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The Efficacy and Mechanisms of Acupuncture in Depression: A Systematic Review with Meta-Analysis

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Abstract. Conduct a systematic evaluation of acupuncture's effectiveness on depression via modulation of amygdala and hippocampal function using Meta-analysis. Randomized controlled trials (RCTs) on acupuncture for depression published between July 1, 2020, and July 1, 2025, were retrieved from five databases: CNKI, Wangfang, VIP, SinoMed, and PubMed. RevMan 5.4 software was used for Meta-analysis of clinical effectiveness. After inclusion and exclusion, a total of 40 studies involving 3150 cases were included. The effective rates in the treatment group (acupuncture/acupuncture + conventional therapy) and the control group (conventional therapy) were 1434/1578 (90.8%) and 1168/1572 (74.3%), respectively. Meta-analysis showed that acupuncture therapy had a significant effect on depression (RR = 1.22, 95% CI [1.18, 1.26], Z = 12.08, P < 0.00001). No adverse effects were reported in any of the studies. Acupuncture has prominent clinical efficacy in treating depression and significantly improves the effective rate. However, the included study quality was relatively low, necessitating additional high-quality RCTs for future validation.

Keywords: depression, acupuncture therapy, Meta-analysis

1. Introduction

Depression is a prevalent psychiatric disorder characterized by persistent low mood, exhibiting a clinical profile of "four highs and three lows": high disability, high recurrence, high incidence, and high suicide rates, coupled with low recognition, low consultation, and low treatment rates [1]. Recent epidemiological trends demonstrate a progressive increase in depression prevalence, with particularly concerning rises among younger populations [2]. Concurrently, psychological distress affects up to 85% of elderly individuals, creating compounded public health challenges as global populations age [3]. These demographic shifts underscore the urgent need for effective preventive and therapeutic interventions. Emerging evidence suggests acupuncture may exert antidepressant effects through multiple mechanisms, including enhanced synaptic plasticity and hormonal regulation [4]. Clinical studies increasingly support acupuncture's therapeutic advantages for depression, notably its significant efficacy and favorable safety profile. However, current research remains limited by methodological constraints, including small sample sizes and variable study quality. This meta-analysis rigorously assesses high-quality RCTs to deliver robust evidence on acupuncture's efficacy and safety for treating depression.

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2. Methods

Electronic searches were conducted in six databases—CNKI, Wangfang, VIP, SinoMed, PubMed, and Web of Science—for RCTs on acupuncture for depression published between July 2020 and July 2025. Search terms were (Subject = acupuncture + conventional acupuncture) AND (Subject = depression). A self-designed "literature data extraction form" was used, and data were extracted according to Cochrane Handbook 5.3. Disagreements were resolved by a third reviewer.

Studies meeting the PICOS principles of evidence-based medicine were included. Exclusion criteria included studies with excessively small sample sizes, theoretical or experimental studies, retrospective studies, reviews or systematic reviews, and non-randomized controlled trials.

RevMan 5.4 software was used for systematic evaluation and data analysis. For continuous data (HAMD scores), standardized mean difference (SMD) was used as the effect size, while for dichotomous variables, odds ratio (RR) with 95% confidence intervals (CI) was used. Using the I^2 statistic for heterogeneity assessment: Values > 50% established significant heterogeneity, necessitating a random-effects model; fixed-effects models were utilized when below this threshold. Significance was set at $P < 0.05$.

3. Results

3.1. Fundamental characteristics of included studies

The search identified 4585 studies. Following deduplication, 1809 studies remained for screening. After title/abstract review, 329 studies were excluded. Further full-text review excluded studies that were duplicates, reviews, or had unusable data, resulting in 40 included studies. Table 1 details the characteristics of included studies.

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Table 1. Basic characteristics of included studies [5-44]

Incorporated literature	Total number of cases	Number of examples		Intervention measures		Course of treatment/wk	Outcome indicators
		Treatment group	Control group	Treatment group	Control group		
Runfen Zhong 2025	65	33	32	Acupuncture+fluoxetine hydrochloride capsules	Fluoxetine Hydrochloride Capsules	8	①②
Xin Xu 2024	100	50	50	Acupuncture+escitalopram oxalate	Escitalopram Oxalate	4	①
Xiaopeng Zhou 2024	60	30	30	Acupuncture+cinnamon twig decoction for dispelling depression	Yue Ju Jie Yu Decoction	4	①
Xiaolei Chen 2023	71	35	36	Acupuncture+sertraline hydrochloride tablets	Sertraline Hydrochloride Tablets	4	①
Qiangyu Wang 2023	80	40	40	Acupuncture+sertraline	Sertraline	8	①
Jinlong Wu 2023	90	45	45	Acupuncture+paroxetine	Paroxetine	8	①
Wenjin Zhao 2023	82	42	40	Electroacupuncture+acupuncture treatment	Fluoxetine Hydrochloride Capsules	8	①

(Note. This table presents only the top 7 results due to space constraints. The complete dataset includes 40 entries.)1) Hamilton Depression Scale (HAMD); 2) Pittsburgh Sleep Quality Index (PSQI score)

A risk of bias evaluation was conducted for the included studies. Regarding randomization bias, all 40 studies were RCTs, of which 32 used random number tables, 1 study used a randomized parallel-group controlled design, while 8 did not specify the randomization method. None of the studies mentioned blinding, which may lead to performance bias and detection bias.

3.2. Analysis of clinical efficacy count data and measurement data and summary of selected acupoints

A total of 40 studies reported total effective rates involving 3,150 cases (1,578 in the experimental group and 1,572 in the control group). Total effective rate heterogeneity testing yielded the following results: $Chi^2 = 28.48$, $P = 0.89$, and $I^2 = 0.0\%$, indicating no heterogeneity. HAMD's heterogeneity testing revealed significant heterogeneity ($Chi^2 = 277.55$, $P < 0.01$, $I^2 = 86\%$). PSQI's heterogeneity testing indicated high heterogeneity ($Chi^2 = 62.58$, $P < 0.01$, $I^2 = 89\%$). A Fixed-effects model was used for meta-analysis of total effective rate, and a random-effects model was applied for meta-analysis of HAMD scores and PSQI scores. The total effective rate forest plot is shown in Fig 1. The diamond of Fig 1 does not intersect with the null line and is positioned on the right, indicating that the experimental group had superior therapeutic effects compared to the control group. The pooled RR was 1.22 (95% CI: 1.18–1.26), with a combined effect test statistic of $Z = 12.08$ ($P < 0.01$). The experimental group improved the total effective rate by 16% compared to the control group, a statistically significant difference. Egger's test revealed no publication bias (Bias

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-0.82, P=0.09), consistent with low heterogeneity (I^2=0%). The HAMD's pooled SMD was -1.30 (95% CI: -1.51 to -1.09), with a combined effect test statistic of Z = 12.11 (P < 0.01). The SPQI's pooled SMD was -1.35 (95% CI: -1.90 to -0.80), with a combined effect test statistic of Z = 4.80 (P < 0.01). The experimental group exhibited a 1.30-point lower HAMD score and a 1.35-point lower PSQI score compared to the control group, with both statistically and clinically significant differences. Egger's test of HAMD confirmed funnel plot asymmetry (intercept=-1.45, P=0.02), indicating potential publication bias. The Egger's test of SPQI confirmed no statistically significant evidence of publication bias (intercept = -1.25, P = 0.184 > 0.05) based on the funnel plot asymmetry analysis.

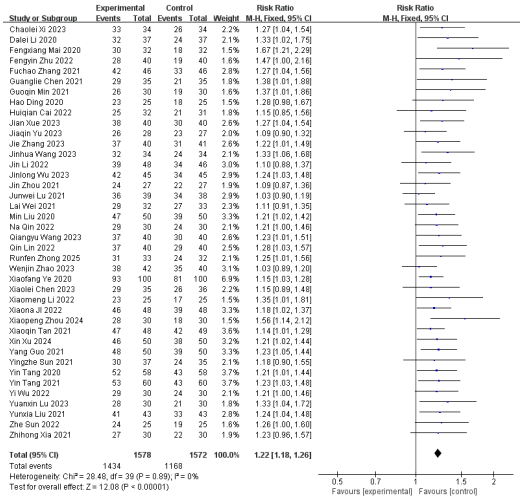


Figure 1. Forest plot of total effective rate for acupuncture/acupuncture + conventional therapy in treating depression

Among the included studies, 15 articles reported adverse reaction assessments, with 13 articles documenting the incidence of adverse events. Two studies employed the Side Effect Rating Scale (SERS) for comparative analysis, while 25 studies did not mention the occurrence of adverse reactions. The reported adverse effects primarily included dry mouth, nausea, decreased appetite, and headache, all of which were mild and resolved spontaneously without intervention.

Frequently used acupoints from the included 40 RCTs are summarized. High-frequency (≥10 studies) and Moderate-frequency (5–9 studies) acupoints:

Baihui (DU20, 28), Yintang (EX-HN3, 18), Shenmen (HT7, 16), Taichong (LR3, 14), Sishencong (EX-HN1, 14), Neiguan (PC6, 13), Sanyinjiao (SP6, 12). Zusanli (ST36, 8), Hegu (LI4, 7), Fengchi (GB20, 6), Shuigou (DU26, 6), Shenting (DU24, 5), and Anmian (EX-HN22, 5).

3.3. Summary of traditional Chinese medicine theory

3.3.1. Treatment based on head and facial regions

In current clinical acupuncture practice for depression, acupoints located on the head and face play a pivotal role. According to TCM theory, the head and brain are regarded as the "residence of essence and intelligence," governing higher cognitive functions such as cognition, thinking, emotion, and memory [45]. Mental disorders are often classified as "yin diseases," and yang meridian acupoints are selected to stimulate yang qi in the body. Abundant yang qi can help regulate mental abnormalities, which is why acupoints from the Governor Vessel (Du Meridian) and Bladder

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Meridian are frequently used in clinical treatment. Yang meridians converge densely on the head and face, making head-region acupoints particularly effective for psychiatric disorders like depression. The Governor Vessel is especially emphasized, aligning with the TCM principle that "for brain disorders, first target the Governor Vessel" [46]. This approach also leverages the "local therapeutic effect" of acupoints.

3.3.2. Treatment based on meridian theory

In TCM clinical practice, some scholars identify "heart-kidney imbalance" as the fundamental pathogenesis of depression [47]. The primary treatment principles include soothing the liver and regulating qi (with Taichong (LR3) as the core acupoint), unblocking the Governor Vessel to relieve depression (using Baihui (DU20) and Shenting (DU24)), calming the mind (via Neiguan (PC6) and Shenmen (HT7)), and harmonizing the heart and kidneys (with Taixi (KI3) and Sanyinjiao (SP6)). This selection of acupoints is consistent with findings from clinical research. Furthermore, TCM holds that the kidneys govern bones, produce marrow, and connect to the brain—the "sea of marrow." As stated in Classified Treatments (Vol. 3): "The kidneys store essence, which generates marrow to nourish the brain" [48], highlighting the vital relationship between the kidneys and brain function. The Yellow Emperor's Inner Canon further elaborates: "The kidneys house willpower" (Suwen•Linglan Midian Lun), "The kidneys store essence, which contains the will; when the kidneys are balanced, the will is regulated" (Lingshu•Benshen).

These texts emphasize that sufficient kidney essence ensures robust brain function, sharp cognition, and strong memory. Conversely, kidney essence deficiency leads to memory decline and mental sluggishness [48]. Thus, from a TCM perspective, the kidneys are closely linked to fear-related emotions, memory, and brain metabolism [49]. And some modern research supports treating mental disorders by targeting kidney meridian acupoints [50].

3.4. Research on the mechanism of acupoint effects in depression treatment

3.4.1. Hypothalamic-Pituitary-Adrenal (HPA) axis and Cortisol (CORT)

Studies have reported that electroacupuncture at "Baihui" (DU20) may reduce HPA axis activity in PTSD rats, repair hippocampal damage, and thereby alleviate anxiety-like behaviors [51]. Electroacupuncture at "Baihui" can also improve learning and memory abilities in stressed rats, regulate HPA axis-related hormones, and correct the abnormal hyperactivity of the HPA axis, potentially influencing the structure and function of the hippocampus to mitigate anxiety and fear behaviors caused by depression or traumatic stress [51]. Clinical studies have also found that acupuncture at "Baihui" (DU20) and "Dazhui" (DU14) exerts antidepressant effects by suppressing HPA axis hyperactivity [51].

Cortisol (CORT), a stress hormone of the HPA axis, is its terminal product [52]. Increased CORT facilitates the rapid development of short-term fear memory into long-term fear memory, promoting the consolidation of fear memory [53]. Additionally, studies indicate that hippocampal volume is negatively correlated with CORT changes, suggesting that excessive CORT may contribute to the consolidation of fear memory in depressed patients by reducing hippocampal volume [54].

Hou Liangqin et al. found that electroacupuncture at "Baihui" (DU20) and "Zusanli" (ST36) in PTSD model rats can effectively modulate HPA axis function, protect hippocampal cholinergic neurons from exogenous CORT damage, and repair damaged hippocampal neurons in model rats [55]. Furthermore, electroacupuncture at "Baihui" (DU20) and "Yintang" (EX-HN3) reduced CORT

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levels in rats with elevated CORT and improved their abnormal emotional states [56]. In the meantime, combined acupuncture at multiple points ("Baihui" (DU20), "Shenting" (DU24), "Yintang" (EX-HN3), "Shenmen" (HT7), and "Sanyinjiao" (SP6)) lowered serum CORT levels in patients. Therefore, the authors propose that this acupuncture treatment may achieve its regulatory effects by inhibiting excessive HPA axis activation [54].

3.4.2. Excitatory (glutamate, GLU) and inhibitory (γ-aminobutyric acid, GABA) neurotransmitters

Emotional processing and regulation critically depend on the excitatory neurotransmitter glutamate (GLU) and inhibitory γ-aminobutyric acid (GABA). Studies have shown that emotional stimuli and prolonged emotional disturbances can disrupt the balance between excitatory and inhibitory neurotransmission, potentially leading to abnormal functional connectivity in brain networks and the emergence of depressive-like symptoms. Excessive GLU can induce excitotoxic damage to hippocampal neurons, resulting in hippocampal volume reduction, suggesting that GLU excitotoxicity may be a key factor in hippocampal atrophy in psychiatric disorders [51,57,58].

Research indicates that stimulating "Baihui" (DU20) and "Dazhui" (DU14) significantly suppresses the expression of GLU and its receptors in the brain tissue of post-stroke depression (PSD) model rats [59]. Additionally, acupuncture at "Baihui," (DU20) "Fengfu" (DU16), "Shenmen" (HT7), and "Taichong" (LR3) can restore neuronal function after cerebral ischemia by modulating GABA and GLU levels in the hippocampal region, thereby improving depressive-like behaviors in model rats [60]. Another study demonstrated that acupuncture at "Sishencong" (EX-HN1) and "Baihui" (DU20) in insomnia model rats significantly increased GABA levels, suggesting that acupuncture enhances the inhibitory effects of neurotransmitters on neurons and reduces neural excitability [61].

The balance between excitatory GLU and inhibitory GABA signaling is essential for sleep-wake regulation [62]. Studies have found an elevated GLU/GABA ratio in the hippocampus of depressed patients, and disruption of GLU-GABA homeostasis can also impair sleep [63]. Furthermore, long-term chronic stress and emotional disturbances reduce GABAergic synaptic input and postsynaptic GABA receptor expression in the amygdala, leading to HPA axis overactivation and elevated CORT levels [64]. Additionally, research has shown that acupuncture at "Shenmai" (BL62) and "Zhaohai" (KI6) effectively modulates sleep-promoting GABA levels, suggesting a potential therapeutic role in improving sleep quality in patients with emotional disorders [65].

3.4.3. Serotonin (5-HT)

Serotonin (5-hydroxytryptamine, 5-HT) is a neurotransmitter associated with positive emotions, primarily regulating energy, mood, and memory. It also serves as a critical neurotransmitter in depression treatment.

Studies have found that after treatment with selective serotonin reuptake inhibitors (SSRIs), PTSD patients exhibit a significant increase in hippocampal volume [66], suggesting that 5-HT is involved in emotional regulation and may be linked to hippocampal volume reduction in depressed patients. Additionally, alterations in 5-HT-related receptors may contribute to hippocampal atrophy and functional impairment, ultimately leading to PTSD-like or depressive-like behaviors [51]. Research has shown that electroacupuncture at "Baihui" (DU20) can influence hippocampal 5-HT expression in rats, mitigating synaptic plasticity damage and thereby improving abnormal emotional states [67]. This indicates that 5-HT modulates hippocampal synaptic plasticity to enhance cognitive

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function and emotional regulation. In another study, music electroacupuncture applied to "Baihui" (DU20) and "Yintang" (EX-HN3) in stressed rats reduced excessive stress behaviors and increased brain 5-HT levels [68]. Further studies demonstrate that acupuncture at "Fengchi" (GB20) can regulate 5-HT levels and related receptor expression in pain modulation pathways [69,70]. It also nourishes hippocampal neurons [71] and enhances neuroplasticity, thereby reducing depression-associated anxiety/somatization scores [72,73]. Similarly, electroacupuncture at "Baihui" and "Dazhui" promoted 5-HT1A receptor expression in stressed rats, restored hippocampal synaptic plasticity, and alleviated depressive behaviors [74].

Other studies indicate that acupuncture at "Zhaohai" (KI6), "Shenmai" (BL62), "Shenmen" (HT7), "Sanyinjiao" (SP6), "Anmian" (Extra), and "Sishencong" (EX-HN1) can modulate 5-HT levels to some extent, improving sleep [75]. Furthermore, "Shenmai"(BL62) and "Zhaohai" (KI6) have been shown to significantly regulate sleep-promoting 5-HT, improving sleep conditions in rats with mood disorders [76].

3.4.4. Modulation of hippocampus-amygdala pathway

Research indicates that depressed patients exhibit enhanced connectivity between bilateral hippocampi and the parahippocampal gyrus with the amygdala [77]. The amygdala plays a crucial role in fear conditioning, while the hippocampus is associated with the consolidation and retrieval of fear memories [78]. Alterations in the connectivity and interactions between these two regions may lead to symptoms such as memory impairment, anxiety, and depression [79].

Zheng Chengqiang employed the "Mind-Regulating and Brain-Awakening" acupuncture technique, stimulating acupoints including Baihui (DU20), Shenting (DU24), Sishencong (EX-HN1), and bilateral Fengchi (GB20) for 12 weeks [80]. Post-treatment assessments involved relevant scale evaluations and resting-state functional magnetic resonance imaging (fMRI). The results demonstrated suppressed connectivity between the left parahippocampal gyrus and right amygdala, along with enhanced functional connectivity between bilateral hippocampi and the right postcentral gyrus/left superior parietal lobule [80]. These findings suggest that electroacupuncture can ameliorate PTSD symptoms to some extent, potentially through mechanisms involving: 1) strengthening hippocampal-parietal lobe connections, 2) inhibiting functional connectivity between the hippocampus and parahippocampal gyrus/amygdala. Concurrently, acupuncture at Baihui (DU20) and Sishencong (EX-HN1) acupoints can modulate deep temporal lobe structures including the amygdala and hippocampal gyrus. This intervention improves cerebral blood flow velocity in corresponding functional cortical areas, promotes neural functional reorganization, maintains cortical cell excitability, and ameliorates associated functional impairments [81].

4. Conclusion

This meta-analysis demonstrates that acupuncture combined with conventional therapy is superior to conventional treatment alone for depression, showing significant improvements in depressive symptoms, sleep quality, and cognitive function, along with a more favourable safety profile. The therapeutic benefits are likely attributable to the synergistic effects of multi-target acupoint stimulation acting through overlapping biological pathways. Specifically, although the therapeutic efficacy of a single acupoint within an individual mechanism may be limited, the overall antidepressant effect of acupuncture likely arises from the cumulative impact of each acupoint acting through multiple distinct pathways. This may explain, at least in part, the clinically observed

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efficacy of acupuncture in treating depression. Nevertheless, further high-quality RCTs are needed to confirm these findings and better elucidate the underlying mechanisms.

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