

A Meta-Analysis on the Efficacy of Acupuncture as an Adjuvant Therapy for Schizophrenia

Cheng Huang¹, Peiming Zhang², Yu Dong¹, Ruchun Chang², Jinxiong Lao^{2,3}, Ziyong Li^{2,3}, Danchun Lan²

¹Acupuncture and Rehabilitation Clinical School of Medicine, Guangzhou University of Chinese Medicine, Guangzhou, People's Republic of China; ²Department of Acupuncture and Moxibustion, Foshan Hospital of Traditional Chinese Medicine, Foshan, People's Republic of China; ³The Eighth Clinical School of Medicine, Guangzhou University of Chinese Medicine, Foshan, People's Republic of China

Correspondence: Danchun Lan, Email Danchun2013@aliyun.com

Objective: To systematically evaluate the efficacy of acupuncture in the treatment of schizophrenia.

Methods: We searched China National Knowledge Infrastructure (CNKI), Wanfang Database, Chongqing VIP Chinese Science and Technology Periodical Database (VIP), China Biology Medicine Database (CBM), PubMed, Embase, Web of Science, Cochrane Library for relevant literature on the acupuncture treatment of schizophrenia published from database inception to May 17, 2023. The evaluation criteria included total effective rate, incidence of adverse reactions, TESS scale, PANSS scale, BPRS scale, SANA scale, SAPS scale. Two researchers independently screened the literature, extracted data, and assessed the risk of bias of the included studies. The RevMan 5.4 software was used for meta-analysis, risk of bias (ROB) evaluation tool was used to evaluate the risk of bias of the studies, and the GRADE evaluation tool was used to evaluate the quality of evidence. The study was registered on PROSPERO, CRD42023416438.

Results: A total of 38 RCTs involving 3143 patients were included in the meta-analysis. The results showed that acupuncture can improve the total effective rate [OR=3.43 (95% CI: 2.71, 4.35), moderate credibility], reduce the incidence of adverse reactions [OR=0.45 (95% CI: 0.32, 0.63), moderate credibility], reduce the TESS score (side effect scale) [MD=-1.83 (95% CI: -2.94, -0.71), very low credibility]. Acupuncture also reduced the PANSS total score [MD=-5.75 (95% CI: -8.08, -3.42), very low credibility], SANA score [MD=-2.66 (95% CI: -6.84, 1.51), very low credibility], SAPS score [MD=-1.26 (95% CI: -2.55, -0.02), very low credibility], and BPRS score [MD=-7.02 (95% CI: -10.59, -3.46), very low credibility].

Conclusion: Existing evidence indicates that acupuncture as an adjunctive therapy can improve the total effective rate of SZ patients, reduce the incidence of adverse reactions, improve clinical symptoms, and alleviate depression and anxiety in SZ patients. However, more high-quality clinical research evidence is still needed to support these findings.

Keywords: acupuncture, meta-analysis, schizophrenia

Introduction

Schizophrenia (SZ) is a chronic mental illness characterized by changes in personality, cognitive, thinking, emotional, and behavioral disorders, as well as a lack of coordination between mental activity and the environment. Its main clinical manifestations are delusions, hallucinations, disordered thinking (speech), obvious disordered or abnormal movements and behaviors, and other symptoms. It affects approximately 20 million people worldwide,¹ and the global prevalence of schizophrenia is estimated to be between 0.33% and 0.75%.¹ The disease is more common in young adults or adults.² At the same time, schizophrenia seriously affects the daily life of patients, and maintaining daily activities is very difficult for schizophrenia patients.

In terms of mechanisms, the etiology of SZ remains elusive to date. Researchers have been searching for biomarkers to aid in the diagnosis and understanding of the pathogenesis of this disease. In recent years, exosomes as a prominent biomarker have garnered widespread attention in this research field. Studies have shown that metabolites derived from

exosomes have significant potential to provide diagnostic information for SZ, highlighting the role of exosomal miRNA dysregulation in the pathophysiology of SZ.³

In clinical practice, drug therapy and psychotherapy are the main treatments for SZ, but their adverse reactions are obvious. Studies have found that second-generation or “atypical” antipsychotics (SGA) can lead to weight gain and significant metabolic changes in patients, indirectly increasing their risk of developing diabetes and increasing circulating cholesterol levels.⁴ In addition, the recurrence rate of this disease is as high as 78–82%.

Acupuncture, as a green therapy, provides another option for SZ without significant side effects. The research findings indicate that acupuncture, by modulating functionally opposing brain networks, enhances the behavior of SZ patients, and this effect is contingent upon psychophysiological responses.⁵ While the effectiveness of acupuncture in treating SZ has been confirmed by several Cochrane systematic reviews,^{6,7} there are limitations in the methodological quality of some included studies, leading to a lack of high-quality evidence. Furthermore, the potential impact factors underlying acupuncture’s therapeutic effects in SZ remain a subject of debate. This study aims to bridge these research gaps, offering more systematic evidence and applying meta-regression to investigate potential factors influencing the efficacy of acupuncture in SZ treatment.

Materials and Methods

The study was registered on PROSPERO (CRD42023416438).

Inclusion and Exclusion Criteria

Inclusion Criteria

(1) Randomized controlled trials (RCTs) of acupuncture treatment (Intervention definition can be found in [Appendix 1](#)) for schizophrenia were included in this meta-analysis. (2) Patients with a clinical diagnosis of schizophrenia according to diagnostic criteria such as Chinese Classification of Mental Disorders (CCMD-2,⁸ CCMD-3⁹), International Classification of Diseases (ICD-10¹⁰), or Diagnostic and Statistical Manual of Mental Disorders (DSM-V¹¹). (3) The intervention group received acupuncture or acupuncture combined with other therapies, and the control group received other therapies except for acupuncture (when the intervention group received acupuncture combined with other adjunct therapies, the control group should receive the same adjunct therapies). (4) The outcome measures must be one of the following, such as total effective rate, incidence of adverse reactions, score on the Treatment Emergent Symptom Scale (TESS), Positive and Negative Syndrome Scale (PANSS), Brief Psychiatric Rating Scale (BPRS), Scale for the Assessment of Negative Symptoms (SANS), and Scale for the Assessment of Positive Symptoms (SAPS).

Exclusion Criteria

(1) Unclear diagnostic criteria or no diagnostic criteria; (2) Studies that did not include outcome measures; (3) Studies with unextractable data or inaccessible full text; (4) Duplicate publications; (5) Reviews, conference abstracts, before-and-after comparison studies, case reports, cohort studies, and other non-randomized studies.

Search Strategy

We searched the China National Knowledge Infrastructure (CNKI), Wanfang Database, Chongqing VIP Chinese Scientific Journal Full-text Database (VIP), China Biology Medicine disc (CBM), PubMed, Embase, Web of Science, and Cochrane Library for relevant literature on acupuncture treatment for schizophrenia. The search time limit was from the establishment of the databases until May 17, 2023. The search terms used included “acupuncture”, “acup*”, “moxibustion”, “electroacupuncture”, “schizophrenia”, “schizo*”, “psychos*” and other relevant terms. Language restrictions were not applied. The specific search formula can be found in [Appendix 2](#)

Literature Screening and Data Extraction

Firstly, two researchers independently screened the retrieved literature based on the inclusion and exclusion criteria. In case of any disputes, a third reviewer cross-checked the articles to reach a consensus. The two researchers extracted relevant information from the included literature, including study identification (first author and year of publication),

general characteristics of patients (gender, age, and sample size), intervention measures, treatment process, and outcome indicators.

Risk of Bias Assessment of Included Studies

The Cochrane risk of bias assessment tool (version 5.4.0) was used to evaluate the risk of bias in the included RCTs. It includes seven items: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases. The risk of bias for each item was classified into three categories: low risk of bias, high risk of bias, or unclear risk of bias. Two reviewers independently assessed the risk of bias of the studies. In case of inconsistent results, a third reviewer made the final decision.

Outcomes and Measures

Primary Outcome

The primary outcome was the total effective rate, which was assessed using the Positive and Negative Syndrome Scale (PANSS), Scale for the Assessment of Positive Symptoms (SAPS), Scale for the Assessment of Negative Symptoms (SANS), Brief Psychiatric Rating Scale (BPRS), Global Assessment of Functioning (GAF), and Pittsburgh Sleep Quality Index (PSQI). In the study, a reduction rate of $\geq 30\%$ in PANSS score, $\geq 20\%$ in BPRS score, $\geq 25\%$ in SAPS excitation score, $\geq 25\%$ in SANS score, an increase rate of $\geq 20\%$ in GAF score, and a reduction rate of $\geq 25\%$ in PSQI score were considered as effective. The evaluation time points included before and after treatment (usually 1–12 weeks).

Secondary Outcomes

The secondary outcome was the PANSS score, which is a scale for evaluating the positive symptoms, negative symptoms, and general psychological symptoms of patients with schizophrenia. The total score ranges from 30 to 210, and includes subscales such as positive symptoms, negative symptoms, and general psychopathology. A threshold of 60 points was used, with higher scores indicating more severe symptoms. The evaluation time points included before and after treatment (usually 1–12 weeks).

BRPS score: The BRPS score was used to evaluate the severity of illness and treatment efficacy in patients with mental illness, with a range of 1–7 points. A score of 1 indicated extremely worsening condition, while a score of 7 indicates complete remission of symptoms. The evaluation time points included before and after treatment (usually 1–12 weeks).

SAPS score: The SAPS score was used to assess the severity and changes in symptoms of mental illness. The scale was consisted of 4 dimensions, including hallucinations, delusions, thought disorders, and affective flattening. The total score ranged from 0–176, with higher scores indicating more severe symptoms. The evaluation time points included before and after treatment (usually 1–12 weeks).

SANS score: The SANS score was used to assess the severity and changes in symptoms of mental illness. The scale was consisted of 5 dimensions, including hallucinations, delusions, thought disorders, affective flattening, and behavioral symptoms, each with multiple scoring indicators. The score range was 0–95, with higher scores indicating more severe symptoms. The evaluation time points included before and after treatment (usually 1–12 weeks).

Effect Size and Heterogeneity Assessment

Meta-analysis was performed using RevMan 5.4 software. With 95% confidence interval (CI), the odds ratio (OR) was used as the effect size (ES) considering the the total effective rate was a dichotomous variable, and the mean difference (MD) was applied for the continuous variables, involving all secondary outcomes.

Effect model: Fixed or random effect models were chosen based on the heterogeneity test results of the studies. Statistical heterogeneity was assessed using I^2 statistic, Cochran's Q test (reporting its between-study variance component τ^2 and corresponding P-value based on the significance level $\alpha=0.1$), and forest plots. If $P > 0.1$ and $I^2 \leq 50\%$, heterogeneity was considered acceptable, and a fixed effect model was used for the pooled effect size. If $P < 0.1$ or $I^2 \geq 50\%$, statistical heterogeneity was considered unacceptable. When the random effects model still could not explain the

heterogeneity well, we attempted to explore the sources of heterogeneity using subgroup analysis, sensitivity analysis, or comparing the specific content of the literature.

Publication Bias

Funnel plots were used to assess potential publication bias when the number of included studies exceeded 10.

Evidence Certainty Assessment

To assess the evidence certainty, we used the GRADEpro online tool (<http://gdt.grade.pro/app#projects>) to perform the evaluation and followed the recommended procedures for grading (high, moderate, low, very low).

Results

Literature Search Results

A total of 1761 relevant articles were obtained in the initial screening, and after a series of selection processes, 38 RCTs¹²⁻⁴⁹ were finally included. The flowchart of literature screening process and results are shown in [Figure 1](#).

Characteristics of Included Studies

A total of 38 randomized controlled trials (RCTs) were included in this review, comprising of 3143 participants. Of these, 1595 were in the treatment group and 1548 were in the control group. The trials were conducted in different countries, including China (37 trials¹²⁻⁴⁸ with 3112 participants) and Tunisia (1 trial⁴⁹ with 31 participants). 36 studies¹²⁻⁴⁷ were published in Chinese, 1⁴⁸ in English, and 1⁴⁹ in French. Sample sizes ranged from 31 to 200 participants, with treatment durations ranging from 1 to 12 weeks. The age of participants ranged from 18 to 65 years. The main interventions in the treatment group included electroacupuncture, manual acupuncture, and scalp acupuncture. The control group included sham acupuncture, psychological health education, clozapine, quetiapine, risperidone, aripiprazole, dextropropoxyphene tablets, paliperidone, haloperidol, olanzapine, sulpiride, chlorpromazine, team psychological intervention, cognitive behavior therapy, and sertraline hydrochloride tablets. The main outcome measures included the total effective rate, and secondary outcome measures included PANSS score, BRPS score, SAPS score, and SANS score ([Table 1](#)).

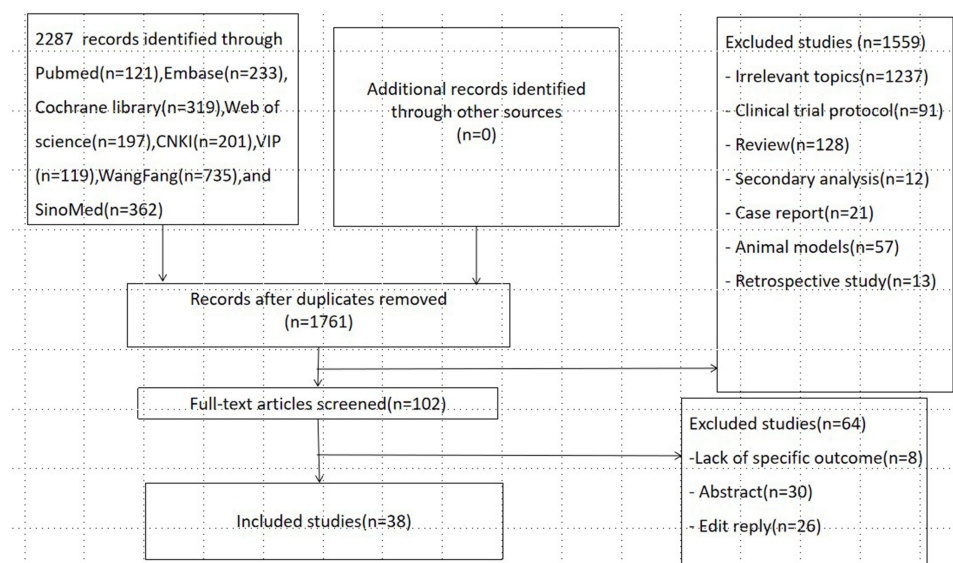


Figure 1 Flowchart of literature search and selection results.

Table I Basic Characteristics of the Included Studies

Study	Sample Size	Age (Year, Mean±SD)	Sex (Male/Female)	Disease course	Methods of Intervention	Comparison	Treatment Duration	Main Outcomes
Yao 2006 ¹²	T:45 C:45	T:31±12 C:29±13	T:28/17 C:22/23	T:8±5m C:9±3m	EA+CI	CI	40d-60d	1,3,5
Jiang 2011 ¹³	T=39 C=39	T:41.6±9.2 C:42.2±8.3	T:21/18 C:17/22	T:12.5±6.8y C:12.8±7.8y	EA+QU	QU	8w	1,2,3
Fan 2015 ¹⁴	T=42 C=42	T:41.3±11.4 C:41.3±11.3	T:28/15 C:29/14	T:3.8±2.7y C:3.9±2.5y	EA+RI	RI	6w	1
Gong 2015 ¹⁵	T=41 C=37	T:42±12.58 C:41±13.48	T:28/13 C:25/12	T:4±1.89y C:3±1.67y	MA+AR	AR	8w	3,7
Liu 2011 ¹⁶	T=30 C=32	T:40±8 C:44±10	T:18/12 C:20/12	T:15.8±8.55y C:19.53±9.50y	EA+CI	CI	4w	4,6,7
Huang 2015 ¹⁷	T=48 C=48	T:41±13 C:41±12	T:25/23 C:24/24	T:15.7±20.3y C:14.9±28.9y	MA+PA	DT+PA	6w	1,2,3
Gao 2014 ¹⁸	T=31 C=31	T:36.2±7.2 C:37.9±8.5	T:17/14 C:16/15	T:23.6±5.7y C:24.5±6.3y	EA+WM+PHE	WM+PHE	4w	3,4
Chen 2015 ¹⁹	T=31 C=31	T:23.3±7.4 C:25.14±6.7	T:18/13 C:17/14	- -	EA+CI	CI	7d	3
CJ 2016 ²⁰	T=62 C=62	T:26.1±8.2 C:27.8±9.1	- -	- -	EA+RA+HA	RA+HA	7d	3
Zhao 2013 ²¹	T=40 C=40	T:27.5±5.6 C:27.3±6.2	T:19/21 C:18/22	T:6.08±2.52y C:6.06±2.43y	MA+OL	OL	5w	2,3
Xiong 2010 ²²	T=40 C=40	T:29.4±11.3 C:28.1±12.2	T:22/18 C:24/16	T:35.2±12.2m C:36.3±13.2m	EA+CI	CI	8W	1,2,3
Du 2011 ²³	T=30 C=30	T:26.81±7.43 C:27.47±6.78	T:18/12 C:16/14	T:6.81±5.42m C:7.73±5.18m	EA+SU	SU	2m	3,4,7
LGH 2012 ²⁴	T=59 C=58	T:32.30±9.41 C:31.30±10.03	T:35/24 C:33/25	T:3.24±1.4y C:3.40±1.5y	MA+RI	RI	8w	3,5
LGH 2006 ²⁵	T=64 C=42	T:31.30±7.8 C:29.5±5.2	T:34/30 C:28/14	T:5.14±2.1y C:4.60±3.2y	WM+EA	WM	3w	3
Xu 2010 ²⁶	T=30 C=30	T:25.67±8.12 C:26.33±7.52	- -	T:5.33±4.02m C:5.04±3.17m	WM+MA	WM	8w	1,3
Cui 2000 ²⁷	T=30 C=30	T:35.1±7 C:35.1±7	T:6/24 C:6/24	T:3.5±2.8y C:3.5±2.8y	EA+CH	CH	6w	3,4
Qu 2014 ²⁸	T=23 C=21	T:39±15 C:38±13	T:14/9 C:13/8	T:3.53±2.5y C:3.62±2.78y	MA+RI	RI	6W	3
Liu 2010 ²⁹	T=47 C=49	T:34.05±8.35 C:35.12±7.57	T:30/20 C:27/23	T:4.27±3.70y C:4.02±3.91y	MA+RI	RI	3m	3,4
Zhao 2018 ³⁰	T=100 C=99	T:32.6±2.3 C:32.4±2.2	T:53/47 C:50/49	T:5.6±0.9y C:5.5±1.1y	MA+RI	RI	3m	3,5
Chen 2017 ³¹	T=48 C=48	T:38.2±7.6 C:39.7±8.1	T:20/28 C:21/27	T:4.4±1.9y C:4.5±1.5y	MA+AR	AR	8w	1
Dang 2017 ³²	T=43 C=26	- -	- -	- -	WM+MA	WM	12w	4
Qin 2017 ³³	T=40 C=40	T:34.5±5.1 C:37.4±5.5	- -	T:5.4±3.2y C:5.0±2.7y	MA+CL	CL	12w	1,2,4
Li 2022 ³⁴	T=30 C=30	T:28.43±5.36 C:33.46±5.78	T:17/13 C:18/12	T:10.43±3.74y C:9.76±3.41y	EA+CL	CL	8w	1,3,5
Ji 2022 ³⁵	T=30 C=30	T:56.2±8.03 C:57.1±5.38	T:16/14 C:18/12	T:2.1±0.79y C:2.67±1.11y	EA+CL	CL	6w	1,2,5
Yang 2022 ³⁶	T=31 C=32	-	-	-	OL+MA	OL	8w	1,3
Li 2021 ³⁷	T=32 C=32	T:37.4±5.3 C:36.4±5.4	T:11/21 C:12/20	T:15.3±1.3m C:16.4±1.1m	EA+QU	QU	8w	3,4,5

(Continued)

Table I (Continued).

Study	Sample Size	Age (Year, Mean±SD)	Sex (Male/Female)	Disease course	Methods of Intervention	Comparison	Treatment Duration	Main Outcomes
Shen 2021 ³⁸	T=41 C=40	T:62.2±5.47 C:61.68±8.38	T:19/22 C:18/22	T:16.94±6.89y C:19.5±7.18y	MA+W/M	W/M	3m	1
Zhon 2021 ³⁹	T=44 C=44	T:37.57±9.73 C:36.92±9.24	T:23/21 C:24/20	T:15.68±9.57y C:15.46±9.43y	AR+MA	AR	8w	3
Zheng 2020 ⁴⁰	T=35 C=35	T:36±8 C:37±8	T:16/19 C:18/17	T:15.58±5.05y C:9.54±4.89y	W/M+MA	W/M	6w	1
LQ 2020 ⁴¹	T=30 C=30	T:39.2±7.1 C:38.3±6.8	T:15/15 C:14/16	- -	MA+RI	RI	30d	1
Pan 2020 ⁴²	T=50 C=51	T:37.56±9.72 C:36.91±9.23	T:28/22 C:27/24	T:15.67±9.56y C:15.45±9.42y	MA+W/M	W/M	12w	1,3,5
LH 2020 ⁴³	T=40 C=40	T:27.25±1.15 C:27.35±1.28	T:28/12 C:27/13	- -	MA+RI	RI	3m	1,4,7
Chen 2020 ⁴⁴	T=100 C=100	T:51.3±7.0 C:52.1±7.3	- -	T:1.2±2.2y C:1.3±2.1y	EA+RI+HA	RI+HA	9d	3
Lj 2020 ⁴⁵	T=59 C=58	T:30±9.1 C:27±8.6	T:29/30 C:30/28	T:9.2±1.5y C:8.8±1.6y	MA+RI	RI	6w	1,2,3
Liao 2019 ⁴⁶	T=35 C=30	T:23–53 C:24–52	T:21/14 C:15/15	T:3–12y C:4–13y	MA+CL	CL	12w	1,3,4,5
Lin 2018 ⁴⁷	T=30 C=30	T:37.4±5.8 C:37.4±5.8	- -	T:2.3±0.7y C:2.3±0.7y	OL+EA	OL	6w	1,3,5
Cheng 2009 ⁴⁸	T=30 C=30	T:31.20±5.79 C:28.97±5.49	T:13/17C:15/15 -	T:10.13±2.89y C:9.03±2.94y	EA	SA	6w	1,3
Bouhlef 2011 ⁴⁹	T=15 C=16	T:36.6 C:36.6	19/12 -	T:12.58y C:12.58y	MA+W/M	SA+W/M	23d	1,6,7

Notes: (1) PANSS (Positive and Negative Syndrome Scale), (2) TESS (Treatment Emergent Symptom Scale), (3) Effectiveness rate, (4) BPRS (Brief Psychiatric Rating Scale), (5) Incidence of adverse reactions, (6) SAPS (Scale for Assessment of Positive Symptoms), and (7) SANS (Scale for Assessment of Negative Symptoms).

Abbreviations: T, treatment; C, control; m, month; w, week; d, day; y, year; MA, Manual acupuncture; SA, sham acupuncture; EA, electro acupuncture; SH, Shallow needling; W/M, Western medicine; PHE, psychological health education; CI, Clozapine; QU, Quiclopine; RI, Risperidone; AR, Aripiprazole; DT, Dextropropionone tablet; PA, paliperidone; HA, haloperidol; OL, olanzapine; SU, sulpiride; SA, scalp acupuncture; CH, chlorpromazine; TPI, Team psychological intervention; CBT, cognitive behavior therapy; SHT, sertraline hydrochloride tablets.

Diagnostic Criteria

Among the 38 studies, three^{34,37,46} did not mention the specific version of the diagnostic criteria, while 35 studies had clear versions of the diagnostic criteria. One study²⁷ used the Chinese Classification of Mental Disorders 2nd edition (CCMD-2), 18 studies^{12,13,15,16,18,21–26,28–30,36,43,44,47} used CCMD-3, 9 studies^{14,17,31,33,35,39–42} used the International Classification of Diseases 10th edition (ICD-10), and 7 studies^{19,20,32,38,45,48,49} used DSM-V.

3.4 Among the 38 studies included in this study, 17 provided sufficient information on randomization and were assessed as having a low risk of selection bias. The randomization methods included random number tables (13),^{14,17–19,23–25,29,30,32,36,39,42} digit tables (1),⁴⁰ drawing lots (1),¹² random allocation tables (1),²⁶ and computer-generated random number sequences (1).⁴⁸ One study⁴⁸ mentioned allocation concealment using sealed opaque envelopes. Two studies^{48,49} mentioned blinding of patients and evaluators. Regarding completeness, two studies^{24,29} out of the 38 did not address the handling of missing data, and we did not find any sources of selective reporting or other bias in all included studies (Figure 2A and B).

Meta-Analysis Results

Primary Results

Overall Effectiveness

A total of 27 RCTs^{12,13,15,17–30,34,36,37,39,42,44–48} with 2367 patients were included. Heterogeneity testing was conducted on the results of the 27 studies. Based on a fixed-effect model, the Meta-analysis showed a statistically significant



Figure 2 Risk of Bias assessment results.

Notes: (A) Graphical representation of the overall risk of bias in the 7 domains. (B) Summary of the risk of bias in 7 domains in the 38 studies. Green (+), yellow (?) and red (-) represent low, unclear and high risk of bias respectively. Length of the rectangles (green, yellow or red) show the percentage of studies with low, unclear, or high risk of bias for the 7 domains analyzed.

advantage in total effectiveness of acupuncture compared to the control group (OR=3.43, 95% CI (2.71, 4.35), $P<0.00001$), with low statistical heterogeneity ($\text{Chi}^2=26.71$, $\text{df}=26$, $P=0.42>0.1$, $I^2=3\%<50\%$) (Figure 3).

Subgroup Analysis

Different Assessment Measures for Overall Response Rate

PANSS

12 studies^{12,13,21,22,26,34,36,39,42,45,47,48} utilized the PANSS scale to evaluate the overall response to acupuncture. The analysis revealed that acupuncture had a significantly greater influence on PANSS scores in comparison to the control group [MD=2.77 (95% CI: 1.93, 3.98), $P<0.00001$, $I^2=34\%$]. (Figure 4)

BPRS

8 studies^{18,24,25,27,29,30,37,46} used the BPRS scale to assess the overall response rate of acupuncture. The analysis showed that acupuncture had a greater impact on BPRS scores compared to the control group [MD=3.57 (95% CI: 2.32, 5.51), $P<0.00001$, $I^2=0\%$]. (Figure 4)

SAPS

3 studies^{19,20,44} employed the SAPS scale to evaluate the overall response to acupuncture. The analysis demonstrated that acupuncture had a greater effect on SAPS scores compared to the control group [MD=5.59 (95% CI: 3.05, 10.26), $P<0.00001$, $I^2=0\%$]. (Figure 4)

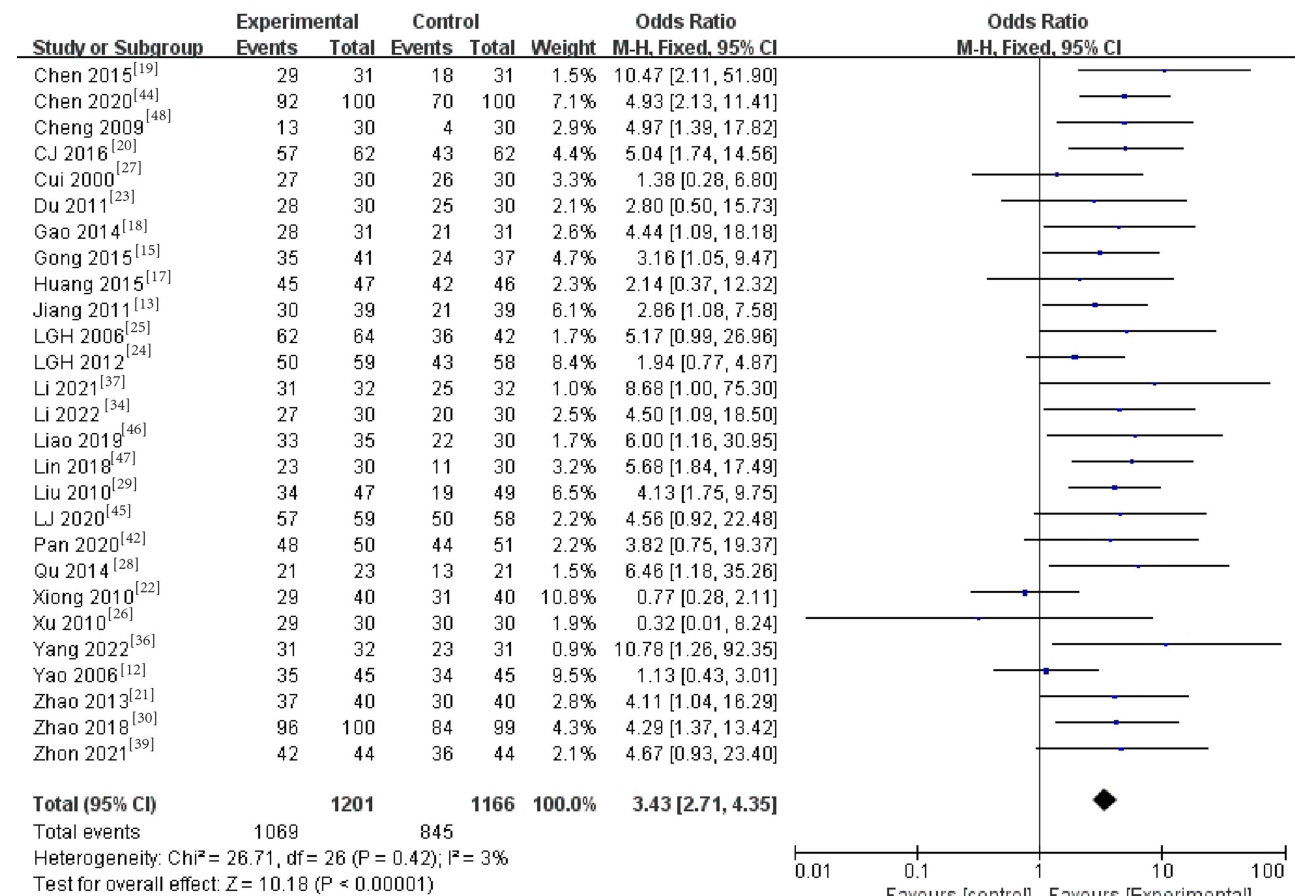


Figure 3 Forest Plot for Overall Response Rate.

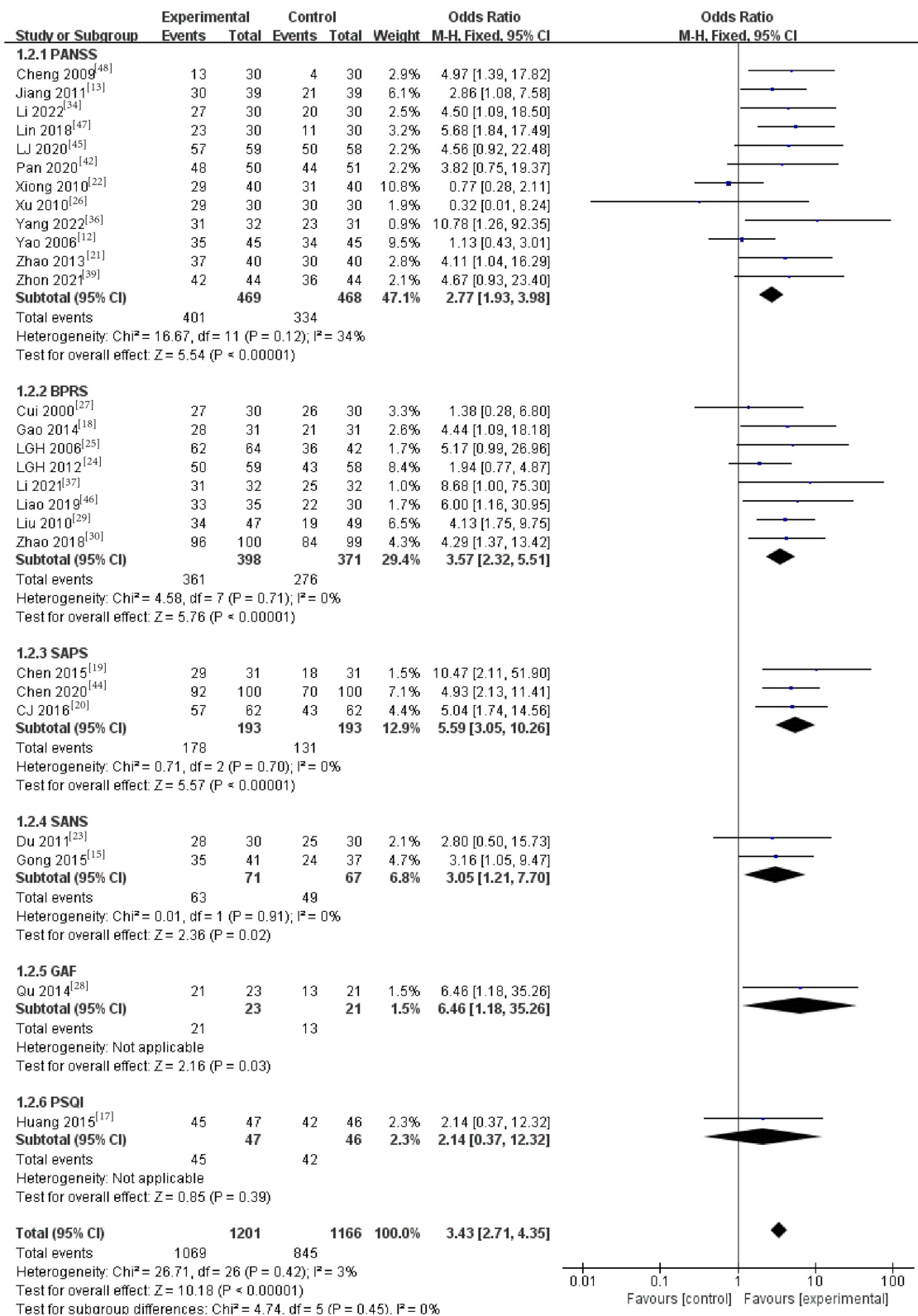


Figure 4 Forest Plot of Total Effective Rate Subgroup Analysis Meta-Regression.

Table 2 Regression Table of Total Effective Rate and Treatment Time

_ES	Exp(b)	Std. Err.	t	P> t	[95% Conf.	Interval]
timeoftherapyday	0.9874736	0.0060944	-2.04	0.052	0.9750013	1.000105
_cons	5.563176	1.541055	6.20	0.000	3.144505	9.842224

SANS

2 studies^{15,23} used the SANS scale to assess the overall response rate to acupuncture. The analysis revealed that acupuncture had a more pronounced effect on SANS scores when compared to the control group [MD=3.05 (95% CI: 1.21, 7.70), $P=0.02$, $I^2=0\%$]. (Figure 4)

One study²⁸ reported the use of GAF to assess the overall response rate (OR: 6.46, 95% CI: 1.18–35.26), and one study¹⁷ mentioned the use of PSQI to assess the overall response rate (OR: 2.14, 95% CI: 0.37–12.32).

Subgroup difference test showed no heterogeneity among different comparison groups ($P=0.45$, $I^2=0\%$).

Meta-Regression

In this study, we used meta-regression analysis to explore the relationship between treatment duration and treatment effectiveness. In a meta-analysis that included 27 studies, we found a negative correlation between treatment duration and treatment effectiveness, but this relationship did not reach statistical significance ($P = 0.052$) (Table 2). Specifically, for every one-day increase in treatment duration, the index level of treatment effectiveness decreased to 0.987. This result was validated in the meta-regression modified by Knapp-Hartung ($b = 5.56$, 95% CI [3.14, 9.84]) (Table 2). The results indicate that for the treatment of schizophrenia, prolonged treatment may not be beneficial to patients' recovery, and further optimization of treatment plans is needed. (Figure 5).

Secondary Outcomes

PANSS has broad applicability and high reliability, which can accurately assess the symptoms of SZ patients. BPRS is a simple and easy-to-use tool that evaluates positive symptoms, negative symptoms, affective symptoms, and cognitive

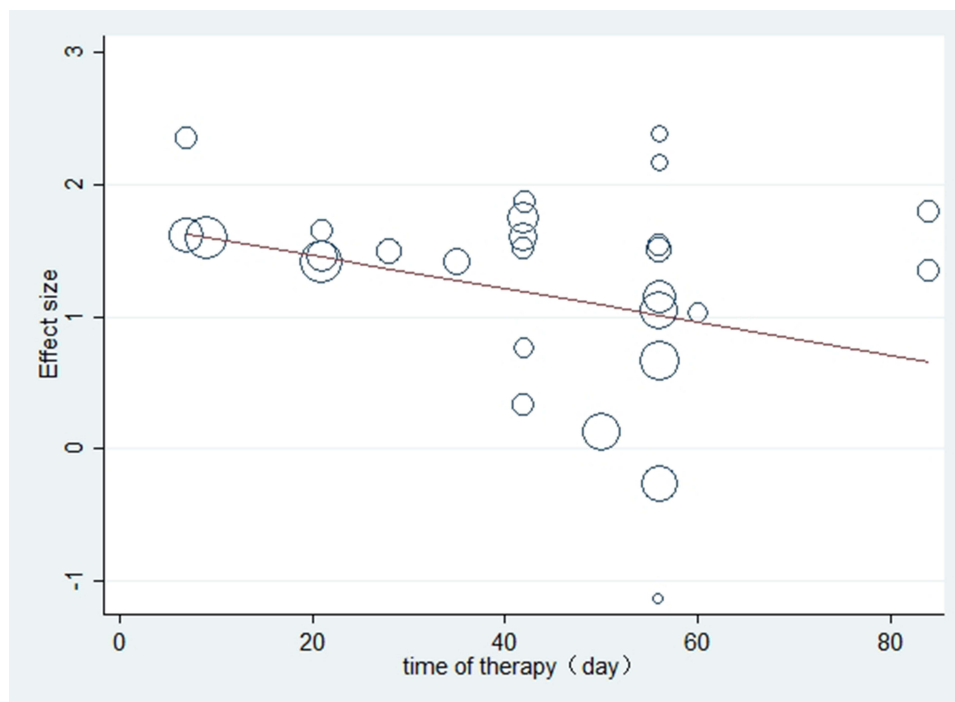


Figure 5 Total response rate and treatment duration regression plot.

symptoms. SANS and SAPS can accurately evaluate the core symptoms of schizophrenia but may not fully reflect the patient’s comprehensive symptoms.

PANSS

PANSS evaluates the severity and changes of patients’ psychotic symptoms before and after treatment to determine the effectiveness of acupuncture. A total of 21 RCTs^{12–14,17,22,26,31,33–36,38,40–43,45–49} with 1566 patients were included in the random effects model meta-analysis. The results showed that compared with the control group, acupuncture treatment for schizophrenia patients had a significant treatment advantage, with MD=−5.75 (95% CI: −8.08, −3.42) and Z=4.84 (P<0.00001). The heterogeneity test showed significant heterogeneity among the included studies (I²=88%, P<0.00001), indicating significant differences among the included studies (Figure 6).

BPRS

The Brief Psychiatric Rating Scale (BPRS) is mainly used to assess the psychopathological symptoms of psychiatric patients to observe the effect of acupuncture on psychiatric symptoms. A total of 10 RCTs^{16,18,23,27,29,32,33,43,46} were included with a total of 698 patients. The random-effects model meta-analysis showed that compared with the control group, acupuncture had a greater impact on BPRS with a MD of −7.02 (95% CI: −10.59, −3.46). The heterogeneity test showed significant heterogeneity among the included studies (I²=94%, P=0.0001) (Figure 7).

SANS

The SANS scale is used to evaluate negative symptoms in patients and assess the effectiveness of acupuncture. A total of 15 RCTs^{13–17,22,23,31,34,38,42,43,47–49} with 1106 patients were included. The random-effects model meta-analysis showed that the effect of acupuncture on SANS was not greater than that of the control group, with no significant difference [MD=−2.66 (95% CI: −6.84, 1.51), P=0.21, I²=99%] (Figure 8).

Subgroup Analysis

Different Intervention Measures

Manual Acupuncture Vs Control

7 studies^{15,17,31,38,42,43,49} conducted a comparison between manual acupuncture and a control group using SANS

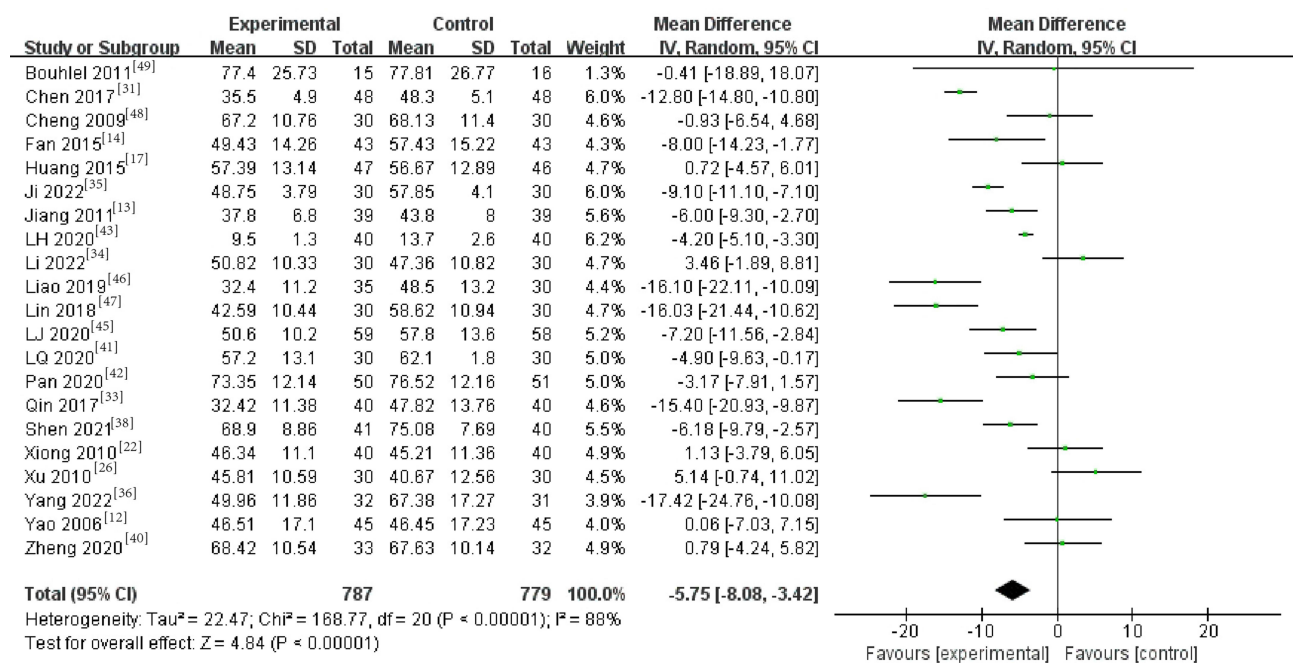


Figure 6 Forest plot of PANSS scores.

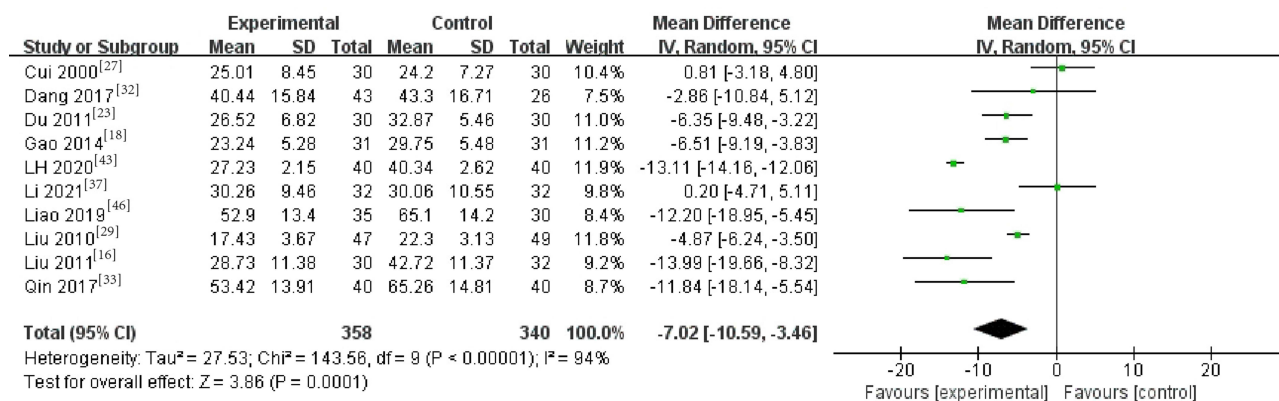


Figure 7 Forest plot of BPRS scores.

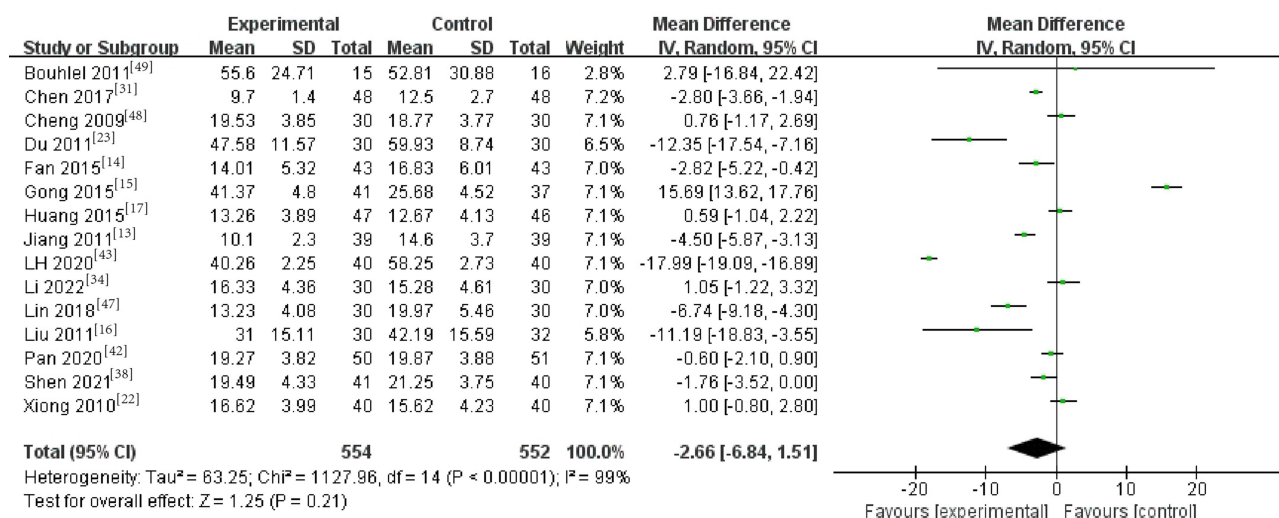


Figure 8 Forest Plot of SANS Scores.

assessment. The analysis revealed that acupuncture did not have a significantly greater impact on SANS scores when compared to the control group [MD: -0.86 (-8.53, 6.80), P=0.82, I²=99%] (Figure 9).

Electroacupuncture VS Control

8 studies^{13,14,16,22,23,34,47,48} compared the effectiveness of electroacupuncture with a control group using SANS assessment. The analysis showed that acupuncture had a greater impact on SANS scores compared to the control group [MD: -3.52 (-6.22, -0.82), P=0.01, I²=90%] (Figure 9).

After the primary meta-analysis, the result of SANS score showed P=0.21, which is greater than 0.05. However, during the subgroup analysis, we divided acupuncture into two groups: electroacupuncture and manual acupuncture. The result revealed that the electroacupuncture group had a P-value of 0.01, which is less than 0.05. Therefore, we can infer that electroacupuncture treatment may be more effective than manual acupuncture in terms of SANS score.

SAPS

The SAPS scale is used to assess positive symptoms and measure symptom changes in patients, aiming to evaluate the effectiveness of acupuncture. A total of 11 RCTs^{13,14,16,17,22,31,34,38,42,48,49} with 828 patients were included in the random-effects model Meta-analysis. The results demonstrated that acupuncture had a greater impact on SAPS compared

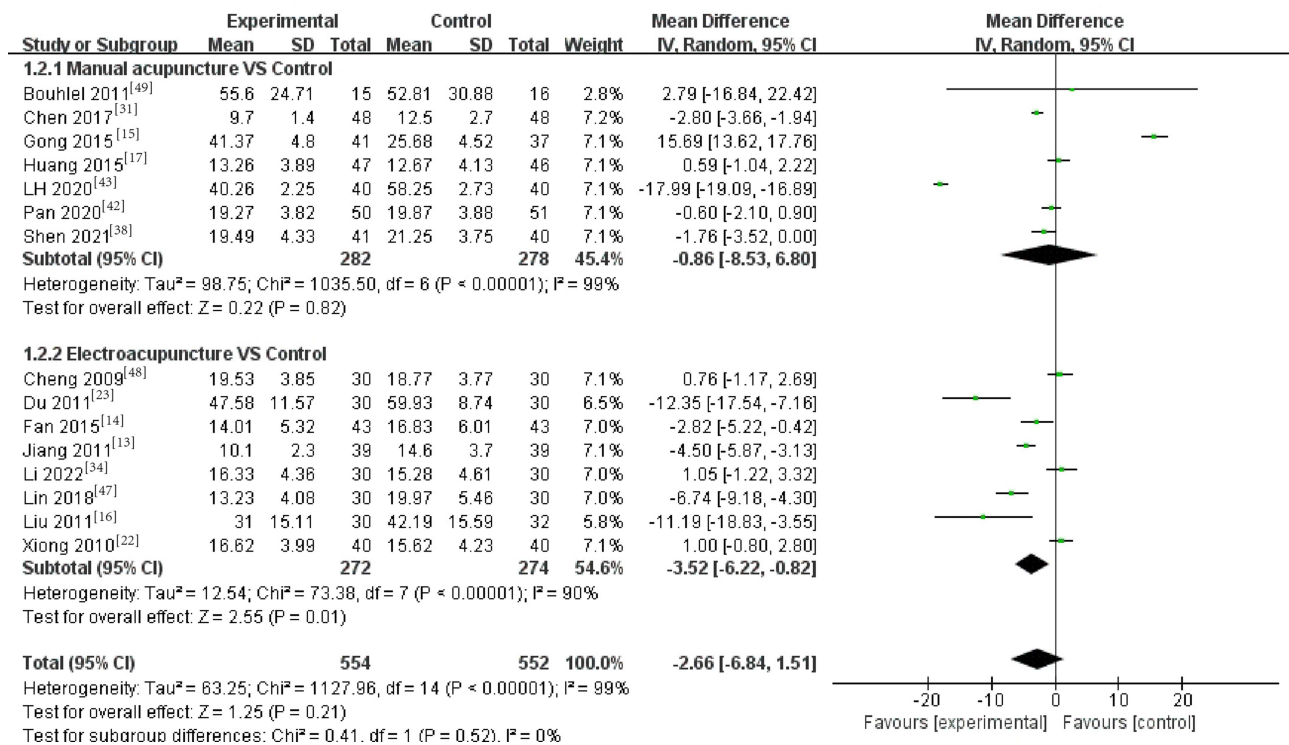


Figure 9 Forest plot of subgroup analysis for SANS.

to the control group, and the difference was statistically significant [MD=-1.26 (95% CI: -2.55, -0.02), P=0.05, I²=86%]. Please refer to Figure 10 for details.

Sensitivity Analysis

To determine the robustness of the summary data for the main outcome measures, we performed a sensitivity analysis by removing each study one by one. The results of the sensitivity analysis showed no significant changes in the combined results, which supports the statistical advantage of acupuncture in overall efficacy (P < 0.0001).

Adverse Events

A total of 15 RCTs^{12,13,17,21,22,24,30,33-35,37,42,45-47} were included, including 1344 patients. 1 study³⁵ reported both count data and continuous data. 9 RCTs^{12,24,30,34,35,37,42,46,47} reported count data and were analyzed using the odds ratio (OR)

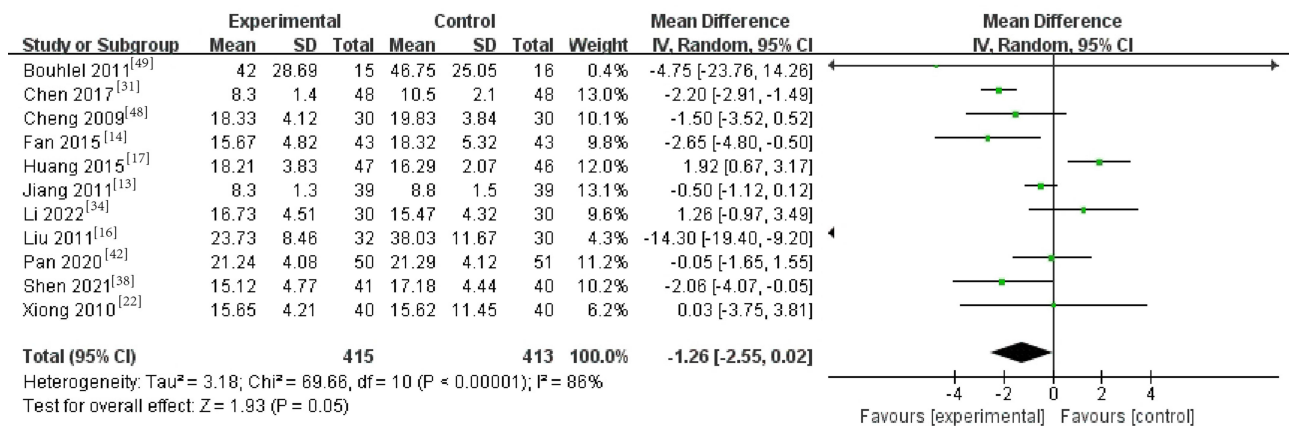


Figure 10 Forest plot of SAPS score.

and its 95% confidence interval (CI). Based on the fixed-effect model, the results of the heterogeneity test of the 9 studies showed statistical advantage of acupuncture over the control group in terms of adverse events (OR=0.55, 95% CI (0.42, 0.71), $P < 0.00001$), with moderate statistical heterogeneity ($Chi^2=13.01$, $df=8$, $P=0.11 > 0.1$, $I^2=39%$) (Figure 11).

7 RCTs^{13,17,21,22,33,35,45} reported continuous data and were analyzed using the mean difference (MD) and its 95% CI. Based on the random-effects model, the results of the heterogeneity test of the 7 studies showed statistical advantage of acupuncture over the control group in terms of adverse events (MD=-1.82, 95% CI (-2.94, -0.71), $P=0.0001$), with high statistical heterogeneity ($Chi^2=50.06$, $df=6$, $P < 0.00001 < 0.1$, $I^2=88%$) (Figure 12).

As can be seen, acupuncture as an adjunctive therapy can effectively reduce adverse reactions in clinical practice.

Publication Bias of Included Literature

Funnel plot and Egger’s test were used to evaluate the publication bias of the overall effective rate. The funnel plot and Egger’s test ($t=1.00$, $P=0.329$) showed no evidence of publication bias. As shown in Figure 13 and Table 3.

GRADE Evidence Quality Assessment

For the adverse reaction incidence rate, we divided it into two outcome indicators based on the different types of variables: incidence rate of adverse reactions for binary variables and TESS score for continuous variables. There were a total of 7 outcome indicators, including Effective rate, incidence rate of adverse reactions, PANSS score, BRPS score, SANS score, SAPS score, and TESS score. The results showed that the quality of Total Effective rate and incidence rate of adverse reactions was Moderate, while the quality of PANSS score, BRPS score, SANS score, SAPS score, and TESS score was very low. Details can be found in Table 4.

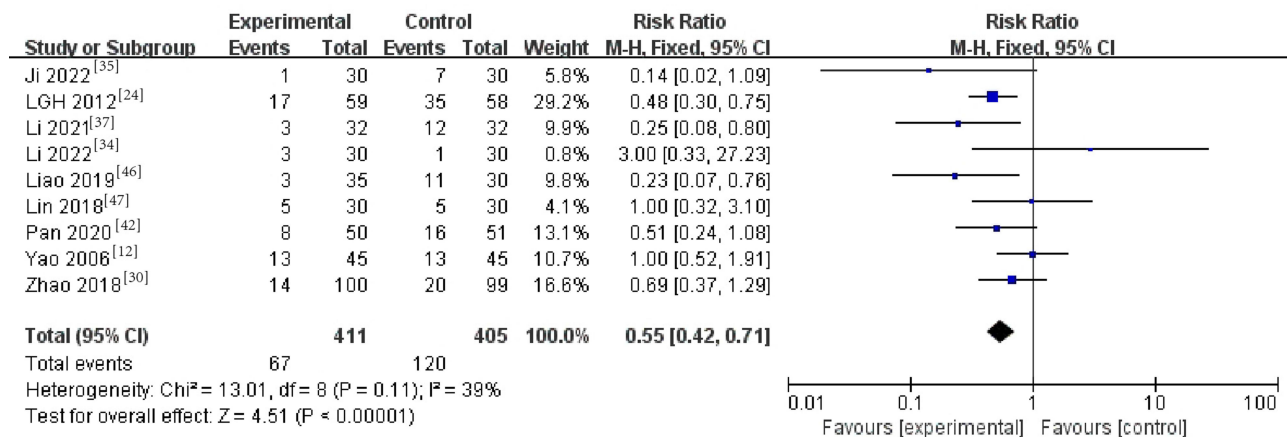


Figure 11 Forest plot of adverse events for binary variables.

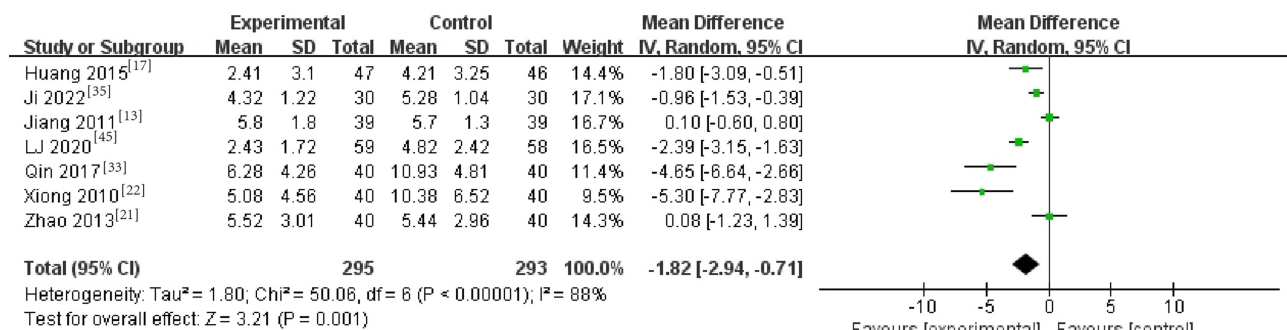


Figure 12 Forest plot of adverse events for continuous variables.

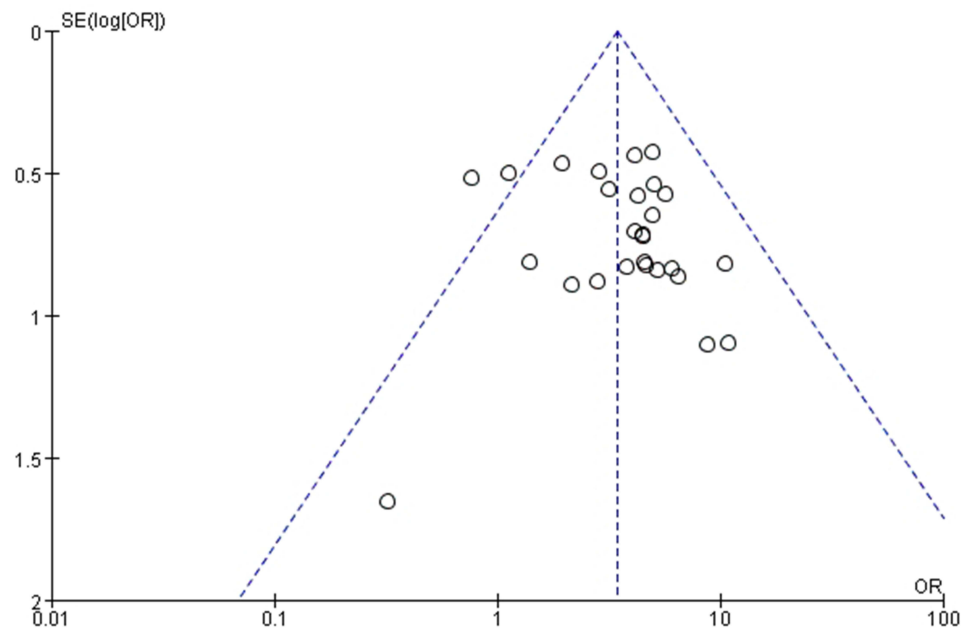


Figure 13 The Funnel plot for publication bias of overall effectiveness.

Discussion

Overview

This meta-analysis included 38 randomized controlled trials with a total of 3143 patients, comparing the efficacy and safety of acupuncture combined with another therapy versus the use of the therapy alone. The results indicated that acupuncture, as an adjunctive therapy in conjunction with Western medicine or other therapies, could improve the overall effective rate of SZ patients ($P < 0.00001$) while reducing the adverse reactions caused by medication. We conducted subgroup analyses on the overall effective rate, comparing different outcome measures, and the results showed no heterogeneity among the different measures ($P = 0.45$, $I^2 = 0\%$), indicating the stability of acupuncture treatment across various outcome measures and its reliability as a treatment option.

Regarding the mechanism of acupuncture in the treatment of schizophrenia, some studies have suggested^{50,51} that structural changes occur in the default mode network (DMN) brain regions of schizophrenia patients, and the dysfunction between the frontoparietal control system and the DMN may be one of the causes of schizophrenia. Acupuncture acts by regulating and normalizing the lateral parietal-occipital network (LPNN), including the default mode network (DMN), thereby balancing bodily functions and improving clinical symptoms in Schizophrenia patients^{5,52}

Comparison with Previous Studies

Compared with previous studies, we have also concluded the effectiveness of acupuncture in the treatment of schizophrenia. In a meta-analysis⁶ published in 2018, researchers found that when comparing acupuncture combined with conventional antipsychotic medication to the use of antipsychotic medication alone, acupuncture combined with antipsychotic medication showed significantly better efficacy in treating SZ. In our study, we focused on the primary

Table 3 Egger's Test for Publication Bias in Overall Effectiveness

Std_Eff	Coef.	Std. Err.	t	P> t	[95% Conf.	Interval]
slope	0.7866153	0.4445966	1.77	0.089	-0.1290485	1.702279
bias	0.6819208	0.6843093	1.00	0.329	-0.7274405	2.091282

Table 4 GRADE Evidence Quality Assessment

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Experimental	Control	Relative(95% CI)	Absolute (95% CI)		
Total effective rate												
27	Randomised trials	Serious ^a	Not serious	Not serious	Not serious	None	1069/1201 (89.0%)	845/1166 (72.5%)	OR 3.43 (2.71 to 4.35)	176 more per 1000 (from 152 more to 195 more)	⊕⊕⊕○ Moderate	CRITICAL
Incidence rate of adverse reactions												
9	Randomised trials	Serious ^a	Not serious	Not serious	Not serious	None	67/411 (16.3%)	120/405 (29.6%)	RR 0.55 (0.42 to 0.71)	133 fewer per 1000 (from 172 fewer to 86 fewer)	⊕⊕⊕○ Moderate	CRITICAL
TESS score												
7	Randomised trials	Serious ^a	Very serious ^b	Not serious	Not serious	None	295	293	–	MD 1.82 lower (2.94 lower to 0.71 lower)	⊕○○○ Very low	CRITICAL
PANSS score												
21	Randomised trials	Serious ^a	Very serious ^b	Not serious	Not serious	None	787	779	–	MD 5.75 lower (8.08 lower to 3.42 lower)	⊕○○○ Very low	IMPORTANT
BRPS score												
10	Randomised trials	Serious ^a	Very serious ^b	Not serious	Not serious	None	358	340	–	MD 7.02 lower (10.59 lower to 3.46 lower)	⊕○○○ Very low	IMPORTANT
SANS score												
15	Randomised trials	Serious ^a	Very serious ^b	Not serious	Not serious	None	554	552	–	MD 2.66 lower (6.84 lower to 1.51 higher)	⊕○○○ Very low	NOT IMPORTANT
SAPS score												
11	Randomised trials	Serious ^a	Very serious ^b	Not serious	Not serious	None	415	413	–	MD 1.26 lower (2.55 lower to 0.02 higher)	⊕○○○ Very low	NOT IMPORTANT

Notes: ^aThere is a large bias in the included studies in randomization, assignment hiding, blind method and other methods. ^bIf the confidence interval overlaps less or the I2 value of the combined result is larger, 50%<I²<75%, minus 1 point, and I²≥75%, minus 2 points. Bolded text indicates statistically significant effect sizes with moderate to high-quality evidence.

Abbreviations: CI, confidence interval; MD, mean difference; OR, odds ratio; RR, risk ratio.

outcome measure of overall effectiveness rate and selected PANSS, BPRS, SANS, and SAPS as secondary outcome measures, providing a more comprehensive reflection of the effectiveness of acupuncture treatment.

In published network meta-analyses,⁷ researchers compared the efficacy of acupuncture combined with Western medicine to the use of Western medicine alone and found that acupuncture had the best efficacy when combined with body acupuncture. In contrast, our meta-analysis has several unique features. Firstly, we performed GRADE evidence grading for each outcome to ensure the reliability of the research findings. Secondly, we conducted subgroup analyses for the overall effectiveness rate to explore differences among different subgroups. Additionally, we performed a meta-regression specifically for the primary outcome measure (overall effectiveness rate) and found that prolonged treatment may not be beneficial for patient recovery.

Clinical Implementation

The findings suggest that acupuncture treatment is an effective adjunctive therapy for schizophrenia and can be used as a supplement or alternative to traditional medication, providing clinicians with a new treatment option.

The Inspiration for Future Directions

Although the meta-analysis results demonstrate the effectiveness of acupuncture, further exploration is needed regarding the treatment mechanisms and long-term effects of acupuncture. Additionally, considering the methodological limitations and quality issues in the studies, more high-quality, large-sample, multicenter clinical trials are required to validate and strengthen these findings. A more comprehensive evaluation of acupuncture's clinical applications in patients with SZ will provide healthcare professionals and patients with more reliable treatment evidence and decision-making support.

Strengths and Limitations

Based on our understanding, this is the first systematic review to evaluate the efficacy and safety of acupuncture as an adjunctive therapy for improving clinical symptoms in patients with schizophrenia.

Our strengths lie in several aspects. First, we selected the total effective rate as the primary outcome measure and conducting subgroup analysis on the primary outcome measure, which allows for a more accurate evaluation of the effect size between different subgroups and further confirms the effectiveness of acupuncture. Second, we performed a meta-regression on the effective rate and found a negative correlation trend between treatment duration and treatment effect, suggesting that longer treatment duration may not be beneficial for patient recovery. Third, we conducted a GRADE assessment on the outcome measures, enhancing the credibility of the results.

We also analyzed the acupoints mentioned in the literature and found that the most frequently mentioned acupoints were Baihui (GV20) (26 times), Neiguan (PC6) (15 times), Yintang (EX-HN3) (13 times), Zusanli (ST36) (13 times), Taichong (LR3) (13 times), Fenglong (ST40) (13 times), Sanyinjiao (SP6) (12 times), Hegu (LI4) (12 times), Shenmen (HT7) (12 times), and Sishencong (EX-HN1) (8 times). Clinical practitioners can use these findings to selectively choose these acupuncture points for acupuncture treatment, aiming to enhance treatment effectiveness. Furthermore, the discovery of these high-frequency acupuncture points provides valuable clues for further exploring the mechanisms of acupuncture treatment and contributes to a deeper understanding of the specific role and pathways of acupuncture in the treatment of SZ.

This study has several limitations: (1) Most of the included studies did not mention the implementation of allocation concealment and blinding, which may introduce selection bias. (2) The interventions included in the studies, such as the types of adjunctive medication, forms of acupuncture, duration of treatment, and techniques used, varied, which could affect the accuracy of the results.

Conclusion

Existing evidence suggests that acupuncture, as an adjunctive therapy used in conjunction with Western medicine or other treatments, can improve the overall effectiveness in patients with SZ, reduce adverse reactions, and improve the mental condition, alleviating the severity of symptoms in SZ patients. However, due to limitations in the quality of the included studies, further high-quality research is needed to validate the above conclusions.

Data Sharing Statement

All data relevant to the study are included in the article or uploaded as [Online Supplemental Information](#). The data used in this review was collected from the thirty-eight eligible studies and therefore available in the public domain.

Author Contributions

All authors have made significant contributions to the work reported, whether in the conception, study design, execution, data acquisition, analysis and interpretation, or in all of these areas. They have all been involved in drafting, revising, or critically reviewing the article, and have given final approval for the version to be published. They have also agreed on the journal to which the article has been submitted and committed to being accountable for all aspects of the work.

Funding

The authors received no financial support for the research, authorship, and/or potential publication of this article.

Disclosure

The authors have no conflicts of interest to declare for this work.

References

- World Health Organization. *Factsheet on Schizophrenia*. World Health Organization Newsroom; 2019.
- Moreno-Küstner B, Martín C, Pastor L. Prevalence of psychotic disorders and its association with methodological issues. A systematic review and meta-analyses. *PLoS One*. 2018;13(4):e0195687. doi:10.1371/journal.pone.0195687
- Du Y, Yu Y, Hu Y, et al. Genome-Wide, integrative analysis implicates exosome-derived MicroRNA dysregulation in schizophrenia. *Schizophr Bull*. 2019;45(6):1257–1266. doi:10.1093/schbul/sby191
- Rognoni C, Bertolani A, Jommi C. Second-generation antipsychotic drugs for patients with schizophrenia: systematic literature review and meta-analysis of metabolic and cardiovascular side effects. *Clin Drug Investig*. 2021;41(4):303–319. doi:10.1007/s40261-021-01000-1
- Hui KK, Marina O, Liu J, Rosen BR, Kwong KK. Acupuncture, the limbic system, and the anticorrelated networks of the brain. *Auton Neurosci*. 2010;157(1–2):81–90. doi:10.1016/j.autneu.2010.03.022
- Zhao J-Q, Ma T-M. Meta-analysis of acupuncture treatment for schizophrenia. *Acupunct Res*. 2018;43(12):806–812. doi:10.13702/j.1000-0607.170716
- Zhaohan H, Yuan F, Xiaolu W, Yue H, Qi YU, Tong W. Effectiveness of acupuncture-related therapies on schizophrenia: a Bayesian network Meta-analysis. *J Tradit Chin Med*. 2023;43(2):239–251. doi:10.19852/j.cnki.jtcm.20221226.001
- Chinese Society of Psychiatry, Chinese Medical Association. *Chinese Classification and Diagnostic Criteria of Mental Disorders*. Vol. 35. Nanjing: Southeast University Press; 1995:64.
- Chen YF. Chinese classification of mental disorders (CCMD-3): towards integration in international classification. *Psychopathology*. 2002;35:171–175. doi:10.1159/000065140
- World Health Organization. *The ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines*. World Health Organization; 1992.
- Edition F. Diagnostic and statistical manual of mental disorders. *Am Psychiatric Assoc*. 2013;21:591–643.
- Feng-Ju Y, Fu-Gen S, Zhi-Hua Z. Short-term curative effect of electroacupuncture as an adjunctive treatment on schizophrenia. *Chin J Integ Tradit West Med*. 2006;26(3):253–255.
- Jiang P-R, Xiao Q, Dai L-Y, et al. Exploring the adjunctive effect of electroacupuncture in the treatment of schizophrenia. *Psychol Doc*. 2011;7:529.
- Fan H. Influence of risperidone combined with electro-acupuncture on the curative effect and P300 of schizophrenic patients. *J Psych*. 2015;28(01):43–45.
- Gong S, Qu Y, Ai C. Effects of acupuncture and moxibustion on living ability in patients with schizophrenia. *J Hubei Univer Chin Med*. 2015;17(04):79–81.
- Liu X-C, Su X-L, Zhao L-Z. Observation on the therapeutic efficacy of electroacupuncture combined with medication in the treatment of schizophrenia. *J Mod Integ Trad Chin West Med*. 2011;20(12):1483–1484.
- Huang Y, Zheng Y. Sleep disorder of schizophrenia treated with shallow needling: a randomized controlled trial. *Chin Acupun Moxibust*. 2015;35(09):869–873.
- Gao L, Wang T-L, Yuan Y-T. Clinical study of intelligent electroacupuncture combined with drug treatment for auditory hallucinations. *Med J Chin People's Health*. 2014;26(12):39–40.
- Chen M-M, Xu Y. Comparative study on the treatment of agitated state in schizophrenia with electroacupuncture combined with olanzapine. *Pract Clin J Integ Tradit Chin West Med*. 2015;15(09):32–34.
- Chen J, Zhou C-M, Chen X-X. Comparative study on the therapeutic effects of risperidone combined with fluphenazine and electroacupuncture in the treatment of agitated state in schizophrenia. *Stra Pharmaceut J*. 2016;28(08):213–214.
- Zhao L, Zhang N, An Y-M, et al. Clinical observation of acupuncture combined with olanzapine in the treatment of 40 cases of schizophrenia. *Hebei J Tradit Chin Med*. 2013;35(10):1533–1534.
- Xiong D-Z, Liu L-L, Liu Y-Y. Observation on the therapeutic effect of electroacupuncture combined with small dose of clozapine in clinical treatment of refractory schizophrenia. *Acupunct Res*. 2010;35(2):134–137.

23. Du Y-J. Efficacy of acupuncture combined with sulpiride in the treatment of schizophrenia dominated by negative symptoms. *Pract Clin Med.* 2011;12(05):19–21.
24. Li G-H, Yan M. Scalp acupuncture with treatment for refractory auditory hallucination in schizophrenia patients—A report of curative effect observation of 60 cases. *Liaoning J Tradit Chin Med.* 2012;39(07):1396–1398.
25. Li G-H, Hu Y-H, Yan M. Clinical efficacy observation of electroacupuncture in the treatment of refractory auditory hallucinations. *Chin J Behav Med Brain Sci.* 2006;2006(11):1015.
26. Xu T-C, Su J, Wang W-N. Effect of three-step acupuncture combined with small dosage antipsychotic in treating incipient schizophrenia. *Chin J Integ Tradit West Med.* 2010;30(11):1138–1141.
27. Cui G-M, Wang P. Clinical study on the treatment of schizophrenia with electroacupuncture combined with chlorpromazine. *J Mod Integ Trad Chin West Med.* 2000; 16:1536–1537.
28. Ou Y-Y, Zhang X-F, Ouyang H-L, Huang Y, Ouyang Q. Therapeutic observation of acupuncture plus moxibustion at shenque(GV 8) for schizophrenia. *Shangh J Acupunct Moxib.* 2014;33(09):795–797.
29. Liu X. Acupuncture treatment for refractory auditory hallucination in schizophrenia patients—a report of 50 cases. *J Tradit Chin Med.* 2010;51(07):621–624.
30. Zhao L-J. Clinical efficacy of traditional Chinese medicine syndrome differentiation acupoint selection acupuncture combined with low-dose risperidone in the treatment of schizophrenia. *Henan Med Res.* 2018;27(24):4553–4554.
31. Chen J. Analysis of the effects of acupuncture combined with aripiprazole on executive function and quality of life in patients with post-schizophrenic depression. *Chin J Pract Med.* 2017;12(03):139–140.
32. Dang Y-M, Cai J-Y, Cui J, et al. Efficacy of acupuncture in treating patients with treatment-resistant auditory hallucinations in schizophrenia and observations on social functioning. *Chin J Clin Res.* 2017;9(19):25–27.
33. Qin L, Chen Z, Wang Y, Nie H, CHEN L. Study on acupuncture combined Clozapine in treatment of refractory schizophrenia. *Med J Chin People's Health.* 2017;29(14):7–10.
34. Li H. Effect of electric needle combined with clozapine in refractory schizophrenia. *Contemp Med.* 2022;28(6):55–57.
35. Ji Y, Li X, Hong Q. Effect of clozapine combined with electroacupuncture in the treatment of refractory schizophrenia. *Tibetan Med.* 2022;43(2):67–69.
36. Yang J, Yang C, Zhang J. Impact of acupuncture combined with medication on cognitive function and serum hcy and nrg-1 in patients with schizophrenia. *Shangh J Acupunct Moxib.* 2022;41(09):883–888.
37. Li H. Clinical observation on the treatment of first-episode schizophrenia with electroacupuncture of Baihui Yintang and antipsychotics. *Contemp Med.* 2021;27(26):23–25.
38. Shen H, Zhao H, Chen J, Lu Y, Pan L. Curative effect of integrated traditional Chinese acupuncture and western medicine on patients with phlegm dampness block schizophrenia. *J Guizhou Med Univer.* 2021;46(11):1338–1342.
39. Zhon L-L, Lin W-Y. Clinical study on the therapeutic effect of acupuncture combined western medicine in patients with schizophrenia of remission. *J Nongken Med.* 2021;43(06):481–483.
40. Zheng W, Zhang L-M, Huang H-X, Lin X-D, Sun Q-Y. The influence of acupuncture therapy on cognitive function in patients with chronic schizophrenia. *Mod Pract Med.* 2020;32(01):75–77.
41. Li Q, Tian Y. The effect of scalp acupuncture combined with electroacupuncture on cognitive function in paranoid schizophrenia patients. *Chin J Mod Drug Applic.* 2020;14(03):104–106.
42. Pan L, Shen H-B, Zhang J, Lu Y, Zhao H. Effect of acupuncture on quality of life of patients with schizophrenia of remission. *World J Integ Tradit West Med.* 2020;15(04):593–596.
43. Li H, Li X. Exploring the effectiveness of acupuncture in the treatment of schizophrenia. *J Contemp Med.* 2020;18(11):196–197.
44. Cheng L, Kang C. Observation and analysis of efficacy and safety of electroacupuncture combined with fluphenazine and risperidone in the treatment of excited state of schizophrenia. *J Integ Tradit Chin West Med Cardio Cerebrov Dis.* 2020;8(29):62–63.
45. Li J, Li X, Liu C, Xu L, Yang P. Clinical observation on the effect of acupuncture with brain-heart concurrent regulation therapy with risperidone on aggressive behavior and cognitive function of schizophrenia. *J Hunan Univer Chin Med.* 2020;40(10):1244–1248.
46. Liao Y. Effect of acupuncture and moxibustion combined with clozapine in the treatment of refractory schizophrenia. *Heilongjiang Sci.* 2019;10(06):50–51.
47. Lin F, Chen M. Clinical analysis of olanzapine combined with electroacupuncture in the treatment of negative symptoms of male schizophrenia: a clinical analysis of 30 cases. *Chin Health Stand Manag.* 2018;9(02):97–99.
48. Cheng J, Wang G, Xiao L, Wang H, Wang X, Li C. Electro-acupuncture versus sham electro-acupuncture for auditory hallucinations in patients with schizophrenia: a randomized controlled trial. *Clin Rehabil.* 2009;23(7):579–588. doi:10.1177/0269215508096172
49. Bouhrel S, El-Hechmi S, Ghanmi L. Apport de l'acupuncture dans le traitement de la schizophrénie: étude randomisée en double-aveugle portant sur 31 patients [Effectiveness of acupuncture in treating schizophrenia: a clinical randomized trial of 31 patients]. *Tunis Med.* 2011;89(10):774–778. French.
50. Camchong J, MacDonald AW, Bell C, Mueller BA, Lim KO. Altered functional and anatomical connectivity in schizophrenia. *Schizophr Bull.* 2011;37(3):640–650. doi:10.1093/schbul/sbp131
51. Pomarol-Clotet E, Canales-Rodríguez EJ, Salvador R, et al. Medial prefrontal cortex pathology in schizophrenia as revealed by convergent findings from multimodal imaging. *Mol Psychiatry.* 2010;15(8):823–830. doi:10.1038/mp.2009.146
52. Fang J, Zhen J, Li K, et al. The salient characteristics of the central effects of acupuncture needling: limbic-paralimbic-neocortical network modulation. *Hum Brain Mapp.* 2009;30(4):1196–1206. doi:10.1002/hbm.20583

Neuropsychiatric Disease and Treatment

Dovepress

Publish your work in this journal

Neuropsychiatric Disease and Treatment is an international, peer-reviewed journal of clinical therapeutics and pharmacology focusing on concise rapid reporting of clinical or pre-clinical studies on a range of neuropsychiatric and neurological disorders. This journal is indexed on PubMed Central, the 'PsycINFO' database and CAS, and is the official journal of The International Neuropsychiatric Association (INA). The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/neuropsychiatric-disease-and-treatment-journal>