Review Article

The Effectiveness and Safety of Manual Acupuncture Therapy in Patients with Poststroke Cognitive Impairment: A Meta-analysis

Wei Liu, Chang Rao, Yuzheng Du, Lili Zhang, and Jipeng Yang

First Teaching Hospital of Tianjin University of Traditional Chinese Medicine, Tianjin, China

Correspondence should be addressed to Yuzheng Du; drduyuzheng@163.com

Wei Liu and Chang Rao contributed equally to this work.

Received 19 June 2020; Revised 7 October 2020; Accepted 28 October 2020; Published 25 November 2020

Academic Editor: Zhen Zheng

Copyright © 2020 Wei Liu et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Background. Poststroke cognitive impairment (PSCI) is a common cause of disability among patients with stroke. Meanwhile, acupuncture has increasingly been used to improve motor and cognitive function for stroke patients. The aim of the present study was to summarize and evaluate the evidence on the effectiveness of acupuncture in treating PSCI.

Methods. Eight databases (PubMed, The Cochrane Library, CNKI, WanFang Data, VIP, CBM, Medline, Embase databases) were searched from January 2010 to January 2020. Meta-analyses were conducted for the eligible randomized controlled trials (RCTs).

Assessments were performed using Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), Barthel Index (BI), or modified Barthel Index (MBI).

Results. A total of 657 relevant RCTs were identified, and 22 RCTs with 1856 patients were eventually included. Meta-analysis showed that acupuncture appeared to be effective for improving cognitive function as assessed by MMSE (mean difference (MD) = 1.73, 95% confidence interval (CI) (1.39, 2.06), \( P < 0.00001 \)) and MoCA (MD = 2.32, 95% CI (1.92, 2.73), \( P < 0.00001 \)). Furthermore, it also suggested that acupuncture could improve the activities of daily life (ADL) for PSCI patients as assessed by BI or MBI (SMD = 0.97, 95% CI (0.57, 1.38), \( P < 0.00001 \)).

Conclusions. Compared with nonacupuncture group, acupuncture group showed better effects in improving the scores of MMSE, MoCA, BI, and MBI. This meta-analysis provided positive evidence that acupuncture may be effective in improving cognitive function and activities of daily life for PSCI patients. Meanwhile, long retention time of acupuncture may improve cognitive function and activities of daily life, and twist technique may be an important factor that could influence cognitive function. However, further studies using large samples and a rigorous study design are needed to confirm the role of acupuncture in the treatment of PSCI.

1. Introduction

Stroke ranks only second to ischemic heart disease as the leading cause of death and the third leading cause of disability-adjusted life-years (DALYs) lost worldwide [1]. In China, with over 2 million new cases annually, stroke has a close relationship with the highest DALYs lost of any disease [2]. Cognitive decline is a major cause of disability in stroke survivors [3]. It is estimated that 11.8 million patients who have had a stroke, 9.5 million of whom have had cognitive impairments after their stroke [4].

Poststroke cognitive impairment (PSCI) contains two different degrees of cognitive impairment, including poststroke cognitive impairment with no dementia (PSCIND) and poststroke dementia (PSD) [5]. In the study [6] which enrolled 620 patients in 12 hospitals with ischemic stroke, of the 506 patients who were followed-up at 3 months after stroke, 353 patients (69.8%) suffered cognitive impairment as measured by the Korean Vascular Cognitive Impairment Harmonization Standards neuropsychological protocol (K-VCIHS-NP). In America, the study on 212 subjects from the Framingham Study suggested that 19.3% of cases...
developed into dementia in 10 years after stroke [7]. PSCI is strongly related to a higher risk of mortality [8], poor functional outcome [9], and poor quality of life [10]. Identifying patients at risk of cognitive impairment is, therefore, important as well as targeting interventions to this group. 

Unfortunately, treatment of PSCI has not been standardized [11]. So far, there are many drugs to improve cognitive, including acetylcholinesterase inhibitors, memantine [12], and nercergoline [13]. But because of the unclear efficacy and side effect, until now, there is a none drug that has been approved by the Food and Drug Administration (FDA) to treat vascular cognitive impairment [14].

In recent years, the spectrum of diseases suitable for acupuncture abroad has been significantly broader, like nervous system, muscular tissue, skeletal system, connective tissue, mental and behavioral disorders, digestive system, and respiratory system [15]. The World Health Organization has also recommended acupuncture as an alternative and complementary strategy for stroke treatment and improvement [16]. In the treatment of apoplexy sequelae, acupuncture is mainly used to treat dyspraxia [17], enhance life quality [18], improve cognition [19], and deal with depression and anxiety [20]. Animal experiments [21] showed that acupuncture could improve cognitive function by stimulating cholinergic enzyme activity and regulating brain-derived neurotrophic factor (BDNF) and cAMP-response element-binding protein (CREB) expression in the rats’ brain; Cai et al. [22] demonstrated that electroacupuncture can improve cognitive impairment in Alzheimer’s disease mice by inhibiting synaptic degeneration and neuroinflammation. 

After searching the database, we found that there were few systematic reviews or meta-analysis focused on the effectiveness of acupuncture in treating PSCI recently, although the number of papers related to this area has an upward trend in the last five years. For instance, the latest meta-analyses on acupuncture treating PSCI were published in 2014 [23] and 2016 [24]. But due to the limitation of sample size and the quality of trials included in the former one, the effectiveness of acupuncture in treating PSCI has not been fully determined. Meanwhile, the later one which also lacked quality randomized controlled trials (RCTs) was merely focused on the effectiveness of scalp acupuncture. Therefore, the purpose of this study is to evaluate the clinical efficacy of acupuncture in the treatment of PSCI by meta-analysis and provide evidence for its rational clinical application.

2. Methods

2.1. Search Methods for Identification of Studies. We searched CNKI, WanFang Data, VIP, CBM, PubMed, Medline, Ebase, and The Cochrane Library to collect randomized controlled trials of acupuncture in the treatment of PSCI published in both Chinese and English. The retrieval time was from January 2010 to January 2020. Searching terms included stroke, cerebral infarction, encephalorrhagia, cognitive impairment and so on. For example, the searching strategy we used on Pubmed is (((((cognitive[Title/Abstract]) OR Cognition[Title/Abstract])) AND (((((stroke[Title/Abstract]) OR cerebral infarction[Title/Abstract]) OR apoplexy[Title/Abstract]) OR hematemephalon[Title/Abstract]) OR encephalorrhagia[Title/Abstract]) OR cerebral hemorrhage[Title/Abstract]) OR infarct of brain[Title/Abstract]) AND acupuncture[Title/Abstract]).

2.2. Inclusion/exclusion Criteria. Relevant clinical trials were included if the following criteria were met: (1) they were randomized controlled trials (RCTs); (2) they included patients diagnosed with poststroke cognitive impairment; (3) they use cognitive function as an outcome measure; (4) the difference of interventions between experimental and control groups is whether they use acupuncture or not. To be more precise, the intervention of experimental group is acupuncture therapy plus another therapy or standard treatment; the intervention of control group is standard treatment or the therapy which also be used in the experimental group except acupuncture therapy. If trials which met above criteria contained more than two groups, the group receiving acupuncture was chosen as the experimental group, and the nonacupuncture treatment group was chosen as the control group.

Trials were excluded if they met any of the following criteria: (1) acupuncture were used in the control group; (2) neither the Mini-Mental State Examination (MMSE) nor the Montreal Cognitive Assessment (MoCA) was used as cognitive function evaluation scale; (3) specific type of acupuncture treatment was used in the experimental group, such as electroacupuncture and laser needles for acupuncture.

2.3. Data Extraction. Two reviewers (L.W. and R.C.) independently extracted the general information of the included trials and reached consensus on all items. Extracted data included authors, year of publication, sample size, source of diagnosis, interventions, main outcomes, and information about acupuncture treatment (including course, frequency, and retention time).

Measures of the outcome evaluation that were reported in the included studies were Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), Barthel Index (BI), or modified Barthel Index (MBI). MMSE which contains domains of orientation, memory, attention, language, and visuospatial ability is the most common used screening scale [25, 26]. MoCA, which is also a cognitive screening and tracking tool, is more useful for the mild stages of the cognitive impairment [27]. It is composed of several cognitive domains such as memory, executive function, attention, language, abstraction, naming, delayed recalls, and orientation [28]. BI is one of the most widely used outcome measures to assess functioning for the patients who have neurological disorders [29, 30]. It consists of 10 others’ rated questions which are for the purpose of evaluating the ability of daily life [31].

2.4. Quality Assessment. The methodological quality and the risk of bias of the included studies were evaluated by the risk of bias 2.0 (ROB 2.0) tool. One author assessed the risk of bias of included studies by using ROB 2.0, and the other author confirmed the judgment. The following items were categorized as having high, low, or unclear risk of bias:
randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result and overall.

2.5. Statistical Analysis. The Review Manager software (version 5.3 Cochrane Collaboration, Oxford, United Kingdom) was used to perform most of the statistical analysis. The mean difference (MD) which was used as the effect analysis statistics for continuous data was calculated with a 95% confidence interval (CI).

The $I^2$ statistic was used to analyze the heterogeneity between the data of included trials. If the figure of $I^2$ was above 50%, which means significant heterogeneity, sensitivity analysis would be performed to analysis the source of heterogeneity. Random-effects model was applied to calculate the study results with significant heterogeneity, while a fixed effect model is used if the statistical heterogeneity was apparent. Publication bias was detected using a funnel plot.

3. Results

3.1. Study Description. Our search identified 657 articles after removing duplicates. Among them, 22 RCTs met our inclusion criteria and were included in this study (Figure 1). The articles included in the analysis are summarized in Table 1. There are 2 in English [32, 33] and 20 articles in Chinese [34–53].

3.2. Study Quality. The risk of bias assessment of the included RCTs is illustrated in Figure 2. With regard to randomization process, 4 studies had a low ROB, and 18 studies had an unclear ROB. With regard to deviations from intended interventions, all RCTs had a low ROB. With regard to missing outcome data, 16 studies had a low ROB, and 6 studies had a high ROB. With regard to measurement of the outcome, 2 studies had a low ROB, and 20 studies had an unclear ROB. With regard to selection of the reported result, 1 study had a low ROB, and 21 studies had an unclear ROB.

3.3. Descriptions of Acupuncture Treatment. The acupuncture interventions of the included trials varied across the 22 trials. The majority of the studies [32, 35–39, 42–45] used acupuncture with medicine, such as cholinesterase inhibitor or lipid-lowering medication, as the intervention of the experiment group. Eight studies [34, 41, 46–48, 50–52] used acupuncture with cognitive training; two studies [33, 53] used acupuncture alone; two studies [42, 49] used acupuncture with rehabilitation training.

In terms of acupoint selecting, single area acupuncture points were used in five studies [39, 40, 45, 49, 50], including the eye, ear, and scalp acupuncture. Special acupuncture therapy, Jin three-needle therapy, and tri-jiao therapy were also used in three studies [46, 47, 53]. Apart from that, a total of 33 acupoints were selected in other 14 studies. Acupoints used for cognitive impairment in most trials were DU 20 (Bai Hui) and DU24 (Shen Ting) (Figure 3).

3.4. Effects of Acupuncture Treatment According to MMSE Assessment Scales. A total of 17 studies reported MMSE scores, including 1389 patients. Heterogeneity test results showed high heterogeneity between groups ($I^2 = 95\%, P < 0.00001$). Sensitivity analysis was done by using the leave-one-out approach; five studies [40, 46, 48, 51, 53] were found
Table 1: Summary of randomized controlled trials of acupuncture for PSCI.

| Author (year) | Sample size | Participants | Source of diagnostic | Intervention group regimen | Control group regimen | Main outcomes | Acupuncture course | Acupuncture frequency | Acupuncture retention time |
|---------------|-------------|--------------|----------------------|----------------------------|-----------------------|--------------|--------------------|-----------------------|--------------------------|
| Wang 2016 [32] | 79          | a65.2 ± 7.1  | a26/14               | Acupuncture                | Nimodipine            | 1. MoCA      | 12 weeks           | 5 times per week       | 30 min                   |
|               |             | b60.6 ± 6.7  | b26/13               |                           |                       |              |                    |                       |                          |
|               |             | a61.58 ± 9.71| a25/27               | Stroke: CT or MRI          | Acupuncture            | Conventional treatment | 1. MMSE   | 12 weeks           | 5 times per week       | 30 min                   |
|               |             | b60.53 ± 9.19| b24/25               |                           | Conventional treatment |              |                    |                       |                          |
| Wang 2018 [34] | 115         | a52.37 ± 8.43| a30/25               | Acupuncture                | Conventional treatment | Cognitive training | 1. MMSE  | 3 months           | Daily                 | Scalp acupuncture: 6 h  |
|               |             | b52.72 ± 9.65| b28/22               |                           | Conventional treatment |              |                    |                       | Body acupuncture 0.5 h |
| Bao 2012 [35]  | 60          | a63 ± 6      | a19/11               | Stroke: CT or MRI          | Acupuncture            | Donepezil    | 2 months           | 6 times per week       | 50 min                   |
|               |             | b64 ± 6      | b21/9                |                           | Conventional treatment |              |                    |                       |                          |
| Zhang 2017 [36] | 84         | a63.28 ± 10.68| a27/15              | Stroke: CT or MRI          | Acupuncture            | Atorvastatin  | 1. MMSE  | 4 weeks           | 5 times per week       | 20 min                   |
|               |             | b63.07 ± 10.59| b28/14              |                           | Conventional treatment |              |                    |                       |                          |
| Wang Q 2019 [37] | 118      | a68.88 ± 3.64| a36/23               | Stroke: CT or MRI          | Acupuncture            | Atorvastatin  | 1. MMSE  | 30 days           | Daily                 | 30 min                   |
|               |             | b67.71 ± 3.02| b32/27               |                           | Conventional treatment |              |                    |                       |                          |
| Yang 2015 [38]  | 72          | a65.89 ± 3.276| a25/11              | Stroke: CT or MRI          | Acupuncture            | Nimodipine   | 1. MMSE  | 3 months           | 6 times per week       | 30 min                   |
|               |             | b65.97 ± 3.308| b21/15              |                           | Conventional treatment |              |                    |                       |                          |
| Du 2017 [39]   | 60          | a64.60 ± 2.84 | a16/14               | Stroke: CT or MRI          | Acupuncture            | Donepezil    | 1. MMSE  | 6 weeks           | 7 times per week       | 30 min                   |
|               |             | b64.43 ± 3.27 | b14/16               |                           | Conventional treatment |              |                    |                       |                          |
|               |             | a59.47 ± 8.62| a36/19               | Stroke: CT or MRI          | Eye acupuncture        |              |                    |                       |                          |
| Author (year) | Sample size | Participants | Source of diagnostic | Intervention group regimen | Control group regimen | Main outcomes | Acupuncture course | Acupuncture frequency | Acupuncture retention time |
|--------------|-------------|--------------|----------------------|---------------------------|-----------------------|--------------|-------------------|-------------------|------------------------|
| Teng 2018 [40] | b58.65 ± 8.17, b35/20 | CI: MMSE and LOTCA | Standard treatment Cognitive training | Standard treatment Cognitive training | 2. LOTCA | | | | |
| Qiu 2018 [41] | 60, a54.18 ± 4.137, a17/11 | Stroke: MRI | Acupuncture | Standard treatment | 1. MoCA | 1 month | 5 times per week | 30 min |
| Li 2019 [42] | 80, a66.9 ± 5.9, a18/22 | Stroke: CT or MRI | Acupuncture | Standard treatment Donepezil | 1. MoCA | 6 weeks | 5 times per week | 30 min |
| Ding 2019 [43] | 110, a66.9 ± 11.1, a39/19 | Stroke: standard [ii] | Acupuncture | Compound musk injection | 1. GCS | 3 weeks | 5 times per week | 30 min |
| Nie 2019 [44] | 63 | Stroke: CT or MRI | Acupuncture | Butyphthalide | 1. MoCA | 40 days | Daily | 30 min |
| Bai 2012 [45] | 60, a60 ± 6, a16/14 | Stroke: CT or MRI | Acupuncture | Piracetam | 1. MMSE | 4 weeks | 5 times per week | 6 h |
| Author (year) | Sample size | Participants | Sex (male/female) | Source of diagnostic | Intervention group regimen | Control group regimen | Main outcomes | Acupuncture course | Acupuncture frequency | Acupuncture retention time |
|--------------|-------------|--------------|-------------------|---------------------|----------------------------|-------------------------|---------------|-------------------|---------------------|--------------------------|
| Zeng 2018 [46] | 80 | —— | a22/18 | Stroke: imaging | Acupuncture | Standard treatment | 1. MMSE | 4 weeks | 6 times per week | 30 min |
| | | | b24/16 | CI: MMSE | Cognitive training | 2. Barthel | | | | |
| Zhang 2019 [47] | 70 | a59.95 ± 8.71 | a20/15 | Stroke: standard | Acupuncture | Cognitive training | 1. MMSE | 8 weeks | 6 times per week | 30 min |
| | | b61.12 ± 9.62 | b19/16 | CI: MMSE | Computer aided treatment | Standard treatment | 2. Barthel | | | |
| Wang Z 2019 [48] | 208 | a62 ± 7 | a62/42 | Stroke: CT or MRI | Acupuncture | Cognitive training | 1. Hcy | 30 days | 5 times per week | 30 min |
| | | b62 ± 7 | b61/43 | CI: MMSE | Cognitive training | 2. hs-CRP | | | | |
| | | | | | | 3. CPI | | | | |
| | | | | | | 4. VILIP-1 | | | | |
| | | | | | | 5. BDNF | | | | |
| | | | | | | 6. GFAP | | | | |
| | | | | | | 7. MMSE | | | | |
| | | | | | | 8. ADL | | | | |
| Mao 2019 [49] | 78 | a57.3 ± 15.6 | a18/21 | Stroke: CT or MRI | Acupuncture | Standard treatment | 1. MoCA | 6 weeks | 5 times per week | 6 h |
| | | b58.2 ± 16.2 | b19/20 | CI: MoCA | Rehabilitation | 2. Barthel | | | | |
| Liu 2016 [50] | 63 | a68.07 ± 2.82 | a16/14 | Stroke: CT or MRI | Eye acupuncture | Standard treatment | 1. MMSE | 4 weeks | 7 times per week | 30– 40 min |
| | | b67.83 ± 3.35 | b18/12 | CI: standard | Cognitive training | 2. Barthel | | | | |
| Author (year) | Sample size | Participants | Source of diagnostic | Intervention group regimen | Control group regimen | Main outcomes | Acupuncture course | Acupuncture frequency | Acupuncture retention time |
|--------------|-------------|--------------|----------------------|---------------------------|-----------------------|---------------|-------------------|----------------------|--------------------------|
| Song 2017 [51] | 62 | a 56.37 ± 1.27, b 58.19 ± 1.24 | a 24/7, b 19/12 | Stroke: CT or MRI | Acupuncture | Standard treatment, Cognitive training | 1. MMSE | 12 weeks | 5 times per week | 30 min |
| Zhang 2018 [52] | 63 | a 59.03 ± 6.066, b 58.17 ± 6.539 | a 14/16, b 13/17 | Stroke: MRI | Acupuncture | Standard treatment, Cognitive training | 1. MMSE | 4 weeks | 6 times per week | 30 min |
| Li 2012 [53] | 60 | a 67.31 ± 10.98, b 66.24 ± 12.53 | ——, b 62.24 ± 12.53 | Stroke: CT or MRI | Acupuncture | Standard treatment | 1. MMSE | 3 weeks | 6 times per week | 30 min |

[i]Experimental group; [ii]control group. [iii]Key points for diagnosis of various cerebrovascular diseases. [iv]National Institute of Neurological Disorders and Stroke-Canadian stroke network vascular cognitive impairment harmonization standards. [v]Spectrum of disease in vascular cognitive impairment.
that patients without cognitive impairment, but low educational level were included in the studies. In addition, another two [46, 53] of them that we removed could significantly vary the direction of the combined estimates (test for subgroup differences: \( \chi^2 = 187.08, df = 1 (P < 0.00001), I^2 = 99.5\% \)) (Figure 4). After studying the full articles carefully, we found that the difference between these two and other article is that they both used Jin 3-needle technique which has a unique twist technique. This indicated that the source of heterogeneity might be related to the frequency and duration of twist technique. It also illustrated that twist technique may influence the effect of improving cognitive function, as the studies used Jin 3-needle technique \( (MD = 11.82, 95\% CI (10.41, 13.23), P < 0.00001, I^2 = 0\%) \) had better outcomes than the studies did not \( (MD = 1.73, 95\% CI (1.39, 2.06), P < 0.00001, I^2 = 50\%) \). However, further research is still needed due to the small number of included studies using Jin 3-needle technique.

Finally, after sensitivity analysis, a total of 12 studies were included for evaluating the effect of acupuncture treatment according to MMSE. The fixed effect model was used for analysis on the basis of heterogeneity test \( (I^2 = 50\%) \). The results of meta-analysis showed that the MMSE score of the acupuncture treatment group was higher than that of the control group \( (MD = 1.73, 95\% CI (1.39, 2.06), P < 0.00001) \). According to subgroup analysis based on treatment duration, meta-analysis results showed that MMSE score of the acupuncture treatment group was higher than that of the treatment group in \( \leq 7\)-week subgroup \( (MD = 1.63, 95\% CI (1.28, 1.99), P < 0.00001, I^2 = 60\%) \). MMSE score in the \( > 7\)-week subgroup was higher than that in the treatment group \( (MD = 2.36, 95\% CI (1.43, 3.29), P < 0.00001, I^2 = 0\%) \) (Figure 5). It illustrated that the duration of acupuncture treatment was also a factor that could influence heterogeneity but have few effect on the outcomes. We also conducted subgroup analysis based on retention time and frequency of acupuncture, but those did not have much influence on heterogeneity or outcomes.

3.5. Effects of Acupuncture Treatment According to MoCA Assessment Scales. There are nine [32, 33, 38, 41–44, 49, 52] trials that used MoCA to compare the cognitive function between acupuncture group and nonacupuncture group. A high statistical heterogeneity was observed \( (I^2 = 84\% > 50\%) \).
After using sensitivity analysis of studies, we found one article [49] that had relatively large impact on statistical heterogeneity. What distinguishes it from other studies is the retention time of acupuncture, so we conducted subgroup analysis based on retention time (Figure 6). It shows that the score of MoCA in the acupuncture group was observed to be higher than that...
also illustrated that retention time may also influence the effect of improving MoCA score, as the study with retention time of 6h (MD = 6.32, 95% CI (4.81, 7.83), I^2 = 83%) had better outcomes than the studies with retention time of 0.5h (MD = 2.15, 95% CI (1.39, 2.91), P < 0.00001, I^2 = 64%). However, further research is still needed due to the small number of included studies with long retention time.

### 3.6. Effects of Acupuncture Treatment According to Activities of Daily Living

There are nine [35, 42–44, 46, 47, 49, 50, 52] trials that used Barthel Index or modified Barthel Index to compare ADL between acupuncture group and nonacupuncture group. The other two trials [48, 53] also mentioned they evaluated ADL but did not specified what kind of scale they used; therefore, we did not include them in this analysis. A high statistical heterogeneity was observed (I^2 = 83% > 50%). Therefore, random-effects model analysis

| Study or subgroup | Experimental | Control | Weight | Mean difference | Std. mean difference |
|-------------------|--------------|---------|--------|-----------------|---------------------|
|                   | Mean (SD)    | Mean (SD) |     | IV, random, 95% CI | Year |
| **3.1.1 acupuncture retention time is 0.5 hour** | | | | | |
| Bao 2012          | 51.2 (11.5)  | 44.6 (10.3) | 30   | 11.1% | 0.60 (0.08, 1.11) | 2012 |
| Liu 2016          | 64.83 (16.16) | 54.67 (16.13) | 30   | 11.1% | 0.62 (0.10, 1.14) | 2016 |
| Zhang 2018        | 53.2 (3.94)  | 47.8 (3.8)  | 30   | 10.7% | 1.38 (0.81, 1.94) | 2018 |
| Zeng 2018         | 21.73 (1.95) | 18.84 (2.79) | 35   | 11.1% | 1.18 (0.67, 1.70) | 2018 |
| Li 2019           | 68.61 (9.62) | 64.04 (9.03) | 40   | 11.6% | 0.49 (0.04, 0.93) | 2019 |
| Zhang 2018        | 58.47 (9.61) | 56.47 (9.61) | 30   | 11.1% | 0.21 [-0.31, 0.72] | 2019 |
| Nie 2019          | 78.31 (3.98) | 74.67 (4.78) | 30   | 11.0% | 0.82 (0.29, 1.35) | 2019 |
| Ding 2019         | 68.45 (15.25) | 52.35 (15.6) | 55   | 12.0% | 1.04 (0.64, 1.44) | 2019 |
| Subtotal (95% CI) | 277          | 280       | 89.6% | 0.79 (0.53, 1.05) | |
| Heterogeneity: tau^2 = 0.08; chi^2 = 15.52, df = 7 (P = 0.03); I^2 = 55% Test for overall effect: Z = 5.90 (P < 0.00001) | | | | | |

| Study or subgroup | Experimental | Control | Weight | Mean difference | Std. mean difference |
|-------------------|--------------|---------|--------|-----------------|---------------------|
|                   | Mean (SD)    | Mean (SD) |     | IV, random, 95% CI | Year |
| **3.1.2 acupuncture retention time is 6 hour** | | | | | |
| Mao 2019          | 74.08 (5.62) | 58.76 (6.12) | 39   | 10.4% | 2.58 [1.97, 3.19] | 2019 |
| Subtotal (95% CI) | 39           | 39       | 10.4% | 2.58 [1.97, 3.19] | |
| Heterogeneity: not applicable Test for overall effect: Z = 8.32 (P < 0.00001) | | | | | |
| Total (95% CI)    | 316          | 319      | 100.0% | 0.97 [0.57, 1.38] | |
| Heterogeneity: tau^2 = 0.32; chi^2 = 46.46, df = 8 (P < 0.00001); I^2 = 83% Test for Overall affect: Z = 4.70 (P < 0.00001) Test for subgroup differences: chi^2 = 28.26, df = 1 (P < 0.00001), I^2 = 96.5% | | | | | |
was chosen to conduct meta-analysis. After using sensitivity analysis of studies, we found one article [49] that had relatively large impact on statistical heterogeneity. What distinguishes it from other studies was the retention time of acupuncture, so we conducted subgroup analysis based on retention time (Figure 7). Therefore, we divided the 9 articles into 2 groups according to the acupuncture retention time. It shows that the score in the acupuncture group was observed to be higher than that in the nonacupuncture group (SMD = 0.97, 95% CI (0.57, 1.38), P < 0.00001); the difference is statistically significant. It also showed that longer acupuncture retention time may lead to better result in activities of daily life (0.5 hours: SMD = 0.79, 95% CI (0.53, 1.05), P < 0.00001; 6 hours subgroup: SMD = 2.58, 95% CI (1.97, 3.19), P < 0.00001).

3.7. Safety. Safety of acupuncture therapy was reported in nine [32, 33, 37, 39, 42–44, 48, 50] of the included articles. Six [32, 33, 37, 39, 43, 48] of the articles reported no adverse events related to acupuncture therapy happened during the trials. One article [50] reported one case of adverse event but did not mention the reason. One article [42] reported one case of subcutaneous hematoma in the experiment group and three cases of fainting in the control group. Another article [44] reported one case of fainting during acupuncture and two cases of subcutaneous hematoma.

3.8. Publication Bias. We used STATA V.15.1 to evaluate publication bias. For MMSE, publication bias was assessed using Begg’s test (Figures 8 and 9) and Egger’s test (Figures 10 and 11), which did not show significant publication bias in the included studies. For MoCA and Barthel, the publication bias could not be assessed as less than ten articles were included.

4. Discussion

After searching PubMed, the Cochrane Library, CNKI, WanFang Data, VIP, CBM, Medline, and Embase databases, 657 relevant RCTs were found in this meta-analysis, and 22 RCTs with 1856 patients were eventually included. According to this study, more evidence was provided to prove that acupuncture treatment is beneficial to PSCI patients in terms of cognitive function and ability of daily life. PSCI, which has high prevalence rate, is a result of mixed damage mechanisms [55]. Jeremy’s study [56] suggested that ongoing ischemic vascular processes were the main mechanism which also emphasized the importance of management for vascular risk factor. Apart from that, there is no established therapy for prevention for PSCI so far. Hence, it is of vital importance for us to explore an effective and highly compliant treatment for PSCI patients.

There were a few relevant meta-analyses about acupuncture treatment for cognitive impairment. Liu et al. [57] searched RCTs that used acupuncture in the treatment of PSCI before February 2012 and included 21 RCTs with a total of 1421 patients. Due to the high risk of bias and lack of unified scale for evaluating cognitive function of the included studies, it is hard to reach reliable conclusions on the effect of acupuncture. Furthermore, it did not focus on analyzing the effects of acupuncture alone but on the combined treatment with acupuncture, which made it difficult to objectively evaluate the effect of acupuncture treatment for PSCI. Kim et al. [58] searched the RCTs on mild cognitive impairment (MCI) patients from October 2007 to August 2017 and
compared the effect of electroacupuncture (EA) to western medication. Their study, which included 5 RCTs with 257 patients, showed that EA had a higher score on MMSE and MoCA than western medications. But the weak methodological quality of the studies and small sample size may affect the reliability of the results.

This present review offered several significant perspectives. Firstly, a common deficiency of previous RCTs and reviews is the lack of attention to ADL. There were only 9 RCTs that we included used BI or MBI to evaluate ADL on PSCI patients. ADL is one of the most important measures to evaluate how severe PSCI is and an essential measure to distinguish PSCIND and PSD [12]. Moreover, PSD has a significantly higher fatality rate than PSCIND [55]. Therefore, we strongly recommend future studies to focus on the ability of daily life for PSCI patients and explore if acupuncture has the benefit of preventing PSCIND progressing to PSD whenever possible. Secondly, it may cause false increase in patients’ test results by using the same version of scale to evaluate cognitive function before and after the treatment. In order to ensure accuracy of MoCA test, we completed MoCA’s official standardized training and certification program online. We learned from the official website (https://www.mocatest.org/training-certification/) that the delay between administration should be sufficient to decrease the risk of a possible learning effect when administering the MoCA to the same subject; the alternative/equivalent versions of the MoCA should be used to decreased possible learning effects when the MoCA is administered, respectively. Therefore, we suggest using different versions of MoCA, such as 7.1, 7.2, or 7.3 versions at different stages of assessment. Thirdly, more attention should be paid to the standardized use of the scale. For instance, in this review, three articles were found incorrect using of MMSE. The wrong use of the scale may lead to serious errors in screening and evaluation of patients. Furthermore, most of the included RCTs have unclear bias of randomization process, measurement of the outcome, and selection of the reported results, which have a significant impact on the evaluation of the results. It is true that the nature of the acupuncture made it difficult for investigators to blind participants and almost impossible to blind the therapists; all the RCTs we included likewise did not blind the participants or therapists. However, we should attach more importance to the blinding on outcome assessors, especially the scale evaluators whose judgement may have a large influence on the outcome. We also advise that all the RCTs which study the effect of acupuncture should have a protocol with complete information prior to the start of trials. The protocol should provide detailed information according to the CONSORT statement and STRICTA recommendations in order to minimize the performance and assessment bias of RCTs.

This review also had certain limitations. Firstly, although we searched the trials written in Chinese or English, all the trials included were conducted in China. This is related to the less application of using acupuncture treatment on PSCI in countries other than China, and it may limit the universality of the results. Moreover, our study mainly focused on the effect of acupuncture alone but neglected the synergistic effect between acupuncture and other effective treatment, such as medication or cognitive training. In addition, this study did not consider the possible placebo effect of
acupuncture as no sham/placebo-controlled trials were included. Furthermore, significant heterogeneities were observed in our study. Experimental design, various acupoint selecting, and therapist skill difference can contribute to the high heterogeneity. Problems about which acupoints are most effective for PSCI and how long the treatment should last need to be resolved in future studies.

5. Conclusions

Compared with the nonacupuncture group, the acupuncture group showed better effects in improving the scores of MMSE, MoCA, BI, and MBI. This meta-analysis provided positive evidence that acupuncture may be effective in improving cognitive function and activities of daily life for PSCI patients. Meanwhile, long retention time of acupuncture may improve cognitive function and activities of daily life, and twist technique may be an important factor that could influence cognitive function. However, further studies using large samples and a rigorous study design are needed to confirm the role of acupuncture in the treatment of PSCI.

Abbreviations

- DALYs: Disability-adjusted life-years
- PSCI: Poststroke cognitive impairment
- PSCIND: Poststroke cognitive impairment with no dementia
- PSD: Poststroke dementia
- K-VCIHS-NP: Korean Vascular Cognitive Impairment Harmanization Standards neuropsychological protocol
- RCTs: Randomized controlled trials
- FDA: The Food and Drug Administration
- BDNF: Brain-derived neurotrophic factor
- CREB: cAMP-response element-binding protein
- CNKI: China National Knowledge Infrastructure
- CBM: China Biology Medicine disc
- VIP: China Science and Technology Journal Database
- RCT: Randomized controlled trial
- MMSE: Mini-Mental State Examination
- MoCA: Montreal Cognitive Assessment
- BI: Barthel Index
- MD: Mean difference
- CI: Confidence interval
- RCTs: Randomized controlled trials
- MOI: Mean di
- BB: Barthel Index
- BBD: Barthel Index
- MBD: Barthel Index
- CI: Confidence interval
- RCT: Randomized controlled trial
- MMSE: Mini-Mental State Examination
- MoCA: Montreal Cognitive Assessment
- BI: Barthel Index
- MD: Mean difference
- CI: Confidence interval
- RCT: Randomized controlled trial
- MOI: Mean di

Data Availability

The datasets generated during and analysed during the current study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Authors’ Contributions

Wei Liu and Chang Rao developed the study concept and design, performed the data acquisition and analysis, and drafted the manuscript. Jipeng Yang and Lili Zhang modified the manuscript. Yuzheng Du read, modified, and approved the final manuscript for submission.

Acknowledgments

This study was financially supported by the Tianjin Science and Technology Project (NO. 18PTLC5Y00060).

Supplementary Materials

Supplemental Files: PRISMA Checklist (the 27 checklist items pertain to the content of a systematic review and meta-analysis, which include the title, abstract, methods, results, discussion, and funding). (Supplementary Materials)

References

[1] G. J. Hankey, “Stroke,” Lancet, vol. 389, no. 10069, pp. 641–654, 2017.
[2] S. Wu, B. Wu, M. Liu et al., “Stroke in China: advances and challenges in epidemiology, prevention, and management,” Lancet Neurology, vol. 18, no. 4, pp. 394–405, 2019.
[3] D. A. Levine, A. T. Galecki, K. M. Langa et al., “Trajectory of cognitive decline after incident stroke,” Journal of the American Medical Association, vol. 314, no. 1, pp. 41–51, 2015.
[4] L. Jia, M. Quan, Y. Fu et al., “Dementia in China: epidemiology, clinical management, and research advances,” Lancet Neurology, vol. 19, no. 1, pp. 81–92, 2020.
[5] Q. Guo, Q. Guo, B. Luo et al., “Expert consensus on the management of cognitive impairment after stroke,” Chinese Journal of Stroke, vol. 12, no. 6, pp. 519–531, 2017.
[6] H. Y. Yu, S. J. Cho, M. S. Oh et al., “Cognitive impairment evaluated with vascular cognitive impairment harmonization standards in a multicenter prospective stroke cohort in Korea,” Stroke, vol. 44, no. 5, pp. 786–788, 2013.
[7] C. S. Ivan, S. Seshadri, A. Beiser et al., “Dementia after stroke: the Framingham study,” Stroke, vol. 35, no. 6, pp. 1264–1268, 2004.
[8] K. B. Rajan, N. T. Aggarwal, R. S. Wilson, S. A. Everson-Rose, and D. A. Evans, “Association of cognitive functioning, incident stroke, and mortality in older adults,” Stroke, vol. 45, no. 9, pp. 2563–2567, 2014.
[9] H. Jokinen, S. Melkas, R. Ylikoski et al., “Post-stroke cognitive impairment is common even after successful clinical recovery,” European Journal of Neurology, vol. 22, no. 9, pp. 1288–1294, 2015.
[10] J. H. Park, B. J. Kim, H. J. Bae et al., “Impact of post-stroke cognitive impairment with no dementia on health-related quality of life,” Journal of Stroke, vol. 15, no. 1, pp. 49–56, 2013.
[11] J. H. Sun, L. Tan, and J. T. Yu, "Post-stroke cognitive impairment: epidemiology, mechanisms and management," *Annals of Translational Medicine*, vol. 2, no. 8, p. 80, 2014.

[12] M. D. Mijailović, A. Pavlović, M. Brainin et al., "Post-stroke dementia - a comprehensive review," *BMC Medicine*, vol. 15, no. 1, p. 11, 2017.

[13] M. Fioravanti, L. Flicker, and Cochrane Dementia and Cognitive Improvement Group, "Nicergoline for dementia and other age associated forms of cognitive impairment," *Cochrane Database of Systematic Reviews*, vol. 2001, no. 4, article CD003159, 2001.

[14] P. B. Gorelick, A. Scuteri, S. E. Black et al., "Vascular contributions to cognitive impairment and dementia: a statement for healthcare professionals from the American Heart Association/American Stroke Association," *Stroke*, vol. 42, no. 9, pp. 2672–2713, 2011.

[15] Y. Guo, M. Xiangwen, L. Yihong et al., “Comparison and analysis on the development of acupuncture and moxibustion medicine in recent years,” *Chin J Inf Tradit Chin Med*, vol. 20, no. 4, pp. 1–5, 2013.

[16] L. M. Chavez, S. S. Huang, I. MacDonald, J. G. Lin, Y. C. Lee, and Y. H. Chen, “Mechanisms of acupuncture therapy in ischemic stroke rehabilitation: a literature review of basic studies,” *International Journal of Molecular Sciences*, vol. 18, no. 11, p. 2270, 2017.

[17] M. Mukherjee, L. K. McPeak, J. B. Redford, C. Sun, and W. Liu, "The effect of electro-acupuncture on spasticity of the wrist joint in chronic stroke survivors," *Archives of Physical Medicine and Rehabilitation*, vol. 88, no. 2, pp. 159–166, 2007.

[18] P. Chou, H. Chu, and J. G. Lin, "Effects of electroacupuncture treatment on impaired cognition and quality of life in Taiwanese stroke patients," *Journal of Alternative and Complementary Medicine*, vol. 15, no. 10, pp. 1067–1073, 2009.

[19] U. Ghafoor, J. H. Lee, K. S. Hong, S. S. Park, J. Kim, and H. R. Yoo, "Effects of acupuncture therapy on MCI patients using functional near-infrared spectroscopy," *Frontiers in Aging Neuroscience*, vol. 11, 2019.

[20] Z. J. Zhang, H. Y. Chen, K. C. Yip, R. Ng, and V. T. Wong, "The effectiveness and safety of acupuncture therapy in depressive disorders: a systematic review and meta-analysis," *Journal of Affective Disorders*, vol. 124, no. 1-2, pp. 9–21, 2010.

[21] B. Lee, B. Sur, J. Shim, D. H. Hahn, and H. Lee, "Acupuncture stimulation improves scopolamine-induced cognitive impairment via activation of cholinergic system and regulation of BDNF and CREB expressions in rats," *BMC Complementary and Alternative Medicine*, vol. 14, no. 1, 2014.

[22] M. Cai, J. H. Lee, and E. J. Yang, "Electroacupuncture attenuates cognition impairment via anti-neuroinflammation in an Alzheimer’s disease animal model," *Journal of Neuroinflammation*, vol. 16, no. 1, p. 264, 2019.

[23] Z. Dan, L. Zuowei, and L. Ping, "Systematic review of different acupuncture methods in the treatment of post-stroke cognitive impairment," *Journal of Sichuan of Traditional Chinese Medicine*, vol. 32, no. 6, pp. 155–158, 2014.

[24] C. Liazao, L. Wu, J. Wang et al., "Meta-analysis on the treatment of post-stroke cognitive impairment with head acupuncture," *Guiding Journal of Traditional Chinese Medicine and Pharmacy*, vol. 22, no. 22, pp. 84–87, 2016.

[25] H. Brodaty, M. H. Connors, C. Loy et al., "Screening for dementia in primary care: a comparison of the GPCOG and the MMSE," *Dementia and Geriatric Cognitive Disorders*, vol. 42, no. 5-6, pp. 323–330, 2016.

[26] M. F. Folstein, S. E. Folstein, and P. R. McHugh, "‘Mini-mental state’. A practical method for grading the cognitive state of patients for the clinician," *Journal of Psychiatric Research*, vol. 12, no. 3, pp. 189–198, 1975.

[27] Z. S. Nasreddine, N. A. Phillips, V. Bédirian et al., "The Montreal cognitive assessment, MoCA: a brief screening tool for mild cognitive impairment," *Journal of the American Geriatrics Society*, vol. 53, no. 4, pp. 695–699, 2005.

[28] Y. L. Chang, M. W. Bondi, L. K. McEvoy et al., "Global clinical dementia rating of 0.5 in MCI masks variability related to level of function," *Neurology*, vol. 76, no. 7, pp. 652–659, 2011.

[29] S. Kwon, A. G. Hartzema, P. W. Duncan, and S. Min-Lai, "Disability measures in stroke," *Stroke*, vol. 35, no. 4, pp. 918–923, 2004.

[30] H. Houlden, M. Edwards, J. McNeil, and R. Greenwood, "Use of the Barthel index and the functional Independence measure during early inpatient rehabilitation after single incident brain injury," *Clinical Rehabilitation*, vol. 20, no. 2, pp. 153–159, 2016.

[31] B. Prodinger, R. O’Connor, G. Stucki, and A. Tennant, "Establishing score equivalence of the functional Independence measure motor scale and the Barthel index, utilising the international classification of functioning, disability and health and Rasch measurement theory," *Journal of Rehabilitation Medicine*, vol. 49, no. 5, pp. 416–422, 2017.

[32] S. Wang, H. Yang, J. Zhang et al., "Efficacy and safety assessment of acupuncture and nimodipine to treat mild cognitive impairment after cerebral infarction: a randomized controlled trial," *BMC Complementary and Alternative Medicine*, vol. 16, no. 1, p. 361, 2016.

[33] C. Jiang, S. Yang, J. Tao et al., "Clinical efficacy of acupuncture treatment in combination with RehaCom cognitive training for improving cognitive function in stroke: a 2 × 2 factorial design randomized controlled trial," *Journal of the American Medical Directors Association*, vol. 17, no. 12, pp. 1114–1122, 2016.

[34] W. Lina and L. Fang, "Effect of atorvastatin combined with acupuncture on patients with mild cognitive impairment after stroke," *GuangDong Medical Journal*, vol. 39, no. 23, pp. 3557–3561, 2018.

[35] B. Yu, Z. Wei, and S. Xiaowei, "Therapeutic observation on acupuncture for mild cognitive impairment after cerebral infarction," *Shanghai Journal of Acupuncture and Moxibustion*, vol. 31, no. 7, pp. 470–472, 2012.

[36] Z. Xiaojian, Z. Yuan, G. Zechun et al., "Effect of acupuncture at cervical Jiapin and Du Channel point combined with atorvastatin on hemodynamics in patients with mild cognitive impairment after stroke," *Journal of Hunan Normal University (Medical Sciences)*, vol. 14, no. 2, pp. 131–134, 2017.

[37] W. Qin, D. Juncheng, and S. Liangying, "Effects of acupuncture combined with atorvastatin on Hemorheology and cognitive status of elderly patients with mild cognitive impairment after ischemic stroke," *Chinese Journal of Gerontology*, vol. 39, no. 21, pp. 5180–5183, 2019.

[38] Y. Hongling, Z. Jiangang, L. Tao et al., "Therapeutic observation on acupuncture combined with Nimodipine for mild cognitive impairment after cerebral infarction," *Journal of Clinical Acupuncture and Moxibustion*, vol. 31, no. 3, pp. 33–36, 2015.
Observation on the Curative Effect or Acupuncture of Ear-Well Acupoint on Treatin Mild Vascular Cognitive Impairment after Stroke, Master, Anhui University of Chinese Medicine, Anhui, China, 2017.

Clinical study on post stroke cognitive impairment by eye acupuncture, "Guid J Tradit Chin Med Pharm," vol. 24, no. 12, pp. 67–69, 2018.

Effect of Acupuncture on Attention Function in Post-Stroke Patients with Cognitive Impairment Based on EEG Signal, Fujian University of Traditional Chinese Medicine, Fujian, China, Master, 2018.

Effects of acupuncture combined with donepezil on cognitive impairment after stroke in elderly patients. Chinese journal of prevention and control of chronic, "Diseases," vol. 27, no. 8, pp. 617–620, 2019.

Kidney and medullary acupuncture combined with compound musk injection for the treatment of cognitive impairment after stroke, "Chinese Journal of General Practice," vol. 17, no. 3, pp. 416–418 +499, 2019.

Study on the Effect and Therapeutic Effect of Tongdu Tianwen Acupuncture on Platelet Microparticles in Patients with Ischemic Stroke, Master, Anhui University of Chinese Medicine, Anhui, China, 2019.

Therapeutic observation on cluster needling at scalp Acupoints plus cognition training for post-stroke cognitive impairment, "Shanghai J Acup Moxi," vol. 31, no. 10, pp. 711–713, 2012.

Clinical effects of Jin’s 3-needle combined with cognitive rehabilitation training in the treatment of convalescent cerebral apoplexy with cognitive impairment, "Shandong Journal of Traditional Chinese Medicine," vol. 37, no. 5, pp. 367–370, 2018.

Clinical observation of triple energizer acupuncture combined with computer aided cognitive training in treatment of cognitive impairment after acute stroke, "Shandong Journal of Traditional Chinese Medicine," vol. 38, no. 12, pp. 1118–1122, 2019.

Efficacy of acupuncture plus cognitive rehabilitation training for post-stroke cognitive impairment and its effect on cytokines, "Shanghai J Acup Moxi," vol. 38, no. 10, pp. 1098–1102, 2019.

Treatment of 39 patients with cognitive impairment after stroke with acupuncture combined with modern rehabilitation training, "Traditional Chinese Medicine Research," vol. 32, no. 10, pp. 47–49, 2019.

Effect of Eye Acupuncture Combined with Cognitive Training on Vascular Cognitive Impairment after Stroke, Master, Liaoning University of Traditional Chinese Medicine, Liaoning, China, 2016.

Effects of Acupuncture Combined with Cognitive Training on the Expression of Synapse Related miRNAs in Patients with Post-Stroke Cognitive Impairment, Master, Fujian University of Traditional Chinese Medicine, Fujian, China, 2017.

Acupuncture Combined with Cognitive Rehabilitation in the Treatment of Cognitive Impairment after Stroke, Master, Shanxi University of Chinese Medicine, Shanxi, China, 2018.

Efficacy observation of Bianjing Cijing combined with Nie’s 3-needle in the treatment of cognitive impairment in acute stroke. Clinical," Journal of Traditional Chinese Medicine, vol. 24, no. 11, pp. 1059–1061, 2012.

Comparison of the mini-mental state examination and Montreal cognitive assessment executive subtests in detecting post-stroke cognitive impairment," Geriatrics & Gerontology International, vol. 17, no. 12, pp. 2329–2335, 2017.

Prevalence of post-stroke cognitive impairment in China: a community-based, cross-sectional study," PLoS One, vol. 10, no. 4, article e0122864, 2015.

Vascular and neurodegenerative markers for the prediction of post-stroke cognitive impairment: results from the TABASCO study," Journal of Alzheimer's Disease, vol. 70, no. 3, pp. 889–898, 2019.

A meta-analysis of acupuncture use in the treatment of cognitive impairment after stroke," The Journal of Alternative and Complementary Medicine, vol. 20, no. 7, pp. 535–544, 2014.

Cognitive improvement effects of electro-acupuncture for the treatment of MCI compared with Western medications: a systematic review and meta-analysis," BMC Complementary and Alternative Medicine, vol. 19, no. 1, p. 13, 2019.