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Comparison of multiple acupoints combination in the treatment of post-stroke cognitive impairment

A network meta-analysis

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Abstract

Background: To evaluate the efficacy of multiple acupoint combinations for the treatment of post-stroke cognitive impairment (PSCI) using a network meta-analysis method.

Methods: Searches for clinical randomized controlled trials (RCTs) of various types of acupuncture treatments for post-stroke cognitive dysfunction were conducted, data were extracted from studies selected according to the inclusion criteria, and the RCTs included in the analysis were assessed separately for risk of literature bias. Network meta-analysis was performed using Stata 14.0.

Results: Sixteen RCTs involving 1257 patients were included, which involved 9 groups of acupoint treatment plans. The best treatment plan for improving the mini-mental state examination score of PSCI was a cephalic plexus spur (99.7%). The best treatment option for improving the montreal cognitive assessment score for PSCI was Zishen Yisui acupuncture therapy (ZSYSA) (77.3%). The best option for improving the barthel index score of PSCI was ZSYSA (99.2%). In terms of improving the overall clinical outcomes of PSCI, the best treatment option for improving the overall clinical effectiveness of PSCI is ZSYSA Therapy (92.2%).

Conclusion: The analysis of all results shows that ZSYSA can significantly improve PSCI compared to other acupuncture therapies.

Strengths and limitations of this study: This is the 1st study on the treatment of PSCI with different acupoint combinations based on a network meta-analysis method, which provides a reference for clinical rehabilitation workers; all included studies were randomized controlled trials, which increased the reliability of this study. Limitations; The number of relevant clinical studies retrieved was too small, and all included clinical trials were located in China; therefore, there is a great possibility of publication bias; Most of the included studies did not clearly explain the random distribution mode, follow-up, distribution concealment, or other experimental conditions. Therefore, selection and reporting biases cannot be excluded, suggesting that the quality of the literature is not high; Because of the strict inclusion criteria, the number of studies was limited, and subgroup analysis could not be performed according to the time of onset and the length of the disease course.

Abbreviations: BI = Barthel index, CA = common acupuncture, CI = confidence interval, CPS = cephalic plexus spur, IF = inconsistency factors, JSZA = Jin San Zhi acupuncture, MD = mean difference, MMSE = mini-mental state examination, MoCA = Montreal cognitive assessment score, OR = odds ratio, PSCI = post-stroke cognitive impairment, SMD = standardized mean difference, SUCRA = the surface under the cumulative ranking curve, TCM = traditional Chinese medicine, TDTSA = Tongdu Tiaoshen acupuncture, TRTDA = Tiaoren Tongdu acupuncture, TSTLA = Tiaoshen Tongluo acupuncture, WQA = Wu Quan acupuncture, YZKQA = Yizhi Kaiqiao acupuncture, ZSYSA = Zishen Yisui acupuncture.

Keywords: acupuncture, network meta-analysis, post-stroke cognitive impairment, RCTs

R-YL and LX contributed equally to this work.

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Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

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1. Introduction

Stroke, 1 of the main causes of death worldwide, is also the main cause of disability in adults. It has a high incidence rate, high disability rate, high mortality rate, and high recurrence rate.[1,2] The progression is accompanied not only by motor function impairment but also by the decline of cognitive function,[3] a condition known as post-stroke cognitive impairment (PSCI). Although the mortality rate of stroke is declining, PSCI still places a huge burden on patients' daily lives, families, and society. Therefore, it is particularly important to revamp the prevention and treatment schemes for cognitive impairment after stroke.[4]

At present, drug treatment for PSCI mainly includes cholinesterase inhibitors, noncompetitive N-methyl-D-aspartate receptor antagonists, and nicergoline, nimodipine, and butylphthalide, but it has some problems such as poor curative effect and high price. As a traditional therapy in traditional Chinese medicine (TCM), the efficacy of acupuncture in the treatment of PSCI has been confirmed in many clinical studies.[5] In addition to the conventional key points for stroke treatment, such as Hegu (LI4), Taichong (LR3) and Neiguan (PC6),[6] several theoretical systems that propose to stimulate a particular set of acupoints with specific needling techniques have been summarized by famous practitioners during the course of TCM development, including the acupuncture method of "Tiaoren Tongdu" which is mainly based on the acupoints of Ren and Du, and the acupuncture method of "Zishen Yisui" which aims at kidney treatment. Although these approaches show positive clinical outcomes in the treatment of stroke, their effectiveness is not fairly comparable, and their pros and cons are not discussed in depth. In this study, the mini-mental state examination (MMSE), Montreal cognitive assessment score (MoCA),[7,8] Barthel index (BI) score, and total effective rate of clinical treatment were used to evaluate the effects of different acupoint combinations on the treatment of PSCI.

2. Materials and Methods

2.1. Registration

This meta-analysis has been registered on INPLASY, registration number INPLASY202130054. This study conforms to all PRISMA guidelines and reports the required information accordingly See the Supplementary Document (PRISMA Checklist, http://links.lww.com/MD/I175, Guidelines Checklist).

2.2. Patient and public involvement

No patient involved.

2.3. Literature search

Various databases were searched, including PubMed, EMBASE, Cochrane Library, CNKI, and WANFANG.

The search strategy was conducted using a combination of subject terms and free words. The search timeframe was from the start date of the database to November 2022. English search terms included Stroke, Cerebrovascular Accident, Cerebrovascular Accidents, CVA (Cerebrovascular Accident), CVA (Cerebrovascular Accident), Cerebrovascular Apoplexy, (Apoplexy, Cerebrovascular), (Vascular Accident, Brain), Brain Vascular Accident, Brain Vascular Accidents, Vascular Accidents, Brain, Cerebrovascular Stroke, Cerebrovascular Strokes, Apoplexy, Cerebral Stroke, Cerebral Stroke, (Cerebrovascular Accident, Acute), Acute Cerebrovascular Accident, Acute Cerebrovascular Accidents, (Cerebrovascular Accidents, Acute), Cognition, Post-stroke cognitive impairment, Cognitions, Cognitive Function, Cognitive Functions,(Function, Cognitive), (Functions, Cognitive), Acupuncture, electroacupuncture, electro-acupuncture, acupoint, transcutaneous electric nerve stimulation, RCTs. References to the included literature were also retrospectively included and hand-searched for meta-analyses related to acupuncture treatment of interest in this study, and their references were screened. The specific search strategy is detailed in the Appendix. See the Supplementary Document (Appendix 1, Supplemental Digital Content, http://links.lww.com/MD/I176).

PubMed:

#1(clinical[tiab] AND trial[tiab]) OR "clinical trials as topic"[mesh] OR "clinical trial"[pt] OR random*[tiab] OR "random allocation"[mesh] OR "therapeutic use"[sh]

#2(Stroke [Mesh] OR Strokes [Title/Abstract] OR Cerebrovascular Accident [Title/Abstract] OR Cerebrovascular Accidents [Title/Abstract] OR CVAs (Cerebrovascular Accident) [Title/Abstract] OR Cerebrovascular Apoplexy [Title/Abstract] OR Apoplexy, Cerebrovascular [Title/Abstract] OR Vascular Accident, Brain [Title/Abstract] OR Cerebrovascular Stroke [Title/Abstract] OR Cerebrovascular Strokes [Title/Abstract] OR Stroke, Cerebrovascular [Title/Abstract] OR Strokes)

#3 Cognitions [Title/Abstract] OR Cognitive Function [Title/Abstract] OR Cognitive Functions [Title/Abstract] OR Function, Cognitive [Title/Abstract] OR Functions, Cognitive [Title/Abstract] OR Cognition [Mesh])

#4(acupuncture [Title/Abstract] OR Pharmacopuncture [Title/Abstract] OR electroacupuncture [Title/Abstract] OR electro-acupuncture [Title/Abstract] OR transcutaneous electric nerve stimulation [Title/Abstract] OR acupoint [Title/Abstract] OR "Acupuncture"[Mesh])

#1 AND#2AND#3AND#4

55

2.4. Study selection

The inclusion criteria were as follows: randomized controlled trial; the study subjects were stroke patients (≥18 years old) by brain CT, MRI and other imaging examinations, and who were confirmed to have cognitive impairment through screening or evaluation (MMSE <27 or MoCA<26); treatment plan: the patient group was given treatment that involves the stimulation of special acupoints, while the control group was stimulated at acupoints commonly used for PSCI, including Hegu (LI4), Baihui(GV20), Taichong(LR3), Neiguan(PC6), Zusanli (ST36), Sanyinjiao (SP6), Yintang (EX-HN3), et cetera.[6] Operation: The patient generally adopts lateral lying position and long needle retention method (needle retention time exceeds 30 minutes); Outcome indicators: MMSE and MoCA were the primary indicators; BI index and the total clinical effectiveness rate were secondary indicators.

2.5. Study exclusion

The exclusion criteria were as follows: literature with non-clinical patients as study subjects; duplicated literature; and unclear diagnostic criteria or relevant outcome indicators.

2.6. Data extraction

The publications were thoroughly and independently reviewed and cross-referenced by 2 evaluators. In cases of disagreement, a third party was used to arbitrate the assessment. Data items extracted: title, name of the 1st author, baseline characteristics of included studies (sample size, patient age, treatment measures, etc.), year of publication, factors associated with risk of bias (randomization method, blinding, etc.), and outcome data (MMSE, MoCA, BI, overall effectiveness). MMSE, MoCA, BI outcome data were included in the before-and-after change difference (i.e., the difference between indices after treatment and before treatment). If not mentioned in the original text, it can be calculated from the given data. The formula is as follows, where corr is usually 0.5: MMSE, MoCA, BI, and the total effective rate of clinical treatment.

$$SD_{E.change} = \sqrt{SD^2_{E.baseline} + SD^2_{E.final} - (2 \times Corr \times SD_{E.baseline} \times SD_{E.final})}$$

If there is any ambiguity in the data, we will contact the 1st author of the original article for additional information.

$$\mathbf{Mean_{E.change} = Mean_{E\ final} - Mean_{E\ baseline}}$$

2.7. Statistical analysis

The statistical method of network meta-analysis was based on the frequency framework, and all outcome indicators were analyzed using the random effects model.[9] If the evaluation metrics of this study were continuous variables, MMSE and MoCA, the mean difference (MD) was adopted as the effect size. When BI was the outcome index of continuous variables, standardized mean difference (SMD) was used, considering that some of the measurement methods in the literature were improved. If it was a dichotomous variable, the odds ratio (OR) was used as the effect size and the corresponding 95% confidence interval (CI) was calculated. STATA 14.0 software (STATA Corporation, Lakeway, Texas) was used to plot the network evidence relation diagram, forest diagram, rank probability diagram, funnel diagram, and corresponding statistical results.[9] In the global consistency test, no global inconsistency was considered if the difference was not statistically significant ($P > .05$.[10] To evaluate local inconsistency, this study calculated the inconsistency factors (IF) and 95% CI for each closed ring in the network. In this calculation method, the ifplot command in Stata was used to detect loop inconsistency. If the lower limit of the 95% confidence interval was contained or close to 0, the local comparison, *that is,* direct comparative evidence, was considered consistent with indirect comparative evidence. Use the Review Manager 5.3 software for traditional meta analysis. The heterogeneity test is mainly determined by I^2. If there is no significant heterogeneity between the research results ($I^2 \leq 70\%$), the fixed effect model is used for meta analysis; If there is heterogeneity ($I^2 > 70\%$) among the research results, further analyze the source of heterogeneity and use the random effect model for meta analysis. In this study, The surface under the cumulative ranking curve (SUCRA) was used to calculate the cumulative ranking probability of each treatment plan. A larger SUCRA value, which resulted from a larger area under the curve of the cumulative probability ranking graph, indicated that the intervention had a better effect.

2.8. Methodologic quality

The quality of the included studies was assessed according to the risk of bias table, a quality assessment scale recommended in the Cochrane Handbook 5.1.0, which included reporting bias, detection bias, performance bias, selection bias, attrition bias, and other biases. Quality assessment included 6 components: reporting bias, detection bias, performance bias, selection bias, attrition bias, and other biases. Each part of the evaluation was judged as high, medium, or low risk according to the criteria in Cochrane Handbook 5.1.0.

3. Results

3.1. Characteristics of the included trials

A total of 2184 related articles were obtained in the preliminary examination. After eliminating irrelevant literature based on the title and abstract, there were 260 articles in total. After eliminating duplicate articles and strictly following the inclusion criteria, 16 RCTs were finally included,[11–26] all of which were double-arm trials with a total of 1257 patients. A total of 9 sets of acupuncture groups were used in these studies, including common acupuncture (CA), tiaoshen tongluo acupuncture (TSTLA), Tongdu Tiaoshen acupuncture (TDTSA), Jin San Zhi acupuncture (JSZA), cephalic plexus spur (CPS), Zishen Yisui acupuncture (ZSYSA), tiaoren tongdu acupuncture (TRTDA), Wu Quan acupuncture (WQA) and Yizhi Kaiqiao acupuncture (YZKQA). The literature screening process and results are shown in Figure 1A, and basic information of the included literature is shown in Table 1.

3.2. Risk of bias

The included studies were evaluated using the Cochrane Manual 5.1.0 Bias Risk Assessment Tool. Random assignment was conducted in the bias risk assessment of all included studies, among which 5 studies[13,20–22,25] used the random number envelope method as their allocation method, 5 studies[11,12,15,16,18] used the random number table method, 1 study[26] used the central random method, and 1 study[17] used the random lottery method. Three literatures[20,21,26] used a single-blind method. Other studies have not clearly described its random distribution pattern, blind method, distribution concealment, and so on. The outcome data of all studies were complete, *that is,* the number of patients lost was clear. One literature[21] had an incorrect outcome index name, which was confirmed after inquiring the author. The bias risk assessment of the included studies is shown in Figure 1B.

3.3. Evidence network

A total of 12 studies reported the MMSE as the outcome indicator and involved 8 groups of acupoints. Eight studies reported MoCA as the outcome indicator and involved 7 groups of acupuncture points. Eight studies reported BI as the outcome indicator and involved 7 groups of acupuncture points. Six studies reported the total effective rate as the outcome indicator and involved 6 groups of acupuncture points. Network evidence is shown in Figure 1C. The line between the 2 points suggests that evidence of direct comparison between the 2 groups of acupoints is available, whereas the lack of connection suggests otherwise, but the results can be obtained through indirect comparison. The thickness of the line between 2 points indicates the number of studies that used these 2 groups of acupuncture points among all included studies, and the size of the dot indicates the sample size using this group of acupoints among all included studies.

3.4. Inconsistency test

The MMSE scores of the 8 groups of acupuncture points formed a closed ring. The overall consistency result showed $P = .2099 > 0.05$, suggesting that there was no overall inconsistency. IF detection, 95% CI, and inter-cycle heterogeneity parameter T2 were detected in each characteristic cycle, as shown in Figure 1D. The results showed that the inconsistency factor IF was 2.39, and the lower limit of 95% CI was 0 or close to 0, indicating that the consistency of each closed loop was good. These results imply that the comparison method (direct vs indirect comparison) had little impact on the results of the entire reticular meta-analysis, and the statistical results of the total effective rate of the reticular meta-analysis were highly reliable. The other 3 indicators (MoCA, BI, and total effective rate) did not form a closed loop, so there was no need to conduct a closed-loop inconsistency test. The results of the inconsistency test are shown in Figure 1D.

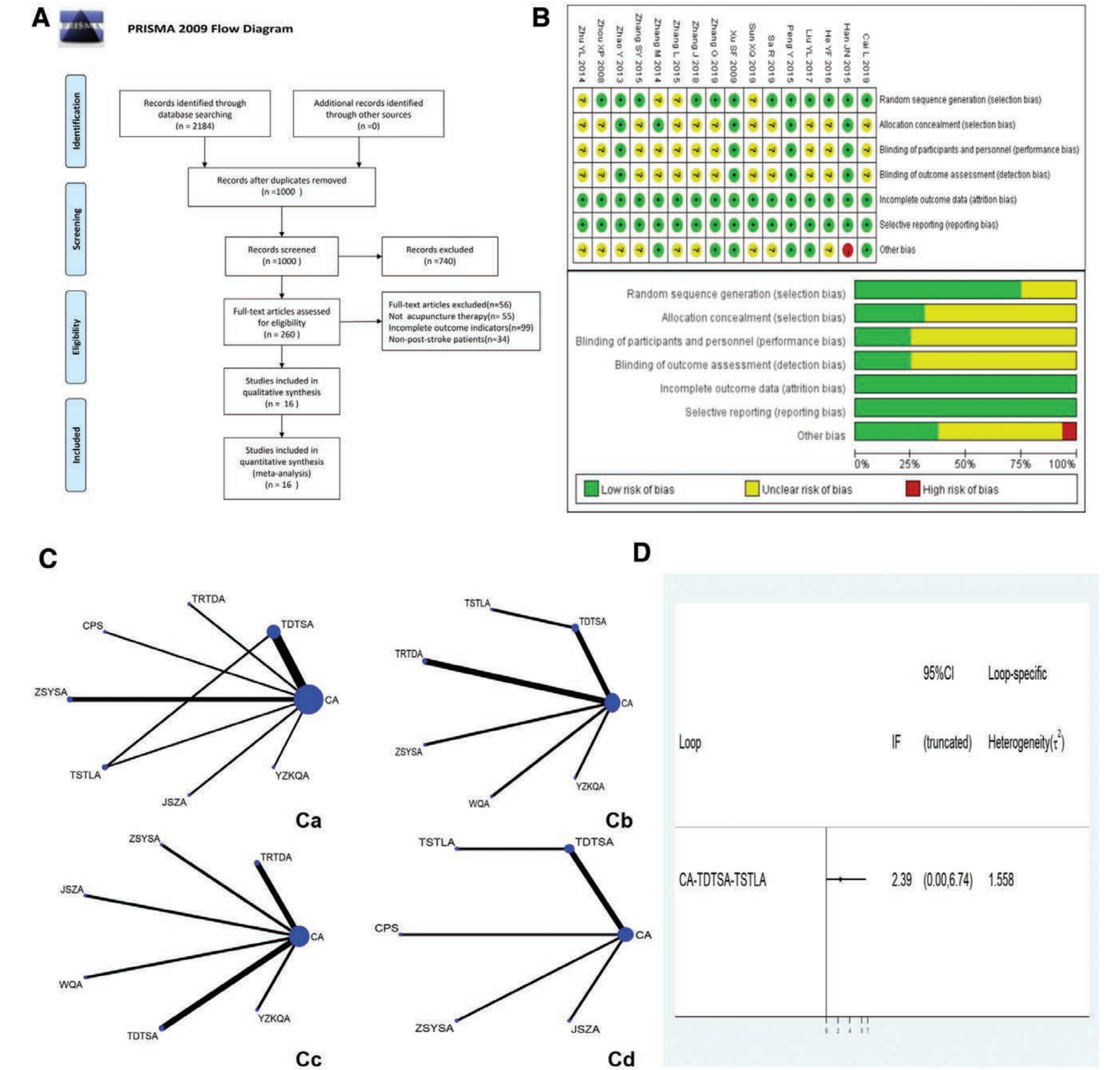

Figure 1. (A) Flow chart of literature screening; (B) risk of bias graph; (C) network diagram (Ca: MMSE; Cb: MoCA; Cc: BI; Cd: total effective rate); D: Inconsistency of total effective rate. MMSE = mini-mental state examination, MoCA = Montreal cognitive assessment score.

3.5. Traditional meta-analysis

3.5.1. MMSE. Under the same conditions of intervention measures, for the comparison of large heterogeneity (TDTSA vs CT, $I^2 > 70\%$), a random effect model was used for meta-analysis. After detailed analysis with other studies, it was found that the source of heterogeneity may be Zhang 2019[11] ($I^2 = 59\%$ after excluding this article), which may be due to the fact that nimodipine was explicitly mentioned as a routine treatment in both the control group and the test group in this study, other studies did not explicitly mention it. The other studies were basically homogeneous ($I^2 < 70\%$), using a fixed effect model. In the 8 acupuncture treatment schemes included, except that there was no statistical difference between TDTSA versus TSTLA and TDTSA versus CT, the MMSE elevation of the other 7 acupuncture treatments was significantly higher than that of the control group ($P < .05$), as shown in Table 2.

3.5.2. MoCA. Under the same conditions of intervention measures, for the comparison of large heterogeneity (TDTSA vs CT, $I^2 > 70\%$), a random effect model was used for meta-analysis. After detailed analysis with other studies, it was found that the source of heterogeneity might be due to the different intervention time of the 2 included literatures, 2 weeks[21] and 4 weeks[17] respectively. The other studies were basically homogeneous ($I^2 < 70\%$), using a fixed effect model. In the 6 acupuncture treatment schemes included, except that there was no statistically significant difference between TDTSA and CT, the MoCA elevation of the other 5 acupuncture treatments was significantly higher than that of the control group ($P < .05$), as shown in Table 3.

3.6. Network meta-analysis

3.6.1. MMSE. Eight acupoint combinations were pairwise compared either directly or indirectly, and 9 comparisons showed statistical differences. Compared to CA, CPS (MD = 6.57, 95% CI [4.13 9.01]) and ZSYSA (MD = 3.20, 95% CI [1.50, 4.90]) significantly increased MMSE scores and had better efficacy. Compared to TDTSA, CPS (MD = 5.72, 95% CI [3.08, 8.36]) and ZSYSA (MD = 2.35, 95% CI [0.38, 4.33]) significantly increased MMSE scores and had better efficacy. Compared to TRTDA, CPS (MD = 6.01, 95% CI [2.80, 9.22]) significantly increased the MMSE score and had better efficacy. Compared with ZSYSA (MD = –3.37, 95% CI [–6.34, –0.69]), TSTLA (MD = –5.32, 95% CI [–8.41, –2.24]), JSZA (MD = –5.05, 95% CI [–8.33, –1.77]), and YZKQA (MD = –4.7, 95% CI [–8.21, –1.19]), CPS significantly increased the MMSE score and had a significant effect, while other comparisons showed no statistical difference (Table 4).

3.6.2. MoCA.

Seven groups of acupoints were pairwise compared either directly or indirectly, and 1 comparison showed a statistical difference. Compared with CA, TDTSA (MD = 2.85, 95% CI [0.49, 5.20]) could significantly increase the MoCA score and have good efficacy, while other comparisons showed no statistical difference, as shown in Table 5.

Table 1

Basic characteristics of trials included.

Author	Year	Number of patients		Age (yr)		Male/female)	Treatment		Intervention period	Outcome indicator
		I	C	I	C		I	C		
Zhu[23]	2014	40	40	56.37 ± 13.26	55.56 ± 13.58	46/34	TDTSA	CA	30D	①,③
Xu[26]	2009	82	80	62.38 ± 8.32	63.73 ± 7.23	105/57	JSZA	CA	5W	①,③,④
Zhang[19]	2015	20	20	-	-	23/17	TDTSA	CA	4W	①
Zhang[18]	2015	30	30	65 ± 5	67 ± 7	37/23	TRTDA	CA	4W	①,②,③
He[17]	2016	30	30	61.78 ± 6.75	62.97 ± 6.51	34/26	TDTSA	CA	4W	②,③
Zhou[25]	2008	30	30	65.17 ± 5.83	64.93 ± 6.29	30/30	TSTLA	CA	3W	①
Zhang[11]	2019	45	45	68.69 ± 13.04	69.53 ± 14.14	44/46	TDTSA	CA	2W	①,④
Liu[16]	2017	30	30	62 ± 6	65 ± 7	32/28	TDTSA	TSTLA	4W	①,②,④
Sa[12]	2019	55	55	67.96 ± 10.12	68.02 ± 9.57	65/45	CPS	CA	15D	①,④
Sun[14]	2019	50	50	60.21 ± 2.12	60.28 ± 2.36	45/55	ZSYSA	CA	4W	③,①,④
Zhang[15]	2018	65	65	59.87 ± 9.78	59.57 ± 8.85	92/38	ZSYSA	CA	4W	①,②
Cai[13]	2019	30	30	61.20 ± 8.02	57.30 ± 9.24	36/24	YZKQA	CA	4W	①,②,③
Peng[20]	2015	30	30	61.80 ± 7.232	64.37 ± 7.972	29/31	TRTDA	CA	21D	②,③
Zhao[24]	2013	31	30	69.16 ± 7.475	67.20 ± 10.978	39/22	TDTSA	CA	2W	①
Zhang[22]	2014	32	32	71.55 ± 8.49	68.89 ± 7.27	36/28	WQA	CA	45D	③,②
Han[21]	2015	30	30	60.25 ± 8.551	62.5 ± 8.339	27/33	TDTSA	CA	8W	②,④

BI = Barthel index, CA = common acupuncture, CPS = cephalic plexus spur, JSZA = Jin San Zhi acupuncture, MMSE = mini-mental state examination, MoCA = Montreal cognitive assessment score, TDTSA = Tongdu Tiaoshen acupuncture, TRTDA = Tiaoren Tongdu acupuncture, TSTLA = Tiaoshen Tongluo acupuncture, WQA = Wu Quan acupuncture, YZKQA = Yizhi Kaiqiao acupuncture, ZSYSA = Zishen Yisui acupuncture.
①MMSE;②MoCA;③BI;④:the total effective rate of clinical treatment; I: Intervention; C: Control.

Table 2

Traditional meta-analysis of MMSE.

Treatment	Numbers of RCTs	MD [95% CI]	I^2/%	Z	P	Effect
TDTSA vs CT	4	0.66 [–0.59, 1.92]	97	1.03	.3	Random
ZSYSA vs CT	2	3.27 [2.35, 4.19]	46	6.94	<.00001	Fixed
YZKQA VS CT	1	1.87 [0.35, 3.39]	–	2.40	.02	Fixed
TDTSA vs TSTLA	1	0.35 [–0.37, 1.07]	–	0.95	.34	Fixed
CPS vs CT	1	6.57 [5.19, 7.95]	–	9.33	<.00001	Fixed
JSZA vs CT	1	1.52 [0.66, 2.38]	–	3.45	.0006	Fixed
TRTDA vs CT	1	0.56 [0.03, 1.09]	–	2.06	.04	Fixed
TSTLA vs CT	1	2.70 [0.50, 4.90]	–	2.41	.02	Fixed

CI = confidence interval, CPS = cephalic plexus spur, JSZA = Jin San Zhi acupuncture, MD = mean difference, MMSE = mini-mental state examination, TDTSA = Tongdu Tiaoshen acupuncture, TRTDA = Tiaoren Tongdu acupuncture, TSTLA = Tiaoshen Tongluo acupuncture, YZKQA = Yizhi Kaiqiao acupuncture, ZSYSA = Zishen Yisui acupuncture.

Table 3

Traditional meta-analysis of MoCA.

Tteatment	Numbers of RCTs	MD [95% CI]	I^2/%	Z	P	Effect
TDTSA vs CT	2	2.86 [–0.36, 6.08]	95	1.74	.08	Random
TRTDA vs CT	2	1.56 [0.84, 2.28]	24	4.25	<.0001	Fixed
YZKQA vs CT	1	2.23 [0.61, 3.85]	–	2.7	.007	Fixed
TDTSA vs TSTLA	1	3.54 [0.23, 6.85]	–	2.10	.04	Fixed
ZSYSA vs CT	1	3.27 [1.65, 4.89]	–	3.94	<.0001	Fixed
WQA vs CT	1	1.34 [–0.17, 2.85]	–	1.74	.08	Fixed

CI = confidence interval, MD = mean difference, MoCA = Montreal cognitive assessment score, TDTSA = Tongdu Tiaoshen acupuncture, TRTDA = Tiaoren Tongdu acupuncture, TSTLA = Tiaoshen Tongluo acupuncture, WQA = Wu Quan acupuncture, YZKQA = Yizhi Kaiqiao acupuncture, ZSYSA = Zishen Yisui acupuncture.

3.6.3. BI. Seven acupoint combinations were pairwise compared directly and indirectly, and 14 comparisons showed statistical differences. Compared with CA, TRTDA (SMD = 0.51, 95% CI [0.14, 0.87]), ZSYSA (SMD = 1.78, 95% CI [1.31, 2.24]), JSZA (SMD = 1.27, 95% CI [0.93, 1.61]) and TDTSA (SMD = 0.76, 95% CI [0.42, 1.10]) could significantly increase BI score with a significant effect; Compared with TRTDA, ZSYSA (SMD = 1.27, 95% CI [0.68, 1.86]) and JSZA (SMD = 0.76, 95% CI [0.26, 1.26]) significantly increased BI score, whereas the BI score of acupuncture WQA (SMD = –0.71, 95% CI [–1.33, –0.1]) was significantly lower than TRTDA. The BI scores for acupuncture WQA (SMD = –1.98, 95% CI [–2.66, –1.31]), TDTSA (SMD = –1.02, 95% CI [–1.60, –0.44]), and YZKQA (SMD = –1.55, 95% CI [–2.24, –0.86]) were significantly lower than those for ZSYSA. The BI scores of acupuncture WQA (SMD = –1.48, 95% CI [–2.07, –0.88]), TDTSA (SMD = –0.51, 95% CI [–0.99, –0.03]), and YZKQA (SMD = –1.05, 95% CI [–1.66, –0.44]) were significantly lower than that of JSZA. Compared with acupuncture WQA, TDTSA (SMD = 0.97, 95% CI [0.37, 1.57]) significantly increased the BI score and had significant efficacy, while other comparisons showed no statistical difference, as shown in Table 6.

3.7. The total effective rate

Six acupoints were pairwise compared directly and indirectly, and 4 points showed statistical differences. The TDTSA (OR = 3.04, 95% CI [1.24, 7.47]), CPS (OR = 4.78, 95% CI [1.47, 15.53]), ZSYSA (OR = 10.29, 95% CI [2.21, 47.90]), and JSZA (OR = 2.50, 95% CI [1.15, 5.44]) were significantly higher than those of CA, and there were no statistical differences in other comparisons, as shown in Table 7.

3.8. SUCRA

3.8.1. MMSE. Based on the SUCRA results, CPS may be the most effective intervention for increasing the MMSE scores in patients. The probability ranking results for SUCRA were as follows: CPS (99.7%) > ZSYSA (80%) > YZKQA (55.9%) > JSZA (49.3%) > TSTLA (44.2%) > TDTSA (34.4%) > TRTDA (27.8%) > CA (8.6%). A cumulative probability-ordering diagram is shown in Figure 2A. The larger the area under the curve, the more effective the curve.

3.8.2. MoCA. According to the SUCRA results, ZSYSA may be the most effective intervention for increasing the MoCA in patients. The probability ranking results for SUCRA were as follows: ZSYSA (77.3%) > TDTSA (74.7%) > YZKQA (61.3%) > TRTDA (50.9%) > WQA (47%) > TSTLA (21%) > CA (17.8%). A cumulative probability-ordering diagram is shown in Figure 2B.

3.8.3. BI. According to the SUCRA results, ZSYSA may be the most effective intervention for increasing the BI in patients. The probability ranking results for SUCRA were as follows: ZSYSA (99.2%) > JSZA (83.7%) > TDTSA (63.6%) > TRTDA (49.3%) > YZKQA (32.1%) > CA (16.4%) > WQA (5.6%). A cumulative probability-ordering diagram is shown in Figure 2C.

3.9. The total clinical effective rate

According to the SUCRA results, ZSYSA may be the most effective intervention for increasing the total clinical response rate in patients with post-stroke cognitive dysfunction. The probability ranking results for SUCRA were as follows: ZSYSA (92.2%) > CPS (73.1%) > TDTSA (57.6%) > JSZA (47.1%) > TSTLA (22%) > CA (7.9%). The cumulative probability ordering diagram is shown in Figure 2D.

3.10. Funnel chart

In this study, we conducted a network meta-analysis. Dots of different colors in the funnel plot of MMSE treated with PSCI at

Table 4

Network meta-analysis of MMSE (MD [95% CI]).

Treatment	YZKQA	JSZA	TSTLA	ZSYSA	CPS	TRTDA	TDTSA	CA
YZKQA	0	–	–	–	–	–	–	–
JSZA	0.35 (–2.99, 3.69)	0	–	–	–	–	–	–
TSTLA	0.62 (–2.53, 3.77)	0.27 (–2.62, 3.16)	0	–	–	–	–	–
ZSYSA	–1.33 (–4.38, 1.71)	–1.68 (–4.45, 1.09)	–1.96 (–4.50, 0.59)	0	–	–	–	–
CPS	–4.70 (–8.21, –1.19)*	–5.05 (–8.33, –1.77)*	–5.32 (–8.41, –2.24)*	–3.37 (–6.34, –0.39)*	0	–	–	–
TRTDA	1.31 (–1.96, 4.58)	0.96 (–2.06, 3.98)	0.69 (–2.12, 3.50)	2.64 (–0.04, 5.33)	6.01 (2.80, 9.22)*	0	–	–
TDTSA	1.02 (–1.70, 3.74)	0.67 (–1.74, 3.08)	0.40 (–1.40, 2.19)	2.35 (0.38, 4.33)*	5.72 (3.08, 8.36)*	–0.29 (–2.60, 2.02)	0	–
CA	1.87 (–0.65, 4.39)	1.52 (–0.67, 3.71)	1.25 (–0.64, 3.14)	3.20 (1.50, 4.90)*	6.57 (4.13, 9.01)*	0.56 (–1.52, 2.64)	0.85 (–0.16, 1.85)	0

CA = common acupuncture, CI = confidence interval, CPS = cephalic plexus spur, JSZA = Jin San Zhi acupuncture, MD = mean difference, MMSE = mini-mental state examination, TDTSA = Tongdu Tiaoshen acupuncture, TRTDA = Tiaoren Tongdu acupuncture, TSTLA = Tiaoshen Tongluo acupuncture, YZKQA = Yizhi Kaiqiao acupuncture, ZSYSA = Zishen Yisui acupuncture.
*There was statistical difference between the two ($P < .05$).

Table 5

Network meta-analysis of MoCA (MD [95% CI]).

Treatment	YZKQA	WQA	ZSYSA	TRTDA	TSTLA	TDTSA	CA
YZKQA	0	–	–	–	–	–	–
WQA	0.89 (–4.12, 5.90)	0	–	–	–	–	–
ZSYSA	–1.04 (–6.09, 4.01)	–1.93 (–6.95, 3.09)	0	–	–	–	–
TRTDA	0.65 (–3.63, 4.93)	–0.24 (–4.48, 4.00)	1.69 (–2.59, 5.98)	0	–	–	–
TSTLA	2.92 (–3.35, 9.20)	2.03 (–4.21, 8.28)	3.96 (–2.31, 10.24)	2.27 (–3.40, 7.94)	0	–	–
TDTSA	–0.62 (–4.90, 3.66)	–1.51 (–5.74, 2.73)	0.42 (–3.86, 4.70)	–1.27 (–4.61, 2.07)	–3.54 (–8.13, 1.05)	0	–
CA	2.23 (–1.34, 5.80)	1.34 (–2.18, 4.86)	3.27 (–0.30, 6.84)	1.58 (–0.78, 3.94)	–0.69 (–5.85, 4.47)	2.85 (0.49, 5.20)*	0

CA = common acupuncture, CI = confidence interval, MD = mean difference, MoCA = Montreal cognitive assessment score, TDTSA = Tongdu Tiaoshen acupuncture, TRTDA = Tiaoren Tongdu acupuncture, TSTLA = Tiaoshen Tongluo acupuncture, WQA = Wu Quan acupuncture, YZKQA = Yizhi Kaiqiao acupuncture, ZSYSA = Zishen Yisui acupuncture.
*There was statistical difference between the two ($P < .05$).

Table 6

Network meta-analysis of BI (SMD [95% CI]).

Treatment	YZKQA	TDTSA	WQA	JSZA	ZSYSA	TRTDA	CA
YZKQA	0	–	–	–	–	–	–
TDTSA	−0.53 (−1.15, 0.08)	0	–	–	–	–	–
WQA	0.43 (−0.28, 1.14)	0.97 (0.37, 1.57)*	0	–	–	–	–
JSZA	−1.05 (−1.66, −0.44)	−0.51 (−0.99, −0.03)	−1.48 (−2.07, −0.88)	0	–	–	–
ZSYSA	−1.55 (−2.24, −0.86)*	−1.02 (−1.60, −0.44)*	−1.98 (−2.66, −1.31)*	−0.51 (−1.08, 0.07)	0	–	–
TRTDA	−0.28 (−0.91, 0.34)	0.25 (−0.25, 0.75)	−0.71 (−1.33, −0.10)*	0.76 (0.26, 1.26)*	1.27 (0.68, 1.86)*	0	–
CA	0.22 (−0.28, 0.73)	0.76 (0.42, 1.10)*	−0.21 (−0.70, 0.29)	1.27 (0.93, 1.61)*	1.78 (1.31, 2.24)*	0.51 (0.14, 0.87)*	0

BI = Barthel index, CA = common acupuncture, CI = confidence interval, JSZA = Jin San Zhi acupuncture, SMD = standardized mean difference, TDTSA = Tongdu Tiaoshen acupuncture, TRTDA = Tiaoren Tongdu acupuncture, WQA = Wu Quan acupuncture, YZKQA = Yizhi Kaiqiao acupuncture, ZSYSA = Zishen Yisui acupuncture.
*There was statistical difference between the two ($P < .05$).

Table 7

Network meta-analysis of total effective rate (OR [95% CI]).

Treatment	JSZA	ZSYSA	CPS	TSTLA	TDTSA	CA
JSZA	0	–	–	–	–	–
ZSYSA	0.24 (0.04, 1.36)	0	–	–	–	–
CPS	0.52 (0.13, 2.14)	2.15 (0.31, 14.93)	0	–	–	–
TSTLA	1.94 (0.33, 11.52)	7.99 (0.87, 73.66)	3.71 (0.51, 27.14)	0	–	–
TDTSA	0.82 (0.25, 2.69)	3.38 (0.57, 20.06)	1.57 (0.36, 6.91)	0.42 (0.11, 1.60)	0	–
CA	2.50 (1.15, 5.44)*	10.29 (2.21, 47.90)*	4.78 (1.47, 15.53)*	1.29 (0.26, 6.39)	3.04 (1.24, 7.47)*	0

CA = common acupuncture, CI = confidence interval, CPS = cephalic plexus spur, JSZA = Jin San Zhi acupuncture, OR = odds ratio, TDTSA = Tongdu Tiaoshen acupuncture, TSTLA = Tiaoshen Tongluo acupuncture, ZSYSA = Zishen Yisui acupuncture.
*There was statistical difference between the two ($P < .05$).

8 different acupoint combinations were directly compared, and the number of dots represented the number of studies. Most of the dots in the funnel map of this study are distributed symmetrically about the vertical line with a reasonably good degree of symmetry, but there may still be a certain degree of publication bias towards the right side. Three control studies were distributed outside the 95% CI of the funnel, suggesting the existence of a small-sample effect. There are few experiments of pairwise direct comparisons between other indexes, so there is no bias analysis, as shown in Figure 3.

4. Discussion

PSCI is a common complication of a stroke. Acupuncture, the main treatment for TCM, has a long history. Its application, when combined with modern medicine, has shown significant clinical efficacy. There are many theoretical systems of acupuncture for the treatment of PSCI, and each combination of acupoints represents a theoretical system for the treatment of PSCI.

This network meta-analysis involves a total of 9 acupoint combinations, mainly CA (Baihui (DU20), Hegu (LI4), Neiguan (PC6), Zusanli (ST36), Sanyinjiao (SP6), Xuanzhong (GB39), sishenchong (EX-HN1) et al), tdtsa (Shuigou (DU26), Baihui (DU20), Fengfu (DU16), Shengting (DU24), Dazhui (DU14), Shendao (DU11) et al), TRTDA (Baihui (DU20), Shengting (DU24), Yintang (DU29), Qihai (RN6), Guanyuan (RN4) et al), WQA (3 Acupoints 1 inch on dYongquan (KI1), Lianquan (RN23), left and right, Juquan (EX-HN10) et al), JSZA(the 1st needle is 2 inches above the hair line of ear tip straight, and the second and third needles are 1 inch horizontally forward and 1 inch behind), TSTLA(Fengfu (DU16), Baihui (DU20), Shengting (DU24), Benshen (BG13), Suliao (DU25), Neiguan (PC6), Houxi (SI3), Yanglingquan (GB34), Taixi (KI3) et al), CPS (shenting (DU24), sishentong (ex-hn1), Benshen (BG13), Fengfu (DU16), Fengchi (GB20), Touwei (ST8), Yintang (du29), Shuigou (DU26) et al), zsysa (Dazhong (ki4), Yongquan (KI1), Xuanzhong (GB39), Baihui (DU20), Sishentong (ex-hn1) et al) and YZKQA (Baihui (DU20), Sishentong (EX-HN1), Shenting (DU14), Naohu (DU17), Shenmen (HT7), Hegu (LI4), Sanyinjiao(SP6), Xuanzhong(GB39), Taixi(KI3), Taichong(LR3) et al). Each combination of acupoints represents a theoretical system for treating PSCI. Based on the results of this study, the best 3 acupoint combinations in improving the MMSE score after stroke is CPS, ZSYSA, YZKQA; the best 3 acupoint combinations in improving the MoCA score after stroke was ZSYSA, TDTSA, YZKQA; In improving the BI score after stroke, the best 3 acupoint combinations was ZSYSA, JSZA, TDTSA; In improving the total clinical effective rate of post-stroke cognitive impairment, the best 3 acupoint combinations is ZSYSA, CPS, TDTSA. In the comparison of the 4 outcome indicators included in this study, it was found that there are significant differences in the optimal ranking of each index; therefore, it is difficult to select the optimal acupoint combination scheme. The MMSE is a screening scale originally used for Alzheimer's disease and has been developed as a screening examination and evaluation method for patients with moderate or severe cognitive impairment.[7] The MoCA was developed by Nasreddine et al in Canada based on clinical experience, cognitive items, and MMSE scores. It is more sensitive in screening for mild cognitive impairment.[8] The MMSE and MoCA are usually used as the main indicators of cognitive measurement in PSCI. The BI is usually used as an index to evaluate the ability to perform daily living. Its evaluation scope includes not only cognitive function, but also motor function. Therefore, BI is usually used as a secondary index to evaluate cognitive function after PSCI.[27] The total clinical effective rate is usually the summary of the effective rate of all indicators in clinical research; therefore, it also has important clinical implications.

Based on all rankings, this study found that ZSYSA can significantly improve the MMSE, MoCA, BI, and total clinical effective rate of patients with PSCI. ZSYSA is based on the theory of the brain-kidney axis. It advocates that the treatment of PSCI should also aim to improve and protect renal function, in addition to treating the brain. This may be an important enlightenment in the application of acupuncture in the treatment of PSCI. Many scholars in the field of TCM

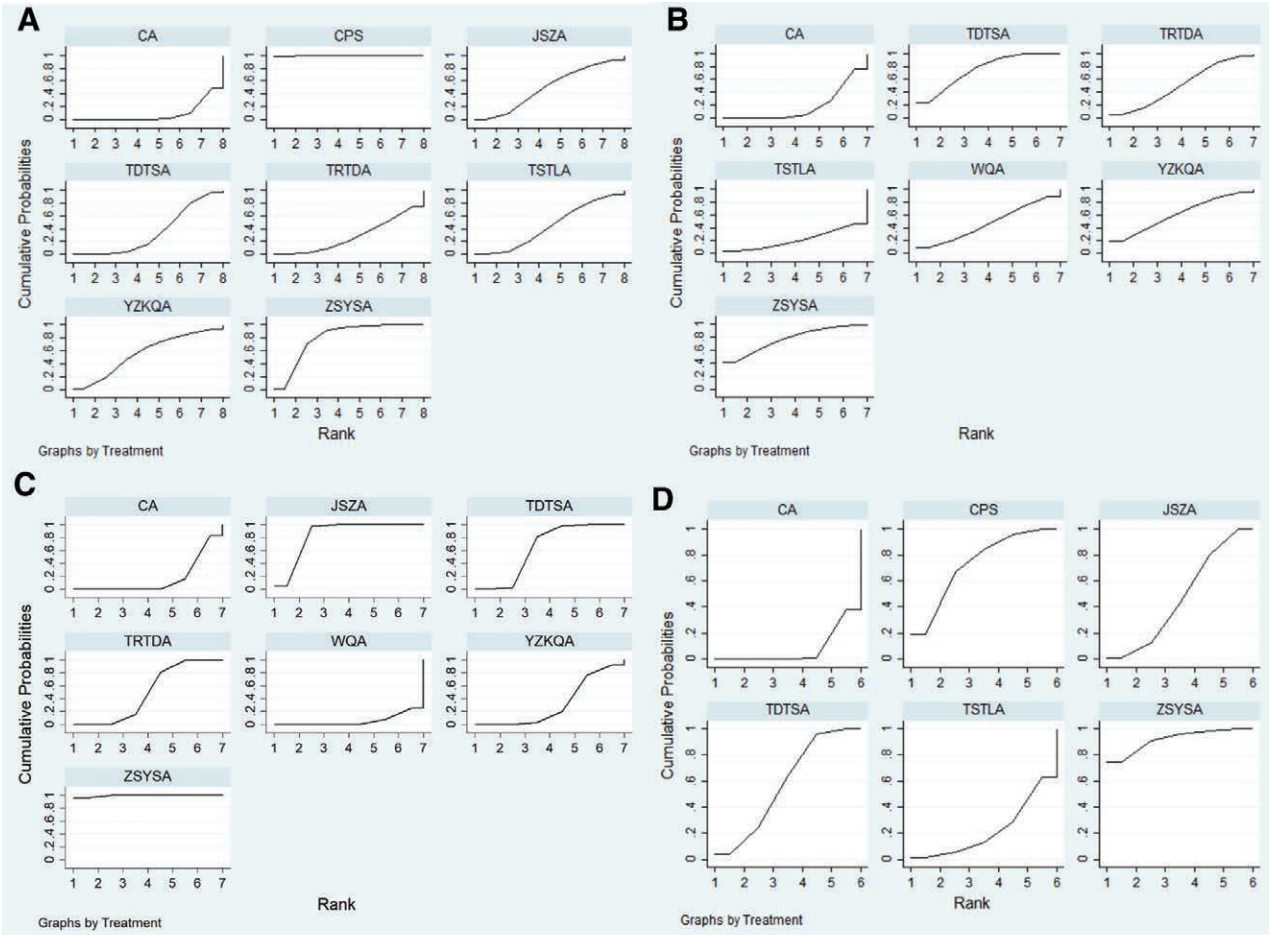

Figure 2. Cumulative probability ranking plot (A: MMSE; B: MoCA; C: BI; D: total effective rate). BI = Barthel index, MMSE = mini-mental state examination, MoCA = Montreal cognitive assessment score.

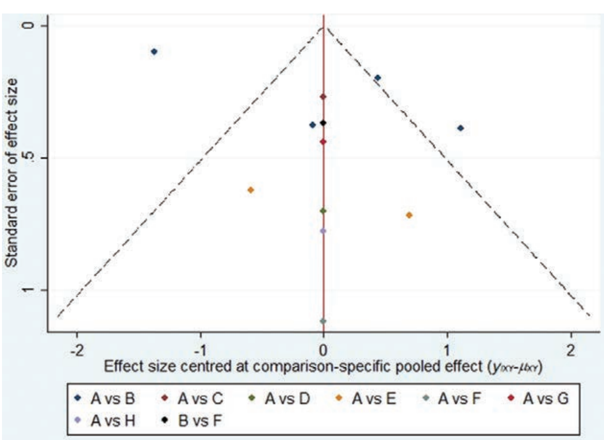

Figure 3. Funnel diagram of MMSE (A: CA; B:TDTSA; C:TRTDA; D:CPS; E:ZSYSA; F:TSTLA; G:JSZA; H:YZKQA). CA = common acupuncture, MMSE = mini-mental state examination, TDTSA = Tongdu Tiaoshen acupuncture, TRTDA = Tiaoren Tongdu acupuncture, TSTLA = Tiaoshen Tongluo acupuncture, YZKQA = Yizhi Kaiqiao acupuncture, ZSYSA = Zishen Yisui acupuncture.

believe that, although the disease occurs in the brain, it is fundamentally in the kidney, and the lack of kidney essence is the main pathogenesis.[28] The formation of the brain-kidney axis theory can be traced back to the pre-Qin era. Su Wen said: "all marrow belongs to the brain" and "kidney governs bone and generates marrow." Ancient Chinese medical experts believe that Sui (a subtle substance closely related to cognition in ancient Chinese medicine) converges in the human brain, while Sui is the essence and metaplasm hidden in the kidney. The meridian connection between the brain and kidney is formed through Du Mai, which is a prototype of the brain-kidney axis theory. Many modern clinical studies have also confirmed the clinical effectiveness of simultaneous treatment of the kidney and brain in PSCI.[29,30] In recent years, modern medicine has been used in many basic and clinical studies of the brain-kidney axis. Some studies have confirmed that acute stroke is likely to be accompanied by varying degrees of abnormal renal function, with some even reaching the degree of acute renal injury.[31] However, there is no consensus on the risk factors of acute renal injury in patients with acute stroke. Some scholars believe that the use of contrast media is an independent risk factor for acute renal injury,[32] and others believe that it is closely related to the use of mannitol and nephrotoxic drugs.[33] Most studies have shown a positive correlation between the index severity of renal injury markers, such as albuminuria, and aggravation of cognitive impairment. Some hypotheses may link albuminuria with the pathogenesis of small cerebral vessels, which is related to the aggravation of cognitive impairment, but the specific pathological mechanism is unclear.[34] In summary, simultaneous treatment of the kidney and brain may be an important breakthrough in the treatment of PSCI using TCM techniques. At the same time, according to the results of this study, it is suggested that clinical workers can perform acupuncture with methods that nourish the kidney and marrow and perform rehabilitation treatment according to the different clinical symptoms and severity of PSCI at the same time to achieve the best therapeutic effect.

This study has the following shortcomings: The number of relevant clinical studies retrieved is too small, and all included clinical trials are located in China, so there is a great possibility of publication bias; most of the included studies did not clearly explain the random distribution mode, follow-up, distribution concealment, or other experimental conditions. Therefore, selection and reporting biases cannot be excluded, suggesting that the quality of the literature is not high; Because of the strict inclusion criteria, the number of studies was limited, and subgroup analysis could not be performed according to the time of onset and the length of the disease course.

5. Conclusion

In conclusion, according to the results of the mesh meta-analysis, the ZSYSA method significantly improved post-stroke cognitive impairment. However, due to the overall quality and quantity of the literature included in the study, it is expected that the above results could benefit from a more reasonable research design, large sample size, and multicenter randomized double-blind controlled trial to provide a basis for different acupoint combinations to improve the clinical efficacy of PSCI.

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