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Original Article

Benefit of electroacupuncture for pulmonary infections in patients with schizophrenia and bipolar disorder: a retrospective study

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Abstract: Objective: Patients with schizophrenia (SP) and bipolar disorder (BD) who are on prolonged medication are particularly vulnerable to pulmonary infections. This study aims to assess the effectiveness of electroacupuncture (EA) in treating pulmonary infections. Methods: For this retrospective study, data of 170 SP/BD patients with pulmonary infections were collected: a control group (85 patients) and an EA group (85 patients). The control group received standard psychiatric care and supportive treatment, while the EA group also underwent electroacupuncture. After two weeks, various factors including blood oxygen saturation (SpO_2), inflammatory cytokine levels, manic symptoms, and cognitive function were compared between the two groups. Results: Beneficial effects of electroacupuncture on SpO_2 and white blood cell counts were observed after two weeks of intervention. Additionally, electroacupuncture was more effective in reducing inflammatory cytokine levels. Patients receiving electroacupuncture also had lower symptom scores for expectoration, panting, coughing, and sputum compared to the control group ($P<0.05$). Logistic regression analysis confirmed the important role of electroacupuncture in promoting patient recovery. However, the improvements in manic symptoms and cognitive function with electroacupuncture were not significant compared to the control group ($P>0.05$). Conclusions: Electroacupuncture can have a beneficial impact on the recovery of SP/BD patients with pulmonary infections.

Keywords: Electroacupuncture, schizophrenia, bipolar disorder, pneumonia, rehabilitation

Introduction

Schizophrenia (SP) and bipolar disorder (BD) are common mental disorders that are often seen in clinical settings. SP patients usually presents with abnormalities in consciousness and behavior. In more severe cases, individuals may also have cognitive and social functioning problems. Failure to promptly address the condition can increase the likelihood of mental disability [1-3]. BD often arises from a combination of genetic predisposition, external environmental triggers, and individual factors. Manic episodes in patients are often characterized by extreme impulsivity and a tendency towards destructive behavior. Additionally, the recurrent nature of the disorder poses specific challenges for treatment [4].

Currently, both SP and BD require ongoing supervision and medication. Drugs such as quetiapine fumarate and olanzapine provide quick-acting benefits and effective sedation to help stabilize patients' mental well-being, but prolonged use may lead to organ dysfunction, hindering overall recovery [5]. Extended medication usage can weaken the physical immunity of many individuals with SP and BD over time. Furthermore, the reduced self-protective abilities of these patients increase their susceptibility to pulmonary infections [6, 7]. Previous epidemiologic studies have shown that BD patients have a higher risk of developing concurrent lung conditions compared to the general population. The prevalence of pulmonary infections among psychiatric patients is around 70%, harming their daily functioning and quality

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of life. This puts a significant financial burden on patients, their families, and society [8, 9]. As the condition worsens, the patient's ability to swallow declines, leading to an increase in pulmonary infections due to frequent aspirations [10-12]. Treating pulmonary infections in patients with SP and BD who have developed such infections presents a greater challenge compared to patients with typical pulmonary infections. This is mainly because of some drug interactions between their psychiatric medications and anti-infection treatments, as well as the risk of lower treatment compliance due to cognitive dysfunction and behavioral abnormalities. Therefore, it is crucial to explore additional treatment options beyond medication for patients with mental disorders who are also dealing with pulmonary infections.

Electroacupuncture (EA) can improve neurologic and endocrine functions in patients by targeting specific acupoints. Studies have shown that electroacupuncture therapy can increase blood circulation, reconstruct = neural function, and be effective in managing various mental health disorders [13, 14]. Jiang's research notes that EA can be used to treat patients with hypertensive intracerebral hemorrhage suffering from pneumonia, since it can increase the effectiveness rate, decrease inflammatory factor levels, and alleviate clinical symptoms [15]. Furthermore, Zhou's animal experiments also suggested that EA pretreatment may have a protective role by promoting macrophage polarization to the M2 phenotype in a septic rat model of lipopolysaccharide -induced acute lung injury [16]. Research has evaluated the effectiveness of combining EA with medication to alleviate symptoms in patients with SP and BD [17]. However, further studies are needed to confirm the clinical benefits of using EA in patients with SP/BD who have pulmonary infections.

Building on the research background discussed earlier, the main goal of this study was to examine the effectiveness of EA as a supplementary therapy for patients with SP and BD who have pulmonary infections. This study seeks to provide new insight on improving the treatment outcomes of pulmonary infections in this patient population.

Patients and methods

Subjects

This was a retrospective study conducted at a single center. **Figure 1** shows a flowchart of the research design. The study focused on individuals with SP and BD who also had pulmonary infections as participants. The data of participants were collected at Huai'an NO. 3 People's Hospital from August 1, 2023, to August 1, 2024. The protocol was approved by the Ethics Committee of Huai'an NO. 3 People's Hospital (Approval NO. 2024-064).

Sample size estimation

The sample size was determined based on the total number of patients with SP and BD cases receiving treatment for pulmonary infections at the hospital. The main focus of this study, as determined by previous research, was to assess the effectiveness of treatment for severe pulmonary infections and to evaluate the occurrence of adverse events. It was hypothesized that patients undergoing combined electroacupuncture therapy in this study will achieve at least as good, if not better, treatment efficacy rates than those observedin previous studies [18]. Assuming asignificance level of α=0.05 and a power of $1\text{-}\beta$=0.90, accounting for a potential dropout rate of 10%, these values were inputted into the Power Analysis and Sample Size 2023 program (NCSS, LLC; East Kaysville, Utah, USA). The analysis indicated that a minimum of 170 patients should be included in the study. Patients were allocated in a 1:1 ratio, with each group requiring a minimum of 85 participants.

Inclusion and exclusion criteria

Criteria for inclusion: (1) Meeting the diagnostic criteria for SP or BD as outlined in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) and the International Classification of Diseases, 10th Edition (ICD-10) (see **Table 1**) [19, 20]; (2) Participants must be 18 years of age or older; (3) Meeting clinical diagnostic criteria for pulmonary infection, including symptoms such as fever, cough, chest pain et al.; chest imaging demonstrated new patchy infiltrates, lobar or segmental consolidation, ground-glass opacities, or interstitial

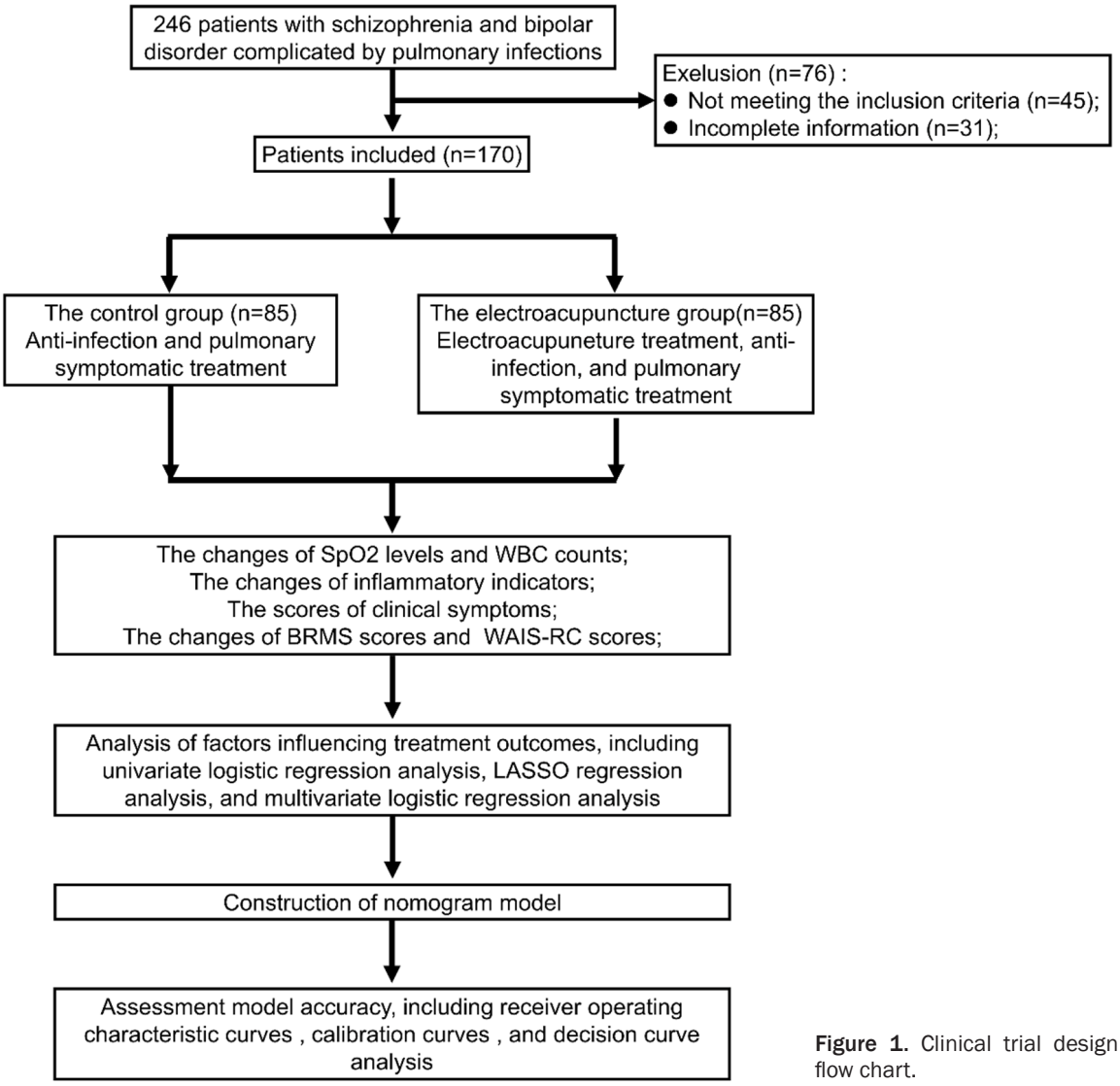

Figure 1. Clinical trial design flow chart.

changes with or without pleural effusion laboratory results showing signs of infection such as elevated white blood cell (WBC) count and inflammatory markers, and positive pathogen identification; (4) Consistently using second-generation antipsychotic drugs and being in a stable condition post-treatment; (5) Ensuring there are no drug-drug interactions between the psychiatric medications being taken and the antimicrobial drugs to be administered; (6) Obtaining informed consent from the patient's immediate family members or guardians.

Criteria for exclusion: (1) Concurrent presence of other infectious illnesses; (2) Presence of long-term lung conditions such as chronic obstructive pulmonary disease; (3) Autoimmune disorders like systemic lupus erythematosus; (4) Cancerous tumors; (5) Patients who stop treatment for any reason during the study; (6) Patients who withdraw from the study group for personal reasons during the intervention period; (7) Instances of mortality during treatment.

Intervention

The control group received Quetiapine Fumarate orally after meals. The treatment began with a dose of 25 mg twice daily and was adjusted to 50 mg every 1 to 3 days until reaching 100 mg per administration, depending on the patient's response. Based on the "Diagnosis and treatment of community-acquired pneumonia in adults: 2016 clinical practice guidelines

Table 1. Definitions of SP and BD according to DSM-5 and ICD-10

Disease	DSM-5	ICD-10
SP	1. Presence of at least two of the following symptoms, each of which has been persisting for a period of time, with at least one of them being symptoms from items 1.1 to 1.3: 1.1. Hallucinations 1.2. Delusions 1.3. Schizophrenic-like disorganized thinking (e.g., incoherent speech or significantly disorganized behavior) 1.4. Marked emotional incoordination or flat affect 1.5. Retreat in behavior or affect (e.g., social withdrawal or reduced emotional expression) 2. A continuous course of the illness, accompanied by impairment in social/occupational functioning or evident negative symptoms (such as flat affect, poverty of speech, or lack of motivation). 3. Exclude mood disorders and schizoaffective disorders, and the symptoms are not due to the effects of substances or a general medical condition. 4. If there is an autism spectrum disorder or another developmental disorder that began in childhood, the diagnosis should be noted as “other disorders related to SP”.	1. At least two of the following symptoms are present, and they have persisted for more than one month: 1.1. Hallucinations 1.2. Delusions 1.3. Disorganized thinking or speech (e.g., frequent incoherent speech or significantly disorganized behavior) 1.4. Marked emotional blunting or inappropriate affect 2. There is marked impairment in social or occupational functioning. 3. The duration of the illness is more than six months, during which the patient has shown at least one of the above symptoms for most of the time, with impaired functioning. 4. Exclude affective disorders, mental retardation, and mental disorders caused by substances or known physical diseases.
Bipolar Affective Disorder	1. Manic Episode: 1.1. A distinct period of abnormally and persistently elevated, expansive, or irritable mood lasting at least one week. 1.2. During this period, three or more of the following symptoms are present to a significant degree and cause marked impairment in social, occupational, or other important areas of functioning, or the symptoms necessitate hospitalization to prevent harm to self or others: (1) Inflated self-esteem or grandiosity. (2) Decreased need for sleep (e.g., feeling rested after only 3 hours of sleep). (3) More talkative (pressured speech) or feeling compelled to speak. (4) Flight of ideas or the feeling that thoughts are racing. (5) Distractibility or an inability to concentrate. (6) Increased goal-directed activity (social, work, sexual, or recreational) or psychomotor agitation. (7) Excessive involvement in activities that have a high potential for painful consequences (e.g., uncontrolled shopping, reckless sexual behavior, foolish business investments). 2. Hypomanic Episode: 2.1. A distinct period of abnormally and persistently elevated, expansive, or irritable mood lasting at least 4 days. 2.2. During this period, three or more of the symptoms described for a manic episode are present, but the symptoms are not severe enough to cause marked impairment in social or occupational functioning, and no hospitalization is required, and there are no psychotic symptoms. 3. Depressive Episode: The criteria for a depressive episode in BD are similar to those for major depressive disorder, but the diagnosis of BD requires at least one manic or hypomanic episode.	1. Manic Episode: 1.1. There is a marked elevation in mood, inflated self-esteem, reduced need for sleep, increased talkativeness, flight of ideas, distractibility, and excessive involvement in activities that could lead to painful consequences. 1.2. The symptoms last for at least one week. 2. Depressive Episode: 2.1. There is a pronounced low mood, loss of interest or pleasure, fatigue or decreased energy, reduced speech, slowed thinking, difficulty concentrating, sleep problems, low self-esteem, feelings of hopelessness, and thoughts of death or suicide. 2.2. The symptoms last for at least two weeks. 3. Bipolar Affective Disorder: The diagnosis requires at least one manic episode and one depressive episode, and no other mental disorder better explains these episodes.

by the Chinese Thoracic Society, Chinese Medical Association", [21] the control group patients were given standard care such as blood pressure and blood sugar management, anti-infection medication, and optimal intracranial pressure control. Additionally, patients received supportive symptomatic treatment like atomization, sputum drainage, and oxygen inhalation therapy based on their individual needs. The treatment duration for all patients was two weeks.

On the basis of treatment in the control group, patients in the EA group further administered EA therapy, the EA group was treated with the ZCEA type electroacupuncture device from Beijing Zhongke Electroacupuncture Research Institute (Beijing, China). Feiyu (BL13), Baihui (GV20), Quchi (LI11), Hegu (LI4), and Yintang (EX-HN3) acupoints were stimulated using electroacupuncture at a frequency of 2 Hz. The intensity of stimulation was adjusted based on each patient's tolerance level. Each 45-minute session of electroacupuncture was performed once daily for five sessions, making up one treatment course. After a 2-day break, the next course began, with the entire treatment period lasting 14 days.

Observation index

General information: The researchers collected patient data from hospital records stored in electronic medical systems. The data included information such as patient age, gender, smoking habits, medical history of chronic conditions (such as hypertension and diabetes), specific mental health diagnoses (SP or BD), family history of mental illness, duration of mental health conditions, and length of pulmonary infections episodes.

Blood oxygen saturation: Before and after the intervention, arterial blood gas analysis was conducted for each patient. The radial artery was punctured while the patient remained calm, and 2 ml of arterial blood was obtained using a collection tube containing heparin. The blood specimen was promptly transferred to an arterial blood gas analyzer within 15 minutes to determine the patient's blood oxygen saturation (SpO_2) level.

Inflammation indicators: Before and after treatment, 2 mL of fasting venous blood was drawn from each patient and subjected to a two-step centrifugation protocol (1,600 g for 10 min at 4°C followed by 16,000 g for 10 min at 4°C) to separate the upper layer of serum. Subsequently, the levels of C-reactive protein (CRP), procalcitonin (PCT), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α) were measured using a double antibody sandwich enzyme-linked immunosorbent assay (ELISA).

Rehabilitation indicators: Pre-treatment and 14 days after treatment, main symptoms were assessed and recorded on a four-point scale from 0 to 3 (none/mild/moderate/severe), including expectoration, panting, cough, and sputum.

Manic symptoms: Prior to and following the intervention, all individuals underwent an evaluation using the Bech-Rafaelsen Mania Scale (BRMS) [22]. This measurement tool comprises 11 domains: activity level, sexual desire, emotional state, thought process, verbal communication, responsiveness to stimuli, sleep patterns, occupational functioning, antagonistic tendencies, social engagement, and self-assessment, with each domain assigned a score between 0 and 4. Elevated scores indicateheightened manic symptomatology. The BRMS scale demonstrates a *Cronbach's α* value of 0.712 and a split-half reliability of 0.803.

Cognitive function: Two specialized physicians evaluated all patients using the Wechsler Adult Intelligence Scale (WAIS-RC) before and after treatment, following the recommended protocols [23]. The scale includes two aspects: operational capacity and language proficiency. Operational capacity is assessed through five tasks including completing drawings, arranging pictures, recalling digits, building blocks, and composing figures. Language proficiency is measured through six tasks: solving arithmetic problems, recalling digits, demonstrating general knowledge, defining vocabulary, understanding texts, and identifying similarities. Each task score is transformed into a standardized score with an average of 10 and a standard deviation of 3, with higher scores indicating better performance in that area. The WAIS-RC scale exhibits a *Cronbach's α* value of 0.750 for internal consistency and a split-half reliability coefficient of 0.779.

Table 2. Comparison of general clinical data between the two groups [($\bar{x}$±s), n (%)]

Clinical data	Control group (n=85)	Observation (EA) group (n=85)	Z/χ^2 value	*P* value
Age (years)	46.18±9.22	46.94±8.55	0.548	0.584
Gender			0.850	0.357
Male	42 (49.41)	48 (56.47)		
Female	43 (50.59)	37 (43.53)		
Smoking history			0.389	0.533
Yes	37 (43.53)	33 (38.82)		
No	48 (56.47)	52 (61.18)		
Chronic disease history				
Hypertension	29 (34.12)	38 (44.71)	1.995	0.158
Diabetes	28 (32.94)	31 (36.47)	0.234	0.629
Types of mental illness				
SP	63 (74.12)	57 (67.06)	1.020	0.313
BD	22 (25.88)	28 (32.94)		
Family history of mental illness			0.684	0.408
Yes	12 (14.12)	16 (18.82)		
No	73 (85.88)	69 (81.18)		
Duration of Mental Illness (year)	4.15±0.48	3.98±0.95	0.658	0.510

Quality control

(1) Strictly adhere to the criteria for including and excluding research participants to minimize potential interference. (2) Form a team to conduct research, including determining research objectives, methods, and content, training and evaluating team members. (3) Researchers personally conduct data screening. Before data input, maintain data accuracy through a double validation process to ensure the accuracy of research results.

Statistical analysis

Statistical analyses were conducted utilizing SPSS 23.0. Measured data were tested for normality using the Kolmogorov-Smirnov method. Data were presented as means ± standard deviation ($\bar{x}$±SD) or n (%). Counted data were compared through the chi-square test. Baseline characteristics and inter group data comparison before intervention were evaluated using paired sample t-tests or Mann-Whitney U test. Finally, within-group comparisons were performed using the paired sample t-tests or Wilcoxon test. Covariance analysis was used for inter group comparison of indicators after intervention. Using R software (R Foundation for Statistical Computing, Vienna, Austria) to execute rms, glmnet and rmda packages, univariate and multivariate logistic regression analysis and Least Absolute Shrinkage and Selection Operator Regression (LASSO) regression analysis were used to identify factors closely associated with patient rehabilitation outcomes. Additionally, a predictive nomogram model was generated using the rms package. Using ms, rmda, and pROC packages, decision curve analysis (DCA), receiver operating characteristic (ROC) curves, and calibration curves were performed to assess accuracy of the predictive nomogram model. Statistical significance was set at P<0.05.

Results

General clinical data comparison

The data of 170 participants were collected, including the control group (85 participants) and the EA group (85 participants). 90 partiicpants were male. Among them, 70 individuals had a history of smoking, 67 had hypertension, 59 had diabetes, 120 had SP, 60 had BD, and 28 reported a family history of mental illness. When comparing the age, gender distribution, and prevalence of chronic diseases between the two groups, no significant differences were found (all P>0.05, **Table 2**).

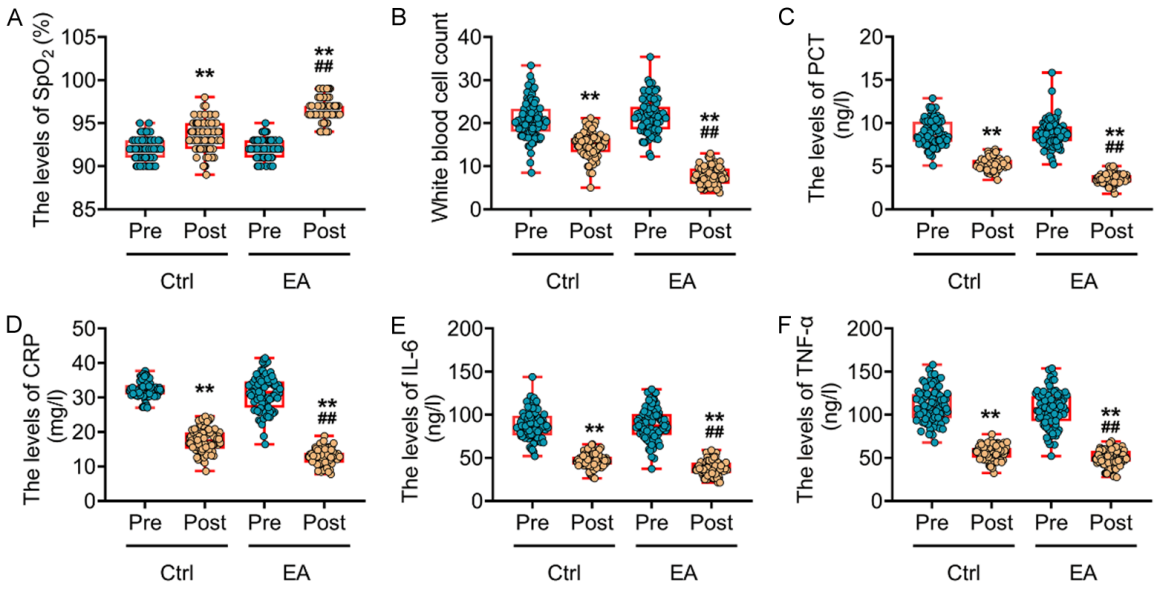

Figure 2. Changes in SpO_2 and inflammatory factors before and after intervention. A. Levels of SpO_2 before and after intervention. B. Levels of WBC count before and after intervention. C. Levels of PCT before and after intervention. D. Levels of CRP before and after intervention. E. Levels of IL-6 before and after intervention. F. Levels of TNF-α before and after intervention. Versus pre-treatment, **P<0.01; Versus post-treatment of the control group, ##P<0.01.

Changes in SpO_2 levels and WBC counts before and after intervention

The initial SpO_2 levels did not show significant differences between the two groups of patients (**Figure 2A**). After treatment, there was a noticeable increase in SpO_2 levels in both groups compared to pre-treatment levels (P<0.05). Using covariance analysis, we found that the SpO_2 levels in the EA group improved significantly more than in the control group after treatment (P<0.05), as shown in **Figure 2A**. Additionally, while there was no initial difference in WBC levels between the two groups of patients (P>0.05), after treatment, patients in both groups experienced a significant decrease in WBC levels. Interestingly, patients in the EA group had a more pronounced decrease than the control group (P<0.05), depicted in **Figure 2B**. These results indicated that incorporating electroacupuncture therapy was more effective in improving the pulmonary function of SP/BD patients with pulmonary infections.

Inflammatory indicators change assessment

To assess the effect of EA on inflammatory reactions in patients, serum inflammatory factors were measured before and after treatment in both groups. Prior to treatment, there were no significant differences in the levels of serum inflammatory factors, including PCT, CRP, PCT, IL-6, and TNF-α between the two groups (all P>0.05, **Figure 2C-F**). After treatment, there was a significant decrease in serum inflammatory factors for all patients, with a notable reduction in the levels of PCT, CRP, PCT, IL-6, and TNF-α observed in the EA group. Additionally, the decline in inflammatory factors in the EA group was greater than in the conventional treatment group (all P<0.05, **Figure 2C-F**). These results suggested that adding EA may reduce the systemic inflammatory response in SP/BD patients with pulmonary infections.

Influence of electroacupuncture on clinical symptoms of patients

We further evaluated the changes in clinical symptoms of patients after EA. No significant differences were observed in any of the outcome measures between the control and EA groups, including expectoration scores, panting scores, cough scores, and gurgling scores of sputum (P>0.05, **Figure 3**). It is noteworthy that from baseline to week 2, significantly lower average scores were observed for expectoration, panting, cough, and gurgling sputum in the EA group than the control group (all P<0.05,

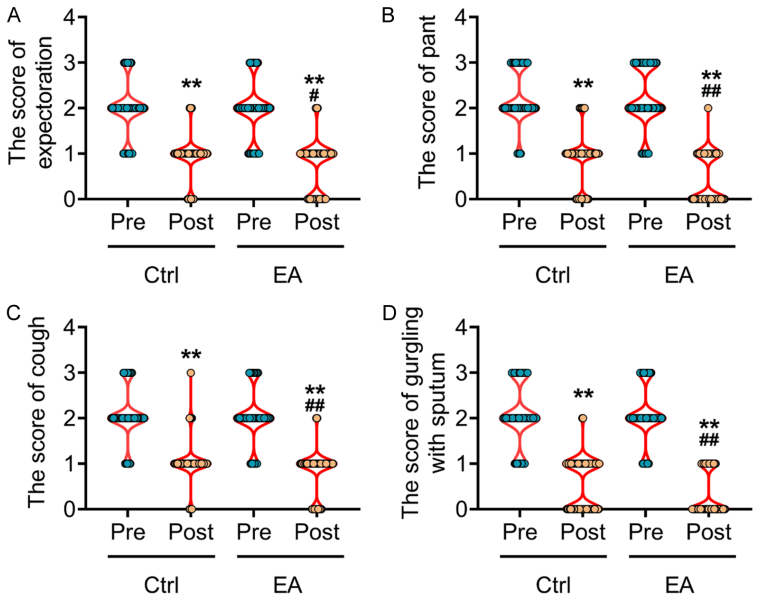

Figure 3. Difference in clinical symptoms between the control group and the EA group. A. Scores of expectoration in the control group and the EA group. B. Scores of pant in the control group and the EA group. C. Scores of cough in the control group and the EA group. D. Gurgling scores of sputum in the control group and the EA group. Versus pre-treatment, **P<0.01; Versus post-treatment of the control group, #P<0.05, ##P<0.01.

Figure 3). EA treatment resulted in a significant reduction in expectoration scores at week 2 compared to conventional treatment (P<0.05, **Figure 3A**). In the EA group, the reduction in pant scores at week 2 was greater than that in the control group (P<0.05, **Figure 3B**). Additionally, a similar trend was observed in cough scores and sputum scores (**Figure 3C**, **3D**). These results showed that adding EA helped reduce respiratory symptoms and manifestations in patients.

Analysis of factors influencing treatment outcome

After two weeks of continuous treatment, recovery outcomes were evaluated based on the patients' clinical symptoms and laboratory test results. The disappearance of symptoms such as cough and sputum, a return to normal body temperature, and a reduction of WBC count, CRP, and PCT to within normal ranges were considered good recovery; other cases were considered poor recovery. Out of the enrolled patients, 129 were classified into the good recovery group, while 41 had poor recovery. A comprehensive assessment of clinical characteristics, inflammation markers, and treatment approaches was conducted for these patients. The results of univariate logistic regression analysis revealed that smoking, diabetes, SpO_2 levels, CRP levels, PCT levels, IL-6 levels, WBC levels, TNF-α levels, and treatment methods affected the recovery outcomes of SP/BD patients with pulmonary infection (all P<0.05, **Figure 4A**). Following the univariate logistic regression analysis, LASSO regression analysis was performed to confirm these variables and prevent gene overfitting (**Figure 4B** and **4C**). Multivariate logistic regression analysis further supported a significant correlation between smoking, diabetes, SpO_2 levels, CRP levels, PCT levels, IL-6 levels, WBC levels, TNF-α levels, treatment method, and clinical outcome in SP/BD patients with pulmonary infection (all P<0.05, **Figure 4D**).

Model construction and efficacy to predict treatment outcome

A nomogram model was developed to predict the recovery of SP/BD patients with pulmonary infection, using smoking, diabetes, SpO_2 levels, CRP levels, PCT levels, IL-6 levels, WBC levels, and TNF-α levels as variables (**Figure 5A**). ROC curve analysis indicated that the nomogram model had an area under the curve (AUC) of 0.991 (95% CI: 0.922-0.976), as shown in **Figure 5B**. Calibration curves demonstrated the nomogram model's reliability by accurately aligning predicted and actual outcomes (**Figure 5C**). Additionally, the DCA in **Figure 5D** consistently outperformed the reference line at various thresholds, emphasizing the clinical utility of the nomogram.

Changes of manic symptoms in both groups after intervention

Using BRMS, we further evaluated whether EA affected manic symptoms in SP/BD patients with pulmonary infections. Although there were similar baseline levels between the two groups, from baseline to week 2, a significant reduction in activity was seen in both observation and control groups (P<0.05). Thedifference

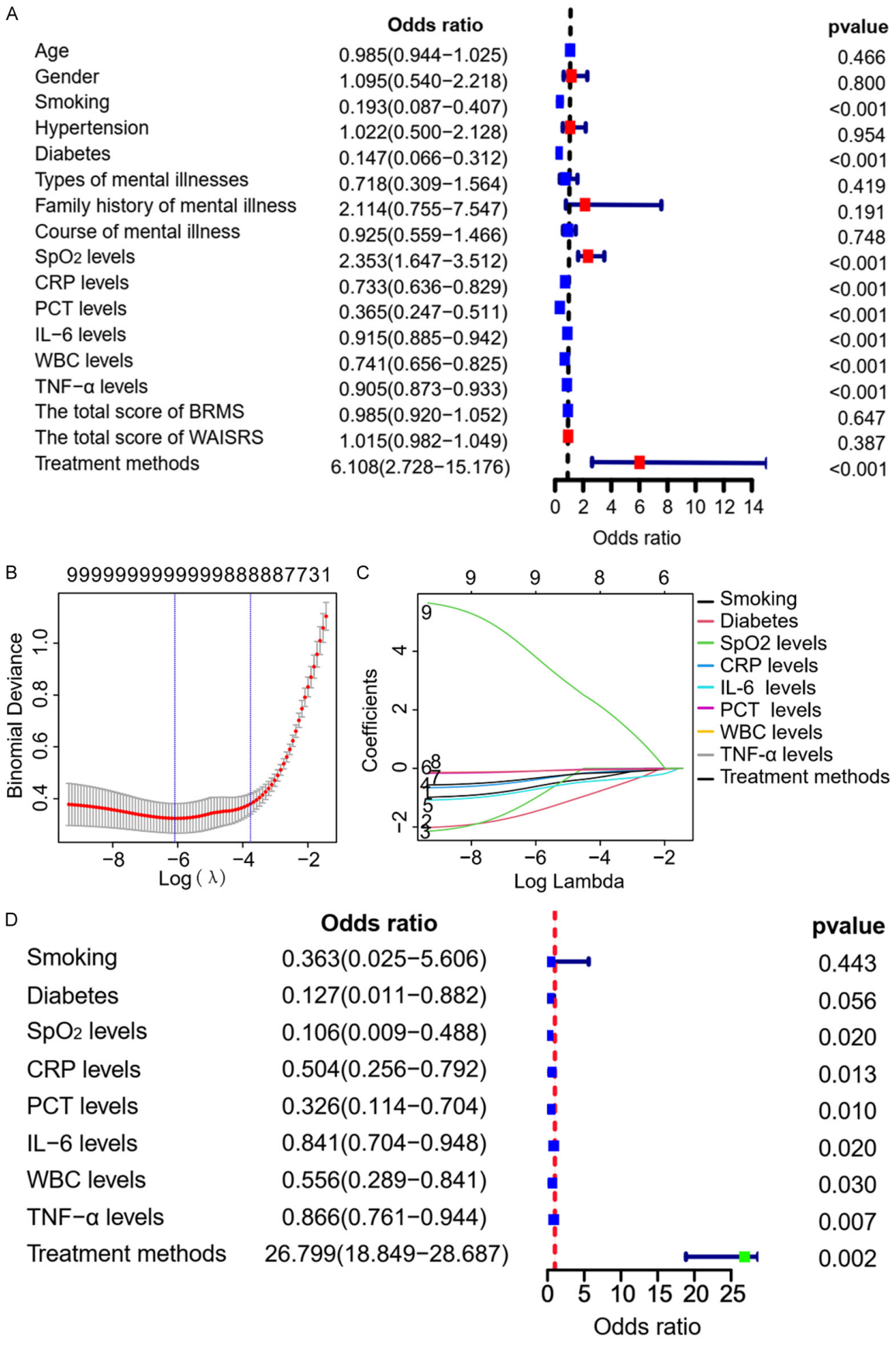
A
Odds ratio
pvalue
Age 0.985(0.944−1.025) 0.466
Gender 1.095(0.540−2.218) 0.800
Smoking 0.193(0.087−0.407) <0.001
Hypertension 1.022(0.500−2.128) 0.954
Diabetes 0.147(0.066−0.312) <0.001
Types of mental illnesses 0.718(0.309−1.564) 0.419
Family history of mental illness 2.114(0.755−7.547) 0.191
Course of mental illness 0.925(0.559−1.466) 0.748
SpO2 levels 2.353(1.647−3.512) <0.001
CRP levels 0.733(0.636−0.829) <0.001
PCT levels 0.365(0.247−0.511) <0.001
IL−6 levels 0.915(0.885−0.942) <0.001
WBC levels 0.741(0.656−0.825) <0.001
TNF−α levels 0.905(0.873−0.933) <0.001
The total score of BRMS 0.985(0.920−1.052) 0.647
The total score of WAISRS 1.015(0.982−1.049) 0.387
Treatment methods 6.108(2.728−15.176) <0.001
0 2 4 6 8 10 12 14
Odds ratio
B
99999999999988887731
Binomial Deviance
0.4 0.6 0.8 1.0
−8 −6 −4 −2
Log (λ)
C
9 9 8 6
Coefficients
−2 0 2 4
Log Lambda
Smoking
Diabetes
SpO2 levels
CRP levels
IL-6 levels
PCT levels
WBC levels
TNF-α levels
Treatment methods
D
Odds ratio
pvalue
Smoking 0.363(0.025−5.606) 0.443
Diabetes 0.127(0.011−0.882) 0.056
SpO2 levels 0.106(0.009−0.488) 0.020
CRP levels 0.504(0.256−0.792) 0.013
PCT levels 0.326(0.114−0.704) 0.010
IL−6 levels 0.841(0.704−0.948) 0.020
WBC levels 0.556(0.289−0.841) 0.030
TNF−α levels 0.866(0.761−0.944) 0.007
Treatment methods 26.799(18.849−28.687) 0.002
0 5 10 15 20 25
Odds ratio

Figure 4. Significant associations with clinical outcomes. A. Univariate logistic regression analyses. B, C. LASSO regression analysis and partial likelihood deviance on the prognostic genes. D. Multivariate logistic regression analyses.

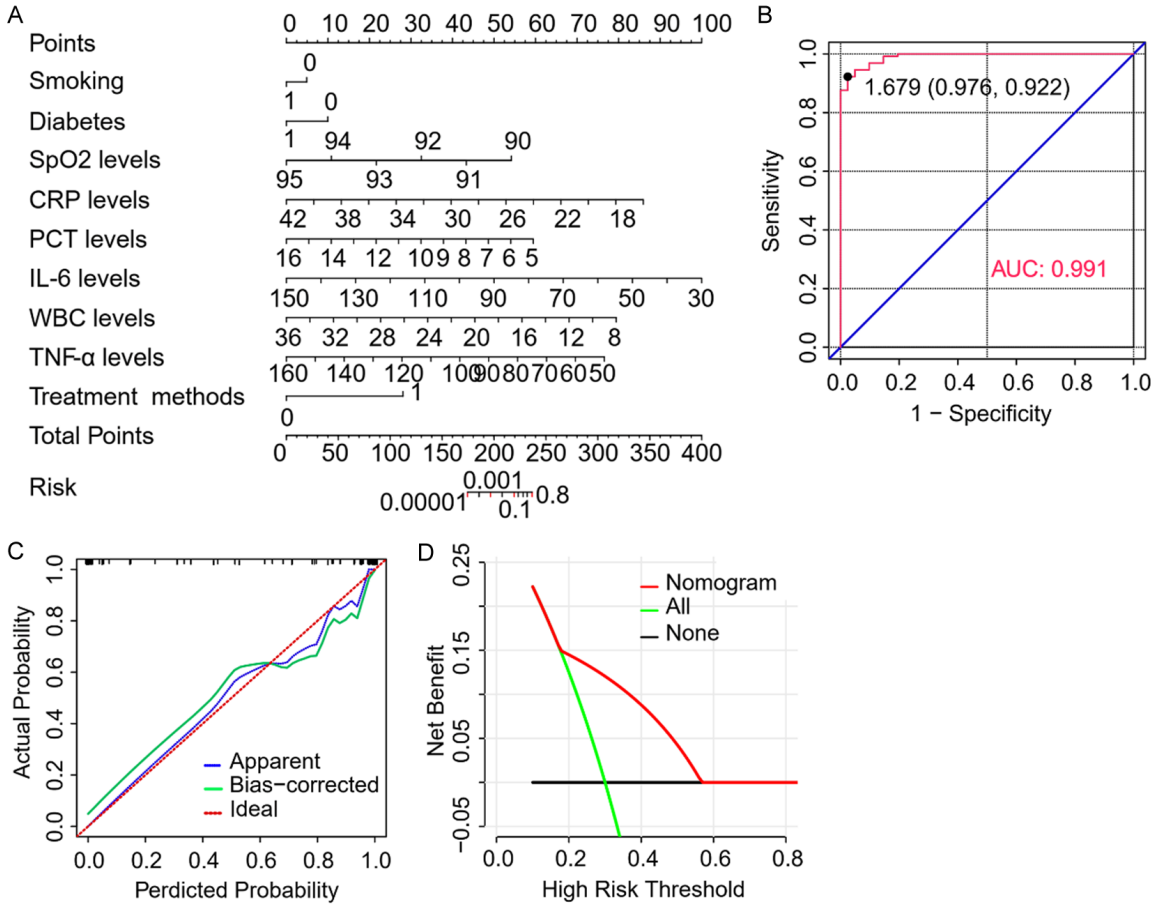

Figure 5. Construction and validation of the nomogram model. A. The nomogram model using clinical features was constructed for predicting outcome of patients with SP/BD and pulmonary infections. B. Receiver operating characteristic analysis for the Nomogram model for predicting the outcome. C. Calibration curves for outcome depict the calibration of nomogram model in terms of the agreement between predicted probabilities and observed outcome. D. Decision curve analysis (DCA) comparing clinical performance of the nomogram model.

between-groups at week 2 was not significant (P>0.05, **Figure 6A**). Considering the similarity of baseline (P>0.05), within-group analyses displayed significant decreases in other scoring entries in two groups, including language, hostility, wrangle, wandering mind, emotion, libido, sleep, self-evaluation, professional, and touch (P<0.05). Nevertheless, there were no significant diffrerences in these scoring entries post-treatment between the two groups (P>0.05), as shown in **Figure 6B-K**. Additionally, there were no significant differences in the total score of BRMS at baseline between the groups (P> 0.05). After finishing treatment, although the total scores of BRMS of the two groups were significantly decreased, EA held no advantage over conventional treatment (P>0.05, **Figure 6L**). These findings implied that adding EA did not confer a significant advantage in ameliorating mania symptoms in SP/BD patients with pulmonary infection, but it is unlikely to impede the efficacy of conventional psychotropic medications.

Evaluation of cognitive function in patients with different interventions

We analyzed operational ability, language proficiency, and WAIS-RC scores to further under-

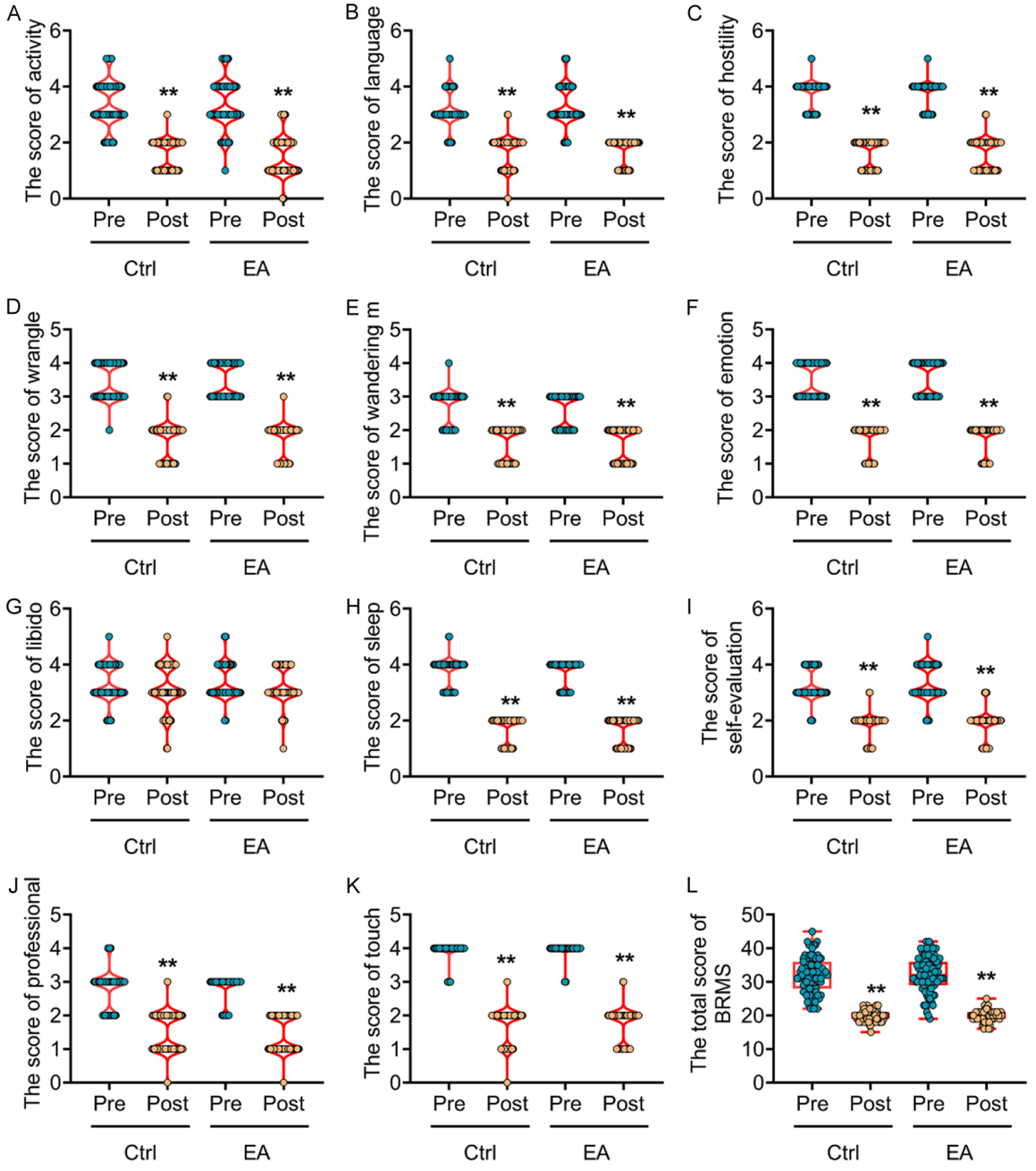

Figure 6. Bech-Rafaelsen Mania Scale (BRMS) scores of patients receiving different interventions. Scores of activity (A), language (B), hostility (C), wrangle (D), wandering mind (E), emotion (F), libido (G), sleep (H), self-evaluation (I), professional (J), and touch (K). (L) Total scores of BRMS. Versus pre-treatment, **P<0.01.

stand the effect of different therapies on cognitive function. For baseline, we observed that operational ability and language proficiency scores were similar between the two groups (P>0.05). After completing treatment, both groups showed improved scores (P<0.05); however, there was no significant difference between the two groups (P>0.05; **Figure 7A** and **7B**). In **Figure 7C**, it was evident that the changes in the total WAIS-RC score reflected those of operational ability and language proficiency. Thus, EA did not affect cognitive function of SP/BD patients with pulmonary infections.

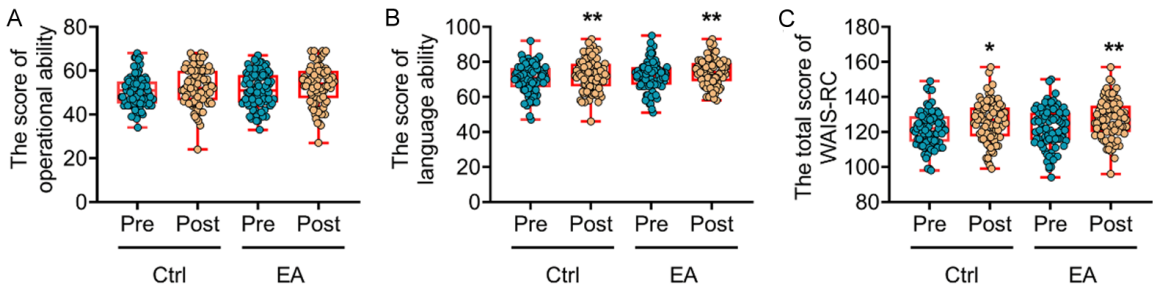

Figure 7. Assessment of cognitive function of patients receiving different interventions. A. Scores of operational ability for patients receiving different interventions. B. Scores of language proficiency for patients receiving different interventions. C. Total scores of the Wechsler Adult Intelligence Scale (WAIS-RC) for patients receiving different interventions. Versus pre-treatment, *P<0.05, **P<0.01.

Discussion

Individuals diagnosed with SP/BD often require long-term medication to maintain stability of their symptoms [24, 25]. Patients with SP/BD frequently suffer from compromised immune function due to extended use of antipsychotic drugs. As a result, these circumstances contribute to a heightened vulnerability to respiratory infections [26-28]. Therefore, it is crucial to explore new approaches with additional therapeutic benefits to enhance the effectiveness of treating patients with SP/BD and concurrent pulmonary infections. This study demonstrated that SP/BD patients receiving electroacupuncture (EA) as supplementary therapy showed higher levels of SpO_2 after treatment compared to before treatment and compared to a control group. In addition, inflammatory markers such as WBC, CRP, PCT, IL-6, and TNF-α were significantly reduced in the EA group. A comprehensive evaluation of treatment outcomes indicated that patients in the EA groupexperienced greater reduction in pulmonary symptoms such as cough and expectoration. Although there were noticeable changes in BRMS and WAIS-RC scores before and after treatment in both groups of patients, post-treatment comparisons did not show a significant difference. Furthermore, logistic regression analysis confirmed that EA improved the recovery outcomes of patients with SP/BD complicated by pulmonary infections.

Previous studies have indicated that long-term use of antipsychotic medications may cause metabolic syndrome, leading to abdominal obesity and affecting the movement of the diaphragm and ventricular diastasis. This ultimately compromises alveolar ventilation and effects the patient's prognosis [29-31]. After two weeks of EA, we found a noticeable increase in SpO_2 levels compared to levels before treatment and to those of the control group. This finding is consistent with results from Jiang's study [15]. The increase in SpO_2 levels provides a foundation for the rehabilitation of SP/BD complicated by pulmonary infection. This improvement may reflect the effectiveness of EA in improving diaphragm function and reducing exercise intolerance. Additionally, our research provides credible evidence that EA had strong effects in lowing WBC levels, which further confirmed its positive effect.

Yuan et al. [32] conducted a systematic evaluation of inflammation-related markers in SP/BD patients, identifying over 30 significantly differing inflammation-related factors in at least one mental disorder when compared to the control group. This underscores the significant involvement of inflammation in the development of these mental disorders. The study conducted by Karimi et al. demonstrated that viral respiratory infections have the ability to trigger the inflammatory pathways of the immune system, affecting the psychological well-being of patients. This highlights the possible connection between inflammation and depression [33]. Although there are currently no reports on acupuncture improving the inflammatory levels in BD or SP patients, a substantial body of research has demonstrated that acupuncture can exert anti-inflammatory effects through multiple pathways of the neuro-endocrine-immune network [34-36]. This research showed that using EA as an additional therapy led to significant improvement in inflammation.

Specifically, levels of inflammatory indicators such as CRP, PCT, IL-6, IL-8, and TNF-α decreased more significantly in the group that received treatment. Additionally, when comparing patients in the treatment group to those in the control group who had similar inflammation levels before intervention, overall expression of the above inflammatory cytokines were notably reduced by addng EA. This is important for promoting the rehabilitation of patients with SP/BD complicated by pulmonary infections. The current from EA will spread to the nearby area and affect the peripheral nerve pulse (i.e. action potential) more strongly. EA produces neuron signals at acupoints and sends them to the spinal cord and brain, which may trigger autonomous regulation of the inflammatory response of target organs, so that the high inflammatory state of patients can be alleviated [37, 38]. These findings imply that the enhanced prognosis seen in patients with SP/BD complicated by pulmonary infection receiving electroacupuncture as an additional therapy may be attributed to the more efficient regulation of inflammatory responses in the body.

Many studies have shown that electroacupuncture can effectively relieve cough, dyspnea, and expectoration in patients with chronic obstructive pulmonary disease or asthma [39, 40]. However, the effect of EA on clinical symptoms in patients with SP/BD complicated by pulmonary infections was limited. In line with these findings [15], we found that adding EA to basic treatment improved expectoration scores, panting scores, cough scores, and sputum scores. Thus, the combination approach with EA helped quickly relieve lung symptoms in patients with lung infections. To assess the benefits of using EA therapy to enhance recovery outcomes for patients with SP/BD complicated by pulmonary infections, our study used univariate and multivariate logistic regression analyses to examine the relationship between EA and clinical outcomes. The results revealed that the predictive nomogram model, which includes “receiving electroacupuncture treatment” among other variables, accurately forecasted positive recovery outcomes for these patients. This further validates the reliability of our findings.

In a retrospective comparative study led by Jia et al., the effectiveness of EA and electroconvulsive therapy as supplementary treatments for inpatients with SP was investigated. The results revealed that both EA and electroconvulsive therapy demonstrated greater efficacy in alleviating positive and negative symptoms in SP patients compared to treatment with antipsychotic drugs alone [17]. Furthermore, a Bayesian network meta-analysis carried out by Zhaohan et al. examined the efficacy of various acupuncture treatments for SP. The results indicated that a holistic approach combining body acupuncture, EA, scalp acupuncture, auricular acupuncture, low-dose medication, and acupuncture point injection and embedding was more beneficial in alleviating symptoms of SP compared to Western approaches alone [41]. Our study found a significant increase in the BRMS and WAIS-RC averages among SP/BD patients receiving EA therapy, indicating improvements in manic symptoms and cognitive function. These improvements may be attributed to the mechanism of EA treatment. The Baihui acupoint, located at the top of the head and part of the Governor Vessel, intersects with points such as Zusanli and the liver meridian during therapy. Baihui is known for its ability to clear heat, unblock orifices, nourish the brain, calm the mind, and alleviate liver-related wind issues. The Yintang acupoint aids in improcing blood circulation, dispelling wind, calming the mind, and promoting mental tranquility. Stimulating these acupoints with an EA instrument enhances cerebral blood flow, providing more oxygen and nutrients to the brain tissue. However, when we compared the scores of individual subscales with those of the control group using t-tests, we did not observe significant differences between the two groups. This discrepancy may be due to notable differences in the characteristics of the SP/BD patients in our study compared to those of previous literature. Specifically, changes in immune response and inflammation levels in patients following pulmonary infection may affect how well psychiatric symptoms improve with pharmacologic or non-pharmacologic interventions, reducing the therapeutic effects of EA on the psychiatric symptoms of these individuals.

This research has some limitations: (1) Since it was a retrospective study, the sample size of patients involved was relatively limited, which may have biased analysis results. Therefore, it is important to interpret the study findings care-

fully; (2) The electroacupuncture adjuvant therapy in this study lasted for two weeks. Further exploration is needed to determine whether there is a recurrence of pulmonary infections after treatment stops; (3) The consistency of clinical efficacy of adjuvant EA among patients with different genders or educational backgrounds requires further detailed examination through stratified analysis.

Conclusion

Our research indicated that adjuvant EA can lead to greater benefits in improving SpO_2 levels, reducing inflammation levels, accelerating recovery, and enhancing the effectiveness of rehabilitation therapy in patients with SP/BD and pulmonary infections. This holistic therapeutic approach could provide new perspectives and strategies for addressing mental health conditions alongside pulmonary infections.

Disclosure of conflict of interest

None.

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References

[1] Olarewaju E, Dumas G and Palaniyappan L. Disorganized communication and social dysfunction in schizophrenia: emerging concepts and methods. Curr Psychiatry Rep 2023; 25: 671-681.

[2] McCutcheon RA, Keefe RSE and McGuire PK. Cognitive impairment in schizophrenia: aetiology, pathophysiology, and treatment. Mol Psychiatry 2023; 28: 1902-1918.

[3] McCutcheon RA, Reis Marques T and Howes OD. Schizophrenia-an overview. JAMA Psychiatry 2020; 77: 201-210.

[4] McIntyre RS, Berk M, Brietzke E, Goldstein BI, López-Jaramillo C, Kessing LV, Malhi GS, Nierenberg AA, Rosenblat JD, Majeed A, Vieta E, Vinberg M, Young AH and Mansur RB. Bipolar disorders. Lancet 2020; 396: 1841-1856.

[5] Tarazi FI, Baldessarini RJ, Kula NS and Zhang K. Long-term effects of olanzapine, risperidone, and quetiapine on ionotropic glutamate receptor types: implications for antipsychotic drug treatment. J Pharmacol Exp Ther 2003; 306: 1145-51.

[6] Morrens M, Overloop C, Coppens V, Loots E, Van Den Noortgate M, Vandenameele S, Leboyer M and De Picker L. The relationship between immune and cognitive dysfunction in mood and psychotic disorder: a systematic review and a meta-analysis. Mol Psychiatry 2022; 27: 3237-3246.

[7] Ermakov EA, Melamud MM, Buneva VN and Ivanova SA. Immune system abnormalities in schizophrenia: an integrative view and translational perspectives. Front Psychiatry 2022; 13: 880568.

[8] Su VY, Hu LY, Yeh CM, Chiang HL, Shen CC, Chou KT, Chen TJ, Lu T, Tzeng CH and Liu CJ. Chronic obstructive pulmonary disease associated with increased risk of bipolar disorder. Chron Respir Dis 2017; 14: 151-160.

[9] Li MS, Hung GC, Yang SY, Pan CH, Liao YT, Tsai SY, Chen CC and Kuo CJ. Excess incidence and risk factors for recurrent pneumonia in bipolar disorder. Psychiatry Clin Neurosci 2018; 72: 337-348.

[10] Kulkarni DP, Kamath VD and Stewart JT. Swallowing disorders in schizophrenia. Dysphagia 2017; 32: 467-471.

[11] Yang Y, Kong D, Li Q, Chen W, Zhao G, Tan X, Huang X, Zhang Z, Feng C, Xu M, Wan Y and Yang M. Non-antipsychotic medicines and modified electroconvulsive therapy are risk factors for hospital-acquired pneumonia in schizophrenia patients. Front Psychiatry 2022; 13: 1071079.

[12] Naruishi K, Nishikawa Y, Kido JI, Fukunaga A and Nagata T. Relationship of aspiration pneumonia to cognitive impairment and oral condition: a cross-sectional study. Clin Oral Investig 2018; 22: 2575-2580.

[13] Zhou Z, Xu G, Huang L, Tian H, Huang F, Liu Y, Sun M and Liang F. Effectiveness and safety of electroacupuncture for depression: a systematic review and meta-analysis. Evid Based Complement Alternat Med 2022; 2022: 4414113.

[14] Wang X, Cai W, Wang Y, Huang S, Zhang Q and Wang F. Is electroacupuncture an effective and safe treatment for poststroke depression? An updated systematic review and meta-analysis. Biomed Res Int 2021; 2021: 8661162.

[15] Jiang A, Wu W, Ma L, Yan M, Zhao Z and Chen Q. Effect of electroacupuncture on the treatment of pneumonia in patients with hypertensive intracerebral hemorrhage. World Neurosurgery 2023; 175: e1124-e1132.

[16] Zhou J, Li L, Qu M, Tan J, Sun G, Luo F, Zhong P and He C. Electroacupuncture pretreatment protects septic rats from acute lung injury by relieving inflammation and regulating macro-

phage polarization. Acupunct Med 2023; 41: 175-182.
[17] Jia J, Shen J, Liu FH, Wong HK, Yang XJ, Wu QJ, Zhang H, Wang HN, Tan QR and Zhang ZJ. Effectiveness of electroacupuncture and electroconvulsive therapy as additional treatment in hospitalized patients with schizophrenia: a retrospective controlled study. Front Psychol 2019; 10: 2306.
[18] Kaal AG, Roos R, de Jong P, Pepping RMC, van den Berg JMW, van Aken MO, Steyerberg EW, Numans ME and van Nieuwkoop C. Oral versus intravenous antibiotic treatment of moderate-to-severe community-acquired pneumonia: a propensity score matched study. Sci Rep 2024; 14: 8271.
[19] First MB. Diagnostic and statistical manual of mental disorders, 5th edition, and clinical utility. J Nerv Ment Dis 2013; 201: 727-9.
[20] Brämer GR. International statistical classification of diseases and related health problems. Tenth revision. World Health Stat Q 1988; 41: 32-6.
[21] Cao B, Huang Y, She DY, Cheng QJ, Fan H, Tian XL, Xu JF, Zhang J, Chen Y, Shen N, Wang H, Jiang M, Zhang XY, Shi Y, He B, He LX, Liu YN and Qu JM. Diagnosis and treatment of community-acquired pneumonia in adults: 2016 clinical practice guidelines by the Chinese Thoracic Society, Chinese Medical Association. Clin Respir J 2018; 12: 1320-1360.
[22] Bech P. The bech-rafaelsen mania scale in clinical trials of therapies for bipolar disorder: a 20-year review of its use as an outcome measure. CNS Drugs 2002; 16: 47-63.
[23] Hartman DE. Wechsler adult intelligence scale IV (WAIS IV): return of the gold standard. Appl Neuropsychol 2009; 16: 85-7.
[24] Correll CU, Martin A, Patel C, Benson C, Goulding R, Kern-Sliwa J, Joshi K, Schiller E and Kim E. Systematic literature review of schizophrenia clinical practice guidelines on acute and maintenance management with antipsychotics. Schizophrenia (Heidelb) 2022; 8: 5.
[25] Yildiz M. Psychosocial rehabilitation interventions in the treatment of schizophrenia and bipolar disorder. Noro Psikiyatr Ars 2021; 58 Suppl 1: S77-S82.
[26] Tew GA, Bailey L, Beeken RJ, Cooper C, Copeland R, Brady S, Heron P, Hill A, Lee E, Spanakis P, Stubbs B, Traviss-Turner G, Walker L, Walters S, Gilbody S and Peckham E. Physical activity in adults with schizophrenia and bipolar disorder: a large cross-sectional survey exploring patterns, preferences, barriers, and motivating factors. Int J Environ Res Public Health 2023; 20: 2548.
[27] Vancampfort D, Firth J, Schuch FB, Rosenbaum S, Mugisha J, Hallgren M, Probst M, Ward PB, Gaughran F, De Hert M, Carvalho AF and Stubbs B. Sedentary behavior and physical activity levels in people with schizophrenia, bipolar disorder and major depressive disorder: a global systematic review and meta-analysis. World Psychiatry 2017; 16: 308-315.
[28] Velelekou A, Papathanasiou IV, Alikari V, Papagiannis D, Tsaras K and Fradelos EC. Factors influencing the duration of hospitalization of patients with schizophrenia. Med Pharm Rep 2022; 95: 290-299.
[29] Ye W, Xing J, Yu Z, Hu X and Zhao Y. Mechanism and treatments of antipsychotic-induced weight gain. Int J Obes (Lond) 2023; 47: 423-433.
[30] Mazereel V, Detraux J, Vancampfort D, van Winkel R and De Hert M. Impact of psychotropic medication effects on obesity and the metabolic syndrome in people with serious mental Illness. Front Endocrinol (Lausanne) 2020; 11: 573479.
[31] Pillinger T, McCutcheon RA, Vano L, Mizuno Y, Arumuham A, Hindley G, Beck K, Natesan S, Efthimiou O, Cipriani A and Howes OD. Comparative effects of 18 antipsychotics on metabolic function in patients with schizophrenia, predictors of metabolic dysregulation, and association with psychopathology: a systematic review and network meta-analysis. Lancet Psychiatry 2020; 7: 64-77.
[32] Yuan N, Chen Y, Xia Y, Dai J and Liu C. Inflammation-related biomarkers in major psychiatric disorders: a cross-disorder assessment of reproducibility and specificity in 43 meta-analyses. Transl Psychiatry 2019; 9: 233.
[33] Karimi Z, Chenari M, Rezaie F, Karimi S, Parhizgari N and Mokhtari-Azad T. Proposed pathway linking respiratory infections with depression. Clin Psychopharmacol Neurosci 2022; 20: 199-210.
[34] Li N, Guo Y, Gong Y, Zhang Y, Fan W, Yao K, Chen Z, Dou B, Lin X, Chen B, Chen Z, Xu Z and Lyu Z. The anti-inflammatory actions and mechanisms of acupuncture from acupoint to target organs via neuro-immune regulation. J Inflamm Res 2021; 14: 7191-7224.
[35] Cui J, Song W, Jin Y, Xu H, Fan K, Lin D, Hao Z and Lin J. Research progress on the mechanism of the acupuncture regulating neuro-endocrine-immune network system. Vet Sci 2021; 8: 149.
[36] Li HL, Zhang Y and Zhou JW. Acupuncture for radicular pain: a review of analgesic mechanism. Front Mol Neurosci 2024; 17: 1332876.
[37] Park JY and Namgung U. Electroacupuncture therapy in inflammation regulation: current perspectives. J Inflamm Res 2018; 11: 227-237.

[38] Liu F, Wang Y, Lyu K, Du X, Zhou M, Shi J, Na R, Guo Y, Wang G and Xu W. Acupuncture and its ability to restore and maintain immune homeostasis. QJM 2024; 117: 167-176.
[39] Chen YM, Xie XL, Xiao PY, Wang QH, Wang JS, Yu XD and Deng S. Acupuncture on treating asthma: a protocol for systematic review and meta analysis. Medicine (Baltimore) 2020; 99: e18457.
[40] Tsai CL, Lan CC, Wu CW, Wu YC, Kuo CY, Tzeng IS, Hsu PS, Lee CT and Hsieh PC. Acupuncture point stimulation treatments combined with conventional treatment in chronic obstructive pulmonary disease: a systematic review and network meta-analysis. Front Med (Lausanne) 2021; 8: 586900.
[41] Zhaohan H, Yuan F, Xiaolu W, Yue H, Qi YU and Tong W. Effectiveness of acupuncture-related therapies on schizophrenia: a bayesian network meta-analysis. J Tradit Chin Med 2023; 43: 239-251.