

# Acupuncture for Post-Stroke Cognitive Impairment: An Overview of Systematic Reviews

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**Background:** Post-stroke cognitive impairment (PSCI) is one of the most common complications after stroke. In recent years, as a complementary alternative therapy, many systematic reviews (SRs) and meta-analysis (MAs) have reported the efficacy and safety of acupuncture in improving cognitive function in patients with PSCI, but the quality of evidence is unknown and therefore needs to be evaluated comprehensively.

**Aim:** We aimed to evaluate the SRs of acupuncture for patients with PSCI, to summarize the evidence quality of SRs to provide scientific evidence.

**Methods:** We searched for relevant SRs and MAs in seven databases up to March 22, 2022. Two reviewers independently completed literature retrieval, screening, and data extraction. We used A Measurement Tool to Assess Systematic Reviews 2 (AMSTAR 2) to evaluate the methodological quality; the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool to determine the strength of evidence; and the ROBIS tool to assess RoB.

**Results:** We identified 14 SRs. The methodological quality of all SRs was low (2/14) or very low (12/14). GRADE results showed 13 were moderate quality (26%), 5 were low quality (10%), and 32 were very-low quality (64%). RoB showed that one SR had a low risk and 13 had a high risk. Moderate quality results showed that combined acupuncture therapy was superior to western medicine or cognitive rehabilitation training in improving cognitive function, the total response rate, and the daily living ability of patients with PSCI.

**Conclusion:** Based on the evidence, acupuncture appears to be effective and safe in improving cognitive function for patients with PSCI, but the overall quality of SRs is not high. High-quality randomized controlled trials are needed to confirm the effectiveness and safety of acupuncture on the cognitive function of patients with PSCI.

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**Keywords:** acupuncture, PSCI, overview, AMSTAR-2, GRADE

## Introduction

Stroke is a leading cause of mortality and disability worldwide.<sup>1</sup> Post-stroke cognitive impairment (PSCI) is one of the most common complications after stroke, mainly manifested as impairments in memory, attention, orientation, and visuospatial function. PSCI refers to a series of syndromes that meet the diagnostic criteria for cognitive impairment after the occurrence of stroke.<sup>2</sup> Two thirds of patients in the acute stage of stroke may have PSCI,<sup>3,4</sup> and more than one third of patients with PSCI develop dementia after stroke recurrence<sup>4</sup> and are easily overlooked.<sup>5</sup> PSCI seriously affects rehabilitation compliance, delays the process of functional recovery, and reduces the quality of life.<sup>6</sup> Therefore, early identification and timely intervention are of great significance to prevent the occurrence of PSCI and to control disease progression.

At present, the main therapeutic objectives for PSCI are to delay the progression of the disease and to prevent risk factors and complications, usually by combining drugs and non-drugs. Western medicine mainly uses calcium channel antagonists, cholinesterase inhibitors, and neurological agents<sup>7</sup> alongside cognitive rehabilitation training. However,

these interventions do not improve clinical efficacy, and the high cost and various adverse drug reactions also affect patient compliance. Therefore, it is necessary to explore other adjuvant treatment modalities.

In recent years, randomized controlled trials (RCTs) have shown the positive effect of acupuncture on improving the cognitive function and daily living ability of patients with PSCI,<sup>8,9</sup> but the quality of evidence in favor of acupuncture for patients with PSCI presented in the relevant systematic reviews (SRs) and meta-analyses (MAs) is unclear. We aimed to collect, analyze, and present descriptive characteristics as well as the quantitative outcome data in SRs on acupuncture in patients with PSCI, and to assess their methodological quality.<sup>10</sup> Our comprehensive evaluation also attempted to clarify the quality of the evidence for acupuncture treatment of patients with PSCI to provide better clinical support.

## Methods

### Search Strategy

We searched the Embase, Cochrane Library, PubMed, CNKI, SinoMed, VIP, and Wanfang databases for SRs published from the beginning to March 22, 2022 without language restriction. We used a combination of subject words and free words, including “stroke”, “post-stroke”, “apoplexy”, “cognitive dysfunction”, “cognition impairment”, “cognitive disorder”, “acupuncture”, “electro acupuncture”, “auricular acupuncture”, “scalp acupuncture”, “systematic review”, “systematic evaluation”, “meta-analysis.” In addition, we manually searched the list of references in the included SRs. The detailed retrieval strategy is shown in [Supplementary document](#).

### Inclusion Criteria

We included SRs and MAs based on RCTs of acupuncture for patients with PSCI. PSCI was diagnosed without restriction for gender, age, and course of disease. The treatment group included traditional acupuncture, electroacupuncture, ear acupuncture, head acupuncture, or acupuncture combined with other treatment. The control group was treated with any other methods except acupuncture, such as sham acupuncture, placebo, conventional therapy, western medicine, and cognitive function training. At least one of these results had to be reported in SRs: total effective rate, Mini-mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), activities of daily living (ADL), P300 peak latency, P300 amplitude, Barthel Index (BI), Loewenstein Occupational Therapy Cognitive Assessment (LOTCA), and Neurobehavioral Cognitive Status Examination (NCSE).

### Exclusion Criteria

We excluded an SR if it met any of the following criteria: (a) the diagnostic criteria were unclear; (b) the intervention was mainly non-acupuncture or the control group received the same acupuncture therapy as the experimental group; (c) repeat publications; (d) unable to obtain the full text or incomplete data presented; (e) other types of research, such as animal experiments, protocols, conference papers, and case reports.

### Study Selection and Data Extraction

According to the comprehensive retrieval strategy, two reviewers independently conducted literature retrieval and screening. The opinion of a third reviewer was sought when there was a disagreement. After identifying eligible studies, two researchers independently extracted relevant data according to standardized extraction tables, such as author, publication year, sample size, diagnostic criteria, interventions, outcomes, adverse reactions, conclusions, etc. Two reviewers cross-checked the extracted content, and a third reviewer was consulted to resolve any discrepancies.

### Assessment of SRs

#### AMSTAR 2

Two reviewers used A Measurement Tool to Assess Systematic Reviews 2 (AMSTAR 2)<sup>11</sup> to evaluate the methodological quality of SRs. This tool includes 16 items in total, with items 2, 4, 7, 9, 11, 13, and 15 considered key items. Items 2, 4, 7, 8, and 9 are rated as yes, no, or partially yes. The rest are rated as yes or no. Finally, the assessment level is divided into high, moderate, low, and very low.

## ROBIS

We used the ROBIS tool<sup>12</sup> to assess the risk of bias (RoB) for SRs. The evaluation process is divided into three stages: (a) evaluating correlation (selected according to the situation); (b) determine the degree of RoB in the SR process; (c) judge the RoB. We systematically evaluated four key areas for the second phase: (a) study eligibility criteria, (b) identification and selection of studies, (c) data collection and study appraisal, and (d) synthesis and findings. Each field consists of 5 or 6 key questions. The third stage judges the overall RoB according to the results of the second stage, and finally divides the risk level into “low risk”, “high risk”, and “unclear risk.” One person assessed RoB, another person checked this assessment, and then both reviewers discussed the results. In the case of a disagreement, a third party was consulted.

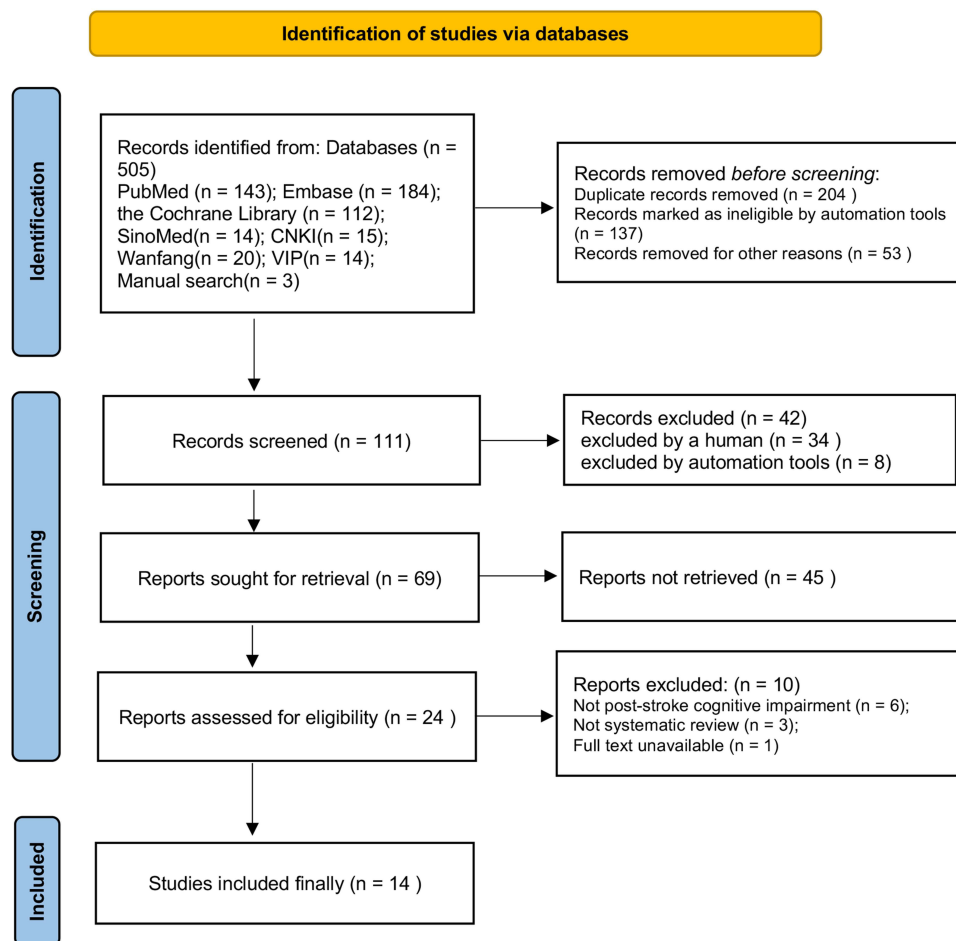
## GRADE

Two researchers independently used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool<sup>13</sup> to evaluate the quality of the evidence. It includes five aspects: RoB, inconsistency, indirectness, imprecision, and publication bias. The two reviewers cross-checked the results, and disputes were decided by a third reviewer. We graded the quality of evidence as “high”, “moderate”, “low”, and “very low.”

## Results

### Search Results

We retrieved 505 related studies from the 7 databases. Of these, we deleted 204 duplicates and then screened 24 studies, followed by full-text evaluation. Finally, we included 14 SRs. The detailed flow chart is shown in [Figure 1](#). The list of exclusions and reasons are shown in Excluded list in the [Supplementary document](#).



**Figure 1** The detailed flow chart.

## Characteristics of the Included SRs

The 14 SRs<sup>14–27</sup> were published from 2015 to 2021; two SRs<sup>19,27</sup> were published in English and the others in Chinese. The SRs comprised a total of 263 RCTs and 19,224 subjects. Each SR included 8–42 RCTs, with a sample size of 506–3069 participants.

Six SRs defined the diagnostic criteria, and three SRs<sup>14,20,21</sup> adopted the Main Points of Diagnosis of Various Cerebrovascular Diseases criteria. Three SRs<sup>18,20,24</sup> adopted the Diagnostic and Statistical Manual of Mental Disorders (4th ed.) criteria. One SR<sup>16</sup> used the Expert Consensus on the Management of Post-stroke Cognitive Impairment criteria. Zhang et al<sup>14</sup> combined the Diagnostic and Therapeutic Criteria of TCM Diseases and Syndromes (ZY/T001.1-94). The remaining SRs did not mention specific diagnostic criteria. The control group usually received conventional treatment, cognitive rehabilitation training, or western medicine, and the treatment group combined traditional acupuncture, electroacupuncture, or ear acupuncture with the treatment received by the control group. The duration was usually 4–12 weeks. Adverse events were reported in six SRs,<sup>16,18,19,23–25</sup> no adverse events were observed in one SR,<sup>22</sup> and adverse events were not mentioned in the remaining SRs. Regarding the methodological quality assessment, four SRs<sup>14,20–22</sup> used the Jadad scale, one SR<sup>15</sup> did not report this information, and the remaining nine SRs used the Cochrane Collaboration's RoB assessment tool. The basic characteristics of the literature are shown in Table 1.

## Methodological Assessment

We used AMSTAR 2 to assess the methodological quality of the SRs. All SRs were low or very-low quality due to one or more serious deficiencies in critical items 2, 4, 7, 9, 11, 13, and 15, and multiple deficiencies in non-critical items.

Among the key items, only one SR reported the research protocol (item 2<sup>19</sup>) and only one SR reported the exclusion list (item 7<sup>16</sup>). The authors conducted a comprehensive database search to identify all relevant literature, but they did not search potential literature that might exist in detail (item 4). In 11 SRs, the authors synthesized data (item 11, except<sup>16,18,25</sup>). In 13 SRs, the authors considered RoB (Item 13, except<sup>15</sup>); 50% of SRs fully investigated and discussed the possible influence of publication bias on research results (item 15).

Among the non-critical items, the included SRs provided reasonable information on the inclusion criteria (item 1), literature screening and data extraction (items 5 and 6, except<sup>15</sup>), and basic characteristics (item 8), and they provided a heterogeneity discussion (item 14, except<sup>14,15</sup>). No SRs reported reasons for inclusion of RCTs (item 3). One SR reported funding source (item 10<sup>16</sup>); 50% of SRs considered the potential impact of RoB on the quality of evidence (item 12). Two SRs claims that there is no conflict of interest.<sup>19,27</sup> The detailed results are shown in Table 2.

## RoB

Only one SR<sup>19</sup> (7.1%) had a low RoB; the remaining 13 SRs (92.9%) had a high RoB. The problems were related to research retrieval and screening, data extraction and quality evaluation, data synthesis, and presentation of the results. Failure to properly interpret and handle RoB may result in a high RoB for SRs, reducing the credibility of results and conclusions. The detailed results are shown in Figure 2 and Table 3.

## Quality of Evidence

We used the GRADE tool to evaluate the evidence quality of 50 outcomes. There were 13 outcomes of moderate quality (26%), 5 of low quality (10%), and 32 of very-low quality (64%); none was high quality. The main influencing factors of demotion were RoB, publication bias, inconsistency, and inaccuracy. The detailed results are shown in Table 4.

## Efficacy of Acupuncture for Patients with PSCI

This overview included three different acupuncture methods: traditional acupuncture (9 SRs), electroacupuncture (3 SRs), and scalp acupuncture (3 SRs). The results showed that these methods could significantly improve the MMSE score of PSCI patients. In addition, traditional acupuncture had a positive effect on improving the quality of life. We analyzed the outcomes, and the results suggested that acupuncture showed certain advantages in improving MMSE (14 SRs), total

**Table 1** The Basic Characteristics of the Literature

Included Studies	Language	Number of RCTs (Participants)	Diagnostic Criteria	Intervention	Comparison	Duration	Adverse Effects (Number of RCTs, A/C)	Primary Outcomes	Methodological Evaluation Tool	Main Conclusion
suZhang (2015) <sup>14</sup>	Chinese	11 (395/394)	①②	A+C	CRT/WM	4–12 weeks	Not reported	①②④⑤⑥	Jadad	The effect of acupuncture combined with CRT was better than that of CRT or drugs alone
Lin (2016) <sup>15</sup>	Chinese	19 (640/635)	Unclear	A	BT	4–12 weeks	Not reported	②③④	Unclear	Acupuncture was better than BT in improving cognitive function of PSCI
Xu (2020) <sup>16</sup>	Chinese	15 (652/649)	③	A or A+C	CRT/Ni	4–12 weeks	Dizziness, hematoma, dizziness, headache, nausea, bruising, vomiting (21/11)	②③④⑦	Cochrane risk of bias tool	Acupuncture could reduce the degree of neurological impairment
Wang (2017) <sup>17</sup>	Chinese	15 (555/530)	Unclear	A or A+C	CRT/Ni	3–12 weeks	Not reported	①②③④	Cochrane risk of bias tool	Combined acupuncture was more beneficial for PSCI
Liu F (2015) <sup>18</sup>	Chinese	42 (1562/1507)	④	A+C	CRT/BT/WM	4–12 weeks	Bleeding, dizziness	②③⑤⑥⑧⑨	Cochrane risk of bias tool	Acupuncture could effectively improve the cognitive function of PSCI
Kuang (2021) <sup>19</sup>	English	28 (1072/1072)	Unclear	A+C	CRT/BT/WM	4–12 weeks	Hematoma, syncope (14/0)	②③	Cochrane risk of bias tool	Acupuncture could be effective and safe for PSCI
Liu WL (2015) <sup>20</sup>	Chinese	9 (293/285)	①④	EA or EA+C	CRT/WM	4–8 weeks	Not reported	①②	Jadad	Electroacupuncture could effectively improve the cognitive function of PSCI
Xiong (2015) <sup>21</sup>	Chinese	13 (475/465)	①	SA or SA+C	CRT/WM	4–10 weeks	Not reported	②⑤	Jadad	The effect of scalp acupuncture on cognitive function of PSCI was not clear

(Continued)

Table 1 (Continued).

Included Studies	Language	Number of RCTs (Participants)	Diagnostic Criteria	Intervention	Comparison	Duration	Adverse Effects (Number of RCTs, A/C)	Primary Outcomes	Methodological Evaluation Tool	Main Conclusion
Chen (2016) <sup>22</sup>	Chinese	8 (252/252)	Unclear	SA+C	WM	3–24 weeks	None	①②	Jadad	The clinical effect of scalp acupuncture on PSCI was better than WM alone
Zhan (2017) <sup>23</sup>	Chinese	14 (450/446)	Unclear	EA+C	CRT/Ni	4–8 weeks	Dizziness, itching (1/1)	①②③⑤⑥⑦	Cochrane risk of bias tool	Electroacupuncture was effective and safe in treating PSCI
Liu F (2018) <sup>24</sup>	Chinese	22 (825/812)	④	A+C	CRT/BT/WM	2–12 weeks	Bleeding	②⑤⑥	Cochrane risk of bias tool	Acupuncture could effectively improve the cognitive function of PSCI
Hu (2020) <sup>25</sup>	Chinese	11 (405/405)	Unclear	A+C	CRT/BT/WM	3–12 weeks	Fluctuation of blood pressure (1/1)	①②③	Cochrane risk of bias tool	Acupuncture could effectively improve the cognitive function of PSCI
Xie (2021) <sup>26</sup>	Chinese	19 (661/666)	Unclear	A+C	CRT/WM	3–12 weeks	Not reported	①②③④⑦⑧	Cochrane risk of bias tool	The clinical effect of scalp acupuncture on PSCI was better than WM or CRT
Zhou (2020) <sup>27</sup>	English	37 (1442/1427)	Unclear	A/EA+C	CRT/BT/WM	2–12 weeks	Not reported	②③	Cochrane risk of bias tool	Acupuncture was effective in improving PSCI

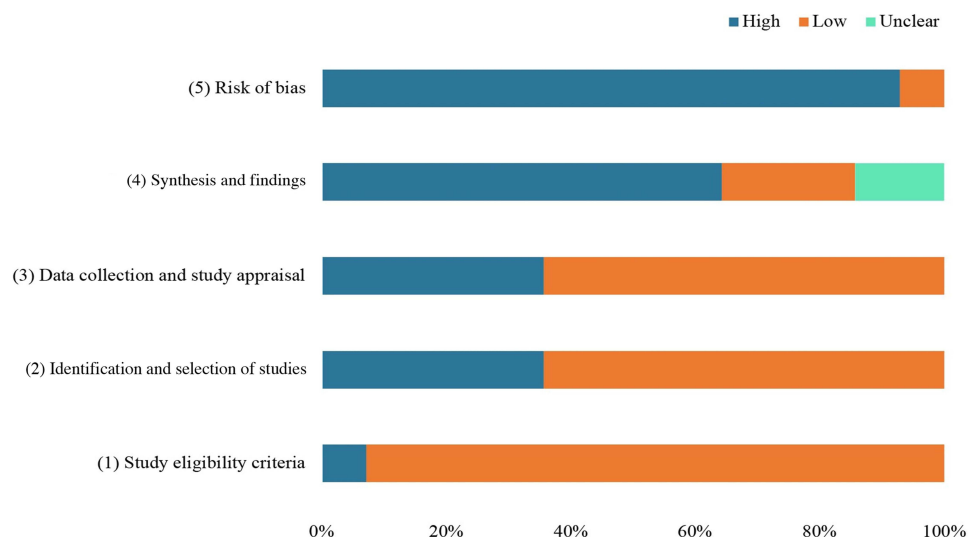
**Notes:** Diagnostic criteria: ① Main points of diagnosis of various cerebrovascular diseases; ② Diagnostic and therapeutic criteria of TCM diseases and syndromes (ZY/T001.1–94); ③ Expert Consensus on the Management of Post-stroke Cognitive Impairment; ④ Diagnostic Statistical Manual of Mental Disorders, 4th Ed. Primary outcomes: ① Total effective rate; ② Mini-mental State Examination, MMSE; ③ Montreal Cognitive Assessment, MoCA; ④ Activities of daily living, ADL; ⑤ P300 peak latency; ⑥ P300 amplitude; ⑦ Barthel Index, BI; ⑧ Loewenstein Occupational Therapy Cognitive Assessment, LOTCA; ⑨ Neurobehavioral Cognitive Status Examination, NCSE.

**Abbreviations:** A, Acupuncture; EA, Electroacupuncture; SA, Scalp acupuncture; C, Comparison; CRT, Cognitive rehabilitation training; Ni, Nimodipine; BT, Basic treatment; WM, Western medicine; PSCI, Post-stroke cognitive impairment.

**Table 2** The Detailed Results of AMSTAR-2

Included Studies	AMSTAR-2																Quality
	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Item 13	Item 14	Item 15	Item 16	
Zhang (2015) <sup>14</sup>	Y	N	N	PY	Y	Y	N	PY	Y	N	Y	Y	Y	N	N	N	Critically low
Lin (2016) <sup>15</sup>	Y	N	N	PY	N	N	N	PY	PY	N	Y	N	N	N	N	N	Critically low
Xu (2020) <sup>16</sup>	Y	N	N	PY	Y	Y	PY	PY	PY	PY	N	Y	Y	Y	Y	N	Critically low
Wang (2017) <sup>17</sup>	Y	N	N	PY	Y	Y	N	PY	Y	N	Y	Y	Y	Y	Y	N	Critically low
Liu F (2015) <sup>18</sup>	Y	N	N	PY	Y	Y	N	PY	PY	N	Y	Y	Y	Y	Y	N	Critically low
Kuang (2021) <sup>19</sup>	Y	Y	N	PY	Y	Y	N	PY	Y	N	Y	Y	Y	Y	Y	Y	Low
Liu WL (2015) <sup>20</sup>	Y	N	N	PY	Y	Y	N	PY	Y	N	N	N	Y	Y	N	N	Critically low
Xiong (2016) <sup>21</sup>	Y	N	N	PY	Y	Y	N	PY	Y	N	Y	N	Y	Y	Y	N	Critically low
Chen (2016) <sup>22</sup>	Y	N	N	PY	Y	Y	N	PY	Y	N	Y	N	Y	Y	N	N	Critically low
Zhan (2017) <sup>23</sup>	Y	N	N	PY	Y	Y	N	PY	Y	N	Y	N	Y	Y	N	N	Critically low
Liu F (2018) <sup>24</sup>	Y	N	N	PY	Y	Y	N	PY	Y	N	Y	N	Y	Y	N	N	Critically low
Hu (2020) <sup>25</sup>	Y	N	N	PY	Y	Y	N	PY	Y	N	N	N	Y	Y	N	N	Critically low
Xie (2021) <sup>26</sup>	Y	N	N	PY	Y	Y	N	PY	Y	N	Y	Y	Y	Y	Y	N	Critically low
Zhou (2020) <sup>27</sup>	Y	N	N	PY	Y	Y	N	Y	Y	N	Y	Y	Y	Y	Y	Y	Low
Y+PY/tota (%)	100	7.14	0	100	92.86	92.86	7.14	100	100	7.14	78.57	50	92.86	85.71	50	14.29	

Abbreviations: Y, yes; PY, partial yes; N, no.



**Figure 2** The detailed results of RoB.

effective rate (7 SRs), MoCA (9 SRs), ADL (5 SRs), P300 peak Latency (6 SRs), P300 amplitude (4 SRs), BI (6 SRs), LOTCA (2 SRs) and NCSE (1 SRs). However, the overall quality of evidence was low. Based on the results of the moderate-quality evidence, four SRs suggested that acupuncture combined with routine therapy is more effective in improving MMSE<sup>14,16,25,27</sup> and MoCA<sup>16,18,19,27</sup> scores. In addition, some studies showed that P300 amplitude<sup>18,24,28</sup> and P300 peak latency<sup>24</sup> in the acupuncture group were better than in the control group. These results indicate that the cognitive function rehabilitation effect of acupuncture is better than western medicine or cognitive rehabilitation training alone. Acupuncture also seems to be effective in improving the total effective rate<sup>25</sup> and daily living ability<sup>14</sup> of patients with PSCI.

**Table 3** The Detailed Results of RoB

Review	Phase 2				Phase 3
	(1) Study Eligibility Criteria	(2) Identification and Selection of Studies	(3) Data Collection and Study Appraisal	(4) Synthesis and Findings	Risk of Bias in the Review
Zhang (2015) <sup>14</sup>	Low risk	Low risk	Low risk	High risk	High risk
Lin (2016) <sup>15</sup>	Low risk	High risk	Low risk	High risk	High risk
Xu (2020) <sup>16</sup>	Low risk	Low risk	Low risk	High risk	High risk
Wang (2017) <sup>17</sup>	Low risk	Low risk	Low risk	High risk	High risk
Liu F (2015) <sup>18</sup>	High risk	Low risk	Low risk	High risk	High risk
Kuang (2021) <sup>19</sup>	Low risk	Low risk	Low risk	Low risk	Low risk
Liu VWL (2015) <sup>20</sup>	Low risk	High risk	High risk	High risk	High risk
Xiong (2016) <sup>21</sup>	Low risk	High risk	High risk	Low risk	High risk
Chen (2016) <sup>22</sup>	Low risk	High risk	High risk	Unclear risk	High risk
Zhan (2017) <sup>23</sup>	Low risk	Low risk	Low risk	High risk	High risk
Liu F (2018) <sup>24</sup>	Low risk	High risk	High risk	High risk	High risk
Hu (2020) <sup>25</sup>	Low risk	High risk	Low risk	Low risk	High risk
Xie (2021) <sup>26</sup>	Low risk	High risk	High risk	Unclear risk	High risk
Zhou (2020) <sup>27</sup>	Low risk	Low risk	Low risk	High risk	High risk



**Table 4** The Detailed Results of GRADE

Included Studies	Outcomes	Number of RCTs (Participants)	Certainty Assessment					Effect Estimate (95% CI)	P-value	Quality of Evidence
			Included Studies	Inconsistency	Indirectness	Imprecision	Publication Bias			
Zhang (2015) <sup>14</sup>	Total effective rate	3 (120/119)	—	—	0	—	—	RR 1.58 (1.10, 2.26)	P = 0.01	Very Low
	MMSE	5 (192/191)	—	0	0	0	0	MD 2.64 (1.78, 3.50)	P < 0.00001	Moderate
	P300 peak latency	4 (122/121)	—	—	0	—	0	MD -18.46 (-30.51, -6.41)	P = 0.03	Very Low
	P300 amplitude	4 (122/121)	—	—	0	—	—	MD 1.23 (0.82, 1.63)	P < 0.00001	Very Low
	ADL	5 (182/182)	—	0	0	0	0	SMD 0.52 (0.31, 0.73)	P < 0.00001	Moderate
Lin (2016) <sup>15</sup>	MMSE	19 (603/598)	—	—	0	0	—	WMD 4.01 (2.32, 5.69)	P < 0.00001	Very Low
	ADL	6 (186/184)	—	—	0	—	—	WMD 9.29 (5.63, 12.95)	P < 0.00001	Very Low
	MoCA	3 (90/90)	—	—	0	—	—	WMD 1.74 (0.84, 2.63)	P = 0.0002	Very Low
	MoCA	9 (397/397)	—	0	0	0	0	MD 2.81 (2.42, 3.20)	P < 0.00001	Moderate
Xu (2020) <sup>16</sup>	MMSE	13 (584/584)	—	0	0	0	0	MD 2.27 (1.60, 2.94)	P < 0.00001	Moderate
	BI	6 (286/283)	—	—	0	—	—	MD 11.35 (7.13, 15.57)	P < 0.00001	Very Low
	ADL	4 (178/178)	—	—	0	—	—	MD -4.3 (-6.05, -2.56)	P < 0.00001	Very Low
	Total effective rate	5 (178/178)	—	0	0	0	—	OR 3.11 (1.76, 5.50)	P < 0.00001	Low
Wang (2017) <sup>17</sup>	MMSE	7 (268/244)	—	—	0	0	—	WMD 2.76 (2.23, 3.29)	P < 0.00001	Very Low
	MoCA	5 (172/173)	—	—	0	0	—	WMD 2.33 (1.15, 3.51)	P = 0.0001	Very Low
	ADL	4 (126/127)	—	—	0	—	—	WMD 9.60 (6.73, 12.48)	P < 0.00001	Very Low
	MMSE	11 (375/372)	—	—	0	0	—	WMD 3.59 (2.19, 4.99)	P < 0.00001	Very Low
	MoCA	6 (209/205)	—	0	0	0	0	WMD 1.48 (0.95, 2.01)	P < 0.00001	Moderate
Liu F (2015) <sup>18</sup>	P300 peak latency	8 (242/239)	—	—	0	—	—	WMD 15.94 (-22.27, -9.60)	P < 0.00001	Very Low
	P300 amplitude	8 (242/239)	—	0	0	0	0	WMD 1.27 (0.95, 1.60)	P < 0.00001	Moderate
	NCSE	2 (60/61)	—	—	0	—	—	WMD 5.63 (3.95, 7.31)	P < 0.00001	Very Low
	LOTCA	2 (65/65)	—	—	0	—	—	WMD 12.09 (3.95, 7.31)	P = 0.002	Very Low
	MoCA	14 (563/562)	—	0	0	0	0	MMD 2.66 (2.18, 3.13)	P < 0.00001	Moderate
Kuang (2021) <sup>19</sup>	MMSE	21 (838/837)	—	—	0	0	0	MM 2.97 (2.13, 3.80)	P < 0.00001	Low

(Continued)

**Table 4** (Continued).

Included Studies	Outcomes	Number of RCTs (Participants)	Certainty Assessment					Effect Estimate (95% CI)	P-value	Quality of Evidence
			Included Studies	Inconsistency	Indirectness	Imprecision	Publication Bias			
Liu WL (2015) <sup>20</sup>	Total effective rate	4 (143/136)	–I	0	0	–I	–I	OR 2.64 (1.40, 5.00)	P < 0.05	Very Low
Xiong (2016) <sup>21</sup>	MMSE	8 (265/265)	–I	–I	0	0	–I	MD 2.12 (0.16, 4.08)	P < 0.00001	Very Low
	MMSE	10 (370/362)	–I	–I	0	0	–I	WMD 2.22 (1.38, 3.07)	P < 0.00001	Very Low
	P300 peak latency	3 (91/89)	–I	–I	0	–I	–I	WMD 1.85 (0.66, 3.04)	p = 0.002	Very Low
Chen (2016) <sup>22</sup>	Total effective rate	2 (45/46)	–I	0	0	–I	–I	OR 14.63 (2.61, 82.16)	P = 0.002	Very Low
Zhan (2017) <sup>23</sup>	MMSE	4 (106/106)	–I	–I	0	–I	–I	MD 5.57 (5.00, 6.13)	P < 0.00001	Very Low
	Total effective rate	3 (81/59)	–I	–I	0	–I	–I	RR 1.37 (0.98, 1.91)	P = 0.04	Very Low
	MMSE	10 (283/278)	–I	–I	0	0	–I	MD 1.78 (0.24, 3.32)	P = 0.02	Very Low
	MoCA	6 (188/176)	–I	–I	0	0	–I	MD 1.92 (0.96, 2.88)	P < 0.0001	Very Low
	P300 peak latency	5 (134/133)	–I	–I	0	–I	–I	MD –11.01 (–18.91, –3.11)	P < 0.00001	Very Low
	P300 amplitude	5 (134/133)	–I	0	0	–I	–I	MD 1.56 (1.14, 1.98)	P < 0.006	Very Low
	BI	4 (156/155)	–I	–I	0	–I	–I	MD 6.38 (–2.41, 15.18)	P = 0.15	Very Low
Liu F (2018) <sup>24</sup>	MMSE	15 (512/488)	–I	–I	0	0	–I	WMD 3.17 (1.7, 5.05)	P < 0.0001	Very Low
	P300 peak latency	6 (198/195)	–I	0	0	0	0	WMD –17.31 (–19.70, –14.93)	P < 0.00001	Moderate
	P300 amplitude	6 (198/195)	–I	0	0	0	0	WMD 1.22 (0.84, 1.59)	P < 0.00001	Moderate
Hu (2020) <sup>25</sup>	Total effective rate	5 (178/177)	–I	0	0	0	0	OR 3.15 (1.81, 5.46)	P < 0.0001	Moderate
	MMSE	8 (308/307)	–I	0	0	0	0	WMD 2.21 (1.01, 3.41)	p = 0.0003	Moderate
	MoCA	4 (125/125)	–I	0	0	–I	–I	WMD 1.84 (0.81, 2.88)	P = 0.0005	Very Low

Xie (2021) <sup>26</sup>	Total effective rate	7 (235/234)	–I	0	0	0	–I	OR 6.3 (3.58, 11.10)	P < 0.00001	Low
	MMSE	8 (261/260)	–I	0	0	0	–I	MD 2.31 (1.86, 2.76)	P < 0.00001	Low
	MoCA	8 (282/282)	–I	0	0	0	–I	MD 3.46 (3.09, 3.84)	P < 0.00001	Low
	BI	4 (158/158)	–I	0	0	–I	–I	MD 7.56 (6.16, 8.97)	P < 0.00001	Very Low
	ADL	2 (71/71)	–I	0	0	–I	–I	MD 11.52 (8.06, 14.98)	P < 0.00001	Very Low
	LOTCA	3 (107/107)	–I	–I	0	–I	–I	MD 9.29 (4.24, 14.33)	P = 0.0003	Very Low
Zhou (2020) <sup>27</sup>	MMSE	31 (1181/1168)	–I	0	0	0	0	MD 2.88 (2.09, 3.66)	P < 0.00001	Moderate
	MoCA	14 (572/557)	–I	0	0	0	0	MD 2.66 (1.95, 3.37)	P < 0.001	Moderate

**Abbreviations:** MMSE, Mini-mental State Examination; MoCA, Montreal Cognitive Assessment; ADL, Activities of daily living; BI, Barthel Index; LOTCA, Loewenstein Occupational Therapy Cognitive Assessment; NCSE, Neurobehavioral Cognitive Status Examination.

## Adverse Events

Seven SRs reported no adverse events, six SRs reported adverse events, and one SR had no mention of adverse events. The main manifestations of the intervention group were subcutaneous hematoma or hemorrhage.<sup>16,18,24</sup> In the control group, the main symptoms were dizziness and headache, nausea and vomiting,<sup>16,18,19,23</sup> occasional itching,<sup>23</sup> and blood pressure fluctuation.<sup>25</sup> No serious adverse events occurred.

## Discussion

### Summary of the Main Results

We conducted a comprehensive and descriptive analysis of 14 SRs of acupuncture for patients with PSCI, involving 263 RCTs and 19,224 participants. Existing evidence suggests that acupuncture combined with cognitive rehabilitation training or western medicine is more effective than cognitive rehabilitation training or western medicine alone in improving the cognitive function of patients with PSCI, and does not cause serious adverse events. However, all SRs had low or very-low methodological quality, and 92.9% (13/14) of SRs were rated as high RoB. The GRADE results suggest that the quality of evidence for the efficacy of acupuncture needs to be improved.

### Results-Based Discussion

A single SR seems to suggest the benefit of acupuncture in improving cognitive function in patients with PSCI, and the ROBIS assessment results indicate that the RoB for SRs are high. There is currently insufficient evidence to claim the efficacy and safety of acupuncture for improving cognitive function in patients with PSCI.

The methodological quality of SRs was low or very low according to AMSTAR 2. Of note, 92.9% (12/14) of SRs did not provide the previous protocol, meaning that we could not guarantee whether the research plan was followed strictly in the production process of SR, thus increasing the RoB. Moreover, 92.9% (12/14) of SRs did not list exclusions and reasons, which may have increased selection bias. Half of the SRs did not fully consider the impact of RoB on the results of the included studies, and the possibility of publication bias was not fully investigated when quantitative synthesis was carried out, which may affect the reliability of the results. In addition, 85.7% (12/14) of SRs did not declare potential conflicts of interest; hence, we could not determine whether the research conclusions were affected by potential interests.

According to the results of the evidence quality grading conducted by GRADE, only 26% of the results (13/50) were moderate. There are many factors contributing to the deterioration of evidence quality. First, the high RoB in all RCTs is the primary reason for the degradation of evidence quality. Factors such as study design, diagnostic criteria, course of disease, interventions, and acupuncture details may contribute to the high heterogeneity of RCTs, thereby increasing RoB in the original study, and thus reducing the reliability of the results of acupuncture for patients with PSCI. Publication bias (35/50), inconsistency (27/50) and inaccuracy (23/50) of SR also reduced the quality of evidence. The small number of RCTs with positive results, or the asymmetry of the funnel plot may lead to a large publication bias in outcomes. Inconsistency is mainly manifested in poor overlap of confidence intervals between different studies and high heterogeneity of the combined results ( $I^2 > 50\%$ ), or the researchers did not provide reasonable explanation for results that had high heterogeneity. The small sample size and the small number of RCTs resulted in a wide 95% confidence interval, and 46% of the results were degraded due to inaccuracy.

Based on the results of all the evaluations, we propose several important recommendations to address the existing problems: (a) In order to further clarify the conclusions of the efficacy and safety of acupuncture in improving cognitive function in patients with PSCI, it is necessary for researchers to improve the quality of RCTs and to follow relevant clinical trial norms. According to the Consolidated Standards of Reporting Trials (CONSORT) and the STandards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA2010), clinical trials should be strictly designed, implemented, and reported to reduce the possibility of false positive results or RoB. (b) Authors should conduct comprehensive quality control of SR using AMSTAR 2, ROBIS, and GRADE tools to improve the stability and reliability of the evidence. (c) In particular, researchers should consider the persistent effects of acupuncture and pay attention to the long-term follow-up results. In addition, the effect of acupuncture has been controversial, and researchers

need to clarify the specific efficacy of acupuncture on improving cognitive function in patients with PSCI, to ensure that positive outcomes are not due to the placebo effect.

## Mechanism of Acupuncture to Improve Cognitive Function

For nearly 20 years, acupuncture has been widely studied for the treatment of pain, arthritis, neoplasms/cancer, pregnancy or labor, mood disorders, stroke, nausea, sleep, and paralysis/palsy,<sup>29</sup> and as a means to regulate overall human health.<sup>30</sup> Psychiatric manifestations of patients with dementia have been well documented in neuroimaging and neuropathological studies.<sup>31</sup> Acupuncture had a synergistic effect on the recovery of upper limb dysfunction after stroke.<sup>32</sup> Although the underlying mechanism of acupuncture treatment for cognitive dysfunction has not been fully elucidated, studies have shown that acupuncture can affect cognitive function by inhibiting the accumulation of toxic proteins in nervous system diseases, regulating glucose generation, reducing neuronal apoptosis, and providing neuroprotection.<sup>33</sup> Animal experiments have shown that acupuncture could improve the cognitive ability of vascular dementia rats by increasing the content of 5-hydroxytryptamine (5-HT) in the hippocampus to regulate nerve conduction function.<sup>34</sup> Moxibustion could reduce the expression of presenilin-1 (PS-1) mRNA and beta-site APP cleaving enzyme 1 (BACE-1) mRNA in the brain, subsequently block the production of amyloid $\beta$ -protein (A $\beta$ ) and reduce the level of serum IL-6, thereby inhibiting the chronic neuroinflammatory cascade.<sup>35</sup> In addition, electroacupuncture can increase the expression of Beclin-1 in the brain tissue of ischemia-reperfusion model rats, and regulate the damage of autophagy network system to nerve cells.<sup>36</sup> Functional magnetic resonance imaging (fMRI) results suggest that acupuncture tended to be associated with greater activation in the basal ganglia, brainstem, cerebellum, and insula, and more deactivation was seen in the so-called “default mode network” and limbic brain regions such as the amygdala and hippocampus. This suggests that the activity of specific brain regions induced by acupuncture is associated with the therapeutic effect of acupuncture on cognitive function.<sup>37</sup>

## Discussion Based on Cognitive Function Assessment Scales

The MMSE, MoCA, NCSE, and LOTCA are commonly used and distinct tools to evaluate cognitive function. The MMSE was developed by Marshal and Susan Folstein of New York Hospital-Cornell Medical Center in NY, USA, in 1975.<sup>38</sup> In 1988, Katzman et al<sup>39</sup> adapted it to Chinese, and it is currently one of the most widely used scales by researchers to evaluate overall cognitive function. The scale contains seven domains: time orientation, place orientation, immediate memory, delayed memory, attention and computation, language, and visual space. It is simple and rapid and has good test-retest reliability. However, there are some limitations, such as lack of content to assess executive ability or poor sensitivity to mild cognitive impairment (MCI).<sup>38,40</sup> Therefore, Nasreddine et al<sup>41</sup> (Charles LeMoyne Hospital, Canada) developed the MoCA, which added an executive function score to the entry details of the MMSE to screen patients with MCI or MMSE usually within the normal range. This method can also quickly and reliably distinguish patients with MCI from patients with intact cognitive function, and has a high sensitivity and specificity for MCI, which can fill the deficiency of the MMSE. However, it is difficult to evaluate PSCI comprehensively and accurately using the MMSE or MoCA alone, so it is often recommended to combine multiple scales or scales in different cognitive function fields for comprehensive evaluation.<sup>42</sup>

The NCSE was compiled in 1983 and is divided into three general factors (level of consciousness, attention and orientation) and five major areas of cognitive function (language ability, structural ability, memory, computational ability, and reasoning ability). The NCSE adopts a functional profile to reflect different cognitive impairments and can also reflect the dynamic characteristics of cognitive function, with high sensitivity and reliability.<sup>43,44</sup> However, the sensitivity is average for assessing reasoning, judgment, and structural abilities.<sup>45</sup>

The LOTCA was developed primarily for patients with acquired brain injury (ABI). One of its key advantages is the ability to assess a range of intact and impaired cognitive abilities,<sup>46</sup> thus enhancing the design and planning of therapeutic interventions. At present, the scale is widely used in schizophrenia,<sup>47</sup> stroke,<sup>48</sup> and cognitive rehabilitation assessment of healthy children, adults, and the elderly.<sup>49</sup> The main domains include containing orientation, visual perception, spatial perception, motor praxis, visuomotor organization, thinking operations, attention, and concentration; it has good internal consistency and inter-rater reliability.<sup>50</sup>

In this study, all SRs used the MMSE, and nine SRs used the MoCA. Four results for each scale were rated as moderate quality. Two SRs used the LOTCA and one SR used the NCSE; the evidence was very low quality. Therefore, the existing evidence cannot confirm that acupuncture improves the cognitive function of patients with PSCI, and the good effect obtained from clinical experience or small-scale application is not sufficient for application to evidence-based medicine. We need more large-sample and high-quality RCTs to prove the efficacy of acupuncture in patients with PSCI.

## Selection of Acupoints

Only 3 SRs listed the characteristics of acupoint selection in detail. Based on the existing results and statistics, the top five acupoints used frequently are baihui (GV20), sishencong (EX-HN1), shenting (GV24), fengchi (GB20), and fengfu (GV16), which mainly involve the governor meridian and the Gallbladder meridian of foot-Shaoyang. The lesion site of PSCI is in the brain, so the main acupoints selected are concentrated in the brain. GV20, GV24 and GV16 belong to the governor meridian, which are closely connected with the brain and are important acupoints for regulating brain function. GB20 belongs to the Gallbladder meridian of foot-Shaoyang. It is good at treating mental diseases such as stroke, insomnia and epilepsy, and cooperated with EX-HN1 to treat mental disorders. These acupoints jointly regulate PSCI.

## Strengths and Limitations

SRs based on high-quality RCTs are critical for clinical decision-making in evidence-based medicine. However, the marked increase in the number of SRs has questioned their quality. In recent years, many SRs showing that acupuncture improves cognitive function in patients with PSCI have been published. To our knowledge, this is the first comprehensive assessment of different SRs through inclusive retrieval and use of internationally recognized assessment tools. We have systematically assessed the methodological quality, RoB, and quality of evidence of relevant SRs by using the AMSTAR 2, ROBIS, and GRADE tools, respectively. We can intuitively understand the overall quality of SRs and the reliability of the results.

The limitation of our overview is that we could only synthesize and describe all the data quantitatively. Differences in RCT study designs and the details of acupuncture interventions may result in high RoB for SRs, which reduces the quality of the evidence and the methodology. Finally, we must point out that due to subjective factors, there could have been some deviations in our understanding of the assessment tools, but we have tried to minimize the errors in the assessment results.

## Conclusion

Based on the collected evidence, acupuncture appears to be effective and safe in improving cognitive function in patients with PSCI, although the quality of the evidence from the original study and the methodological quality of the SRs reduced the reliability of the conclusions and the overall quality is not high. However, based on existing results, we still support the value of acupuncture as an adjunctive intervention for improving cognitive function in PSCI. In future research, it is necessary to confirm the efficacy and safety of acupuncture in patients with PSCI and to provide more reliable and scientific data that contributes to evidence-based medicine.

## Disclosure

None of the authors stated any conflicts of interest in this study, and there were no potential commercial or financial relationships.

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