doi.org/10.36721/PJPS.2025.38.5.REG.13925.1

Clinical efficacy and safety of repetitive transcranial magnetic stimulation (RTMS) in combination with antipsychotic medications in patients with schizophrenia

Jiahui Yin[1], Bojian Dai[1], Ruru Chen[1], Lingyi Dai[1] and Lixue Qiu[2]*

[1]Department of General Psychiatry, the Seventh People's Hospital of Wenzhou, China
[2]Department of Geriatric Psychiatry, the Seventh People's Hospital of Wenzhou, China

Abstract: The global prevalence of schizophrenia is about 0.40% and in some parts of my country it is 0.54%-0.94%. Its treatment faces many difficulties. Antipsychotic drugs are commonly used treatments, but they have many side effects; repetitive transcranial magnetic stimulation (rTMS), as a non-invasive physical therapy, has a certain effect in improving mental and living abilities. This study used a randomized controlled trial to divide 100 patients into an experimental group (rTMS + drugs) and a control group (drugs only) and evaluated them with multiple scales. The relapse rate during the 24-month follow-up period was compared to evaluate rehabilitation and economic value. The results showed that the experimental group had lower Positive and Negative Syndrome Scale (PANSS), higher efficacy and lower relapse rates after treatment; both groups had improved quality of life and cognitive function-related indicators and the experimental group was more significant; the experimental group had higher Wisconsin Card Sorting Test (WCST) scores and better economic benefits; there were no serious adverse events in both groups. In summary, rTMS combined with antipsychotic drugs has good efficacy and safety in the treatment of schizophrenia, can improve patients' quality of life and economic benefits and provide a better choice for clinical treatment.

Keywords: Schizophrenia, antipsychotics, efficacy, repetitive transcranial magnetic stimulation, safety

Submitted on 23-12-2024 – Revised on 02-05-2025– Accepted on 09-05-2025

INTRODUCTION

Schizophrenia (SP) is occurrence and development are closely related to dopamine receptor dysfunction, but the exact mechanism remains unclear (Goff DC, 2021). According to WHO statistics, the global prevalence of SP is 0.40%, including 0.42% and 0.38% in developed and developing countries, respectively. In surveys in some areas of China, the prevalence of schizophrenia is between 0.54% and 0.94% (Mccutcheon RA and Reis Marques T, 2020, Brandt SJ *et al*., 2021). In recent years, people have a more in-depth understanding of the cognitive dysfunction of schizophrenia patients, the damage of cognitive function often involves many aspects, of which attention, memory and executive function are the most important three aspects, at the same time, the patient's speech function, abstract thinking and sensory processing will also appear the corresponding damage (Haiyu C *et al*., 2025). Cognitive impairment is one of the most important clinical manifestations of schizophrenia, which is an important index to evaluate the therapeutic effect, measure the degree of rehabilitation and predict the prognosis (Caicai S *et al*., 2025). The improvement of the patient's cognitive function can effectively improve the patient's long-term quality of life, social work and mobility (Haiyuan W *et al*., 2024). Regarding the research on drug treatment of schizophrenia, many countries (regions) in Asia have conducted large-scale cross-sectional surveys on first- and second-generation antipsychotics. Among them, first-generation antipsychotics accounted for 31.3%, second-generation antipsychotics accounted for 42.6%, third-generation antidepressants accounted for 11.7%, fourth-generation benzodiazepines accounted for 13.7% and fourth-generation anticholinergics accounted for 45.6% (Kahl M *et al*., 2020). After drug treatment, there will be a variety of adverse reactions, such as extrapyramidal reaction, sedentary, late-onset dyskinesia, metabolic abnormalities and weight gain. However, male and female patients differ in this respect (Gongquan L *et al*., 2025). Whether it is developing countries such as Uganda and Vietnam, or developed countries such as France and Australia, no matter what the situation, the government will give priority to low-cost drugs, even if these drugs have a large side effect and will not choose a new generation of sedatives (Nobuyuki N *et al*., 2025).

rTMS is a method of multi-level conduction of the brain using pulse stimulation, which can significantly improve the mental state of patients, improve the ability of patients to live and reduce the recurrence rate of patients (Suzhen Y *et al*., 2025). In recent years, it has been widely used as a non-invasive physical therapy method and a series of studies have been carried out in the world and some experts have reached a consensus (Mamidipalli Sai S *et al*., 2024). There seems to be an abnormal cortical inhibition in schizophrenia, which is consistent with the transmitter abnormalities found in studies of GABA and dopamine (Bingqian L *et al*., 2024). Although the cortical response to

**Corresponding author:* e-mail: docter365day@126.com

rTMS is different in schizophrenia patients, rTMS can improve this inhibition by affecting GABA and dopamine neurotransmission. Thus, it plays a positive role in the improvement of patients' symptoms. Yang C *et al*. (Yang C *et al*., 2021) have shown that the improvement of cognition is mainly the impairment of working memory, which may be related to the partial recovery of dorsolateral prefrontal cortex dysfunction.

Schizophrenia (SP) is a common clinical disease mainly in young adults and its incidence is increasing year by year (Zhenjiang G, 2025). Clinical diagnosis and treatment has become a major health problem that needs to be solved urgently. The occurrence of schizophrenia (SP) is closely related to genetics, psychological and social environment and nutritional status. It is a complex disease and there is still a lack of effective treatment. The disease has the characteristics of repeated attacks and long-term uninterrupted, which has caused a heavy economic burden to the family and society and seriously affected the daily life of patients. Therefore, it is important to find a drug that is both effective and can bring more financial benefits to patients. Therefore, we intend to combine rTMS with traditional drug therapy and traditional rTMS to explore its efficacy, health and economic significance and safety and open up new ideas for its clinical treatment.

MATERIALS AND METHODS

Research design

This study adopts a randomized controlled trial design to clearly compare the effects of antipsychotic drugs alone and in combination with repetitive transcranial magnetic stimulation (rTMS) in the treatment of schizophrenia. 100 eligible patients with schizophrenia were screened from hospitalized patients from July 1, 2019 to June 30, 2021 and were divided into an experimental group and a control group using a random number table method, with 50 cases in each group. The control group was treated with antipsychotic drugs alone, using the drugs in accordance with the drug instructions and taking corresponding symptomatic treatment. The experimental group was treated with rTMS in combination with antipsychotic drugs. During the treatment period, the patients were evaluated using multiple scales such as the PANSS score sheet and the Schizophrenia Quality of Life Scale (SQLS-R4) before and 1, 4 and 8 weeks after treatment to fully understand the improvement of patients' symptoms and changes in quality of life. During the 24-month follow-up period, the relapse rate of the two groups of patients was compared. In addition, the rehabilitation benefits and economic value of the two groups of patients were evaluated in depth by integrating the scores of the Personal and Social Function Scale (PSP), the Family Burden Scale (FBS) and labor value, cost and other data and then the advantages and disadvantages of the two treatment plans were comprehensively and objectively evaluated.

Inclusion and exclusion criteria

Inclusion criteria

In order to ensure the homogeneity of the research subjects and the reliability of the research results, this study set strict inclusion criteria. Patients must meet the professional diagnostic criteria for schizophrenia and have the ability to accept cognitive ability tests in order to accurately evaluate the impact of treatment on cognitive function. At the same time, patients are required to be accompanied by independent guardians after discharge and be able to cooperate with the 2-year follow-up. In terms of the course of the disease, it is stipulated that it should not exceed 60 months; when visiting the doctor, the patient did not take antipsychotic drugs or took them for no more than 14 days to reduce drug interference factors. In addition, the PANSS score is above 60 points to ensure that the patient's symptoms reach a certain severity and it is easier to observe the treatment effect.

Exclusion criteria

Patients who may affect the accuracy of the research results or increase the risk of the research will be excluded. Data collection may be biased for patients who are unable to fill out the scale by themselves due to mental retardation; patients with strong violent and suicidal behaviors have higher safety risks during treatment; pregnant and lactating women have special physiological conditions that may affect drug metabolism and treatment effects; patients with malignant tumors or other serious illnesses have complex conditions that may interfere with the judgment of the treatment effect of schizophrenia; patients with poor drug compliance and unwillingness to cooperate are difficult to ensure the smooth implementation of the treatment plan; patients whose medication plans are too different from other patients will increase the heterogeneity of the data and these patients are excluded from the study.

Sample size calculation

In this study, the determination of the sample size has been rigorously considered. Referring to many similar studies on the treatment effect of schizophrenia, we focus on the changes in PANSS. By analyzing previous research data, it is estimated that there will be a clinically significant difference in the mean PANSS between the experimental group and the control group after treatment and this difference is set to 5 points. At the same time, combined with the fluctuation of PANSS in previous studies, the standard deviation is determined to be 6 points.

We use the sample size calculation formula for comparing two sample means to determine the sample size, which is: The sample size required for each group $n = 2\times[(\text{two-sided quantile } Z(1-\alpha/2) \text{ of the standard normal distribution} + \text{one-sided quantile } Z(1-\beta) \text{ of the standard normal distribution})^2\times \text{standard deviation } \sigma^2]\div(\text{expected difference between the two group means } \delta^2)$

In this formula, the two-sided test level is set to $\alpha = 0.05$ and the corresponding two-sided quantile $Z(1-\alpha/2)$ of the

standard normal distribution is 1.96; the test power is 1-β = 0.8 and the one-sided quantile Z(1-β) of the standard normal distribution is 0.84. Substituting these data into the formula, it is found that approximately 47 samples are required for each group.

However, considering that the follow-up period of schizophrenia patients is long and there may be loss of follow-up during the period, in order to ensure the reliability of the research results, we estimated the loss of follow-up rate according to 10% and finally determined to include 50 patients in each group, with a total of 100 patients in the two groups.

Ethical approval

This study attaches great importance to ethical standards and has been approved by the Ethics Committee of Wenzhou Seventh People's Hospital (NO.: 20210427).

Methods of treatment

In this study, the treatment plans of the control group and the experimental group were rigorously designed, taking into full account the standardization, pertinence and innovation of drug treatment and aiming to accurately evaluate the differences in the efficacy of different treatment methods for patients with schizophrenia.

The control group was treated with classic antipsychotics and atypical antipsychotics according to the clinical treatment guidelines of psychiatry. The specific drugs and dosages are as follows:

Chlorpromazine

For patients with milder illness, first onset, younger age and lighter weight, the starting dose is set at 200 mg/d, taken orally in 2-3 times. During the treatment, the dose is adjusted weekly according to the patient's symptom relief and adverse drug reactions, with each adjustment of 50 mg/d. If the patient has good tolerance and the symptoms are not significantly improved, the dose can be gradually increased to 600 mg/d; if the patient has obvious adverse reactions, such as severe extrapyramidal reactions, excessive sedation, etc., the dose should be appropriately reduced.

Sulpiride

For patients with mainly negative symptoms, the starting dose of sulpiride is 300 mg/d, taken orally in 3 times. Evaluate the patient's condition every 3-5 days. If the treatment effect is not good and there are no obvious adverse reactions, the dose can be gradually increased to a maximum of 1000mg/d.

Perphenazine

The usual starting dose is 8mg/d, taken in 2 divided doses. According to the changes in the patient's symptoms, adjust the dose every 5-7 days, increase by 4mg/d each time and the general therapeutic dose range is 16-32mg/d.

Haloperidol

For patients with obvious excitement and agitation, the starting dose of haloperidol is 4mg/d, which can be increased by 2mg/d every day according to the patient's tolerance and symptom control. The commonly used therapeutic dose is 6-15mg/d.

Clozapine

In view of the fact that clozapine may cause more serious adverse reactions, such as agranulocytosis, the starting dose is set at 50mg/d, taken at bedtime. Increase by 25mg/d every 3-5 days and gradually increase to the therapeutic dose. The general effective therapeutic dose is 300-500mg/d. During treatment, the patient's blood routine, liver and kidney function and other indicators need to be closely monitored.

Olanzapine

The starting dose is 5mg/d, taken orally once a day. According to the patient's condition and tolerance, increase 2.5-5mg/d every week and the commonly used therapeutic dose is 10-20mg/d.

Aripiprazole

The starting dose is 10mg/d, taken orally once a day. If the patient tolerates the drug well, the dose can be increased to 15mg/d after 2-3 weeks. Some patients may need to further increase the dose to 30mg/d to achieve better therapeutic effects.

Risperidone

For first-episode patients, the starting dose of risperidone is 1mg/d, taken in 2 divided doses. Increase 0.5mg/d every 3-4 days and the therapeutic dose is generally 2-6mg/d.

Quetiapine

The starting dose is 100mg/d, taken orally in 2 divided doses. Increase 100mg/d every 2-3 days and the effective therapeutic dose is usually 300-750mg/d.

At the same time, corresponding symptomatic treatment is carried out for various symptoms that patients experience during treatment, such as anxiety, insomnia, water and electrolyte disorders, malnutrition, etc. For example, benzodiazepines (such as clonazepam, alprazolam, etc.) are used to relieve anxiety and insomnia symptoms; water and electrolyte balance is maintained through intravenous rehydration; nutritional support therapy is given to patients with malnutrition, etc. The medication time of both groups of patients strictly follows the routine treatment course of schizophrenia to ensure the comparability of the research results.

The experimental group received antipsychotic drug treatment (the type of drug, dosage and course of treatment were the same as those of the control group) and combined with repetitive transcranial magnetic stimulation (rTMS) for intervention. The British Magstimrapid 2 magnetic

stimulator was selected for rTMS treatment. This device is widely used in the treatment of clinical mental illness and has stable performance. The stimulation position is precisely located in the left dorsal prefrontal cortex, a brain area that is closely related to cognitive function, emotion regulation and positive and negative symptoms in patients with schizophrenia. The stimulation intensity is set at 85% of the motor threshold, which can not only ensure that the stimulation has an effective effect on brain neural activity, but also minimize the patient's discomfort and risk of adverse reactions. The stimulation frequency is 10Hz, which has been shown in previous studies to have a good effect on improving the negative symptoms and cognitive function of patients with schizophrenia. Each treatment is performed 30 times, each shock contains 50 pulses and the pulse interval is 30 seconds. One treatment is performed per day, 5 consecutive days per week and a total of 4 weeks of treatment. During the treatment, the patient's response is closely observed, such as whether there are adverse reactions such as headache, dizziness and local skin discomfort, so as to adjust the treatment plan in time or give corresponding treatment to ensure the safety and effectiveness of the treatment.

Assessment of efficacy

The patient's condition was evaluated by PANSS (Songping Z *et al*.,2025), which includes three dimensions of negative, positive and general psychopathology, a total of 30 dimensions, 1-7 is "no symptoms" to "extreme symptoms", the higher the score, the more severe the symptoms. Measurements were made at different time points before treatment and 1, 4, 8 weeks after treatment.

According to the PANSS score reduction rate, the treatment effect was judged: ＞75% for complete cure, 50%-75% for significant improvement, 25%-49% for progress, ＜25% were ineffective. Recurrence rate comparison: After 24 months of follow-up, the recurrence rate was compared with the situation at the end of follow-up. A relapse was considered if any of the following occurred: 1) rehospitalization due to worsening psychiatric symptoms; ② PANSS evaluation scale hallucination, suspicion, abnormal thinking, association, any item more than 5 points, or more than 4 points, PANSS total score more than 60 points.

The Schizophrenia Quality of Life Scale (SQLS-R4) was used to evaluate the quality of life of patients, including 33 questions, each question is represented by 0-4 points: never, rarely, sometimes, often, always, the score needs to be converted to 0-100 points, the higher the score, the higher the quality of life. Measurements were made at different time points before treatment and 1, 4, 8 weeks after treatment.

Personal and social Performance Scale (PSP) and Family Burden Scale of Disease (FBS) scores were carried out for patients (Gong J *et al*.,2020), which were combined with PANSS score, SQLS-R4 score and labor value to evaluate the total rehabilitation benefits and economic value of patients. The specific calculation was related to relevant literature. The difference with other methods is that this paper sets the cost of each recurrence to 12,000 yuan according to the actual local cost (Xingmei D *et al*., 2024). Benefit-cost ratios were used to assess the health economic value of patients at 6,12,18 and 24 months after treatment.

STATISTICAL ANALYSIS

SPSS22.0 software was used to analyze the data. Count data were analyzed by t test. $P<0.05$ was considered as significant difference between the two groups.

RESULTS

The PANSS scale was compared between the two groups

Before treatment, there were no significant differences in PANSS between the two groups ($P>0.05$). After 1, 4 and 8 weeks, the treatment group showed significantly lower general psychopathology scores ($P<0.05$) and after 4 and 8 weeks, the positive and negative symptom scores were also significantly lower ($P<0.05$). See table 1.

Comparison of treatment effects in patients

The total effective rate was 92.0% in the treatment group and 68.0% in the control group ($P<0.05$). After 2 years of follow-up, the recurrence rate was 32.0% in the experimental group and 54.0% in the control group, with a significant difference ($P<0.05$). See table 2.

Comparison of PANSS total scores between the two groups during the follow-up period

The PANSS total score of the experimental group was significantly lower than that of the control group at 6 months, 12 months, 18 months and 24 months after discharge ($P< 0.05$). As shown in table 3.

Comparative analysis of patients' quality of life

Before treatment, no significant differences were found between the groups ($P>0.05$). After 1 and 4 weeks, there were no significant differences. After 8 weeks, all parameters in the treatment group were significantly reduced ($P<0.05$). See table 4.

Value versus cost of patient labor

At 6, 12, 18 and 24 months, the treatment group had significantly higher cumulative labor value and lower costs than the control group (P<0.05). See table 5.

Cost-effectiveness ratio for patients

At 6, 12, 18 and 24 months post-discharge, the experimental group had higher income, better benefit-cost ratio and lower costs than the control group ($P<0.05$). See table 6.

Comparison of CT and WMS-RC

Before treatment, there were no significant differences in CT and WMS-RC scores between the two groups ($P>0.05$), while after treatment, both groups showed improvements in CT net score, error rate reduction, WMS-RC total score and memory quotient ($P<0.01$). After treatment, the CT net score, error rate, WMS-RC total score, memory quotient and other indicators of the two groups were significantly improved ($P<0.05$) table 7.

Comparison of WCST scores

Before treatment, there were no significant differences in WCST scores ($P>0.05$). After treatment, both groups showed reduced errors and responses ($P<0.01$), with the experimental group also showing improved correct responses and completed categories ($P<0.05$). The experimental group had a significant reduction in errors and responses ($P<0.05$ and $P<0.01$) table 8.

Side effects

There were no significant changes in blood and urine routine, blood biochemistry, blood glucose and electrocardiogram after treatment. During the treatment, one patient in the experimental group experienced headache and one patient experienced dizziness. These patients said they could tolerate them and no special treatment was given. After resting, the patients were able to relieve themselves and continue with the treatment. No other significant adverse reactions occurred.

DISCUSSION

For patients with newly diagnosed schizophrenia, if they have not received relevant treatment before and have not developed resistance to antipsychotic drugs, drug treatment is usually the first choice. In actual clinical practice, most patients will take typical or atypical antipsychotic drugs in sufficient doses and for a sufficient course of treatment. After a period of treatment, when the patient's condition tends to stabilize, the doctor will adjust the dosage of the medication and give a relatively stable maintenance dose to consolidate the treatment effect and prevent relapse.

Studies have shown that 80-90% of patients with schizophrenia have severe cognitive impairment; therefore, improving patients' cognitive ability and improving their positive and negative symptoms have become important targets for their treatment (Zhao SW *et al*., 2021). Due to the unique mechanism of action of rTMS, single drug can improve the clinical symptoms of patients, therefore, the combination of drugs to improve the cognitive function of patients, improve the self-care ability, reduce the recurrence rate and other aspects of the role will be more significant. This project intends to use the method of combining antipsychotic drugs and rTMS to further clarify the effect of the combination of the two and to further improve the health and economic interests of patients.

The alternating electromagnetic energy of rTMS directly enters the deep tissue of the brain and generates an alternating electric wave. The direct action of the electric wave on brain cells can improve the permeability of cells and facilitate the transfer of neurotransmitters and other substances in the intracellular and extracellular. It can promote local microcirculation of cerebral blood vessels, improve local blood and oxygen supply and promote the recovery of nerve function. Our previous study found that rTMS could enhance the gamma resonance activity in the brain, which is a key trigger mechanism for higher cognitive functions such as memory and logical thinking. Cui LB *et al*. (Cui LB *et al*., 2021) In animal experiments, we found that rTMS could improve the secretion of dopamine and glutamate in the frontal brain region, thereby improving the negative symptoms of patients.

Therefore, we plan to use chlorpromazine, sulpiride, perphenazine, haloperidol, clozapine, olanzapine, aripiprazole, risperidone and quetiapine in combination with rTMS to treat schizophrenia in clinical practice and comprehensively evaluate their clinical efficacy in terms of patient symptom improvement, changes in cognitive function, relapse rate, improvement in quality of life and health economic indicators. Previous studies by our research group have found that the combination of antipsychotic drugs and rTMS can significantly improve the clinical symptoms of patients with schizophrenia, with significant improvements in positive symptoms, negative symptoms and general psychopathological symptoms.

The efficacy of this combined treatment is significantly better than that of antipsychotic drugs alone. During the follow-up period, the PANSS total score of the experimental group was significantly lower than that of the control group. This result is of great significance. It not only confirms the advantage of combined rTMS and antipsychotic drug treatment in improving patients' clinical psychological symptoms, but also provides a strong basis for the optimization of clinical treatment plans. Cognitive impairment is common in patients with schizophrenia and the treatment compliance is poor due to the extrapyramidal reaction and obesity caused by drug therapy, which makes it difficult to standardize the implementation of treatment regimens, thus affecting the efficacy of drug therapy.

One of the main effects of rTMS is to improve the patient's cognitive ability, thereby improving the patient's medication compliance, which indirectly enhances the patient's efficacy against the disease. In the comparison of quality of life, the improvement of the medical group was significantly better than that of the control group, indicating that rTMS can improve the living ability of patients with schizophrenia, which is consistent with the research results of Dollfus *et al*. (Gong J *et al*, 2020).

Table 1: PANSS of the two groups of patients ($\bar{x}\pm s$)

The project	Groups	n	Before treatment	The treatment lasted for 1 week	Treatment for 4 weeks	Treatment for 8 weeks
Positive symptoms	Experimental group	50	22.7±3.8	19.2 ±2.6	15.0±2.6	12.5±2.4
	Control group	50	23.4±3.1	20.0 ±2.8	17.1±3.0	14.6±2.1
P			0.182	0.095	<0.05	<0.05
Negative symptoms	Experimental group	50	21.1±4.2	18.2±3.1	14.0±3.0	13.1±2.7
	Control group	50	20.4±4.0	18.8±3.4	16.2±2.8	14.6±3.1
P			0.221	0.201	<0.05	<0.05
General psychopathology score	Experimental group	50	43.4±6.8	39.1 ±5.6	32.4 ±5.1	24.8±5.0
	Control group	50	44.1±7.0	41.5±6.0	35.8 ±4.2	28,2±4.5
P			0.322	<0.05	<0.05	<0.05

Table 2: Response rate and recurrence rate in the two groups (n, %)

Groups	n	Recovery from illness	Remarkable progress	progress	Void of effect	Total effective rate	Relapse
Experimental group	50	27	11	8	4	46(92.0)	16(32.0)
Control group	50	18	10	6	16	34(68.0)	27(54.0)
x^2						6.643	4.553
P						0.010	0.033

Table 3: Total PANSS scores in the two groups during the follow-up period ($\bar{x}\pm s$)

Groups	n	Discharge from hospital 6 months	Discharge from hospital 12 months	Discharge from hospital 18 months	Discharge from hospital 24 months
Experimental group	50	36.1±4.6	37.2 ±5.5	39.4±7.0	41.0±8.1
Control group	50	39.0±5.8	42.7±8.1	48.5±8.6	48.4±9.5
t		2.484	3.564	5.241	3.795
P		0.006	0.000	0.000	0.000

Table 4: Comparison of SQLS-R4 scores between the two groups ($\bar{x}\pm s$)

The project	n	Before treatment	Treatment for 1 week	Treatment for 4 weeks
Social Psychology				
Experimental group	50	45.1±7.4	44.0±8.1	36.6±5.8
Control group	50	46.7±7.0	44.8±6.1	38.1±6.3
t		1.008	0.511	0.968
P		0.156	0.304	0.166
Motivation/energy				
Experimental group	50	22.5±4.3	20.7±5.1	17.0±4.1
Control group	50	21.8±4.6	20.0±4.6	17.5±3.7
t		0.705	0.650	0.575
P		0.240	0.257	0.282
Symptoms, Adverse reactions				

Table 5: Comparison of the value and cost of labor in the two groups (in ten thousand yuan, $\bar{x}\pm s$)

Groups	n	Discharge from hospital 6 months	Discharge from hospital 12 months	Discharge from hospital 18 months	Discharge from hospital 24 months
Value of labor					
Experimental group	50	6.6±1.2	11.4±2.6	19.1±4.0	25.3±5.6
Control group	50	4.1±1.1	6.7±1.6	12.4±3.1	18.7±4.2
t		9.217	9.712	8.660	6.065
P		0.000	0.000	0.000	0.000
Medical expenses					
Experimental group	50	3.6±0.7	8.0±2.0	12.7±3.1	17.0±4.1
Control group	50	4.2±0.6	9.5±2.6	17.4±3.8	23.4±3.7
t		3.687	3.211	6.026	7.374
P		0.000	0.001	0.000	0.000
Non-medical expenses					
Experimental group	50	1.0±0.1	1.8±0.2	4.1±1.1	7.4±1.7
Control group	50	1.5±0.2	3.4±0.5	8.4±2.0	13.8±3.1
t		8.921	15.248	11.396	11.171
P			0.000	0.000	0.000

Table 6: Overall benefits, costs, and benefit-Cost comparison between the two groups ($\bar{x}\pm s$)

Groups	n	Discharge from hospital 6 months	Discharge from hospital 12 months	Discharge from hospital 18 months	Discharge from hospital24 months
Total benefit					
Experimental group	50	60.8±11.3	72.2±15.1	77.4±12.0	79.1±15.2
Control group	50	55.7±10.7	63.7±15.8	66.8±10.7	65.0±14.8
t		2.116	2.510	4.266	4.266
P		0.017	0.006	0.000	0.0O0
Total cost					
Experimental group	50	5.4±1.1	11.1±2.3	18.7±4.5	27.1±6.4
Control group	50	6.3±1.1	14.5±3.3	28.6±6.5	40.1±7.6
t		3.450	5.572	7.925	8.224
P		0.000	0.000	0.000	0.000
Benefit-cost ratio					
Experimental group	50	11.0±2.5	6.5±1.3	4.0±1.0	2.8±0.5
Control group	50	8.6±2.1	4.3±1.1	2.2±0.5	1.5±0.3
t		4.607	7.801	9.504	11.871
P		0.000	0.000	0.000	0.000

Table 7: Comparison of CT and WMS-RC scores between the two groups before and after treatment ($\bar{x}\pm s$)

Groups	Time	n	CT		WMS-RC	
			Net score	Rate of error	Total score	Quotient of memory
Experimental group	Before treatment	50	106.0±19.1	24.1±14.8	94.6±16.2	88.7±14.0
	After treatment	50	122.3±15.1*#	13.3±8.0*#	107.4±12.2*#	104.0±14.4*#
Control group	Before treatment	50	105.0±16.0	23.2±11.1	95.1±15.7	87.8±14.1
	After treatment	50	114.2±12.6*	17.2±5.7*	100.0±13.8*	95.3±13.0*

Note: * indicates the difference between the two groups, $P<0.01$; # indicates the difference between the treatment group before and after treatment, $P<0.05$.

Table 8: WCST scores for both groups before and after treatment ($\bar{x}$±s)

Groups	Time	n	Total number of responses	Number of correct responses	Number of persistent errors	Random error number	Number of classifications completed
Experimental group	Before treatment	50	106.1±12.8	51.1±9.1	31.7±13.1	23.0±1.8	4.6±1.2
	After treatment	50	89.2±9.93$^{*\triangle}$	53.1±6.2$^{\alpha}$	21.0±6.0$^{*\#}$	14.8±5.33$^{*\triangle}$	5.0±1.0$^{\alpha}$
Control group	Before treatment	50	105.3±14.4	50.1±9.6	32.8±14.0	22.1±10.1	4.5± 1.4
	After treatment	50	95.8±13.8*	50.5±9.4	25.8±9.7*	19.2±9.7$^{\alpha}$	4.5±1.1

Note: * indicates the difference between the two groups, $P < 0.01$; # indicates the difference between the experimental group before and after treatment, $P < 0.05$; a indicates the difference between the two groups, $P < 0.05$; △ indicates the difference between the experimental group and the control group after treatment, $P < 0.05$.

An important feature of schizophrenia is recurrent episodes, the need for continuous treatment and high demands on both the patient's family and social security. The implementation of this project can not only relieve the economic burden of patients, but also optimize social medical resources and benefit patients to the maximum extent. In recent years, the health economic research on schizophrenia has received increasing attention, but the economic impact of the combination of drugs and rTMS on patients with schizophrenia is still unclear. On this basis, we used five psychological, physiological, social and social dimensions including PSP, FBS, PANSS and SQLS-R4 to comprehensively evaluate the health economic value of patients and verify its importance by considering the five dimensions including health status, quality of life, social function, labor value and family burden.

The CT and WMS-RC scores indicating that the treatment can partially improve the attention function, memory function and partial executive function of schizophrenia.

The experimental group receiving antipsychotic drugs and rTMS shows that patients can produce greater labor value and overall benefit after receiving rTMS. Combining with previous studies, we believe that this may be because the patients' condition is significantly improved. Their cognitive functions such as thinking, perception and learning are also improved accordingly and their self - care ability is enhanced, which is helpful for their participation in daily work to produce more labor value. Buechler R *et al*. (Buechler R *et al*., 2020) show that recurrence, hospitalization after recurrence and special care of family members are the main costs of schizophrenia. The experimental group has lower expenses and a higher benefit - cost ratio than the control group, likely due to the improved patient condition, better quality of life and lower recurrence rate, resulting in greater health and economic benefits.

CONCLUSION

In conclusion, for patients with schizophrenia, in addition to the use of antipsychotic drugs, rTMS treatment can also be combined. This combination aims to improve the efficacy of patients, reduce their symptoms and enhance their quality of life. At the same time, this combination therapy enables patients to obtain more health - economic benefits, thus reducing the economic burden on patients and society. It is a new method worthy of clinical promotion.

Conflict of interest

The authors declare that there is no conflict of interests.

Funding

This study was supported by the Wenzhou Basic Scientific Research Project Fund (No.: Y20190484).

REFERENCES

Bingqian L, Hao Y, Shanling J and Jinguo Z (2024). Brain mechanisms and intervention measures for cognitive impairment in schizophrenia. *J. Psychiatry*., **37**(03): 319-324

Brandt SJ, Oral HY and Arellano- Bravo C (2021). Repetitive transcranial magnetic stimulation as a therapeutic and probe in schizophrenia: An examining the role of neuroimaging and future directions. *Neurother.*, **18**(2): 827-844.

Buechler R, Wotruba D and Michels L (2020). Cortical volume difference ences in subjects at risk for psychosis are driven by surface area. *Schizophr Bull*, **46**(6): 1511-1519.

Caicai S, Hailing J, Lili Z, Yunshu Z and Keqing L (2025). Research progress on the correlation between cognitive function and sleep spindles in schizophrenia. *J. Neurosci. Ment. Health*., **25**(02): 103-108.

Cui LB, Fu YF and Liu L (2021). Baseline structural and functional magnetic resonance imaging predicts early detection and evaluation of early detection and evaluation of early detection.magnetic resonance imaging predicts early treatment response in schizophrenia with radiomics strateg. *Eur. J. Neurosci*., **53**(6): 1961-1975

Goff DC (2021). The pharmacologic treatment of schizophrenia. *JAMA*, **325**(2): 175-176.

Gong J, Cui LB and Xi YB (2020). Predicting response to electrocon- vulsive therapy combined with antipsychotic therapy.vulsive therapy combined with antipsychotics in schizophrenia using multi- parametric magnetic resonance imaging. *Schizophr. Res*., **216**: 262-271

Gongquan L, Linjia C and Qingfang X (2025). Comparison of the clinical effects of lurasidone and olanzapine in the treatment of schizophrenia and their effects on patients' cognitive function. *J. Clin. Res*., **42**(03): 437-440

Haiyu C, Jinjun L, Tianxiang Z, Ziwei T, Yue Q, Renrong W, Yeliang Y, Kai F, Wenjuan J, Yunxia J, Riyong Z, Jianzhong M, Jian L and Jing H (2025). Effects of sulforaphane on negative symptoms and cognitive impairments in chronic schizophrenia patients: A randomized double-blind trial. *J. Psychiat. Res*., **184**: 464-472.

Haiyuan W, Jianbo C, Ming Y and Yonghou Z (2024). Research progress on the regulation of PI3K/Akt signaling pathway by traditional Chinese medicine in the prevention and treatment of schizophrenia. *Chin. J. Exp. Tradit. Med. Formulae*., **30**(08): 280-289

Kahl M, Wagner G, De La Cruz F (2020). Resilience and cortical thickness: a MRI study. *Eur. Arch. Psychiatry. Clin. Neurosci*., **270**(5): 533- 539

Mamidipalli Sai S, Anirudh B, Shobit G, Rajshekhar B and Sai Krishna T (2024). Predictors of response to rTMS in severe mental illnesses- schizophrenia and bipolar disorder. *Curr. Behav. Neurosci*., **11**(3): 146-163

Mccutcheon RA, Reis Marques T and Howes OD (2020). Schizophrenia- an o-verview. *JAMA Psychiatry*, **77**(2): 201-210

Nobuyuki N, Spyridon S, Johannes Schneider T, Lasse B, Jinyoung P, Orestis E, Josef P, John MD, Hiroyoshi T, Stefan L (2025). The trajectory of sedative adverse events caused by antipsychotics: A meta-analysis of individual participant data from randomised, placebo-controlled, clinical trials in acute phase schizophrenia. *Lancet Psychiat*., **12**(4): 266-275

Songping Z, Jiangjiang C and Xin Z (2025). Comparison of the efficacy and safety of clozapine and aripiprazole in the treatment of schizophrenia. *Med. Innovation. Chin*., **22**(08): 114-117

Suzhen Y, Bailing W, Heling S, Meihong X and Fengchun W (2025). Association between white blood cell counts and the efficacy on cognitive function after rTMS intervention in schizophrenia. *Schizophrenia*., **11**(1): 41.

Xingmei D, Zhongting Y, Deng Rui D, Chen Ying C, Zhang Hui Z and Huang Yuan H (2024). Cost-effectiveness analysis of five drug regimens for the treatment of schizophrenia. *Chin. J. New Drugs*, **33**(19): 2067-2074

Yang C, Tang J and Liu N (2021). The effects of antipsychotic treatment on the brain of patients with first- episode schizophrenia: A selective review of longitudinal MRI studies. *Front Psychiatry*, **12**: 593703

Zhao SW, Xu X and Wang XY (2021). Shaping the Trans-scale proper ties of schizophrenia via cerebral alterations on magnetic resonance imaging and single- nucleotide polymorphisms of coding and non-coding regions. *Front Hum Neurosci*., **15**: 720239

Zhenjiang G (2025). Effects of mindfulness-based stress reduction on young and middle-aged patients with schizophrenia. *Chin. J. Urban Rural Enterp. Hyg*., **40**(04): 68-70.