Systematic Review and Meta-Analysis

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# Comparison between acupuncture and antidepressant therapy for the treatment of poststroke depression

## Systematic review and meta-analysis

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**Abstract**

**Background:** In this paper, a systematic review and meta-analysis of published randomized controlled trials (RCTs) was conducted to compare the efficacies of acupuncture and antidepressant therapy for the treatment of poststroke depression (PSD).

**Methods:** The research team searched RCTs published on PubMed; Medline; Cochrane library; Chinese National Knowledge Infrastructure (CNKI); Wanfang; Embase; Scopus, and Sinomed from their respective establishments to January 2019. We evaluated the Hamilton Depression Rating Scale (HAMD) scores, Treatment Emergent Symptom Scale (TESS) scores, National Institute of Health Stroke Scale (NIHSS) scores, and total clinical efficacy using fixed effects models.

**Results:** Fourteen RCTs, representing a total of 1124 patients, were studied. Results showed that acupuncture was more effective in improving HAMD scores at 3 weeks after administration (mean difference [MD] = −1.17, 95%CI = −2.18 to −0.16), at 4 weeks (MD = −4.44, 95% CI = −5.64 to −3.23), at 6 weeks (MD = −1.02, 95% CI = −1.68 to −0.36), and at 8 weeks (MD = −4.33, 95% CI = −4.96 to −3.70). Similarly, acupuncture more dramatically decreased NIHSS scores (MD = −2.31, 95% CI = −2.53 to −2.09), and TESS scores (MD = −4.70, 95% CI = −4.93 to −4.48) than conventional Western medicinal therapy. Further, the total clinical efficacy in the acupuncture group was significantly higher than in the antidepressants group (risk ratio [RR] = 1.15, 95% CI = 1.08–1.21).

**Conclusions:** The results of this study suggest that acupuncture not only can reduce the severity of PSD, but also has significant effects on decreasing the appearance of other adverse events.

**Abbreviations:** 5-HT = serotonin, CCMD = Chinese classification and diagnostic criteria of mental disorders, CNKI = Chinese National Knowledge Infrastructure, DSM = diagnostic and mtatistical manual of mental disorders, HAMD = Hamilton Depression Rating Scale, MD = mean difference, NIHSS = National Institute of Health Stroke Scale, PSD = poststroke depression, RCTs = randomized controlled trials, RR = risk ratio, TCM = traditional Chinese medicine, TESS = Treatment Emergent Symptom Scale.

**Keywords:** acupuncture, antidepressants, meta-analysis, poststroke depression

## 1. Introduction

Poststroke depression (PSD),which is mainly characterized by emotional instability, decreased interest, anxiety, and even suicidal tendencies, is common following stroke.[1] According to relevant literature, the incidence of PSD is 33% in the acute stage and 34% in the long term after stroke.[2] Studies have shown that PSD not only affects the recovery of stroke, but also causes disability and low standard of living.[3,4] Currently, PSD is commonly treated with antidepressants.[5] However, patient staking antidepressants may experience adverse reactions, such as headache, nausea, agitation, diminished mental acuity, memory loss, weight gain, and

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metabolic abnormalities.[6,7] Studies also showing that antidepressants can damage the nervous system, liver, and heart of patients, as well as causing patients to experience life-threatening side effects through suicide.[8–10] Additionally, antidepressants have also been found to be unresponsive in some patients.[2] Therefore, it is necessary to seek safe and effective treatment, with few adverse reactions, to replace antidepressants.

Presently, acupuncture is becoming more widely used in the treatment of PSD. At present, the pathogenesis of PSD is mainly considered as "primary endogenous theory" and "reactive mechanism theory".[11] The former thought that after stroke, norepinephrine neurons and 5-hydroxytryptaminergic neurons were damaged, which significantly reduced the levels of these 2 neurotransmitters, resulting in the disorder of brain regulatory function and depression. Acupuncture at corresponding acupoints can improve cerebral blood flow or promote the absorption of intracerebral hematoma, repair noradrenergic neurons and 5-hydroxytryptamine neurons, awaken brain nerve cells and gradually restore their functions, and also promote the release of norepinephrine and 5-hydroxytryptamine.[12] Zhang et al (2010, 2012) found that acupuncture was more effective than antidepressants in treating PSD, but did not standardize the criteria of PSD.[4,13] Thus, the current meta-analysis examined PSD, strictly in accordance with corresponding diagnostic standards, for determining the efficacy and safety evaluation results of acupuncture treatment, and comparing these results with antidepressant treatments.

## 2. Methods

### 2.1. Patient and public involvement

There was no patient and public involvement in present meta-analysis. An ethical approval is not necessary for a meta-analysis.

### 2.2. Eligibility criteria

After retrieval in the initial search, references were subsequently checked for eligibility. Candidate studies were selected that metal of the following criteria:

1. strokes were diagnosed according to the *Diagnostic Points for Various Cerebrovascular Diseases* adopted by the Fourth National Congress of Cerebrovascular Diseases of the Chinese Medical Association in 1995,and confirmed by computed tomography or magnetic resonance imaging;
2. depression was diagnosed in accordance with the Chinese classification of mental disease (CCMD-2,CCMD-3) or diagnostic and statistical manual of mental disorders (DSM-III, DSM-IV, DSM-V);
3. comparison of acupuncture and antidepressants;
4. no limit imposed to the acupuncture process, including, but not limited to, different shapes, stimulation methods, acupoint selection, needle retention time, or parameter settings, such as instrument model, stimulation intensity, and / or frequency (in cases of electro-acupuncture; and
5. patient depression occurs after the stroke.

Exclusion criteria were as follows:

1. studies with efficacy and safety data were unavailable;
2. b) no randomized controlled trials (RCTs); and
3. multiple articles that analyzed the same trials.

Further, the above process was completed by 2 reviewers (Weiyan Cheng and Weinan Yang). A flow diagram of the literature selection is shown in Figure 1.

### 2.3. Search strategy

A sensitive literature search was conducted through PubMed; Medline; Cochrane library; Chinese National Knowledge Infrastructure (CNKI); Wanfang; Embase; Scopus, and Sinomed from their respective establishments to January 2021. The following MeSH terms were used: *stroke, depression, acupuncture, zhenci, zhenjiu and zhenfa*. Terms, concluded in the Table 1, were changed depending on the predominant language of the database. For example, the literature search conditions for the CNKI and Wanfang databases were as follows: *zhenciliaofa, zhenci, zhenjiu, zhenfa, yiyu*, and *zuzhong*. The literature search conditions applied to Medline were as follows: (MH "Acupuncture Therapy+") AND (MH "Stroke+") AND (MH "Depression").

### 2.4. Data extraction

Extraction of data was conducted by 2 examiners (Lin-cheng Zhang and Qi-gu Yao) in accordance with the established protocol. Disagreements were discussed and decided upon by a third examiner (Wei-nan Yang). The accuracy of the data were

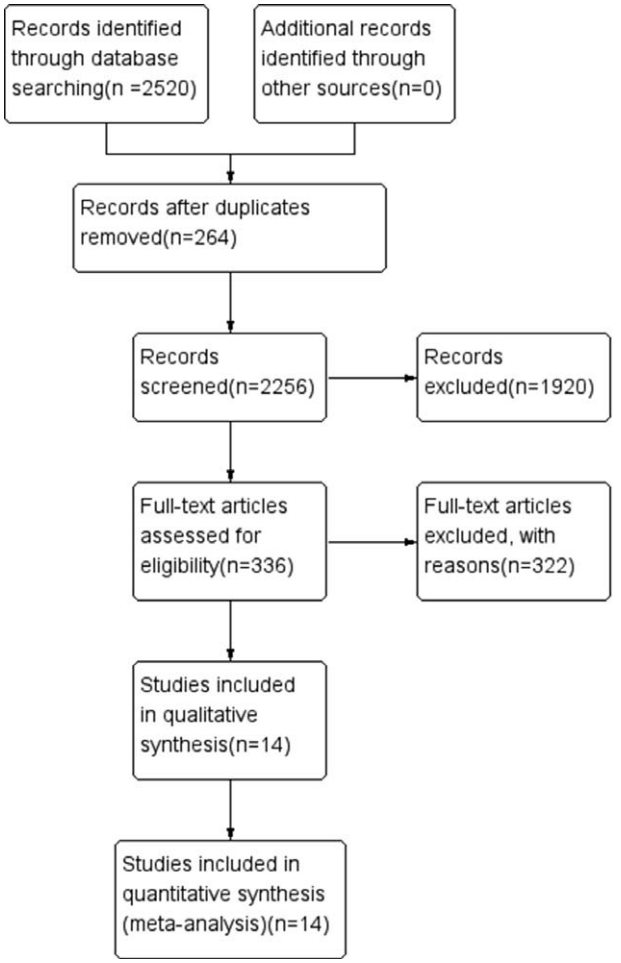


**Figure 1.** Flow chart of literature election.

**Table 1**

**Search strategy.**

| Data source | Search terms |
|---|---|
| PubMed | #1 "Acupuncture" Therapy[Title/Abstract] OR "zhenjiu" [Title/ Abstract] OR "zhenfa"[Title/Abstract] #2 Stroke [Title/Abstract] #3 Depression [Title/Abstract] #4 #1 AND #2 AND #3 |
| Chinese National Knowledge Infrastructure | #1 Zhenciliaofa[MeSH Terms] OR Zhenjiu[MeSH Terms] OR Zhenci [MeSH Terms] OR Zhenfa[MeSH Terms] #2 Zuzhong [MeSH Terms] #3 Yiyu [MeSH Terms] #4 #1 AND #2 AND #3 |
| Wanfang | #1 Zhenciliaofa[MeSH Terms] OR Zhenjiu[MeSH Terms] OR Zhenci [MeSH Terms] OR Zhenfa[MeSH Terms] #2 Zuzhong [MeSH Terms] #3 Yiyu [MeSH Terms] #4 #1 AND #2 AND #3 |
| Sinomed | #1 Zhenciliaofa[MeSH Terms] #2 Zuzhong [MeSH Terms] #3 Yiyu [MeSH Terms] #4 #1 AND #2 AND #3 |
| Scopus | #1 TITLE-ABS-KEY ( acupuncture ) OR TITLE-ABS-KEY ( zhenjiu ) OR TITLE-ABS-KEY ( zhenfa ) OR TITLE-ABS-KEY ( zhenci ) #2 TITLE-ABS-KEY(Stroke) #3 TITLE-ABS-KEY(Depression) #4 #1 AND #2 AND #3 |
| Embase | #1 Acupuncture: ti,ab,kw OR Zhenci: ti,ab,kw OR Zhenjiu:ti,ab, kw OR Zhenfa:ti,ab,kw #2 'cerebrovascular accident':ti, ab, kw #3 Depression: ti, ab, kw #4 #1 AND #2 AND #3 |
| Medline | #1(MH "Acupuncture Therapy+") #2(MH "Stroke+") #3(MH "Depression") #4 #1 AND #2 AND #3 |
| Cochrane library | #1 (Acupuncture Therapy): ti, ab, kw(Word variations have been searched) #2 (Stroke):ti, ab, kw(Word variations have been searched) #3 "Depression": ti, ab, kw(Word variations have been searched) #4 #1 AND #2 AND #3 |

then reviewed by 2 other examiners (Yu-yan Zhang and Lin-cheng Zhang). Extracted data included study design, sample size, intervention, diagnostic criteria of PSD, baseline Hamilton Depression Rating Scale (HAMD) score, publication period, treatment duration, number of acupuncture sessions, study country, HAMD score following treatment, total clinical efficacy, National Institute of Health Stroke Scale (NIHSS) score, and Treatment Emergent Symptom Scale (TESS) score.

### 2.5. Assessment of method logical quality for included studies

Two examiners (Weiyan Chen and Lan He) used the Cochrane Collaboration stool[14] to evaluate the risk of bias of the included trials based on the following 7 aspects: random sequence generation (selection bias); allocation concealment (selection bias); blinding of participants and personnel (performance bias); blinding of outcome assessment (detection bias); incomplete outcome data (attrition bias); selective reporting (reporting bias); as well as other forms of bias.

Two examiners (Lin-cheng Zhang and Weinan Yang) used the Jadad score form to assess the methodological quality of included trials, which contained: randomization; random packet sequence generation; double blinding (participant and researcher); allocation concealment; the describing of the withdrawal, and loss of follow-up. If any of the above points were met, the study was awarded 1 point, for a maximum score of 5 points. A score greater than or equal to 3 was classified as high quality.

### 2.6. Statistical analysis

To compare the efficacy of acupuncture and antidepressants in PSD, were respectively used the mean difference (MD), risk ratio (RR), and 95%CI to evaluate HAMD scores, NIHSS scores, TESS scores, and total clinical efficacy. The reduction rate of the HAMD scale was used to calculate clinical efficacy. Specifically, total clinical efficacy = (total HAMD score before treatment-total HAMD score after treatment)/total HAMD score before treatment × 100%. Studies were considered to be clinically effective if their total clinical efficacies ≥25%. Higgins $I^2$ tests were performed to estimate heterogeneity among studies. Heterogeneity was classified into 4 levels: no heterogeneity ($0\% \leq I^2 \leq 25\%$), low heterogeneity ($25\% < I^2 \leq 50\%$), medium heterogeneity($50\% < I^2 \leq 75\%$), and high heterogeneity ($I^2 > 75\%$). Based on the heterogeneity of the included studies, the combined effect of MD and RR were calculated by a random-effect model or a fixed-effect model to draw forest plots. For indicators with higher heterogeneity, sensitivity analysis was carried out to determine the origin of heterogeneity. Literature publication bias was performed using a funnel plot, Begg rank correlation test, and Egger linear regression test (with $P < .05$ considered to be statistically significant) for visual and asymmetry tests. STATA[15] version 12.0 and Review Manager Version5.3[16] were utilized to analyze data.

### 2.7. Data availability statement

The dataset analyzed in this study is not publicly available because of restricted access but further information about the dataset is available from the corresponding author on reasonable request.

## 3. Results

### 3.1. Description of included studies

Details of the literature search and screening process are presented in Figure 1. After sufficient screening, 14 studies met criteria and were included in the final analysis.[12,17–29] The main features of the included trials are summarized in Table 2. A total of 1124 patients were available from 14 studies, with a median sample size of 67.5 cases. Two studies allowed the calculation of pooled MD for HAMD scores at week 3 of treatment. Among 3 studies, obtained MD data allowed the calculation of pooled MD for HAMD scores at week 4 of treatment. HAMD scores at week 6 of were obtained from 6 studies, and pooled MD was calculated. Four studies allowed the calculation of pooled MD for HAMD scores at week 8 of treatment. Two studies allowed the calculation of pooled MD for NIHSS scores. Three studies allowed the calculation of a pooled MD for TESS scores. The total clinical efficacy after treatment was obtained from 12 studies, and pooled RR was calculated.

### 3.2. Assessment of methodological quality for included studies

Using the Cochrane Collaboration tool, the risk of bias of the included trials was determined, as shown in Figure 2. All studies were randomized, but 2[19,27] did not address the method of

**Table 2**

**Main characteristic of included randomized controlled trials.**

| Study | Sample size | Diagnostic criteria of PSD | Baseline HAMD | Intervention | Control | No. of EA sessions | Treatment duration | Main outcome | Jadad score |
|---|---|---|---|---|---|---|---|---|---|
| Song et al China 2015[25] | A:30 C:30 | DPVCVD/CCMD/CT/MRI | A:22.65±4.83 C:22.37±4.46 | DU 20 and DU24; 30min; once a day | FLX 20 mg/d | 56 | 8 wks | HAMD score, Total efficiency, TESS score | 3 |
| Guo et al China 2011[19] | A: 32 C: 31 | DPVCD /CCCD/CCMD/HAMD/CT/MRI | A:21.74±5. 50 C:21.08±5.72 | DU 20, DU24, EX-HN3, LI4, EX-HN1 and LR3; 30 min, once a day | FLX 20 mg/d | 30 | 4 wks | HAMD score, SDS score | 3 |
| Sang et al China 2018[7] | A:30 C:30 | CAISIDTG/CCMD/CT/MRI/HAMD | A: 28. 23±5. 56 C: 28. 57±6. 09 | DU 20, EX-HN1, EX-HN3, PC6, HT7, LI4,LR3, SP6; 40 min, once a day | PH 20 mg/day | 28 | 4 wks | HAMD score, Total efficiency | 3 |
| Dong et al China 2017[27] | A:50 C:50 | DPVCVD/CCMD/CT/MRI | A:22.65±4.83 C: 24. 36±4. 10 | DU 20, EX-HN1, EX-HN3, PC6, HT7, LI4, LR3, SP6; 30 min, once a day | FH 20 mg/d | 30 | 30 days | HAMD score, Total efficiency, SDS score | 3 |
| Xu et al China 2015[26] | A:40 C:40 | DPVCD /CCMD/CT/MRI/HAMD | A:30.65±3.98 C:30.96±4.25 | DU 20, EX-HN1, EX-HN3, PC6, HT7, KI3, BL15, LR3, SP6; 30 min, once a day | FLX 20 mg/d | 42 | 7 wks | HAMD score, Total efficiency | 3 |
| Huang et al China 2014[23] | A:31 C:31 | DPVCD CCMD/CT/MRI | A:19.00±2.55 C:19.10±2.46 | DU 20, DU18, GB9; 30 min, 2-100 Hz, once a day | FH 20 mg/day | 30 | 6 wks | HAMD score, Total efficiency | 4 |
| Zhang et al China 2013[22] | A:31 C:31 | DPVCD /CCMD/CT/MRI | A:19.03±2.55 C:19.13±2.46 | DU 20, DU18, BG13, GB9; 30 min, 2-100 Hz, once a day | FH 20 mg/d | 30 | 6 wks | HAMD score, Total efficiency | 4 |
| Dong et al China 2007[17] | A:38 C:34 | DPVCD /CCMD/CT/MRI/DSM | A:24.67±2.59 C:24.12±3.17 | GB5,GB6, DU17,DU18,GB15, GB14, GB8, GB7, DU24, EX-HN3; 30 min, once a day | FH 20 mg/d | 30 | 4 wks | HAMD score, SDS score, 5-HT, Total efficiency | 3 |
| Song et al China 2014[24] | A:100 C:100 | DPVCD /CCMD/CT/MRI/HAMD | A:22.65±3.15 C:22.14±3.06 | DU 20, EX-HN1, DU24; 30 min, once a day | FH 20 mg/d | 28 | 8 wks | HAMD score, NIHSS score, BI score, TESS score, Total efficiency | 3 |
| Liu et al China 2015[12] | A:40 C:40 | DPVCD /CCMD/CT/MRI/DSM | A:21.32±4.15 C:22.10±4.39 | DU 20, LI4, EX-HN3, LR3, LA14, ST36, BL20; 30 min, once a day | FLX 20 mg/d | 20 | 4 wks | HAMD score, TESS score, Total efficiency | 3 |
| Du et al China 2017[28] | A:54 C:54 | DPVCD /CCMD/CT/MRI | A:22.5±3.2 C:22.3±3.1 | DU 20, DU24, EX-HN1; 30 min | FH 20 mg/d | / | 8 wks | HAMD score, NIHSS score, Total efficiency | 3 |
| Li et al China 2011[20] | A:23 C:20 | DPVCD /DSM/CT/MRI | A:24.8±5.0 C:26.7±4.6 | DU 20, EX-HN1, EX-HN3, HT7, LR3, SP6, PC6, KI3, BL15; 30 min, once a day | FH 20 mg/d | 30 | 6 wks | HAMD score, | 5 |
| Zhao et al China 2012[21] | A:40 C:40 | DPVCD /DSM/CT | A:33.5±1.02 C:32.4±5.8 | DU 20, EX-HN1, EX-HN3, HT7, LI4, LR3, PC6; 30 min, once a day | FLX 20 mg/d | 21 | 3 wks | HAMD score, CGI score, Total efficiency | 3 |
| Xin China 2008[18] | A:26 C:28 | DPVCD /CCMD/CT/MRI | A:33.5±1.02 C:32.4±5.8 | DU 20, DU24, EX-HN1, EX-HN3, HT7, LR3, PC6; 20 min, 4/20 Hz once a day | FH 20 mg/d | 20 | 4 wks | BI score, Total efficiency | 3 |

BI = Barthel index, C = control group, CCMD = Chinese classification and diagnostic criteria of mental disorders, CGI = clinical global impression, CLP = citalopram, CT = computed tomography, DPVCD = diagnostic points for various cerebrovascular diseases, DSM = diagnostic and statistical manual of mental disorders, E = electroacupuncture group, FH = fluoxetine hydrochloride, FIM = functional independence measure, FLX = fluoxetine, HAMD = Hamilton Depression Rating Scale, MRI = magnetic resonance imaging, NIHSS = National Institute of Health stroke scale, PSD = poststroke depression, SDS = Self-Rating Depression Scale, TCM = traditional Chinese medicine, TESS = Treatment Emergent Symptom Scale.

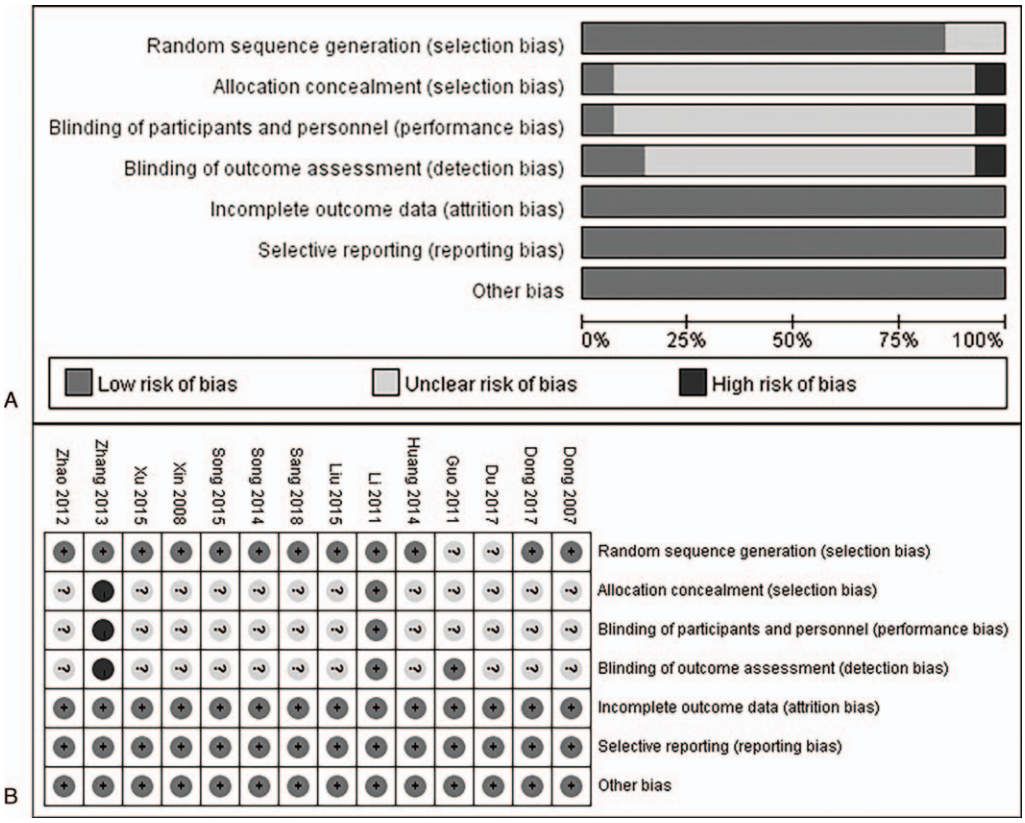


**Figure 2.** (A) Risk of bias: review of authors' judgments about each risk-of-bias item presented as percentages across all included studies; (B) Risk-of-bias summary: review of authors' judgements about each risk-of-bias item for each included study.

random sequence generation. Only 1 study addressed the procedure for allocation concealment, as well as blinding of participants and personnel.[20] Two studies[19,20] did not blind the participants and personnel. All studies were determined to be at low risk of bias in the aspects of incomplete outcome data, selective reporting, and other biases. Utilizing the Jadad score form, the methodological quality of the included trials was assessed, and is shown in Table 2. All 14 studies[12,17–29] received ≥3 points and were included in the meta-analysis.

### 3.3. HAMD score

Thirteen RCTs[12,17,19–29] utilized a HAMD score to evaluate the efficacy of treatment at weeks 3, 4, 6, and 8 (Figs. 3–6). Two RCTs,[21,22] representing 140 patients measured HAMD score at week 3. Pooled data from these studies showed that acupuncture more dramatically decreased HAMD scores when compared to antidepressants (MD = −1.17, 95%CI = −2.18 to −0.16, $P = .02$, $I^2 = 0\%$), with no heterogeneity observed in the fixed-effects models.

Similarly, acupuncture demonstrated a benefit in decreasing HAMD scores at week 4, as determined by 3 RCTs, representing 175 patients (MD = −4.44, 95%CI = −5.64 to −3.23, $P < .00001$, $I^2 = 83\%$), with high heterogeneity in the fixed-effects models. After sensitivity analysis, we found that heterogeneity came from Li et al (2011).[20] When this study was excluded, the heterogeneity changed significantly (MD = −5.22, 95% CI = −6.51 to −3.92, $P < .00001$, $I^2 = 0\%$). The nonacupoint acupuncture performed in the control group may have demonstrated a certain effect, which may have been the source of the heterogeneity observed. As for HAMD scores at weeks 6 and 8 of treatment, authors obtained the same results as above (MD = −1.02, 95%CI = −1.68 to −0.36, $P < .003$, $I^2 = 93\%$; MD = −4.33, 95%CI = −4.96 to −3.70, $P < .00001$, $I^2 = 0\%$). HAMD scores at weeks 6 and 8 involved 6 RCTs, representing 406 patients, with high heterogeneity in the fixed-effects models, and 4 RCTs representing 448 patients, with no heterogeneity in fixed-effects models, respectively. After sensitivity analysis, we found that heterogeneity of the HAMD scores at week 6 came from Dong et al (2017).[27] When this study was excluded, the heterogeneity changed (MD = 0.52, 95%CI = −0.31 to 1.34, $P < .22$, $I^2 = 7\%$). Upon further review, we found that the RCTs included only patients with a HAMD score greater than >20. This was likely the origin of the high heterogeneity.

### 3.4. NIHSS score

Acupuncture was significantly associated with reducing NIHSS score compared to antidepressants (MD = −2.31, 95%CI = −2.53 to −2.09, $P < .00001$, $I^2 = 32\%$) with low heterogeneity in the fixed-effects models, which involved 2 RCTs,[24,28] including 308 patients (Fig. 7). Since there were few studies included, it was not possible to find the source of the heterogeneity.

### 3.5. TESS score

Acupuncture was significantly associated with reducing TESS scores compared to antidepressants (MD = −4.70, 95%CI = −

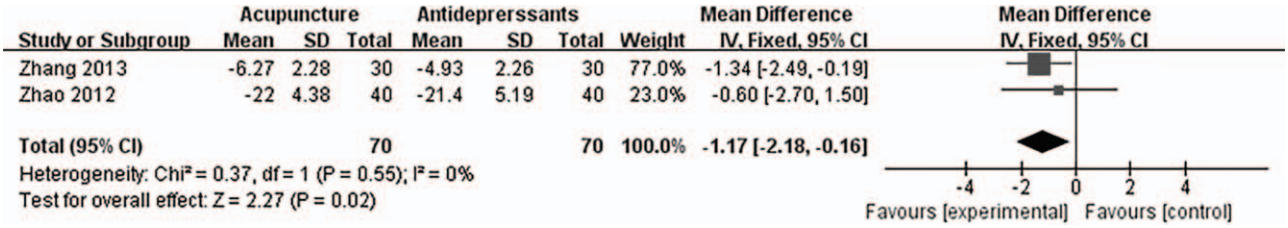


**Figure 3.** (A) Forest plot representing acupuncture therapy vs antidepressants for PSD: HAMD scores at week 3 of treatment; (B) Funnel plot identifying a paper with no significant publication bias in the assessment of HAMD scores at week 3 of treatment.

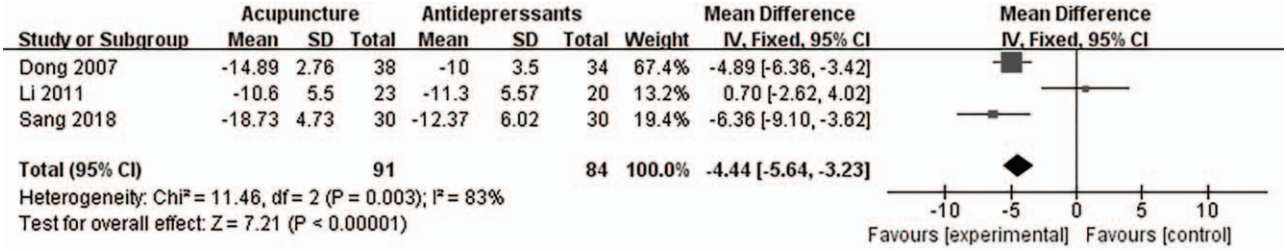


**Figure 4.** (A) Forest plot representing acupuncture therapy vs antidepressants for PSD: HAMD score at week 4 after treatment; (B) A funnel plot identifying a paper with no significant publication bias in the assessment of HAMD score at week 4 after treatment; (C) Funnel plot excluding the Li et al 2011: HAMD score at week 4 after treatment.

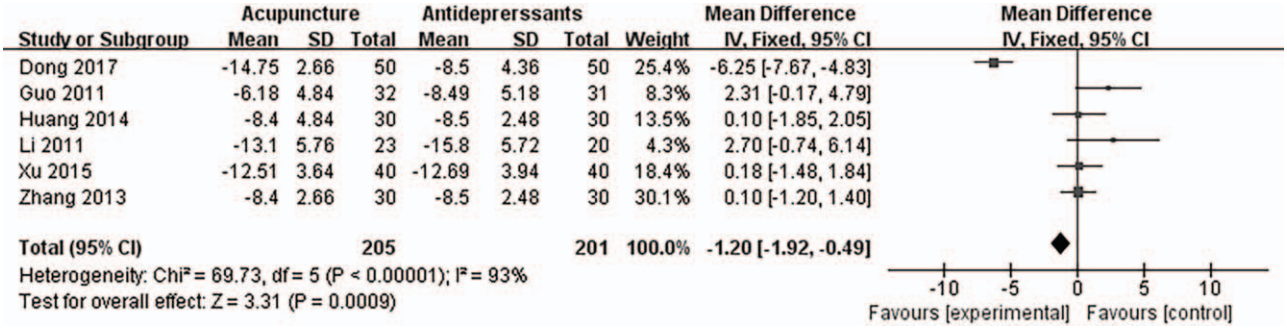


**Figure 5.** (A) Forest plot representing acupuncture therapy vs antidepressants for PSD: HAMD score at week 6 after treatment; (B) A funnel plot identifying a paper with no significant publication bias in the assessment of HAMD score at week 6 after treatment; (C) Funnel plot excluding the Dong et al 2017: HAMD score at week 6 after treatment.

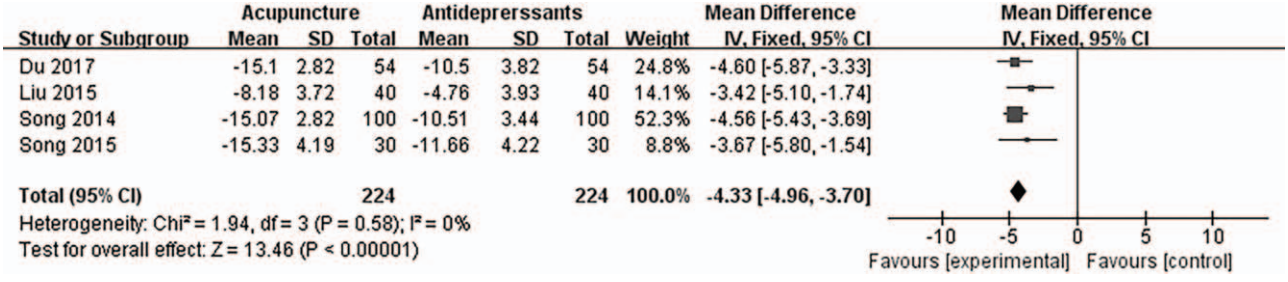


**Figure 6.** (A) Forest plot representing acupuncture therapy vs antidepressants for PSD: HAMD score at week 8 after treatment; (B) A funnel plot identifying a paper with no significant publication bias in the assessment of HAMD score at week 8 after treatment.

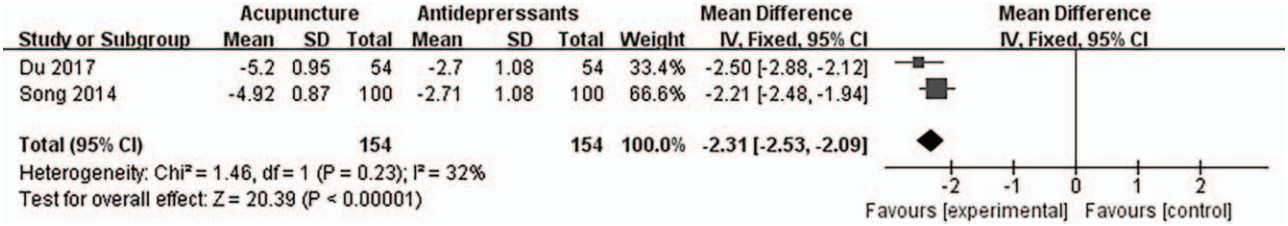


**Figure 7.** (A) Forest plot representing Acupuncture therapy vs antidepressants for PSD: NIHSS score after treatment; (B) A funnel plot identifying a paper with no significant publication bias in the assessment of NIHSS score after treatment.

4.93 to −4.48, $P < .00001$, $I^2 = 87\%$), with high heterogeneity in the fixed-effects models, which involved 3 RCTs,[19,24,25] including 323 patients (Fig. 8). Because of the lack of literature, it was impossible to determine the source of the high heterogeneity. Therefore, we further performed a Begg test ($P = 1.000 > .05$) and an Egger test ($P = .850 > .05$) using STATA version12.0, whose results both showed no significant publication bias.

### 3.6. Total clinical efficacy

Acupuncture was significantly associated with increasing total clinical efficacy compared to antidepressants (RR = 1.15, 95% CI = 1.08–1.21, $P < .00001$, $I^2 = 24\%$), with no heterogeneity in the fixed-effects models, which involved 12 RCTs,[12,17,18,21–29] including 1010 patients (Fig. 9**A**). A funnel plot of the NIHSS score after treatment showed potential publication bias (Fig. 9**B**). Therefore, we performed a Begg test ($P = 1.000 > .05$) and an Egger test ($P = .125 > .05$) using STATA version12.0, showing no apparent publication bias.

## 4. Discussion

PSD is a common neuropsychiatric complication of stroke, severely affecting the quality of life of one third of stroke patients.[2,30] Currently, antidepressant drugs, represented by selective serotonin reuptake inhibitors, are the most common treatments. However, the efficacy of antidepressants is limited and accompanied by a variety of adverse reactions.[31] In recent years, acupuncture has been proposed to treat PSD and has begun to be applied clinically. Zhang et al (2010) summarized the efficacy of acupuncture on PSD through meta-analysis.[13] However, while searching the literature, no clear standard was used for the diagnosis of stroke. This may have resulted in heterogeneity, and publication bias to some extent. Zhang et al (2012) also did not have an unified diagnostic criteria for PSD.[4]

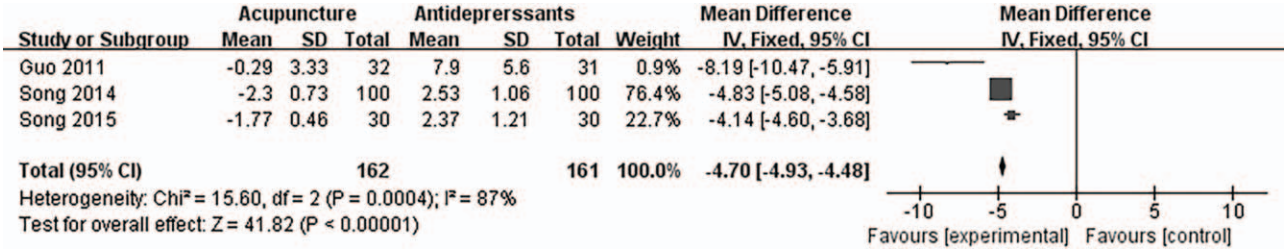


**Figure 8.** (A) Forest plot representing acupuncture therapy vs antidepressants for PSD: TESS score after treatment; (B) A funnel plot identifying a paper with no significant publication bias in the assessment of TESS score after treatment.

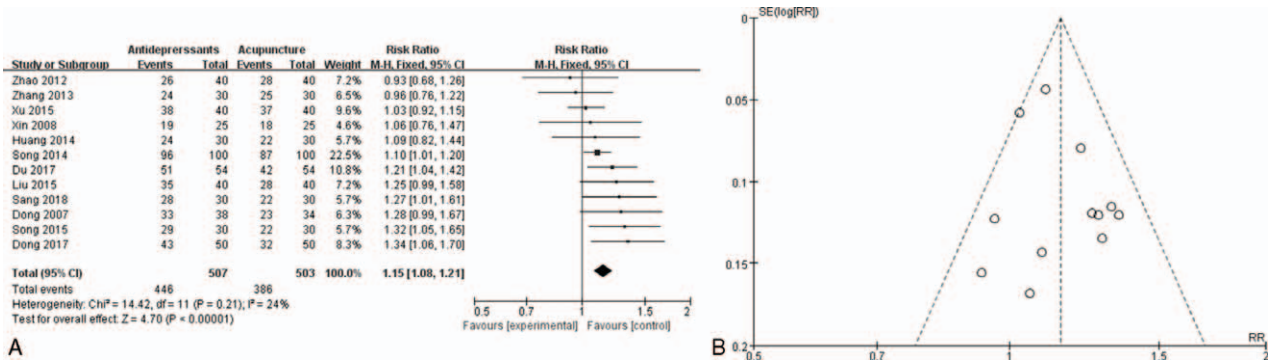


**Figure 9.** (A) Forest plot representing acupuncture therapy vs antidepressants for PSD: Clinical totally efficiency of depression after treatment; (B) A funnel plot identifying a paper with no significant publication bias in the assessment of clinical totally efficiency after treatment.

Therefore, a systematic evaluation of the efficacy and safety of acupuncture therapy for PSD was urgently needed.

A total of 14 studies were included in this study to assess the efficacy and safety of acupuncture vs antidepressant medication for the treatment of PSD. This study measured HAMD scores at different time points for fixed-effects models (3, 4, 6, and 8 weeks after beginning treatment; Fig. 3**A**, 4**A**, 5**A**, and 6**A**, respectively). We use the fixed effect model for the research with little heterogeneity and use sensitivity analysis to analyze those with high heterogeneity. Because the sources of these heterogeneity are well described, we did not show the results of the random effect model. Data indicated that acupuncture was superior to antidepressants in reducing HAMD scores at the above time points. These outcomes were consistent with the initial findings reported in Zhang et al (2010),[11] but were different than the findings reported by Li et al (2018).[2] From the data analysis results of the TESS score, acupuncture more effectively reduce TESS scores when compared to antidepressants (Fig. 8**A**). This suggested that acupuncture had fewer adverse events than antidepressants, also confirmed by Li et al (2018).[2] Similarly, the total clinical efficacy across the 12 RCTs was significantly different between the 2 groups in favor of acupuncture (Fig. 9**A**).

An advantage of the current study was that the NIHSS score was obtained after commencement of treatment (Fig. 7**A**). Acupuncture was superior to antidepressants in decreasing NIHSS scores. Therefore, we concluded that acupuncture did well in treating issues caused by stoke, which was consistent with the findings of other researchers.[32,33] Results suggest that acupuncture plays an important role in both depression and stroke at the same time. This finding is in line with the idea of treating both symptoms and root causes of mental dysfunction, which is common in traditional Chinese medicine (TCM).

According to past studies, a variety of neurotransmitters play an important role in the pathogenesis of depression. Currently, common antidepressant drugs, such as selective eserotonin-reuptake inhibitors and serotonin (5-HT) norepinephrine reuptake inhibitors exert therapeutic effects through their respective neurotransmitters.[34–36] Related studies have shown that electroacupuncture can significantly improve cerebral cortical activity in the corresponding area of stroke patients.[37–39] Also, electroacupuncture can adjust 5-HT and NE levels in the needled area.[40] However, whether the mechanism of acupuncture treatment of PSD was through an increase in the release of 5-HT and/or NE is unknown. This unknown variable can be considered a limitation of the current study, as shortage of the analyzed studies examined changes in 5-HT and NE before and after acupuncture and antidepressant treatment. Future research should seek to clarify the mechanism of acupuncture treatment in PSD.

At present, antidepressant drugs and psychological and physical methods are mainly used in clinical treatment.[41] There are many deficiencies in drug therapy, such as great side effects, high price, and poor long-term effect.[42] There are also studies on the treatment of PSD by scalp electro-acupuncture, which has achieved good results. Various studies reported acupuncture procedures in are similar. For example, according to the relevant standards in "meridian position,"[8] DU20, DU18, BG13, and GB9 acupoints were selected. After the above acupoints are connected to the electronic acupuncture apparatus, the acupoints are stimulated with electric current of density wave, frequency of 2 to 100 Hz and intensity of 0.1 to 1 mA, the intensity is in accordance with the patient's tolerance, and the retention time is 30 minutes. Course of treatment: 5 times a week, 3 weeks as a course of treatment, a total of 2 courses.[23]

The current study contained some additional limitations. First, the included studies did not carry out or indicate whether single blindness was achieved, which may have resulted in potential heterogeneity. Next, the current study did not limit the different shapes, uses, stimulation methods, acupoint selection, needle retention time, or parameter settings (e.g., instrument model, stimulation intensity, or frequency in electro-acupuncture studies). This possibly was one of the origins of the heterogeneity observed. To this end, the research design should be more standardized in the future, so that it is completely in accordance with standards for reporting interventions in clinical trials of acupuncture guidelines.[43] According to the theory of TCM, the roles of different acupoints on the 12 regular meridians have "commonness" and "personality." The correct application of the "commonness" and "personality" of acupoints was the key to improving the clinical efficacy of acupuncture.[44] Zhang et al (2013) and Sun (2015)[45,46] analyzed the literature on acupuncture treatment of PSD in recent years, and found that LR3 and DU20 have the highest frequency of application. Sun (2015) found using "TCM inheritance auxiliary platform" software that the most commonly selected meridian acupoints in the 14 main meridians were in the pericardium. The 6 common syndromes were summarized. Based on unsupervised entropy hierarchical clustering, new prescriptions were obtained: RN6, RN12, DU26, DU26, DU23, BG13, SP4, DU20, BL4, and GB40. Based on the software clustering analysis of "TCM inheritance auxiliary platform" software, 2 groups of new prescriptions were acquired. The first was titled "New prescriptions for acupuncture and moxibustion treatment of PSD deficiency syndrome" (RN6, RN12, RN4 DU26, and DU23), and the second was titled "New prescriptions of acupuncture and moxibustion for empirical syndrome of PSD" (BG13, SP4, DU20, BL4, and GB40).[46] Based on the dialectical thinking of TCM, we should choose acupoints according to the specific diseases of patients. Therefore, future research should conduct comparative studies on the effect of different acupuncture points on the treatment of PSD. It should be noted that, due to the experience and manipulation of acupuncture operators, there will be differences in therapeutic effect.

## 5. Conclusions

Based our result, we find that acupuncture is superior to antidepressants in the treatment of PSD and reduces the incidence of adverse events. Therefore, acupuncture may be a meaningful treatment for PSD. Future research should be conducted on the selection of acupuncture points and the underlying mechanisms for the treatment of PSD and use standardized protocols.

## Author contributions

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