07, 2.56)	-2.33 (-7.98, 3.36)	-3.19 (-6.92, 0.58)	-1.01 (-8.92, 6.88)	-0.47 (-8.39, 7.44)	-1.93 (-7.35, 3.45)	1.14 (-6.01, 8.27)	-0.85 (-3.6, 1.87)	1.14 (-3.08, 5.36)	AC		
-8.75 (-16.75, -0.76)	-5.83 (-11.22, -0.42)	-6.68 (-10.16, -3.18)	-4.5 (-12.23, 3.2)	-3.96 (-11.7, 3.77)	-5.43 (-10.73, -0.13)	-2.35 (-9.3, 4.58)	-4.34 (-6.64, -2.05)	-2.36 (-6.21, 1.52)	-3.49 (-5.19, -1.79)	WM	
-14.43 (-22.81, -6.08)	-11.51 (-17.85, -5.17)	-12.35 (-17.11, -7.62)	-10.19 (-18.59, -1.83)	-9.64 (-18.1, -1.21)	-11.11 (-17.28, -4.99)	-8.02 (-15.73, -0.34)	-10.02 (-14.04, -6.04)	-8.03 (-13.17, -2.94)	-9.17 (-12.17, -6.22)	-5.68 (-9.04, -2.33)	UC

NOTE: The estimates of mean difference of treatments in the columns versus rows presented in the lower diagonal elements (while those of the row treatments vs. column treatments are presented in the upper diagonal elements). The MD of significant difference was presented in bold font. AC, Acupuncture; AM, Acupuncture and moxibustion; TCM, Traditional Chinese medicine; WM, Western medicine; UC, Usual care; RTMS, Repetitive transcranial magnetic stimulation; CT, Cognitive therapy.

Table 3. Ranking probability of different interventions.

	Treatments	Cumulative Probability
1	AC+RTMS	49.43%
2	AC+TCM+WM	10.99%
3	AC+TCM	10.62%
4	AC+Tai Chi	10.30%
5	AC+CT	8.10%
6	TCM	7.48%
7	AM	2.53%
8	AC+WM	0.37%
9	AM+WM	0.16%
10	AC	0.01%
11	WM	0.00%
12	UC	0.00%

NOTE: AC, Acupuncture; AM, Acupuncture and moxibustion; TCM, Traditional Chinese medicine; WM, Western medicine; UC, Usual care; RTMS, Repetitive transcranial magnetic stimulation; CT, Cognitive therapy.

Table 4. The GRADE table for depression scores.

Comparison	Number of studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
AC vs AC with RTMS	1	Major concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Low
AC vs AC with TCM	1	No concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	High
AC vs AC with WM	2	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
AC vs TCM	1	No concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Moderate
AC vs UC	7	Some concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Moderate
AC vs WM	20	Some concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Moderate
AC with CT vs WM	1	Some concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Moderate
AC with TCM vs TCM	2	Major concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Low
AC with TCM vs WM	4	Major concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Low
AC with TCM with WM vs WM	2	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
AC with Tai Chi vs WM	1	Major concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Low
AC with WM vs WM	11	Some concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	Moderate
AM vs AM with WM	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
AM vs WM	1	Some concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Moderate
AM with WM vs WM	4	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
TCM vs WM	1	Major concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Low
UC vs WM	1	Some concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Moderate

NOTE: AC, Acupuncture; AM, Acupuncture and moxibustion; TCM, Traditional Chinese medicine; WM, Western medicine; UC, Usual care; RTMS, Repetitive transcranial magnetic stimulation; CT, Cognitive therapy.

Figures

Figure 1

Network plot. NOTE: AC, Acupuncture; AM, Acupuncture and moxibustion; TCM, Traditional Chinese medicine; WM, Western medicine; UC, Usual care; RTMS, Repetitive transcranial magnetic stimulation; CT, Cognitive therapy.

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