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REVIEW

Efficacy of Acupuncture Therapy in Treating Non-Motor Symptoms of Parkinson's Disease: A Systematic Review and Network Meta-Analysis

Xiaoyan Li, Peng Chen, Shaosong Wang, Chunchen Wang, Bin Li, Huilin Liu

Department of Acupuncture and Moxibustion, Beijing Hospital of Traditional Chinese Medicine, Capital Medical University, Beijing Key Laboratory of Acupuncture Neuromodulation, Beijing, People's Republic of China

Correspondence: Huilin Liu, Beijing Hospital of Traditional Chinese Medicine, Capital Medical University, Beijing Key Laboratory of Acupuncture Neuromodulation, No. 23, Behind Art Museum Street, Dongcheng District, Beijing, People's Republic of China, Tel +86 13681395789, Email liuhuilin@bjzhongyi.com

Purpose: Recently, research on the management of Parkinson's disease (PD), particularly non-motor symptoms (NMS), has been increasingly reported. This systematic review and network meta-analysis (NMA) aimed to evaluate the efficacy of acupuncture interventions for NMS in PD patients to identify the most effective strategy.

Methods: Randomized controlled trials (RCTs) on acupuncture for NMS in PD were retrieved up to July 31, 2024, across eight databases: PubMed, Embase (OVID), Cochrane Library, Web of Science, China National Knowledge Infrastructure, Chinese Biomedical Literature Database, VIP Database, and Wanfang Database. The quality of the included studies was assessed using the Cochrane handbook for systematic reviews.

Results: 77 RCTs were included, involving 5538 PD patients. The NMA indicated that acupuncture_training_usual ([SUCRA] = 84.18%) was the best intervention for improving the anxiety state of PD patients. Abdominal_acupuncture_usual (94.15%) was a preferred intervention for improving the depressive state. Scalp_acupuncture_usual (99.98%) and Scalp_electroacupuncture (94.28%) can significantly improve the sleep quality of PD patients. Heat_sensitive_moxibustion_usual (94.65%) and Warm_acupuncture_moxibustion_usual (99.995%) can significantly improve the quality of life of PD patients. Acupuncture_usual (94.02%) may be considered a promising intervention for improving the psychological, emotional and cognitive functions. Additionally, shallow_acupuncture_usual (99.17%) was the safest option. Notably, acupuncture_moxibustion (98.24%) was the most effective intervention involving the largest number of participants.

Conclusion: This analysis identifies the most effective acupuncture interventions for improving NMS in PD patients, including anxiety, depression, sleep quality, and overall quality of life, as well as additional benefits in pain management and gastrointestinal function. Future large-scale RCTs are needed to confirm these findings.

Keywords: Parkinson's disease, non-motor symptoms, acupuncture, network meta-analysis, systematic review

Introduction

Parkinson's disease (PD) is a neurodegenerative disorder,[1] primarily characterized by motor symptoms and non-motor symptoms (NMSs). Typical motor symptoms involve bradykinesia, resting tremor, muscle rigidity, and postural instability.[2] However, before motor symptoms appear, PD patients often experience NMSs for several years. Over the past few years, the prevalence of PD has been on the rise, and it has become one of the most prevalent neurodegenerative diseases globally. In the United States alone, nearly one million individuals are diagnosed with PD. Moreover, the related economic costs are estimated to surpass 50 billion dollars,[3] imposing noticeable financial and emotional burdens on both patients and their caregivers. Currently, the treatment for PD primarily encompasses pharmacological therapy, surgical intervention, and physical rehabilitation.[4] However, prolonged use of medications can lead to drug resistance, and long-term pharmacological treatment may indirectly increase the risk of NMS in PD patients.[5] To date, there is no definitive

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evidence demonstrating that any medication can relieve PD.[6] Surgical treatments, like deep brain stimulation, have achieved certain effects in some patients. However, these treatment methods may cause surgical risks and are only suitable for patients with surgical indications.[7,8] Physical therapies like rehabilitation training are beneficial in maintaining the motor function of patients to a certain degree. Nonetheless, it is difficult to comprehensively address the complex symptoms of PD.[9] Despite the ongoing research focus on motor abnormalities in PD, there is increasing evidence emphasizing the importance of NMS.[10] Recent research[11] has found that genetic factors play a significant role in the occurrence and development of NMS in PD. Mutations in certain specific genes may be closely tied to NMS, such as sleep disorders, depression, and cognitive decline, further highlighting the complexity and diversity of NMS in PD. NMS is prevalent among PD patients and has a more profound effect on their quality of life than motor symptoms.[12] Therefore, it is imperative to identify an effective therapeutic approach for alleviating NMS in PD.

NMS in PD encompasses a range of conditions, including olfactory dysfunction, sleep disturbances, constipation, depression, and autonomic nervous system disorders. In the management of PD, a multidisciplinary approach is recommended for NMS, including non-pharmacological interventions.[2] Acupuncture, as a traditional Chinese medicine (TCM) therapeutic approach, is related to minimal side effects. In recent years, it has been increasingly used in the treatment of PD. A study indicates that acupuncture can help alleviate NMS in PD patients by regulating the nervous system to activate corresponding neuronal areas, improving blood circulation, and relieving pain.[13] Although previous research[14] has explored the impact of acupuncture on NMS in PD, they have some limitations. In terms of study design, most existing studies have small sample sizes and are limited to specific regions or populations, without large-scale and multi-center designs. Moreover, previous studies have only focused on one or two common acupuncture methods without exploring other potential approaches, thus failing to fully reveal the advantages and differences of various acupuncture techniques in treating different NMSs. Additionally, traditional meta-analysis methods cannot simultaneously compare multiple interventions, limiting the comprehensiveness and applicability of conclusions. Unlike traditional meta-analysis, NMA can simultaneously integrate direct and indirect comparison evidence of multiple acupuncture interventions, thereby providing a more comprehensive evaluation of the relative efficacy of different therapies and offering more reliable evidence for clinical decision-making. Hence, to address these issues and summarize evidence in this field, this study employs NMA. Randomized controlled trials (RCTs) worldwide are searched to ensure a wide range of samples from multiple countries and regions. This helps to enhance the representativeness of the samples and reduce the potential biases caused by geographical limitations. Regarding interventions, we included diverse acupuncture approaches, encompassing not only traditional methods like manual acupuncture, moxibustion, and electroacupuncture, but also novel technique combinations such as heat-sensitive moxibustion and warm acupuncture, to more thoroughly compare the efficacy of various acupuncture methods. Through NMA, we can simultaneously compare the effectiveness of multiple acupuncture interventions for different NMSs in PD. Unlike previous studies focusing on a single symptom, our analysis encompassed a broad spectrum of NMSs, including anxiety, depression, sleep disturbances, quality of life, cognitive impairment, and gastrointestinal dysfunction. This NMA design allows for a more comprehensive assessment of the effect of acupuncture on NMSs in PD patients compared to previous studies. This study aims to compare the effectiveness of different acupuncture therapies for treating NMS in PD through a systematic review and NMA, to provide a stronger scientific guidance for clinical practice and offer new insights into comprehensive treatment strategies for PD patients.

Methods

This study adhered to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Network Meta-Analysis (PRISMA-NMA),[15] and was registered with the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42024575721).

Literature Search

Chinese and English publications were systematically retrieved until July 31, 2024, from eight databases: Pubmed, Embase (OVID), Cochrane Library, Web of Science, China National Knowledge Infrastructure, Chinese Biomedical Literature Database, VIP Database, and Wanfang Database. The search strategy primarily consisted of two components:

the disease ("Parkinson Disease", "Parkinson's Disease", "Parkinsonism", "Parkinsonian Syndrome", "Parkinsonian Diseases", "Paralysis Agitans", "Shaking Palsy", "Lewy body Parkinsons disease", "Lewy bodies of Parkinsons disease") and interventions ("Acupuncture Therapy", "acupuncture", "electroacupuncture", "Moxibustion", "Acupotom*", "Auriculoacupuncture", "Auriculotherapy", "blood letting", "electrical acupoint stimulation", "needle", "needling", "pharmaco puncture", "Pharmacoacupuncture", "Thermoacupuncture"). The final search terms were formed by combining medical subject headings and free-text terms. The complete retrieval strategy can be found in Table S1.

Inclusion and Exclusion Criteria

The principles of Population, Intervention, Comparison, Outcomes and Study were rigorously applied. Articles That Met the Following Criteria Were Included

(i) Population: Participants must meet the clinical diagnostic criteria for PD by referring to internationally recognized standards, such as the UK Parkinson's Disease Society Brain Bank clinical diagnostic criteria[16] and Movement Disorder Society clinical diagnostic criteria for Parkinson's disease.[10] No restrictions were applied on age, sex, disease duration, Hoehn & Yahr staging, or disease severity.

(ii) Interventions: Participants in the experimental group received acupuncture therapy as the primary intervention. Acupuncture therapy was defined as a technique that involved the stimulation of specific acupoints, based on TCM theory. This therapy included various techniques, such as manual acupuncture, moxibustion, electroacupuncture, warm acupuncture, fire needle, dry needling, and heat-sensitive moxibustion. These techniques were employed alone or combined in pairs. Additionally, treatments combining acupuncture therapy with conventional Western medicine or rehabilitation training were also considered. Detailed information can be found in Table S2.

(iii) Comparison: The control group received no intervention, placebo, conventional physiotherapy exercise, conventional western medicine alone or in combination with usual treatment, or an acupuncture modality that was inconsistent with the experimental group.

(iv) Outcome measures: An appropriate assessment method was selected based on NMS in participants. For primary outcome indicators, the Hamilton Anxiety Scale (HAMA) was used for assessing anxiety, Hamilton Rating Scale for Depression (HAMD) for depression, Parkinson's Disease Sleep Scale (PDSS) and Pittsburgh Sleep Quality Index (PSQI) for the quality of sleep, 39-item Parkinson's Disease Questionnaire (PDQ-39) and Patient Assessment of Constipation Quality of Life scale (PAC-QOL) for the quality of life, and Unified Parkinson's Disease Rating Scale (UPDRS) for psychological, emotional and cognitive functions. Secondary outcome indicators included other scales related to NMSs (eg, sleepiness, pain, constipation, swallowing function, cognition, autonomic function).

(v) Study design: RCTs.

Exclusion Criteria Were as Follows

(i) Duplicates (when similar studies by the same authors were identified, the latest publications or those presenting high-quality evidence were selected);

(ii) Non-RCTs, such as animal experiments, meta-analyses, reviews, conferences, and dissertations;

(iii) Interventions that involved acupoint injection and acupoint application (utilizing certain pharmacological components), TCM herbs, Tuina, and Qigong;

(iv) Studies with outcome indicators that were inconsistent with this study, those not focused on NMS in PD, or studies with incomplete outcome indicators;

(v) Participants with other comorbid diseases;

(vi) Studies without an inaccessible full text.

Study Selection and Data Extraction

Two investigators employed EndNote X9 to select studies and extract data. Initially, titles and abstracts were read to exclude studies that clearly did not meet the inclusion criteria. If the eligibility of the studies could not be determined through the above process, the full texts would be obtained and reviewed. Subsequently, relevant data were extracted from the eligible studies, including i) basic information, such as study author, publication year, and study source; ii)

patient information, like age, sex, case number, and main symptoms; iii) interventions, such as intervention type, duration, and frequency; iv) outcome indicators, encompassing both primary and secondary outcomes that were extracted as mean and standard deviation (mean ± SD). If study data were missing, corresponding authors were contacted by Email or phone to obtain complete data. Study screening and data extraction were conducted independently by two investigators. In the event of any discrepancies, a third investigator would be invited to discuss and resolve them.

Risk of Bias (ROB) and Quality Assessment

Two investigators independently employed the Cochrane risk-of-bias tool to assess ROB in the included RCTs. The Jadad scale was applied to evaluate the quality of each study. The Cochrane risk-of-bias tool[17] includes seven domains: random sequence generation, allocation concealment, blinding of patients, therapists, and outcome assessors, incomplete outcome data, selective reporting, and other sources of bias. Each domain can be categorized into three levels: a low, high risk, or unclear ROB. If a study had a low ROB in four or more domains, it was defined as high quality. The Jadad scale[18] is a widely used tool, which includes four aspects: random sequence generation, allocation concealment, blinding, and withdrawals/dropouts, with a score of 2, 2, 2, and 1, respectively. A total score of 1–3 was considered low quality, while a score of 4–7 was deemed high quality. During the evaluation process, if there were any discrepancies, they would be resolved through consultation with a third investigator.

Statistical Analysis

The NMA was conducted utilizing a Bayesian random-effects model to compare the effect size of various interventions and evaluate their effectiveness. This model, based on Bayes' theorem, combines prior distributions and sample data to infer parameters through posterior distributions. Utilizing prior information, it improves the stability and accuracy of estimations and thus is appropriate for complex study designs. The modeling was conducted using the Markov Chain Monte Carlo (MCMC) method, with four Markov chains running simultaneously. The annealing process was set to 20,000 iterations, and the modeling was completed after 50,000 simulation iterations. The MCMC method builds a Markov chain with a stationary distribution that corresponds to the target posterior distribution. It allows for sampling from complex probability distributions to estimate parameters, overcoming the difficulties of traditional complex integral calculations, and approximating the true posterior distribution. Deviance information criterion (DIC) was leveraged to compare model fit and global consistency. The DIC takes into account both the goodness of fit and complexity for the model. A smaller DIC value indicated a better fit and lower complexity, aiding in the selection of the best model. If there was a closed loop in the network, the node-splitting method would be employed to analyze local consistency. Additionally, interventions were ranked based on the surface under the cumulative ranking (SUCRA) curve, and a league table was generated to compare the differences in effect size among various interventions. Funnel plots were used to visually assess the heterogeneity observed across studies. The data analysis was completed in R 4.3.2 (R Development Core Team, Vienna, http://www.R-project.org) and Stata (MP 15.0).

Results

Study Selection

In total, 5941 studies were retrieved from the eight databases. After eliminating 1867 duplicates, 3764 articles were excluded after reading titles and abstracts. Subsequently, after reviewing the full texts, 77 studies[19–95] were included in this meta-analysis, involving 5538 PD patients. The detailed process of the literature screening is illustrated in the PRISMA flow diagram (Figure 1).

Study Characteristics

The basic characteristics of the included studies are presented in Table 1. The sample size varied from 22 to 166 participants. The articles were published from 2012 to 2024, comprising 15 English articles and 62 Chinese articles. Two studies were conducted in Brazil (2.60%), one in Singapore (1.30%), one in the United States (1.30%), and 73 in China (94.80%). Twelve studies[23,24,45,59,65,71,72,76,79,83,84,94] focused on constipation, twelve[28,36,38,40,51,53,54,58,67,85,88,93] on

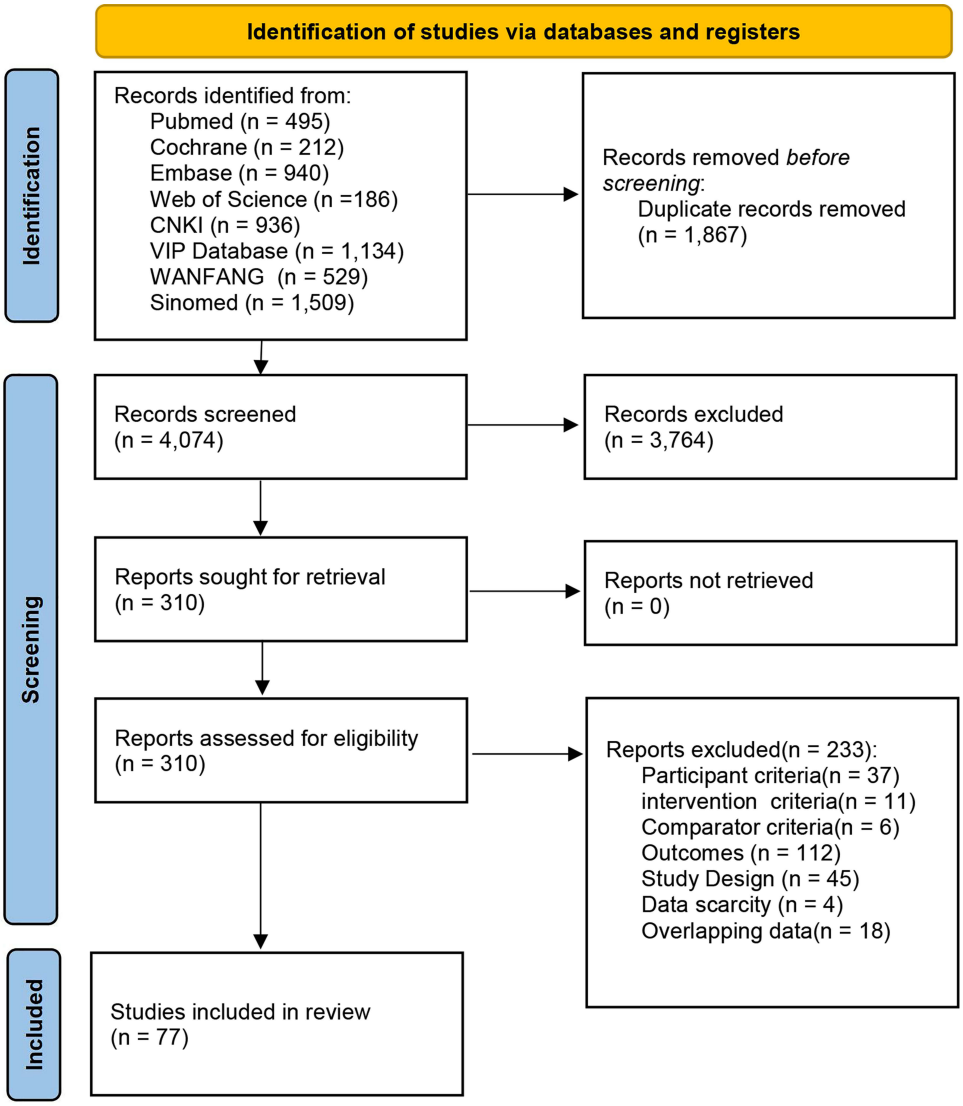

Figure 1 PRISMA flow diagram.

depression, six[35,41,54,77,78,82] on cognitive impairment, eleven[21,33,34,37,44,60–62,74,75,80] on dysphagia, ten[19,30,42,49,55,57,66,73,81,87] on sleep disorders, three on fatigue,[29,31,47] two[64,95] on anxiety, two[20,63] on pain, two[39,48] on overactive bladder syndrome, and two[69,70] on olfactory impairment. The specific details are provided in Table 1.

ROB and Quality Assessment

In this study, the Cochrane risk-of-bias tool was used to analyze the ROB in the included studies. In the included studies, 56 studies provided detailed explanations or descriptions of the randomization methods, while 21 studies[31,32,36,41,53,54,56,63,64,66,69,71,74,78,85–87,90,92–94] only mentioned the term "randomization" or did not describe the randomization methods. Only eleven studies[19,20,23–27,29,31,77,83] provided detailed descriptions of allocation concealment. Due to the specific nature of acupuncture treatment, implementing blinding for physicians was quite challenging. 14 studies[9–29,31,49,57] were classified as high risk. Among them, only eleven studies[19,20,22,23,26,27,29,31,42,45,49] reported single blinding for participants, while thirteen[19,20,23,24,26–29,31,33,40,49,60] studies mentioned blinding of data analysts. Regarding follow-up and reporting biases, ten studies[27,32,33,47,49,51,56,58,68,91] exhibited attrition bias. Moreover, the ten studies reported incomplete data, indicating a high ROB. According to the Jadad scale, 24 studies were classified as high-quality

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Table 1 Study Characteristics

Author	Year	Intervention	Characteristics of the Participants			Outcome
			Age	Sex F/M	Sample	
Yan[19]	2024	Real acupuncture	63.8±8.5	20/18	38	(1)(2)(3)(4)(5)(49)
		Sham_acupuncture	64.4±7.5	17/23	40	
Wang[20]	2024	Electroacupuncture_daily medication	64.30±9.76	13/17	30	(6)(7)(8)
		Sham electroacupuncture_daily medication	64.30±7.99	15/14	29	
Gao[21]	2024	Tongue acupuncture g_routine interventions	55.8±0.6	14/18	32	(9)(49) (57)
		Electrical stimulation_routine interventions	57.6±0.7	15/17	32	
Tahara[22]	2023	Dry Needling (DN)	62.2±7.69	7/11	18	(10)(13)
		Sham Dry Needling	64.9±7.79	5/14	19	
Li[23]	2023	Acupuncture_daily medication	63.9±7.34	22/17	39	(11)(12)(15)
		Sham acupuncture_daily medication	63.74±9.24	21/18	39	
Li[24]	2023	Electroacupuncture_conventional pharmacological	67.3±8.1	38/45	83	(5)(7)(12)(14)(15)(49)
		Conventional pharmacological treatment	66.9±7.1	40/43	83	
Nazarova[25]	2022	Electroacupuncture_conventional drug	70.1±6.2	6/9	15	(1)(3)(12)(13)(16)
		Conventional drug	66.9±7.8	8/7	15	
Li[26]	2023	Qihuang needle_conventional drug		19/15	15	(3)(5)
		Sham acupuncture_conventional drug			19	
Xu[27]	2020	Electroacupuncture_madopar	61.73±10.28	18/15	33	(1)(13) (17)(49)(57)
		Madopar	61.95±9.77	16/21	37	
Wang[28]	2020	Heat-sensitive moxibustion_levodopa and benserazide hydrochloride Tablets	64.2±7.8	24/16	40	(5)(8)(13)(49)(57)
		Levodopa and benserazide hydrochloride Tablets	65.9±8.0	22/18	40	
Kong[29]	2018	Acupuncture	66.4 ± 6.5	14/6	20	(2)(5)(18)
		Sham acupuncture	62.9 ± 9.7	13/7	20	
Aroxa[30]	2018	Acupuncture_daily medication	65±10	4/7	11	(1)
		Daily medication	56±12	4/7	11	
Kluger[31]	2016	Acupuncture	64.4±10.3	17/30	47	(1)(2)(19)(20)(49)
		Sham acupuncture	63.0±13.0	18/29	47	
Wang[32]	2015	Electroacupuncture_daily medication	62.1 ± 8.7	15/13	28	(4)(8)(21)(22)(23)
		Daily medication	59.1 ± 12.4	11/9	20	
Feng[33]	2023	Acupuncture_onventional medication therapy_rehabilitation training	71±5	13/15	28	(24)(25) (26)
		Conventional medication therapy_rehabilitation training	72±6	14/13	27	

(*Continued*)

Table 1 (Continued).

Author	Year	Intervention	Characteristics of the Participants			Outcome
			Age	Sex F/M	Sample	
Wu[34]	2021	Acupuncture_onventional medication therapy_rehabilitation training	63±10	17/11	28	(27)(57)
		Conventional medication therapy_rehabilitation training	65±7	18/10	28	
Ye[35]	2016	Acupuncture_cognitive function training		10/20	30	(22)(23) (57)
		Donepezil hydrochloride Tablets		11/19	30	
Xie[36]	2016	Acupuncture_triple viable bacteria_routine therapy		47/61	53	(8)(13) (57)
		Routine therapy			53	
Zhao[37]	2015	Needle warming moxibustion_rehabilitation training		13/17	30	(57)
		Rehabilitation training		11/17	28	
Xia[38]	2012	Electroacupuncture_routine therapy	72±7	8/22	30	(8)(57)
		Routine therapy	72±8	10/20	30	
Chen[39]	2012	Electroacupuncture_tolterodine_Madopar	65.60±3.79	11/19	30	(29)(49)
		Tolterodine_Madopar	61.93±3.67	13/17	30	
Chu[40]	2024	JIN's three-needle regulating Shen acupuncture_basic treatment	65.60±3.79	11/19	35	(1)(5)(8) (49)
		Basic treatment	61.93±3.67	13/17	35	
Zhang[41]	2024	Scupuncture-levodopa	64.25±4.64	26/43	69	(13)(30)
		Levodopa	64.85±5.01	29/40	69	
Zhao[42]	2023	Integrated acupuncture and moxibustion	59.97±9.05	12/18	30	(1)(21) (57)
		Sham integrated acupuncture and moxibustion	58.40±9.52	15/15	30	
Zhao[43]	2023	Acupuncture_Madopar	69.18±12.33	20/19	39	(32)(49)
		Madopar	68.29±13.67	17/22	39	
Tang[44]	2023	Acupuncture_rehabilitation training	69.18±12.33	17/18	35	(25)(26) (57)
		Rehabilitation training	68.29±13.67	11/18	29	
Song[45]	2023	Acupoint catgut	70±6	17/23	40	(12)(33) (49)(57)
		Sham stimulation treatment	71±6	18/22	40	
Luo[46]	2023	Acupuncture_daily medication	42.81±11.25	17/13	30	(4)(5)(8) (21)
		Daily medication	41.22±10.75	19/11	30	
Liu[47]	2024	Acupuncture and moxibustion_daily medication	66.45±6.41	23/37	60	(5)(17) (31)(49)
		Daily medication	68.00±7.47	24/36	60	
Jiang[48]	2023	Electroacupuncture_daily medication	67±8	17/15	32	(29)(34) (35)
		Daily medication	68±9	18/14	32	

(*Continued*)

Table 1 (Continued).

Author	Year	Intervention	Characteristics of the Participants			Outcome
			Age	Sex F/M	Sample	
Huang[49]	2023	Scalp electroacupuncture_daily medication	62.11±6.01	12/23	35	(21)(49) (57)
		Shallow acupuncture_daily medication	61.71±6.56	13/22	35	
		Shallow acupuncture_scalp electroacupuncture_daily medication	62.57±5.96	14/21	35	
Zhang[50]	2022	Scalp electroacupuncture_madopar	61.8±4.6	23/20	43	(1)(3)(4) (5)(8)(36)
		Madopar	62.2±4.3	22/21	43	
Lu[51]	2022	Scalp electroacupuncture_madopar	67.81±7.27	16/16	32	(8)(13) (37)(38)
		Madopar	67.36±8.83	15/18	33	
Li[52]	2022	Warm Acupuncture-moxibustion_daily medication	64.36±4.83	23/28	51	(3)
		Daily medication	63.17±4.75	25/26	51	
Cao Long[53]	2021	Scalp acupuncture_daily medication		16/14	30	(8)(57)
		Daily medication		17/13	30	
Qian[54]	2021	Scalp electroacupuncture_daily medication	60.45±2.40	26/26	52	(22)(39) (57)
		Daily medication	60.33±2.37	24/28	52	
Li[55]	2021	Electroacupuncture_madopar	61.56±7.51	23/27	50	(1)(17) (21)(40)
		Madopar	62.49±7.53	24/26	50	
Chen[56]	2021	Acupuncture_rehabilitation robot training_daily medication	67.07±8.75	13/17	30	(1)(3)(4) (8)(36) (41)
		Daily medication	63.28±8.78	15/14	29	
Bai[57]	2021	Acupuncture_daily medication		18/11	29	(4)(21) (57)
		Daily medication		17/12	29	
Yuan[58]	2020	Acupuncture_daily medication	75.5±8.7	15/31	46	(8)(13) (42)(57)
		Escitalopram oxalate Tablets	63.7±7.9	23/28	51	
Jin[59]	2020	Moxibustion_auricular point seed-pressing therapy_conventional nonmedication intervention therapy			60	(12)(28) (57)
		Conventional nonmedication intervention therapy			60	
Wang[60]	2020	Nape acupuncture_swallowing training_conventional drug	54.0±9.2	23/37	60	(25)(26) (43)
		Swallowing training_conventional drug	52.0±11.3	29/31	60	
Wang[61]	2020	Acupuncture_oral sensorimotor training_conventional drug	59±10	16/29	45	(24)(26) (43)(44) (57)
		Oral sensorimotor training_conventional drug	59±10	19/26	45	

(*Continued*)

Table 1 (Continued).

Author	Year	Intervention	Characteristics of the Participants			Outcome
			Age	Sex F/M	Sample	
Wang[62]	2020	Acupuncture_rehabilitation training	63±5.5	11/9	20	(45)(57)
		Rehabilitation training	64±4.5	8/12	20	
Yu[63]	2020	Superficial needling_conventional drug	68.1±14.7	11/9	20	(5)(12) (41)(49)
		Electroacupuncture_conventional drug	58.2±13.4	12/8	20	
Liu[64]	2020	Acupuncture and moxibustion_daily medication	59.31±13		30	(4)(8)(57)
		Conventional drug	54.55±1.21		30	
Jiang[65]	2020	Warm acupuncture-moxibustion _madopar	64.82±12.23	15/18	33	(5)(46)
		Madopar	64.41±11.89	16/17	33	
Cai[66]	2020	Abdominal acupuncture_western medicine	69.10±7.46	11/18	29	(1)(29) (47)(49)
		Western medicine	69.69±7.82	9/20	29	
Zhao[67]	2019	Acupuncture_paroxetine_conventional drug	66.63±5.71	15/17	32	(8)(57)
		Conventional drug_paroxetine	64.85±6.14	15/16	31	
Wang[68]	2019	Madopar	65.43±6.82	15/16	34	(13)(22) (23)(57)
		Acupuncture	65.72±5.67	17/15	33	
		Acupuncture_madopar	66.24±6.09	18/14	33	
Wang[69]	2019	Needle warming moxibustion_daily medication	51.6±2.2	18/28	46	(48)
		Conventional drug	51.4±2.3	20/26	46	
Deng[70]	2018	Needle warming moxibustion_scalp electroacupuncture_daily medication	58±6.0	5/10	15	(48)
		Daily medication	60±5.7	6/9	15	
Peng[71]	2019	Moxibustion_daily medication	55.32±23.11	16/15	31	(13)(36) (46)
		Daily medication	52.32±27.51	13/17	30	
Luo[72]	2019	Electroacupuncture_daily medication	66.31±5.57	12/18	30	(13)(46) (50)(51) (57)
		Daily medication	66.07±5.48	13/17	30	
Li[73]	2019	Acupuncture_psychotherapy			15	(1)(21)
		Daily medication			15	
Chen[74]	2019	Warming Acupuncture Moxibustion_functional training	53.6±9.4	18/22	40	(24)(57)
		Functional training	54.1±9.5	19/21	40	
Wang[75]	2018	Scalp electroacupuncture_levodopa and benserazide hydrochloride Tablets_acupuncture	62.8±8.2	14/16	30	(1)(57)
		Scalp electroacupuncture_acupuncture	63.1±8.5	13/17	30	
		Levodopa and benserazide hydrochloride Tablets_acupuncture	62.6±7.2	15/15	30	

(*Continued*)

https://doi.org/10.2147/NDT.S541627

Table 1 (Continued).

Author	Year	Intervention	Characteristics of the Participants			Outcome
			Age	Sex F/M	Sample	
Liu[76]	2018	Electroacupuncture_compound carbidopa Tablets and phenolphthalein Tablets	65.28±7.32	20/28	48	(45)(46) (51)(57)
		Compound carbidopa Tablets and phenolphthalein Tablets	64.58±7.33	23/25	48	
Lin[77]	2018	Electroacupuncture_cognitive training and drug treatment	58.3±4.6	7/12	19	(23)(37) (49)
		Cognitive training_drug treatment	59.2±4.4	5/13	18	
Li[78]	2019	Acupuncture_madopar	72.16±5.41	11/19	30	(22)(23)
		Madopar	73.36±6.18	16/14	30	
Li[79]	2018	Acupuncture_daily medication	69.82±8.42	10/37	47	(13)(51) (57)
		Polyethylene glycol	70.73±8.88	12/34	46	
Li[80]	2018	Electroacupuncture_functional training_daily medication	59.37±4.89	14/29	43	(43)
		Functional training_daily medication	58.46±4.32	15/28	43	
Dong[81]	2018	Scalp electroacupuncture_madopar	60.25±6.376	17/19	36	(1)(57)
		Madopar	59.06±7.830	15/21	36	
Cao[82]	2018	Acupuncture_blood letting_function training	56.31±9.62	20/28	48	(22)(23)
		Function training	55.93±10.08	19/29	48	
Li[83]	2017	Press-needle	76.77±11.50	13/17	30	(12)(51) (57)
		Mosapride Tablets	75.77±11.30	16/14	30	
Zhou[84]	2017	Press-needle	76.77±11.50	13/17	30	(1)(49)
		Mosapride Tablets	75.77±11.30	16/14	30	
Yu[85]	2016	Scalp electroacupuncture_daily medication	66.38±11.48	11/13	24	(8)
		Paroxetine hydrochloride	65.77±11.87	16/10	26	
Li[86]	2016	Acupuncture and moxibustion_daily medication	63.30±5.82	14/16	30	(57)
		Deanxit	64.35±5.64	13/17	30	
Huang[87]	2014	Scalp acupuncture_madopar	61±8	7/13	20	(21)(57)
		Madopar	59±9	8/12	20	
Xia[88]	2013	Electroacupuncture_conventional drug	71.84±7.22	8/22	30	(8)(57)
		Conventional drug	71.93±8.12	10/20	30	
Huang[89]	2012	Moxibustion_daily medication	67.2±7.5	14/17	31	(29)(52) (57)
		Daily medication	66.9±7.0	14/16	30	
Liang[90]	2014	Acupuncture_madopar	62.43±6.25	16/19	35	(1)(5)(57)
		Madopar	60.57±9.25	18/17	35	

(*Continued*)

Table 1 (Continued).

Author	Year	Intervention	Characteristics of the Participants			Outcome
			Age	Sex F/M	Sample	
Li[91]	2024	Acupuncture_daily medication_	61±7	16/15	31	(53)(54) (55)(57)
		Daily medication	62±8	18/15	33	
Gu[92]	2023	Acupuncture_daily medication_	51.37±7.26	24/28	52	(4)(8)(49) (56)(57)
		Daily medication	52.07± 7.56	21/30	51	
Cai[93]	2023	Abdominal acupuncture_western medicine	70.26±10.15	14/24	38	(5)(8)(13)(49)
		Venlafaxine hydrochloride capsules	72.55±8.00	15/23	38	
Qiao[94]	2022	Warm acupuncture-moxibustion _madopar	76.67±4.67	16/13	29	(12)(36) (46)
		Madopar	76.83±4.65	15/14	29	
Fan[95]	2022	Real acupuncture	61.03±9.80	13/19	32	(4)(5)(13)
		Sham acupuncture	62.66±6.94	17/15	32	

Notes: (1)PDSS, (2)Epworth Sleepiness Scale (ESS), (3)Non-motor Symptoms Scale (NMSS), (4)HAMA, (5)PDQ-39, (6)King's Parkinson's Pain Scale (KPSS), (7)Visual Analog Scale (VAS), (8)HAMD, (9)Eating Assessment Tool (EAT-10), (10)Lung volume and capacity, (11)Constipation Symptom and Efficacy Assessment Scale (CSEAs), (12)PAC-QOL, (13)UPDRS I, (14) Constipation Classification Score (CCS), (15)Spontaneous Bowel Movements (SBMs), (16)Bristol Stool Form Scale (BSFS), (17)Self-Rating Depression Scale (SDS), (18)Multidimensional Fatigue Inventory (MFI), (19)Modified Fatigue Impact Scale (MFIS), (20Hospital Anxiety and Depression Scale (HADS), (21) PSQI, (22)Montreal Cognitive Assessment (MoCA), (23Mini Mental State Examination (MMSE), (24)Wada Drinking Test, (25)Wada Drinking Test, Salivary Secretion Amount (SSA), (26)Swallowing Quality of Life (SWAL-QOL), (27)Fluoroscopy, (28)Wexner Constipation Score (WCS), (29)Bladder Diary, (30)Event-Based Prospective Memory (EBPM), Time-Based Prospective Memory (TPBM), (31)Fatigue Severity Scale (FSS), (32)Gastrointestinal Symptom Rating Scale (GUSS), (33)Patient Assessment of Constipation Symptoms (PAC-SYM), (34)Overactive Bladder Symptom Score (OABSS), (35)Urodynamics, (36)Scales for Outcomes of Parkinson's disease-Autonomic (SCOPA-AUT), (37)Trail Making Test (TMT), (38)Traditional Chinese Medicine Quality of Life (TCM-QOL), (39) Emotion Regulation Questionnaire (ERQ), (40)Self-Rating Anxiety Scale (SAS), (41)Short Form McGill Pain Questionnaire (SF-MPQ), (42)Beck Depression Inventory-II (BDI-II), (43)Videofluoroscopic Swallow Study (VFSS), (44) Functional Oral Intake Scale (FOIS), (45)Short Form Health Survey (SF-36), (46)Constipation Severity Score (CSS), (47)Nocturia Quality of Life (N-QOL), (48)Zhao's Olfactory Dysfunction Scoring (ZODS), (49)Adverse Events (AEs), (50)Time to Resolution of Constipation, (51)Time to Resolution of Constipation, Anorectal Manometry (ARM), (52)Barthel Index Subitem Scores, (53)Systolic Blood Pressure (SBP), (54)Diastolic Blood Pressure (DBP), (55)Oral Health Quality of Life (OHQ), (56)Yale-Brown Obsessive Compulsive Scale (YBCS), (57) The total effective rate.

(Jadad score ≥ 4), with three studies[19,23,29] with a score of 7, six studies[20,22,26,31,45,95] with a score of 6, and three studies[27,42,77] with a score of 5. Further details are available in Figures 2 and 3.

Network Meta-Analysis results

Network Plot

In this study, network plots were drawn for outcome indicators including HAMA, HAMD, PDSS, PSQI, PDQ-39, PAC-QOL, UPDRS I, AEs, and the total effective rate. These indicators involved different intervention measures, covering various types such as acupuncture_usual, scalp_electroacupuncture, warm acupuncture_ moxibustion, and acupoint catgut embedding. Specifically, HAMA involved 7 interventions; HAMD involved 9 interventions; PSQI involved 6 interventions; PDSS involved 10 interventions; PDQ-39 involved 10 interventions; PAC-QOL involved 7 interventions; UPDRS I involved 8 interventions; the total effective rate involved 19 interventions, and AEs involved 11 interventions. In the figure, larger nodes indicate larger sample sizes, and thicker lines indicate a greater number of studies. The details are shown in Figure 4A–I).

Anxiety

Nine studies[19,32,46,50,56,57,64,92,95] used the HAMA score to assess anxiety levels in PD patients after interventions, involving 616 patients. According to the SUCRA (Table S3A and Figure 5A), acupuncture_training_usual (84.18%) ranked first, followed by acupuncture_usual (84.02%) and acupuncture_moxibustion_usual (76.50%). Acupuncture_training_usual may be the optimal intervention for reducing the HAMA score. The league table (Table S3B) indicated that acupuncture_moxibustion_usual (mean difference [MD] = −4.51, 95% credible interval [CrI]: −6.1 ~ −2.94), acupuncture_training_usual (MD = −5.05, 95% CrI: −8.07

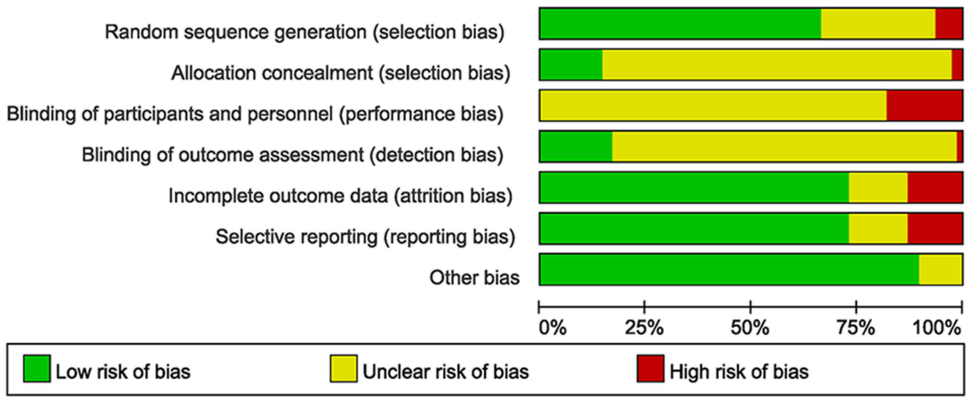

Figure 2 Risk of bias graph.

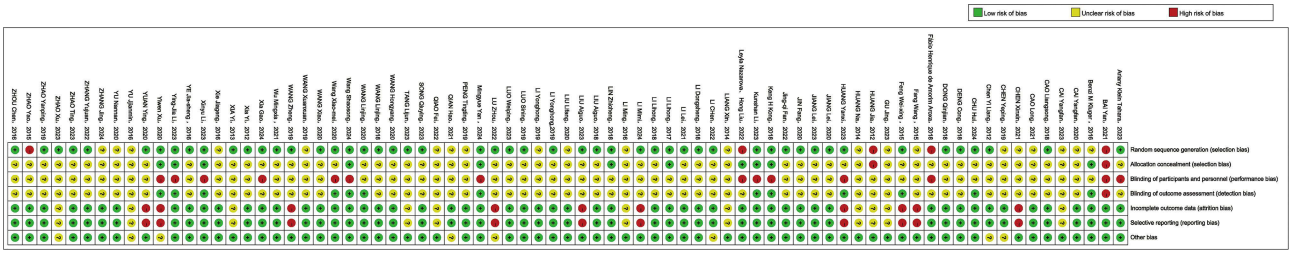

Figure 3 Risk of bias summary.

~ −1.99), and acupuncture_usual (MD = −4.81, 95% CrI: −6.38 ~ −3.23) were more effective in reducing the HAMA score compared to acupuncture. Additionally, compared to usual treatment, acupuncture_moxibustion_usual (MD = −2.95, 95% CrI: −3.89 ~ −2.01), acupuncture_training_usual (MD = −3.49, 95% CrI: −6.23 ~ −0.72), acupuncture_usual (MD = −3.25, 95% CrI: −4.17 ~ −2.31) also notably reduced the HAMA score. Furthermore, acupuncture_usual was also more effective than scalp_-electroacupuncture_usual in reducing the HAMA score (MD = −2.25, 95% CrI: −4.29 ~ −0.21).

Depression

A total of 18 studies[20,28,32,36,38,40,46,50,51,53,56,58,64,67,85,88,92,93] utilized the HAMD score to assess depressive symptoms among PD patients, involving 1262 participants. The SUCRA results revealed that abdominal_acupuncture_usual (94.15%) performed best in reducing HAMD scores, followed by acupuncture_moxibustion_usual (80.17%) and heat_sensitive_moxibustion_usual (75.93%) (Table S4A and Figure 5B). The league table (Table S4B) demonstrated that abdominal_acupuncture_usual reduced the HAMD score more effectively than electroacupuncture_usual (MD = −7.25, 95% CrI: −12.46 ~ −1.99), sham_acupuncture_usual (MD = −10.25, 95% CrI: −16.17 ~ −4.29), and usual treatment (MD = −6.54, 95% CrI: −11.59 ~ −1.45). Acupuncture_moxibustion_usual outperformed acupuncture_usual (MD = −2.18, 95% CrI: −3.28 ~ −1.07), electroacupuncture_usual (MD = −4.44, 95% CrI: −6.05 ~ −2.81), sham_acupuncture_usual (MD = −7.43, 95% CrI: −10.7 ~ −4.18), and usual treatment (MD = −3.73, 95% CrI: −4.7 ~ −2.75) in decreasing the HAMD score.

Sleep Quality

Eight studies[32,42,46,49,55,57,73,87] used the PSQI score to assess the sleep quality in PD patients, involving 497 patients. According to the SUCRA (Table S5A and Figure 5C), scalp_acupuncture_usual (99.98%) ranked first, followed by acupuncture_usual (71.17%) and acupuncture_moxibustion (68.84%). This result implied that scalp_acupuncture_usual could be a superior choice in the clinical treatment of sleep disorders in PD patients. The league table (Table S5B) indicated that, in reference to the minimal clinically important difference (MCID) for PSQI (2.5),[96] compared to usual treatment, acupuncture_moxibustion (MD = −4.03, 95% CrI: −5.1 ~ −2.95) and acupuncture_usual (MD = −3.91, 95%

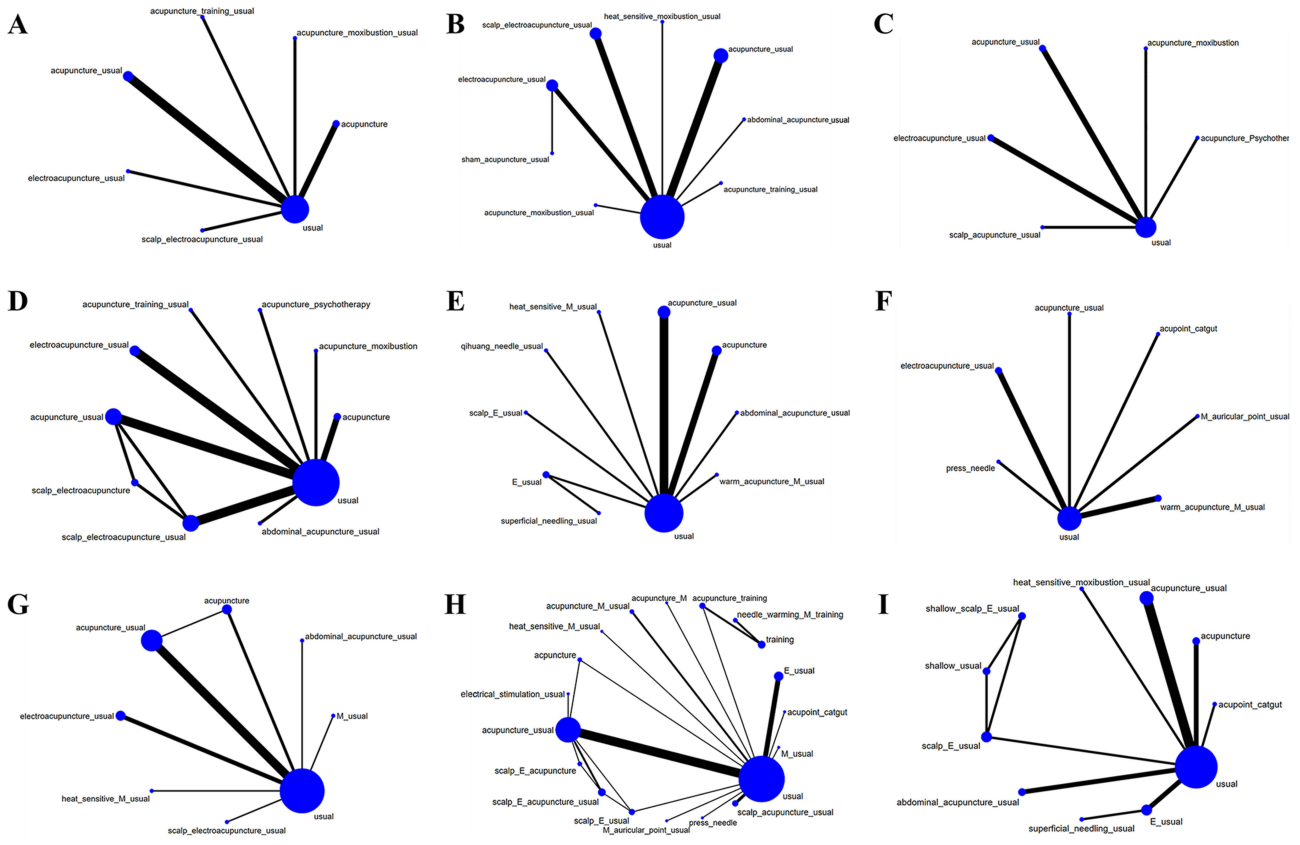

Figure 4 Network plot. (**A**) HAMA; (**B**) HAMD; (**C**) PSQI; (**D**) PDSS; (**E**) PDQ-39; (**F**) PAC-QOL; (**G**) UPDRS I; (**H**) The total effective rate; (**I**) AEs.
Abbreviations: M, moxibustion; E, electroacupuncture.

CrI: −4.99 ~ −2.83) were more effective in lowering the PSQI score, which exceeded the MCID, thus having clear clinical significance in improving sleep quality. Moreover, scalp_acupuncture_usual was more effective in reducing the PSQI score, with a difference higher than the MCID.

16 studies[19,25,27,30,31,40,42,50,55,56,66,73,75,81,84,90] utilized the PDSS score to assess the sleep quality in PD patients, involving 1116 patients. According to the SUCRA (Table S6A and Figure 5D), scalp_electroacupuncture (94.28%) ranked first, followed by scalp_electroacupuncture_usual (90.38%) and acupuncture_moxibustion (69.80%). The league table (Table S6B) indicated that scalp_electroacupuncture was more efficacious for improving the PDSS score than acupuncture (MD = 31.75, 95% CrI: 24.77 ~ 38.75), acupuncture_psychotherapy (MD = 12.33, 95% CrI: 3.36 ~ 21.27), acupuncture_training_usual (MD = 10.78, 95% CrI: 1.63 ~ 19.85), acupuncture_usual (MD = 24.43, 95% CrI: 20.89 ~ 27.94), electroacupuncture_usual (MD = 8.29, 95% CrI: 2.2 ~ 14.37), and usual treatment (MD = 18.77, 95% CrI: 14.71 ~ 22.82). Notably, the mean difference (MD=31.75) between scalp_electroacupuncture and acupuncture far exceeded the MCID (3.44)[97] for the PDSS score. The results indicated that the effect size of this intervention was statistically significant and it was capable of significantly improving patients' sleep quality in daily life.

Quality of Life

16 studies[19,25,27,30,31,40,42,50,55,56,66,73,75,81,84,90] selected the PDQ-39 score to evaluate the quality of life in PD patients, involving 1048 patients. According to the SUCRA (Table S7A and Figure 5E), heat_sensitive_moxibustion_usual (94.65%) ranked first, followed by superficial_needling_usual (85.16%) and abdominal_acupuncture_usual (71.94%). The league table (Table S7B) revealed that, in reference to the MCID for PDQ-39 (4.72),[98] heat_sensitive_moxibustion_usual outperformed acupuncture (MD = −17.07, 95% CrI: −22.15 ~ −11.99), Qihuang_needle_usual (MD = −57.33,

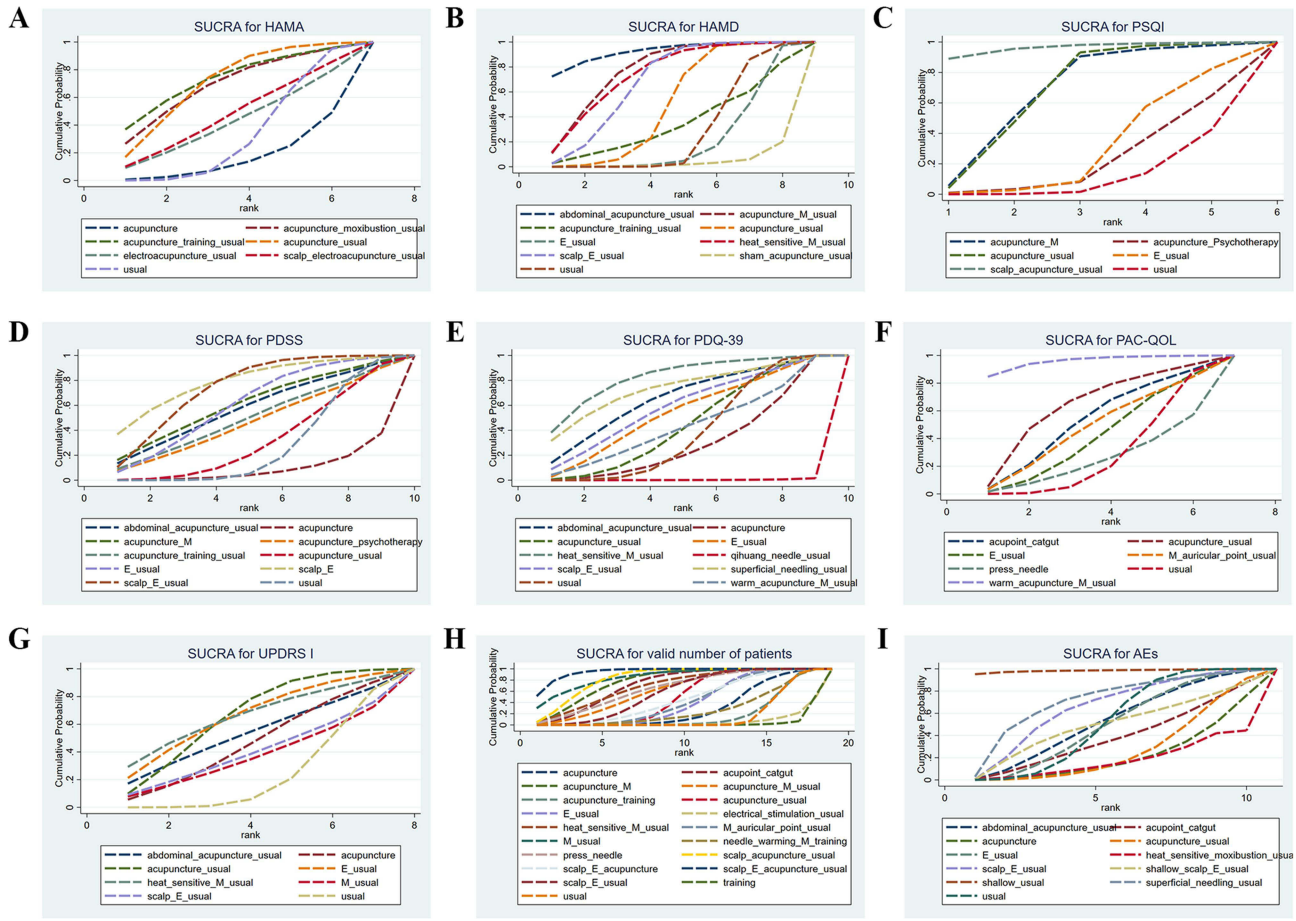

Figure 5 Cumulative probability graphs. (**A**) HAMA; (**B**) HAMD; (**C**) PSQI; (**D**) PDSS; (**E**) PDQ-39; (**F**) PAC-QOL; (**G**) UPDRS I; (**H**) The total effective rate; (**I**) AEs.
Abbreviations: M, moxibustion; E, electroacupuncture.

95% CrI: −69.17 ~ −45.68), and usual treatment (MD = −12.73, 95% CrI: −16.29 ~ −9.15) in reducing the PDQ-39 score, with a difference far higher than the MCID.

Eight studies[23–25,45,59,65,83,94] selected the PAC-QOL score to evaluate the quality of life in PD patients, involving 658 patients. According to the SUCRA (Table S8A and Figure 5F), warm_acupuncture_moxibustion_usual (99.995%) ranked first, followed by acupuncture_usual (76.36%) and acupoint_catgut_embedding (60.76%). It could serve as a key intervention for improving the quality of life of PD patients in clinical settings. The league table (Table S8B) implied that warm_acupuncture_moxibustion_usual outperformed electroacupuncture_usual (MD = −23.51, 95% CrI: −31.78 ~ −15.31), moxibustion_auricular_point_seed_pressing_usual (MD = −21.91, 95% CrI: −32.27 ~ −11.48), acupoint_catgut_embedding (MD = −21.01, 95% CrI: −29.54 ~ −12.52), and acupuncture_usual (MD = −17.73, 95% CrI: −27.76 ~ −7.7) in reducing the PAC-QOL score.

UPDRS I

14 studies[23,25,27,28,36,41,51,58,68,71,72,79,93,95] chose the UPDRS I score to assess the psychological, emotional, and cognitive functions in PD patients, involving 1113 patients. According to the SUCRA (Table S9A and Figure 5G), acupuncture_usual (94.02%) ranked first, followed by heat_sensitive_moxibustion_usual (85.55%) and abdominal_acupuncture_usual (59.54%). The league table (Table S9B) indicated that abdominal_acupuncture_usual (MD = −0.97, 95% CrI: −1.84 ~ −0.12), acupuncture (MD=−0.74, 95%CrI:-1.27~-0.21), acupuncture_usual (MD = −1.67, 95% CrI: −1.86 ~ −1.48), and heat_sensitive_moxibustion_usual (MD = −1.52, 95% CrI: −1.99 ~ −1.05) were more efficacious in lowering the UPDRS I score than usual treatment. Acupuncture_usual (MD = −0.93, 95% CrI: −1.47 ~ −0.38) and

heat_sensitive_moxibustion_usual (MD = −0.78, 95% CrI: −1.5 ~ −0.07) outperformed acupuncture in decreasing the UPDRS I score.

Total Effective Rate

36 studies[27,28,34–38,42,44,45,49,53,54,57–59,61,62,64,67,68,72,74–76,79,81,83,86–92] reported the total effective rate, involving 2655 patients. According to the SUCRA (Table S10A and Figure 5H), acupuncture_moxibustion (98.24%) ranked first, followed by acupoint_catgut_embedding (95.43%) and scalp_electroacupuncture_acupuncture_usual (78.44%). The league table (Table S10B) revealed that acupuncture_moxibustion outperformed acupuncture (RR = 3.33, 95% CrI: 1.65 ~ 8.1), acupuncture_moxibustion_usual (risk ratio [RR] = 2.8, 95% CrI: 1.49 ~ 6.42), acupuncture_training (RR = 3.41, 95% CrI: 1.5 ~ 8.86), acupuncture_usual (RR = 2.83, 95% CrI: 1.53 ~ 6.43), electroacupuncture_usual (RR = 3.04, 95% CrI: 1.64 ~ 6.89), electrical_stimulation_usual (RR = 3.64, 95% CrI: 1.91 ~ 8.51), heat_sensitive_moxibustion_usual (RR = 2.57, 95% CrI: 1.33 ~ 5.95), moxibustion_auricular_point_seed_pressing_usual (RR = 2.64, 95% CrI: 1.38 ~ 6.15), moxibustion_usual (RR = 2.32, 95% CrI: 1.16 ~ 5.45), needle_warming_moxibustion_training (RR = 2.67, 95% CrI: 1.1 ~ 7.26), press_needle (RR = 2.53, 95% CrI: 1.28 ~ 5.92), scalp_acupuncture_usual (RR = 2.3, 95% CrI: 1.21 ~ 5.31), scalp_electroacupuncture_acupuncture (RR = 2.79, 95% CrI: 1.44 ~ 6.54), scalp_electroacupuncture_acupuncture_usual (RR = 2.26, 95% CrI: 1.21 ~ 5.2), scalp_electroacupuncture_usual (RR = 2.74, 95% CrI: 1.46 ~ 6.27), training (RR = 4.23, 95% CrI: 1.82 ~ 11.16), usual treatment (RR = 3.37, 95% CrI: 1.84 ~ 9.65) in improving NMS in PD.

AEs

18 studies[19,21,24,27,28,31,39,40,43,45,47,49,63,66,77,84,92,93] reported AEs, while 202 individuals reported AEs. According to the SUCRA (Table S11A and Figure 5I), shallow_acupuncture_usual (99.17%) ranked first, followed by superficial_needling_usual (SUCRA = 85.54%) and scalp_electroacupuncture_usual (SUCRA = 77.71%). The league Table (Table S11B) indicated that shallow_acupuncture_usual was related to a lower risk of AEs compared to heat_sensitive_moxibustion_usual (RR = 0.01, 95% CrI: 0 ~ 0.42). The risk of AEs with superficial_needling_usual was lower than that of abdominal_acupuncture_usual (RR = 0.22, 95% CrI: 0.05 ~ 0.85), acupoint_catgut_embedding (RR = 0.1, 95% CrI: 0.01 ~ 0.74), acupuncture (RR = 0.11, 95% CrI: 0.03 ~ 0.34), acupuncture_usual (RR = 0.14, 95% CrI: 0.03 ~ 0.51), electroacupuncture_usual (RR = 0.32, 95% CrI: 0.1 ~ 0.76), heat_sensitive_moxibustion_usual (RR = 0.02, 95% CrI: 0 ~ 0.2), and usual treatment (RR = 0.22, 95% CrI: 0.06 ~ 0.64).

Secondary Outcome

Electroacupuncture_usual showed positive effects. Li et al[24] Nazarova et al[25] Luo et al[72] and Liu et al[76] collectively demonstrated that it outperformed conventional interventions or medication alone in alleviating intestinal dysfunction, with benefits observed in various assessments of gastrointestinal function. Li et al[23] and Li et al[79,83] found that acupuncture_usual and press-needle improved gastrointestinal function compared to western medicine or medication alone. Jin et al[59] reported favorable outcomes with moxibustion_auricular point seed-pressing. Qiao et al[94] and Song et al[45] noted that warm acupuncture-moxibustion and acupoint catgut embedding, respectively, alleviated gastrointestinal symptoms ($P < 0.05$).

Several studies have shown that various interventions can improve cognitive and memory functions in patients with PD. Wang Zheng et al[68] Li et al[78] and Zhang et al[41] confirmed that acupuncture_usual could effectively improve patients' cognitive and memory functions. Wang et al[32] Lin et al[77] and Lu et al[51] reported that electroacupuncture-related interventions, such as electroacupuncture_ training_usual, and scalp_electroacupuncture_usual, all have positive effects on improving cognitive functions. Ye et al[35] indicated that acupuncture_cognitive function training was more effective than conventional Western medicine. Cao et al[82] found that acupuncture_blood letting function training could improve cognitive function. Qian et al[54] confirmed that scalp_electroacupuncture_daily medication improved cognitive function.

Xu et al[27] and Li et al[55] showed that eight-week electroacupuncture_madopar notably reduced SDS and SAS scores compared to madopar ($P < 0.05$). Liu et al[47] Yuan et al[58] and Gu et al[92] confirmed that acupuncture_daily medication more significantly reduced emotion-related scores compared to daily medication alone. Gu et al[92] observed a notable decrease after 3 months of treatment ($P < 0.05$). Kluger et al[31] indicated that acupuncture alone significantly relieved

anxiety and depression levels in the HADS score after 6 weeks of treatment. Qian et al[54] showed that scalp_electroacupunctur_daily medication increased the cognitive reappraisal score and reduced the expressive suppression score in the Emotion Regulation Questionnaire.

Kong et al[29] Kluger et al[31] and Liu et al[47] all confirmed that acupuncture and acupuncture_daily medication could relieve fatigue in PD patients. In addition, Yan et al[19] Kong et al[29] and Kluger et al[31] found that acupuncture could reduce the ESS index ($P < 0.05$), which could alleviate drowsiness in patients.

Chen et al[39] Huang et al[49] Cai et al[66] and Huang et al[89] selected medication treatment as the control group. Their results revealed that electroacupuncture_daily medication, abdominal acupuncture_daily medication, and moxibustion_daily medication were superior to the control group in reducing the frequency of urination within 24 hours, decreasing the average number of urinary incontinence episodes over 24 hours, and elevating the average single urine volume over 24 hours.

In addition, eight studies[21,33,43,44,60,61,74,80] confirmed that acupuncture and related therapies such as electroacupuncture, abdominal acupuncture, warming acupuncture moxibustion, tongue acupuncture combined with training or conventional treatment were superior to conventional treatment or rehabilitation training alone in improving swallowing function in patients with PD. However, due to the numerous outcome indicators, NMA cannot be performed.

Regarding other NMSs, three studies[51,62,76] showed that combined interventions such as scalp_electroacupuncture, acupuncture, and electroacupuncture with medication or training were more effective in improving quality of life-related scores than single treatment or training alone. Four studies[20,24,56,63] indicated that combined interventions like electroacupuncture, acupuncture, and superficial needling with medication or training were superior to medication alone in improving pain-related scores. Six studies[19,25,26,50,52,56] demonstrated that combined interventions including acupuncture, electroacupuncture, and warm acupuncture-moxibustion with medication or training could reduce NMSS scores compared to medication alone. Four studies[50,56,71,94] showed that combined interventions such as scalp electroacupuncture, warm acupuncture-moxibustion, and moxibustion could reduce SCOPA-AUT scores. In addition, acupuncture_ medication could improve blood pressure-related indicators.[91] Dry needling could enhance lung function.[22] Furthermore, combined interventions like warm acupuncture moxibustion could improve olfactory function.[69,70]

Publication Bias

Funnel plots were utilized to assess publication bias. For the scores of PDQ-39, PDSS, PAC-QOL, and the total effective rate, the included studies were generally symmetrically distributed on both sides in the funnel plots, suggesting no publication bias (Figure 6A–D). For studies on the HAMA and PSQI scores, no publication bias was observed; moreover, the majority of the studies included were concentrated in the lower part of the plot, indicating a potential presence of small sample events (Figure 6E and F). Regarding studies on the HAMD score, no publication bias was found; furthermore, most of the studies included were concentrated in the lower part of the plot, indicating the potential presence of small sample events (Figure 6G); additionally, a limited number of studies were located outside the plot, indicating the potential presence of heterogeneity (Figure 6G). In terms of the UPDRS I score and AEs, overall publication bias may exist (Figure 6H and I).

Discussion

The motor symptoms of PD have been widely investigated in previous studies.[99] In contrast, studies on NMSs are limited and incomplete. In total, 76 eligible studies are incorporated in our analysis, encompassing a wide variety of common NMSs, thereby providing crucial references for clinical practice.

The mental state of PD patients has long been a complex issue, which contributes to an increased burden on healthcare systems.[100] The findings of this study suggest that acupuncture_training_usual exhibits great effects in addressing anxiety in PD patients. This approach may be considered a promising intervention for addressing anxiety in PD patients, possibly because it combines training and acupuncture, which more effectively regulates mental state and neurological function. The HAMA scale is utilized to assess anxiety. While a meta-analysis of 20 RCTs[101] indicates that moxibustion is the most effective for reducing HAMA scores, existing studies on PD have not fully explored moxibustion, highlighting the need for further research. Depression is also prevalent among PD patients.[102] Depressive symptoms

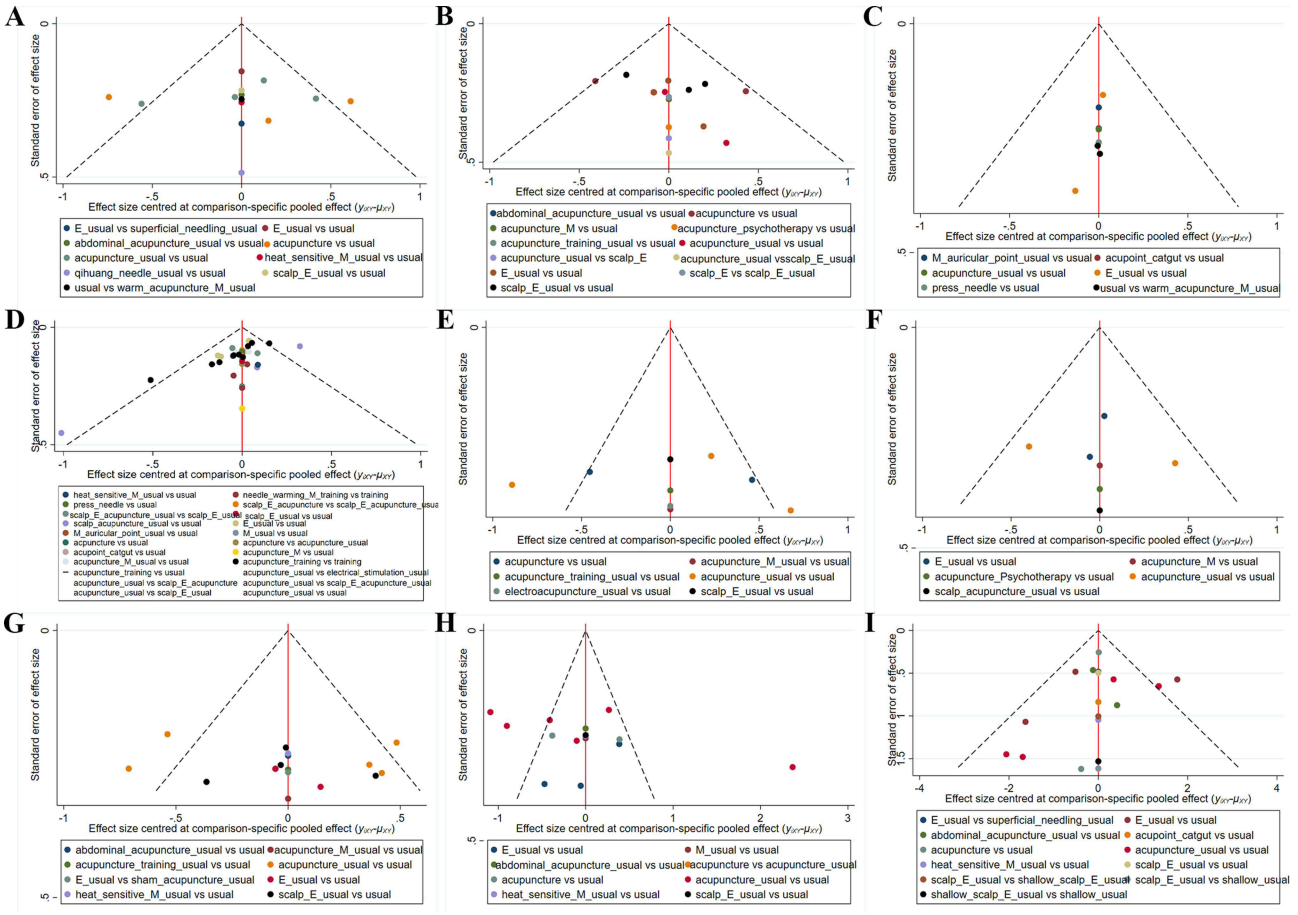

Figure 6 Funnel plot. (**A**) PDQ-39; (**B**) PDSS; (**C**) PAC-QOL; (**D**) The total effective rate; (**E**) HAMA; (**F**) PSQI; (**G**) HAMD; (**H**) UPDRS I; (**I**) AEs.
Abbreviations: CNKI, China National Knowledge Infrastructure; VIP Database, Chinese Science and Technology Periodical Database; SUCRA, Surface Under the Cumulative Ranking Curve; HAMA, The Hamilton Anxiety Scale; HAMD, The Hamilton Rating Scale for Depression; PDSS, The Parkinson's Disease Sleep Scale; PSQI, The Pittsburgh Sleep Quality Index; PDQ-39, The 39-item Parkinson's Disease Questionnaire; PAC-QOL, The Patient Assessment of Constipation Quality of Life scale; UPDRS, The Unified Parkinson's Disease Rating Scale; M, moxibustion; E, electroacupuncture.

are often coexistent with anxiety. Abnormal activity in the amygdala is considered a key contributor to major depressive disorder and anxiety.[103] One study has found that acupuncture remarkably modulates the functional connectivity between the amygdala and the hippocampus, thereby helping to reduce symptoms of anxiety and depression.[104] Based on the HAMD scale, abdominal_acupuncture_usual is regarded as one of the most effective methods for alleviating anxiety in PD patients. This finding may be explained by the role of the gut-brain axis in the development of PD, as a growing body of evidence indicates that gut microbial dysbiosis causes PD.[105] By modulating gastrointestinal function, abdominal acupuncture may indirectly enhance the emotional state of PD patients. In clinical practice, clinicians should pay attention to the patient's gastrointestinal function and consider using acupuncture in combination with potential gut microbiota modulation techniques to achieve better antidepressant effects.

Two meta-analyses reveal that acupuncture can treat sleep disorders and improve sleep quality in PD patients.[106,107] This is further validated by the study conducted by Zhang et al[108] on acupuncture treatment for insomnia symptoms in hypertensive patients. In addition, according to Jingjun Xie et al, scalp_acupuncture_usual has demonstrated an excellent effect on improving sleep quality,[109] which is consistent with our findings. The scalp acupuncture exhibits sedative and calming effects and is significantly effective in treating brain diseases. Scalp acupuncture also reflects the adjacency principle of TCM that acupuncture at an acupoint can treat diseases at and around the acupoint. One study suggests that electroacupuncture may help improve sleep in PD patients.[110] Our results found that scalp_electroacupuncture was significantly effective in enhancing PDSS scores. This finding is further confirmed since it achieves the MCID of the PDSS score.[96] This result aligns with its underlying mechanisms: by regulating cortical bioelectrical activity and

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modulating neurotransmitters such as serotonin and GABA key to sleep regulation, scalp_electroacupuncture effectively bridges the gap between statistical differences and patient-perceived improvement.[111] Studies with long-term follow-up[19,27] have also confirmed that the positive effects of acupuncture on sleep disorders persist after treatment. For PD, fatigue is moderately linked to drowsiness and sleep disturbances, and it can persist throughout various stages of the disease.[112] Notably, acupuncture did not significantly relieve fatigue and drowsiness in our study, likely due to limited sample size and intervention types. Further RCTs exploring diverse acupuncture-based interventions for these symptoms are warranted.

The NMS of PD patients can notably impact their quality of life.[113] A meta-analysis including 39 studies indicates that acupuncture-related therapies, when combined with conventional medication, are more effective than conventional medication alone in improving quality of life.[114] Our results reveal that moxibustion therapy combined with conventional medication noticeably improves the quality of life. The protective mechanism of moxibustion, an external treatment in TCM, may be linked to the inhibition of ferroptosis.[115] Moxibustion has the potential to enhance antioxidant capacity and regulate neuronal activity, thereby contributing to the treatment of PD. Notably, the five included studies with long-term follow-up indicate a sustained effect of acupuncture on quality of life even after treatment cessation.[19,23,40,47,95] Regarding UPDRS I, our results align with previous evidence[116,117] that acupuncture_usual and electroacupuncture_usual outperform usual treatment. A strong correlation between UPDRS I and NMSS has been reported in a previous study.[118] Likewise, our results found that acupuncture plus usual treatment was more effective in reducing NMSS scores compared to usual treatment alone.

In this study, cognitive function is assessed using not only UPDRS I but also MMSE and MoCA scales. Additional measures such as TMT, EBPM, and TBPM are used to evaluate executive function and memory. The results showed that acupuncture combined with other therapies significantly improved cognitive scores compared to Western medication, cognitive training, or their combination, suggesting a positive role of acupuncture in enhancing cognitive function in PD patients. This finding is consistent with that reported by Zheng et al[68] who have found that acupuncture_madopar is superior to madopar alone in improving cognitive function, but do not compare it to acupuncture alone. Hence, further research is necessary to verify whether combined acupuncture therapies have synergistic effects compared to acupuncture alone.

In addition to the aforementioned issues, gastrointestinal dysfunctions (such as dysphagia, delayed gastric emptying, and constipation) are common in PD patients and may manifest as early as 15 to 24 years prior to the diagnosis of PD. Li et al[119] have proven that acupuncture may be used to treat constipation in PD. However, their study has some limitations. Our study finds that several acupuncture techniques can treat constipation symptoms in PD, with a high safety profile, such as auricular point seed pressing, warm acupuncture moxibustion, and acupoint catgut. However, due to the presence of numerous indicators for assessing constipation symptoms, there is currently no unified outcome measure, making it difficult to evaluate which acupuncture method is more effective. It is important to note that all evidence indicates that acupuncture-related therapies are superior to usual treatment. A study by Zhang et al[120] also finds that acupuncture is feasible for treating PD-related constipation. However, the two studies differ in research paths and focal points. Four studies have demonstrated that electroacupuncture_usual treatment has effectively alleviated constipation symptoms and improved gastrointestinal motility.[24,25,72,76] Electroacupuncture is a novel approach to treating constipation. It promotes the release of glial cell-derived neurotrophic factors in colonic tissue through central cholinergic pathways, thereby protecting intestinal neurons and improving gastrointestinal motility.[121] Moreover, dysphagia is another remarkable manifestation of gastrointestinal dysfunction, characterized by changes in swallowing physiology and the risk of aspiration.[122] In terms of swallowing function, acupuncture combined with swallowing training has achieved favorable clinical results. It has been found that swallowing and breathing are closely related, and swallowing may occur when lung capacity expands.[123] According to Ariany Klein Tahara et al[22] dry needling has a positive impact on lung volume and capacity in PD patients. However, whether it can further improve swallowing difficulties in PD patients requires to be investigated.

The results of this study indicate that shallow_acupuncture_usual has the lowest risk of AEs among all acupuncture interventions, providing a safe and effective option for the clinical treatment of NMS in PD. Shallow needling and superficial needling are relatively safe, possibly because they stimulate shallower layers of the skin or subcutaneous

tissue. Such approaches result in a milder form of stimulation, thereby minimizing potential damage to deeper tissues, blood vessels, and nerves. Consequently, they generally do not induce severe pain. The results of this study reveal that acupuncture_moxibustion demonstrates the highest efficacy rate among all acupuncture-based interventions. It integrates both acupuncture and moxibustion, which can thoroughly regulate physiological and pathological conditions in patients. Acupuncture can stimulate acupoints, regulate the flow of Qi and blood, and improve blood circulation.[5] Moxibustion stimulates the body with heat, enhancing immunity and improving antioxidant capacity.[124] The integrated effects of acupuncture_moxibustion enable it to notably improve NMS in PD patients, including anxiety, depression, sleep disturbances, and overall quality of life. Studies suggest that acupuncture_moxibustion is superior to other acupuncture methods, such as traditional acupuncture, moxibustion, or electroacupuncture, in improving NMS in PD patients. This may be because acupuncture_moxibustion can more comprehensively regulate the patient's physiological and pathological state, thereby more effectively improving the symptoms of PD.

This meta-analysis presents several strengths. First, all included studies are RCTs, which are identified through a comprehensive study search. Furthermore, this study addresses various NMSs related to sleep, the urinary system, and gastrointestinal function. It provides a comprehensive understanding of acupuncture treatment for NMS in PD patients. However, this study has certain limitations. i) The manifestations of NMS in PD are diverse, and thus outcome measures are diverse. Furthermore, these measures are predominantly assessed by subjective scales, and appropriate objective outcome indicators are lacking. ii) The present study only identifies 18 articles that report AEs, with no clear safety evaluation. iii) This analysis includes studies from multiple regions, and the majority of patients (94.80%) are from China, which may introduce cultural biases affecting NMS expression and measurement. Cultural norms can lead to underreporting of mental health-related symptoms due to stigma. Western assessment scales may fail to capture culturally specific NMS manifestations due to linguistic barriers. In China, acupuncture is deeply integrated into healthcare, leading to a greater patient preference for acupuncture-based treatments compared to other regions. This preference may impact sample representativeness and limit the generalizability of the results to non-Chinese populations. iv) Although some long-term follow-up studies have been included, there are remarkable discrepancies in the selection of outcome measures and measurement methods among these studies. Some studies focus on the changes in specific NMSs, while others emphasize the overall quality of life. This makes it difficult to integrate and analyze these outcome indicators in a network meta-analysis. Moreover, the follow-up time points and frequencies vary across different studies, further complicating the pooling and presentation of results. v) Among the included studies, some studies did not provide clear descriptions of the implementation of randomization methods, allocation concealment, and blinding. Additionally, several studies present high-risk factors that contribute to a ROB.

From a clinical perspective, the results of this study provide important references for clinical practice. When choosing acupuncture interventions, clinicians may consider a suitable method, depending on the patient's specific NMS. In PD patients with evident anxiety symptoms, acupuncture_training_usual should be considered a promising intervention; for those with depression, abdominal_acupuncture_usual could be more suitable; for improving sleep, scalp_acupuncture_usual and scalp_electroacupuncture are promising options; for ameliorating life quality, heat_sensitive_moxibustion_usual and warm_acupuncture_moxibustion_usual are essential treatment methods. Acupuncture demonstrates certain advantages in the treatment of NMS in PD. However, it also presents some limitations. In the future, more high-quality, multicenter, large-sample RCTs should be conducted to verify the effects of different acupuncture therapies on NMS in PD. In terms of study design, it is essential to standardize outcome measures, especially for symptoms like gastrointestinal dysfunction, which have multiple assessment indicators, in order to more accurately compare the effectiveness of different acupuncture therapies. Simultaneously, it is necessary to enhance the monitoring and evaluation of AEs, to improve the reliability of safety evaluations. Moreover, it is essential to investigate the mechanisms of acupuncture in treating NMS in PD, exploring its principles from neurobiological, immunological, and other multidisciplinary perspectives, to offer a stronger theoretical basis for clinical practice.

Conclusion

The findings suggest that acupuncture_training_usual may be particularly beneficial for relieving anxiety, abdominal_acupuncture_usual for depression, and acupuncture_usual for psychological, emotional and cognitive functions.

Scalp_acupuncture_usual and scalp_electroacupuncture could enhance sleep quality; heat_sensitive_moxibustion_usual and warm_acupuncture_moxibustion_usual may improve quality of life; and shallow_acupuncture_usual is associated with fewer adverse events. Conventional acupuncture is also beneficial for alleviating pain and other NMSs. However, these findings should be interpreted with caution due to heterogeneous outcomes, potential publication bias, and predominantly Chinese study populations. Further standardized multicenter trials are required to validate these findings.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Study Approval

As this is a meta analysis, ethical approval is not applicable.

Patient and Public Involvement

It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work. Peng Chen acquired funding.

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Disclosure

All authors declare no conflicts of interest in this work.

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