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ORIGINAL RESEARCH

# Clinical Efficacy of Acupuncture Combined with Escitalopram Oxalate in the Treatment of Mild-to-Moderate Post-Stroke Depression

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**Objective:** This analysis observed the clinical effect of acupuncture combined with Escitalopram oxalate in the treatment of mild to moderate post-stroke depression (PSD).

**Methods:** This was a retrospective study of 1:1 matching design. A total of 96 cases of mild to moderate PSD patients were enrolled and divided into 48 cases each in the control group and the observation group. The control group received treatment with Escitalopram oxalate tablets. The observation group received acupuncture combined with Escitalopram Oxalate, both for a duration of 8 weeks. Comparisons were performed in regard clinical efficacy, 17-Item Hamilton Rating Scale for Depression (HAMD-17), National Institutes of Health Stroke Scale (NIHSS), Pittsburgh Sleep Quality Index (PSQI), Barthel Index, neurotransmitters (5-hydroxytryptamine [5-HT], norepinephrine [NE], and dopamine [DA]), and liver function (alanine aminotransferase [ALT], aspartate transaminase [AST], direct bilirubin [DBIL], and total bilirubin [TBIL]). The Side Effect Rating Scale (SERS) scores at weekends 4 and 8 of treatment were counted.

**Results:** The total effective rate was 91.67% (44/48) higher for the observation group than 75.00% (36/48) for the control group ($P < 0.05$). HAMD-17, NIHSS, and PSQI scores decreased in the two groups after treatment, and they were all lower in the observation group than in the control group ($P < 0.05$). The observation group had a higher Barthel index than the control group ($P < 0.05$). Serum 5-HT, NE and DA levels increased in both groups after treatment, and serum markers were higher in the observation group compared with the control group ($P < 0.05$). The differences in SERS scores between the two groups were not significant ($P > 0.05$).

**Conclusion:** Combining acupuncture with Escitalopram oxalate proves to be effective and safe for treating mild-to-moderate PSD, significantly alleviating depression, and enhancing neurological function, sleep quality, and quality of life.

**Keywords:** stroke, depression, acupuncture, Escitalopram oxalate, neurological function

## Introduction

The most common mental health issue among stroke survivors is post-stroke depression (PSD). In the aftermath of a stroke, PSD negatively affects rehabilitation, and recovery of motor and cognitive deficits, and is associated with a significant rise in relapsing neurovascular events.[1] The researchers state that the incidence of PSD is approximately 31% and it has the potential to manifest at any point within the five years following a stroke. Additionally, PSD may elevate the risk of mortality following a stroke and adversely affect the survival rates of stroke survivors.[2] Multifactorial pathophysiology is likely to be involved in PSD, including reduced levels of inflammation, genetics and epigenetics, cerebrovascular deregulation, white matter disease, altered neuroplasticity, and altered glutamate neurotransmission.[3] Comparatively, individuals with PSD are more likely to suffer from more pronounced cognitive deficits, have greater long-term disability odds, and struggle with more suicidal thoughts.[4,5] Identifying PSD effectively and choosing effective treatment options is therefore vital.

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It is generally agreed that antidepressants, including escitalopram and paroxetine, yield significantly higher response and remission rates for PSD compared to placebo.[6] Off-label use of Escitalopram is often prescribed to treat conditions such as posttraumatic stress disorder, premenstrual dysphoria, and postpartum depression.[7] However, there is concern about the efficacy and safety of antidepressants in treating and preventing clinical depression symptoms after stroke.[8] It is noteworthy that in the non-pharmacological treatment of depression, acupuncture has shown promising results.[9,10] A review suggests that acupuncture combined with conventional treatment is beneficial for improving depressive symptoms in patients with PSD. Furthermore, no serious adverse reactions are reported in PSD patients receiving acupuncture in conjunction with traditional therapy.[11] Network meta-analyses confirm, however, that acupuncture plus antidepressants and acupressure plus antidepressants are superior treatments for PSD.[12] When combined with antidepressants, acupuncture showed better results in treating PSD than antidepressants alone.[13] This study combined acupuncture and Escitalopram oxalate to determine if this therapeutic approach is clinically effective in treating patients with PSD. Meanwhile, we hope that the adjuvant effect of acupuncture can alleviate or improve the adverse symptoms associated with Escitalopram oxalate.

# Materials and Methods

## Ethical Statement

This research was permitted by the ethics committee of Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine (approval number: 2021-020). Written informed consent was acquired from all subjects. Additionally, this study adhered to the principles of the Helsinki Declaration.

## General Information

This was a retrospective study of 1:1 matching design, enrolling 96 cases of patients with mild to moderate PSD admitted to Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine from January 2022 to December 2023, which were divided into 48 cases each in the control group and the observation group according to the treatment methods. The difference between the general conditions of the two groups was not significant ($P > 0.05$, Table 1).

**Table 1** Comparison of the General Conditions of the Two Groups [n(%)]

| Indicators | Observation Group (n = 48) | Control Group (n = 48) | $\chi^2$ | P |
|---|---|---|---|---|
| Gender | | | 0.174 | 0.676 |
| male | 20 (41.67) | 18 (37.50) | – | – |
| Female | 28 (58.33) | 30 (62.50) | – | – |
| Age | | | 0.419 | 0.811 |
| < 45 years | 8 (16.67) | 9 (18.75) | – | – |
| 45–64 years | 18 (37.50) | 15 (31.25) | – | – |
| ≥ 65 years | 22 (45.83) | 24 (50.00) | – | – |
| Type of stroke | | | 0.549 | 0.459 |
| Ischemic | 36 (75.00) | 39 (81.25) | – | – |
| Hemorrhagic | 12 (25.00) | 9 (18.75) | – | – |
| Education | | | 0.281 | 0.964 |
| Primary school | 10 (20.83) | 8 (16.67) | – | – |
| Junior high school | 20 (41.67) | 21 (43.75) | – | – |
| High school | 14 (29.17) | 15 (31.25) | – | – |
| College and above | 4 (8.33) | 4 (8.33) | – | – |
| Marital status | | | 0.801 | 0.371 |
| Unmarried/divorced/widowed | 5 (10.42) | 8 (16.67) | – | – |
| Married | 43 (89.58) | 40 (83.33) | – | – |

## Inclusion Criteria

①Patients who met the diagnostic criteria for PSD[14] with a 17-Item Hamilton Rating Scale for Depression (HAMD-17) score of 8 to 23,[15] and who also met the diagnostic criteria for depression in Traditional Chinese Medicine according to the "Guiding Principles for Clinical Research of New Chinese Medicinal Products", specifically the syndrome of liver qi stagnation, characterized by symptoms such as low mood, mental depression, epigastric discomfort with belching, anorexia with little sleep, chest and rib-side pain and distension, irregular bowel movements, thin and greasy tongue coating, and thin and wiry pulse; ②Patients who were not involved in any other medical clinical studies during the same period; ③ Patients with stable vital signs and communication skills; ④ Patients who were able to cooperate with the assessment; ⑤ Patients with medical compliance; ⑥ Patients who provided informed consent, and signed relevant agreements.

## Exclusion Criteria

① Patients who had received antidepressant-related treatment in the past 1 month; ② patients with HAMD-17 $\geq$ 24 points, suicidal/self-abuse tendency, schizophrenia, bipolar disorder and other serious mental illness; ③ patients with obvious aphasia or cognitive impairment; ④ patients with abnormal heart, liver and kidney function; ⑤ patients with acupuncture contraindications or refusal of acupuncture treatment, allergic constitution or pregnancy and lactation; ⑥ patients with tumors, hematological diseases, endocrine diseases, infectious diseases, infectious diseases, epilepsy and other neurological diseases; ⑦ patients with a history of abuse of tobacco, alcohol and other psychoactive substances.

## Methods

(1) Control group: ESC tablets (10 mg/tablet; H20103327; Jewim Pharma, Shandong, China) were administered orally at night, beginning with a 10 mg daily dose, which was progressively raised to a maximum of 20 mg per day based on the patient's condition severity and their response to the treatment. The medication was continued for 8 weeks.

(2) The observation group was given combined acupuncture treatment on the basis of the control group. Among the main acupoints were Baihui, Yintang, bilateral Shenmen, and bilateral Neiguan. Acupuncture was necessary for patients with liver qi stagnation and spleen deficiency in Taichong, Yinlingquan, and Pishu; Taichong and Danzhong for those with liver qi stagnation; Xinshu, Pishu, and Zusanli for those with heart and spleen deficiencies; Taixi, Ganshu, and Shenshu for those with yin deficiency in liver and kidney; and Xuehai, Geshu, and Zusanli for those with qi deficiency and blood stasis. Patients with insomnia should consider acupuncture in Zhaohai and Shenmai; those with constipation need acupuncture in Zhigou and Tianshu; and those with amnesia should opt for acupuncture in Juegu and Taixi. The needle insertion site was routinely disinfected with 75% ethanol. Transverse or perpendicular needling was performed using 0.3 mm × 25 mm filiform needles at a depth of 15–25 mm and for 30 min. The Qi-guiding acupuncture was used, with even reinforcing-reducing technique. Acupuncture was performed once every other day, 3 times a week for 8 weeks. An acupuncture specialist with at least five years' experience performed the acupuncture operations in this study.

## Observation Indicators

(1) The degree of depression was assessed using HAMD-17, including depressive mood, psychogenic anxiety, somatic anxiety, suicide, guilt, and difficulty falling asleep. According to the scoring system, 0–7 represents no depression, 8–16 represents mild depression, 17–23 represents moderate depression, and 24–52 represents severe depression.

(2) Neurological function was assessed using the National Institutes of Health Stroke Scale (NIHSS), which contains 11 items, including consciousness, language, motor, sensation, and ataxia. Neurological deficits were graded from 0 to 42, with a higher score indicating a more severe problem.

(3) Sleep quality was evaluated using Pittsburgh Sleep Quality Index (PSQI), including 7 items such as sleep quality, efficiency, duration, and time to fall asleep. Sleep quality was measured from 0 to 21, with a higher score representing poorer sleep.

(4) Quality of life was evaluated using Barthel Index (BI). There were 10 assessment items such as eating, bathing, dressing and toileting. Self-care ability scores range from 0 to 100, with higher scores indicating better self-care ability.
(5) Fasting venous blood (4 mL) was collected, and serum 5-hydroxytryptamine (5-HT), norepinephrine (NE), and dopamine (DA) levels were detected with high-performance liquid chromatography (Risun, Shenzhen, China; Thermo Fisher UltiMate 3000).
(6) Fasting venous blood (5 mL) was collected and analyzed with an automatic biochemical analyzer (Perlong, Beijing, China, PUZS-300) to detect serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), direct bilirubin (DBIL), and total bilirubin (TBIL) levels.
(7) The Side Effect Rating Scale (SERS) scores, including 14 entries such as somatic fatigue, headache, sleep disturbance, dizziness, palpitations, and tremor, were evaluated for both groups half an hour after the end of treatment at weeks 4 and 8. Each entry was categorized according to none, mild, moderate and severe, using a 0–3 point scale, with higher scores suggesting more severe side effects.

## Clinical Efficacy

An analysis of the clinical efficacy was performed based upon the reduction rate of HAMD-17 score and the global improvement (GI) in the Clinical Global Impression scale after 8 weeks of treatment. Reduction rate = (pre-treatment total score - post-treatment total score)/pre-treatment total score × 100%. GI was divided into 8 grades: 0 points (not evaluated), 1 point (significant progress), 2 points (progress), 3 points (mild progress), 4 points (no change), 5 points (mild deterioration), 6 points (deterioration), 7 points (serious deterioration). Clinical efficacy criteria: ① Significantly effective: HAMD-17 reduction rate ≥ 50% or HAMD-17 ≤ 7 points, GI = 0–1 points; ② Effective: HAMD-17 reduction rate ≥ 25%, GI = 2–3 points; ③ Ineffective: HAMD-17 reduction rate < 25%, GI = 4–7 points.

## Statistical Analysis

Statistical analyses were performed using SPSS 26.0 and GraphPad Prism 8. Qualitative data were described by [n (%)] with the $\chi^2$ test. Quantitative data were described by $\bar{x} \pm s$ for independent or paired samples *t*-tests, and skewed quantitative data were described by the *M* (*P25, P75*) for *Mann–Whitney U*-test. $P < 0.05$ was considered a statistically significant difference.

# Results

## Clinical Efficacy

An effective rate of 91.67% (44/48) was observed in the observation group, whereas 75.00% (36/48) was recorded in the control group ($P < 0.05$, Table 2).

**Table 2** Comparison of Clinical Outcomes Between the Two Groups [n (%)]

| Clinical Effect | Observation Group (n = 48) | Control Group (n = 48) | $\chi^2$ | P |
|---|---|---|---|---|
| Significantly effective | 26 (54.17) | 17 (35.42) | – | – |
| Effective | 18 (37.50) | 19 (39.58) | – | – |
| Ineffective | 4 (8.33) | 12 (25.00) | – | – |
| Total effective | 44 (91.67) | 36 (75.00) | 4.8 | 0.028 |

## HAMD-17 and NIHSS Scores

Prior to treatment, the difference in HAMD-17 and NIHSS scores between the groups was not statistically significant ($P > 0.05$). Post-treatment, both groups experienced a reduction in HAMD-17 and NIHSS scores, with the observation group showing a lower score compared to the control group ($P < 0.05$, Figure 1).

## PSQI and BI

Statistically significant differences did not exist between the PSQI and BI of the two groups before treatment ($P > 0.05$). Post-treatment, PSQI decreased while BI rose in both groups; and the changes were more obvious in the observation group ($P < 0.05$, Figure 2).

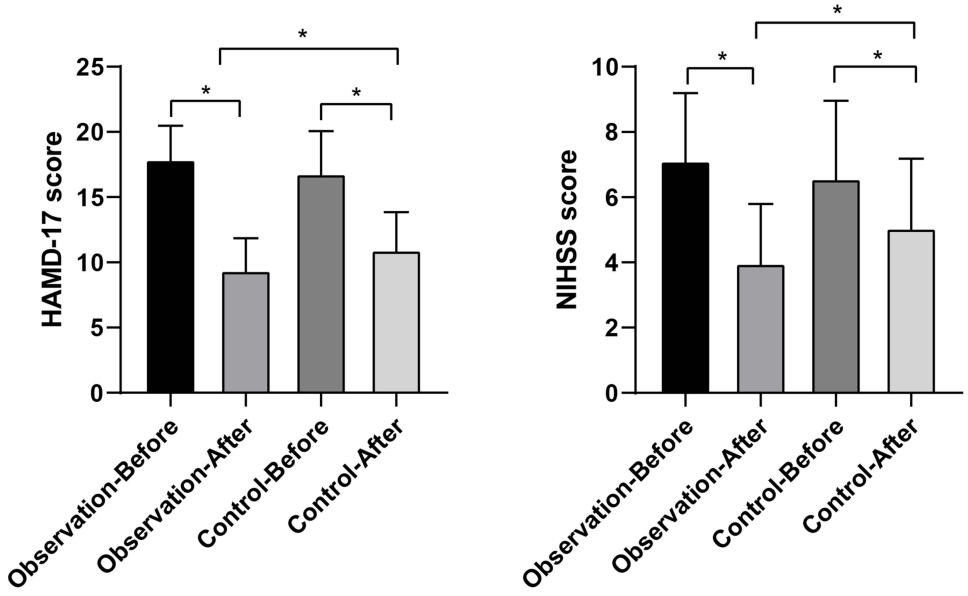


**Figure 1** Comparison of HAMD-17 and NIHSS scores before and after treatment between the two groups. *indicates $P < 0.05$ between the two groups.

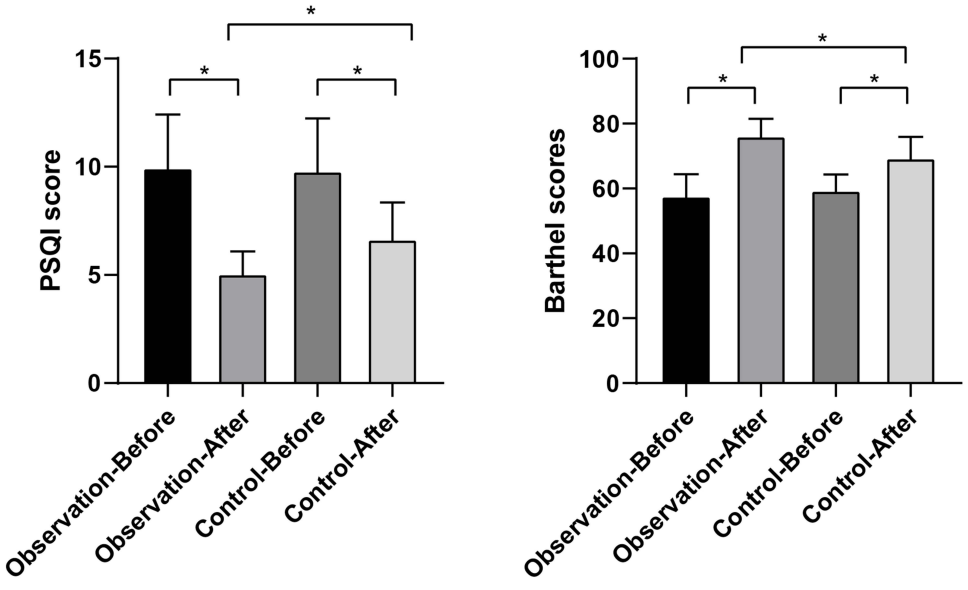


**Figure 2** Comparison of PSQI and Barthel scores before and after treatment between the two groups. *indicates $P < 0.05$ between the two groups.


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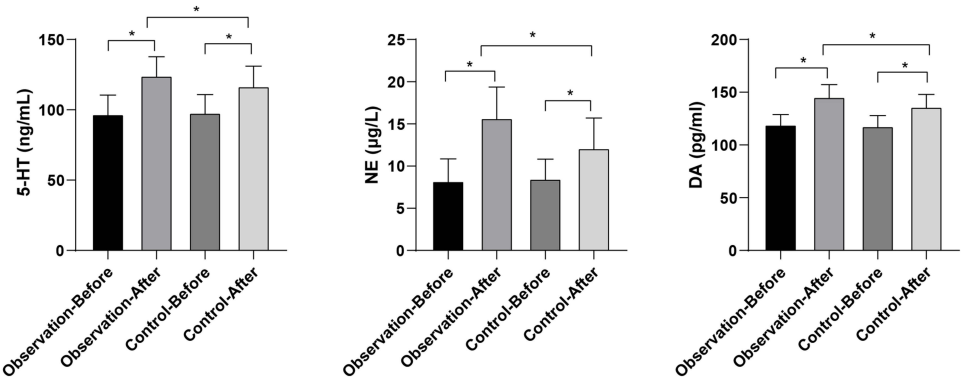


**Figure 3** Comparison of serum levels of 5-HT, NE, and DA before and after treatment between the two groups. *indicates $P < 0.05$ between the two groups.

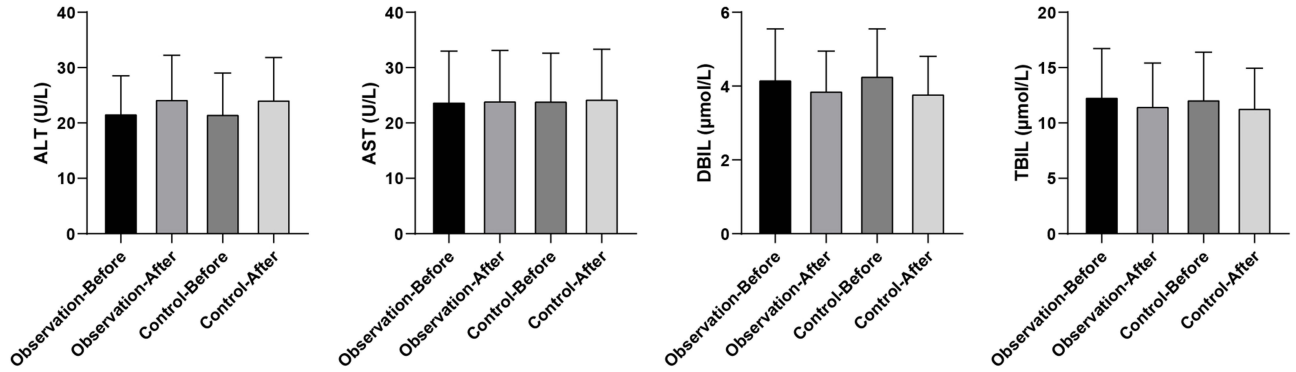


**Figure 4** Comparison of serum levels of ALT, AST, DBIL, and TBIL before and after treatment between the two groups.

## Neurotransmitters

The differences in serum 5-HT, NE and DA levels before treatment between the two groups were not significant ($P > 0.05$); Following treatment, serum 5-HT, NE, and DA levels increased in both groups, with observation levels higher than control levels ($P < 0.05$, Figure 3).

## Liver Function

The differences in serum ALT, AST, DBIL and TBIL levels before and after treatment between the two groups were not significant ($P > 0.05$, Figure 4).

## SERS Scores

There were no significant differences in SERS scores between the two groups at the end of week 4 and week 8 of treatment ($P > 0.05$, Table 3).

**Table 3** Comparison of SERS Scores Between the Two Groups (Points)

| Timing | Observation Group (n = 48) | Control Group (n = 48) | Z | P |
|---|---|---|---|---|
| Weekend 4 of treatment | 16.00 (13.00, 18.75) | 16.50 (13.00, 18.00) | −0.21 | 0.834 |
| Weekend 8 of treatment | 18.00 (15.00, 20.00) | 19.00 (16.00, 21.00) | −0.833 | 0.405 |

**Abbreviation**: SERS, Side Effect Rating Scale.

## Discussion

In addition to negatively affecting social activities and cognitive function, PSD also has a negative effect on stroke rehabilitation. Therefore, minimizing PSD in individuals recovering from a stroke is crucial. In the treatment of PSD, pharmacological and nonpharmacological interventions, as well as combination therapies, have been shown to be effective.[16] This study showed that acupuncture and Escitalopram oxalate, when combined, were more effective than Escitalopram oxalate monotherapy for the treatment of PSD.

Our research results revealed that the total effective rate in the observation group (receiving acupuncture combined with Escitalopram oxalate treatment) was higher than that in the control group (receiving Escitalopram oxalate tablets treatment alone). In terms of clinical efficacy, it suggests acupuncture combined with Escitalopram oxalate is more effective than Escitalopram oxalate alone. As demonstrated by Zheng-Lu Yin et al, the addition of Shugan Tiaoshen acupuncture combined with transcranial magnetic stimulation (TMS) to Escitalopram oxalate treatment can effectively improve cognitive function and sleep quality in patients with PSD, with better outcomes than Escitalopram oxalate treatment alone or TMS combined with Escitalopram oxalate.[17] The research conducted by Fang Yang and others indicates that patients in the PSD group have higher NIHSS scores and Daily Life Ability Scale scores compared to those in the non-PSD group, which may be an independent risk factor for PSD.[18] In this study, there was a reduction in HAMD-17 and NIHSS scores in both groups after treatment, and the observation group scored lower than the control group. It is indicated that combined acupuncture and Escitalopram oxalate treatment for mild-moderate PSD reduces depression and restores neurological function in patients. It has been shown that acupuncture significantly alleviates depression, as evidenced by higher HAMD-17 scores.[19] Moreover, patients with stroke who receive acupuncture in conjunction with conventional rehabilitation show significant improvements in their functional recovery as suggested by improved NIHSS scores during the early subacute stages.[20]

Current research has proven the efficacy of acupuncture to improve sleep quality of stroke-related complications, such as insomnia[21] and PSD.[22] Additionally, interactive dynamic scalp acupuncture has been shown to relieve depression and improve self-care ability for patients with post-stroke cognitive impairment.[23] PSQI is one of the most commonly used sleep quality measures.[24] BI is a widely used tool for assessing functional independence.[25] In the present study, PSQI decreased while BI increased after treatment, with the observation group scoring lower PSQI and higher BI than the control group. This indicates that using acupuncture alongside escitalopram oxalate to treat mild to moderate PSD aids in improving sleep patterns and enhancing quality of life.

Several neurotransmitters are implicated in depression, including serotonin (5-HT, DA, and NE), according to the monoamine hypothesis.[26] 5-HT, NE, and DA monoaminergic neurotransmission regulate mood, reactivity to psychological stress, self-control, and cognitive abilities.[27] Following treatment, serum 5-HT, NE, and DA increased in both groups, with the observation group experiencing a greater increase than the control group. This indicates that acupuncture and Escitalopram oxalate has a restorative effect. Furthermore, antidepressant drugs can cause metabolic disorders, leading to abnormal liver function, which further reduces the effectiveness of drugs or worsens patients' prognosis.[28] The present study showed that the differences in serum ALT, AST, DBIL, and TBIL levels between the two groups before and after treatment were not significant, nor were the differences in SERS scores between the end of the 4th week and the end of the 8th week of treatment. According to our study, acupuncture combined with Escitalopram oxalate in the treatment of mild-to-moderate PSD has a low impact and minimal side effects on liver function. There is no disputing the effectiveness of antidepressants, but side effects should not be ignored.[29,30] Acupuncture with Western medicine often produces better therapeutic effects than Western medicine alone on post-stroke depression, and there are fewer adverse effects.[31] As a result of our research, it was shown that acupuncture in combination with Escitalopram oxalate was not associated with significant side effects, confirming the safety of this regimen in the treatment of PSD.

In conclusion, acupuncture combined with Escitalopram oxalate for the treatment of mild to moderate PSD can alleviate depression severity and promote the recovery of neurological function, sleep quality, and neurotransmitter levels. This combined treatment regimen not only enhances therapeutic efficacy but also helps to mitigate adverse symptoms associated with Escitalopram oxalate. Despite showing promising clinical outcomes in the treatment of PSD, this study still has some limitations. For instance, the limited sample size in this study may lead to certain biases in the

research results. Larger-scale clinical trials are needed in the future to further verify the effectiveness and safety of this combined treatment regimen.

## Data Sharing Statement

The experimental data used to support the findings of this study are available from the corresponding author upon request.

## Ethics Approval

This research was permitted by the ethic committee of Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine (approval number: 2021-020). Written informed consent was acquired from all subjects.

## Consent to Participate

Informed consent was obtained from all individual participants included in the study.

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## Disclosure

The authors have no conflicts of interest to declare that are relevant to the content of this article.

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