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Effects of repetitive transcranial magnetic stimulation combined with risperidone on improving cognitive function and aggressive behavior in patients with schizophrenia and its effects on serum indicators

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Abstract: **Background**: Schizophrenia is a severe mental disorder characterized by hallucinations, delusions and cognitive dysfunction, imposing a substantial burden on individuals and society. While antipsychotic medications such as risperidone effectively control positive symptoms, their efficacy in ameliorating cognitive impairment and aggressive behavior remains limited. Repetitive transcranial magnetic stimulation (rTMS), a non-invasive neuromodulation technique, has recently demonstrated potential in adjunctively improving cognitive and behavioral dimensional symptoms in schizophrenia patients. However, the effects of combined rTMS-risperidone therapy on these symptoms and associated serum biomarkers are not yet adequately supported by clinical evidence. **Objective**: This study aimed to evaluate the effects of repetitive transcranial magnetic stimulation (rTMS) combined with risperidone on cognitive function, aggressive behavior and serum biomarkers in patients with schizophrenia. **Method**: Eighty patients were randomly assigned to a risperidone monotherapy group or a combination therapy group (40 each) for a 4-week intervention. **Results**: Results showed that the combination group achieved significantly greater reductions in cognitive factor scores (11.39±2.44 vs. 12.84±2.13) and aggressive behavior scores compared to the monotherapy group (all $P<0.05$). Serum analysis revealed that the combination group also demonstrated superior modulation of biomarkers, including greater reductions in pro-inflammatory factors (TNF-α, IL-8, IL-18) and greater increases in anti-inflammatory (IL-10) and neurotrophic factors (BDNF, VEGF-A, FGF-2) (all $P<0.05$), while no significant differences were observed in PDGF-BB and HGF between the two groups. **Conclusion**: These findings suggest that rTMS combined with risperidone more effectively improves cognitive and aggressive symptoms in schizophrenia and is associated with favorable changes in serum inflammatory and neurotrophic markers.

Keywords: Aggressive behavior; Cognitive function; Repetitive transcranial magnetic stimulation; Risperidone; Schizophrenia

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INTRODUCTION

Schizophrenia is a complex, chronic mental disorder and one of the leading causes of disability worldwide. Currently, large-scale epidemiological surveys specifically targeting schizophrenia are lacking in China. However, according to a meta-analysis conducted by domestic scholars covering 27 provinces and municipalities, the point prevalence of schizophrenia in China is 3.72% (Wang *et al.,* 2024). Among individuals aged 15-49 (years), mental disorders constitute the dominant cause of years lived with disability (YLDs) globally, with schizophrenia contributing substantially to this disease burden (2022). In addition, recent studies have shown that the incidence of schizophrenia in adolescents and young adults worldwide is showing a slow upward trend (Zhong *et al.,* 2024). This has further exacerbated the disease burden on the global health system.

In the past, clinical treatment for schizophrenia mainly focused on positive and negative symptoms, but more and more clinical evidence shows that cognitive dysfunction is an independent and core pathological feature of schizophrenia and the degree of cognitive impairment is the most critical factor in predicting patients' long-term social and occupational function, quality of life and rehabilitation outcomes (Chen *et al.,* 2019). The current clinical management of schizophrenia mainly follows the guidelines issued by authoritative organizations such as the American Psychiatric Association (Keepers *et al.,* 2020) and the British Society of Psychopharmacology (Barnes *et al.,* 2020). The core recommendations of the above guidelines are highly consistent and all regard antipsychotic drugs as the cornerstone of schizophrenia treatment. They are effective in controlling positive symptoms. However, the improvement of cognitive dysfunction by antipsychotic drugs has not reached the clinical ideal level. It has been pointed out previously in a study that the global composite effect size of antipsychotic drugs is estimated to be between 0.22 and 0.24 (Maroney, 2022). Based on existing clinical studies, although drugs may bring some cognitive benefits, such improvements may not be significant in clinical practice and are far from enough to improve the impact of cognitive impairment on patient prognosis (Allott *et al.,* 2024).

Repetitive transcranial magnetic stimulation (rTMS), a non-invasive brain stimulation technique, has growing evidence for its use in the treatment of schizophrenia.

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Extensive evidence demonstrates that high-frequency rTMS can effectively improve cognitive function, particularly working memory and executive function (Jiang *et al.,* 2019; Xiu *et al.,* 2020). Existing evidence supports the use of rTMS as a combination therapy with risperidone, which can provide more significant cognitive improvements and benefits for patients with schizophrenia. This study sought to evaluate the therapeutic effect of risperidone monotherapy versus its combination with rTMS for schizophrenia. This study sought to compare the effects of risperidone monotherapy versus risperidone combined with rTMS on cognitive function, aggressive behavior and serum biomarker levels in patients with schizophrenia.

MATERIALS AND METHODS

Participants

This single-center, randomized, controlled study aimed to compare the effects of risperidone alone and rTMS combined with risperidone on cognitive function, aggressive behavior and serum markers in patients with schizophrenia. This study was approved by the hospital's ethics committee. The study was based on records of 80 patients diagnosed with schizophrenia between February 2023 and February 2024, as recorded in the electronic medical record system of our Department of Neurology. This trial report adhered to CONSORT reporting standards.

Inclusion criteria:

(1) Age ≥ 18 years.

(2) Patients fulfilled the DSM-5 diagnostic criteria for schizophrenia (First, 2013), that is, met at least two of the characteristic symptoms and each symptom is significantly present within 1 month; the functional level in areas such as work, interpersonal relationships or self-care is significantly lower than the pre-onset state; the symptoms persist for at least 6 months;

(3) Had not received rTMS treatment before enrollment;

(4) Complete medical records and the patient can cooperate with serum marker testing and 12-week follow-up;

Exclusion criteria:

(1) Severe heart, lung, liver, kidney dysfunction or other serious systemic diseases;

(2) Contraindications to rTMS treatment, such as metal implants or electronic devices in the body, a history of epilepsy or a family history of epilepsy, a history of cerebral hemorrhage, cerebral infarction or other cerebrovascular diseases within the past 3 months, etc.;

(3) Comorbidity with other mental disorders (such as bipolar disorder, major depression with suicidal tendencies, etc.);

(4) Cognitive dysfunction is caused by non-schizophrenia factors (such as Alzheimer's disease and post-traumatic dementia);

(5) Pregnant or breastfeeding women;

(6) Use of drugs that may affect cognition or mood (such as benzodiazepines, antidepressants and other antipsychotic drugs) within 2 weeks before enrollment;

(7) Allergy to risperidone ingredients.

Sample size

This study aimed to evaluate the effect of rTMS combined with risperidone on the improvement of cognitive function (cognitive factor score in PANSS) and aggressive behavior (MOAS scale) in patients with schizophrenia. The core outcome indicators were all continuous variables, so the sample size calculation formula for comparison of the means of two independent samples was $n=2\times\frac{(Z_{1-a/2}+Z_{1-\beta})^2\times\sigma^2}{\delta 2}$, α=0.05 (two-sided test), corresponding to $Z_{a/2}$ =1.96; β=0.2 0, corresponding to Z_{β} = 0.84; σ is the pooled standard deviation of the MOAS score change from baseline. Based on preliminary data from our pilot study and similar published research (Shi and Kong, 2025), σ was estimated to be approximately 3.5 points. δ is the minimum clinically important difference (MCID) in MOAS score between groups that we aimed to detect. Considering clinical relevance and preliminary efficacy data (e.g., a reduction of 4-5 points on the MOAS is often associated with a meaningful decrease in aggression risk), δwas set at 2.5 points (Shi & Kong, 2025). Allowing for a 20% dropout, the final group size of 40 was determined.

Participants

Using a computerized random number table function built into statistical software, a random sequence was generated. Eighty patients with schizophrenia enrolled between February 2023 and February 2024 were assigned unique numbers (1 to 80) in the order of their presentation. This was automatically assigned by the software to ensure a final sample size of 40 patients in both groups. After grouping was completed by a non-researcher using the software, the grouping results were placed in a light-proof, sealed envelope. Upon enrollment, the attending physician opened the corresponding numbered envelope to obtain grouping information. To address potential baseline imbalances (such as age), random number table grouping was performed within each stratum to ensure balanced baseline characteristics between the two groups within each stratum and minimize the impact of confounding factors on the evaluation of treatment efficacy.

Instruments

Cognitive factor scores in the PANSS negative symptom scale

Items N5 (Impairment of abstract thinking), N6 (Lack of spontaneity and fluency in conversation) and N7 (Stereotyped thinking) from the PANSS Negative Symptom Scale were used to assess cognitive function.

MOAS scoring

MOAS divides aggressive behavior into four categories. Each category is scored from 0 to 4 points according to severity and the total score is weighted. Scoring criteria: 0 points: no aggressive behavior; 1 point: mild (such as a brief angry expression); 2 points: moderate (such as slamming the door, verbal threats); 3 points: severe (such as breaking glass, physical pushing); 4 points: extremely severe (such as injuring others with weapons, self-harm requiring sutures). The weighted total score = Σ (original score of each category × weight), ranging from0to 40 points; Aggression risk grading: a score of > 4 points is considered significant aggressive behavior; a score of > 15 points is considered to require emergency intervention (such as isolation or drug sedation) (Huang *et al*., 2009).

Serum indicators

Serum levels of tumor necrosis factor-α (TNF-α), interleukin-8 (IL-8), interleukin-10 (IL-10), interleukin-18 (IL-18), brain-derived neurotrophic factor (BDNF), platelet-derived growth factor (PDGF-BB), hepatocyte growth factor (HGF), fibroblast growth factor-2 (FGF-2) and vascular endothelial growth factor (VEGF-A) were measured by enzyme-linked immunosorbent assay (ELISA).

Intervention methods

All participants in both groups were treated with risperidone. The dosage was initiated at 1 mg/day and titrated to a maintenance range of 4-6 mg/day based on clinical response and tolerability, which was sustained for four weeks. The combination treatment group added rTMS to risperidone. The combination group (n=40) underwent 20 Hz rTMS targeting the left DLPFC alongside risperidone medication. During treatment, the coil was tangential to the head, with a stimulation frequency of 20 Hz. Each train lasted 4 seconds, with a 56-second interval. Twenty trains were performed for 20 minutes, with a stimulation intensity of 100% of the cortical motor threshold. rTMS treatment was administered once daily, five times a week, for a total of four weeks. During rTMS treatment, patients sat quietly in a treatment chair and they were instructed to remain awake. Two professional rehabilitation therapists closely monitored the patient's facial expressions in a separate room. If any discomfort was detected, treatment was immediately stopped and intervention was taken (Kang *et al*., 2025).

Statistical analysis

Data analysis was conducted with the Statistical Package for the Social Sciences (SPSS) 27.0 (IBM, Armonk, NY, USA). Categorical and continuous variables were analyzed using the chi-square test and appropriate t-tests (independent or paired), respectively. Results are presented as mean±SD, with a two-sided $P< 0.05$ defining statistical significance.

RESULTS

Baseline characteristics of patients

A total of 80 patients were enrolled in this study. No patients dropped out during treatment and all enrolled patients completed the study (Table 1).

Comparison of cognitive factor scores in the PANSS negative symptom scale

At baseline, cognitive scores were comparable between the medication (15.62±2.47) and combination groups (15.71±2.65) (P=0.876). After 4 weeks, the combination group showed a greater reduction (11.39±2.44) than the medication group (12.84±2.13), with the difference becoming statistically significant (P=0.006). (Table 2 and Fig. 1)

MOAS score

Baseline MOAS scores were comparable between the drug (23.76±3.45) and combination groups (23.72±3.59). After 4 weeks, the combination group showed a greater reduction (14.12±2.75) compared to the drug group (15.77±2.62), with the difference being statistically significant (P=0.007). (Table 3 and Fig. 2).

Serum indicators

Post-treatment serum analysis revealed that the combination therapy led to significantly greater improvements in multiple biomarkers compared to drug treatment alone. While baseline levels were comparable ($P > 0.05$), the combined group showed significantly lower TNF-α (11.25±1.81 vs. 12.76±1.64 pg/mL) and IL-18 (4.20±1.07 vs. 5.39±1.12 pg/mL), but higher IL-10 (11.66±2.95 vs. 10.33±2.62 pg/mL), BDNF (14.39±2.52 vs. 13.14±2.44 pg/mL) and VEGF-A (235.36±23.88 vs. 220.72±23.25 pg/mL) (all $P < 0.05$). IL-8 and FGF-2 also differed significantly between groups. However, PDGF-BB and HGF levels showed no statistically significant intergroup differences after treatment. (Table 4).

DISCUSSION

Cognitive impairment is one of the core symptoms of schizophrenia and is considered to be one of the most critical factors affecting patients' long-term social function, occupational function and quality of life. Recent studies have shown that cognitive impairment in schizophrenia patients is not a simple result of external factors such as drug side effects or hospitalization. It mainly affects patients' executive function, memory, attention/alertness, processing speed, language function and other cognitive areas. The severity of patients' cognitive impairment is closely related to the overall severity and prognosis of the disease (Tschentscher *et al*., 2023).

Table 1: Comparison of basic data between the two groups

Baseline data	Drug treatment group (n= 40)	Combined treatment group (n= 40)	$\chi 2/t$	*P value*
Gender			0.503	0.478
Female	28 (70.00%)	2 5 (62.50%)		
Male	12 (30.00%)	15 (37.50%)		
Age (years)			0.973	0.615
18 - 29	11 (27.50%)	12 (30.00%)		
30 - 39	22 (55.00 %)	18 (45.50%)		
≥40	7 (17.50%)	10 (25.00%)		
Marital status			0.347	0.841
Married	18 (45.00%)	17 (42.50%)		
Unmarried	16 (40.00%)	15 (37.50%)		
Other's	6 (15.00%)	8 (20.00%)		
Family history			0.392	0.531
None	35 (87.50%)	33 (82.50%)		
Have	5 (12.50%)	7 (17.50%)		
Drinking history			0.672	0.412
None	33 (82.50%)	30 (75.00%)		
Have	7 (17.50%)	10 (25.00%)		
Smoking history			0.238	0.626
None	29 (72.50%)	27 (67.50%)		
Have	11 (27.50%)	13 (21.60%)		

Table 2: Comparison of cognitive factor scores between the two groups before and after treatment

Cognitive factor score	Drug treatment (n= 40)	Combination therapy (n= 40)	*t*	*P*
Before treatment	15.62 ± 2.47	15.71 ± 2.65	-0.157	0.876
4 weeks after treatment	12. 84 ± 2. 13	11.39 ± 2.44	2.831	0.006

Note: $^{*}P < 0.05$

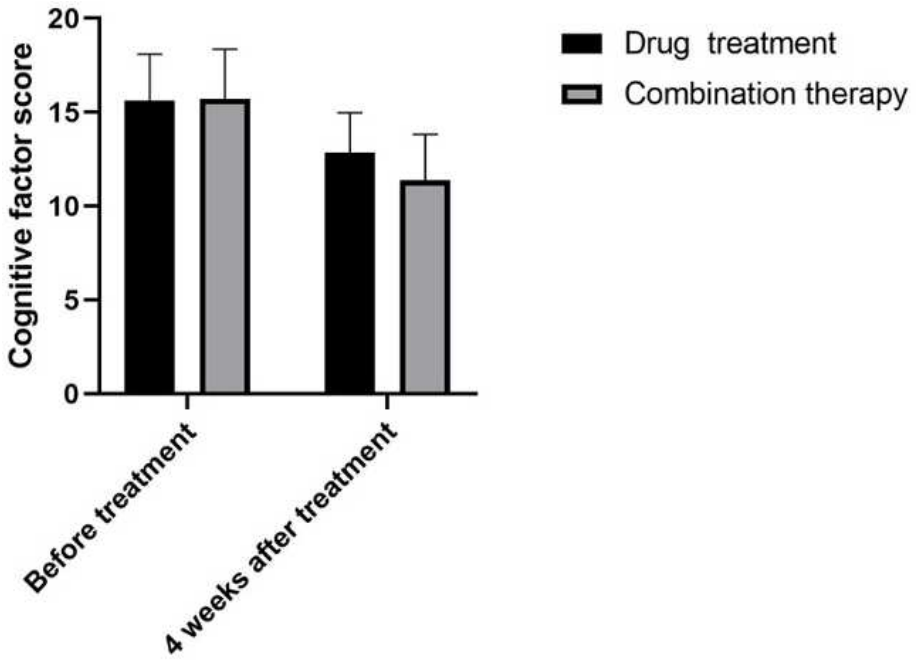

Fig. 1: Comparison of cognitive factor scores between the two groups before and after treatment.
Bar chart comparing the cognitive factor scores (derived from PANSS items N5, N6, and N7) between the drug treatment group and the combination therapy group (risperidone + 20 Hz rTMS targeting the left DLPFC) after the 4-week intervention. As shown in table 2, the combination therapy group achieved a significantly lower mean score (11.39 ± 2.44) compared to the drug treatment group (12.84 ± 2.13) at week 4 (P = 0.006). Data are presented as mean ± SD.

Table 3: Comparison of MOAS scores between the two groups before and after treatment

MOAS scores	Drug treatment (n= 40)	Combination therapy (n= 40)	*t*	*P*
Before treatment	23.76 ± 3.45	23.72 ± 3.59	0.051	0.960
4 weeks after treatment	15.77 ± 2.62	14. 12 ± 2. 75	2.747	0.007

Note: $^{*}P < 0.05$

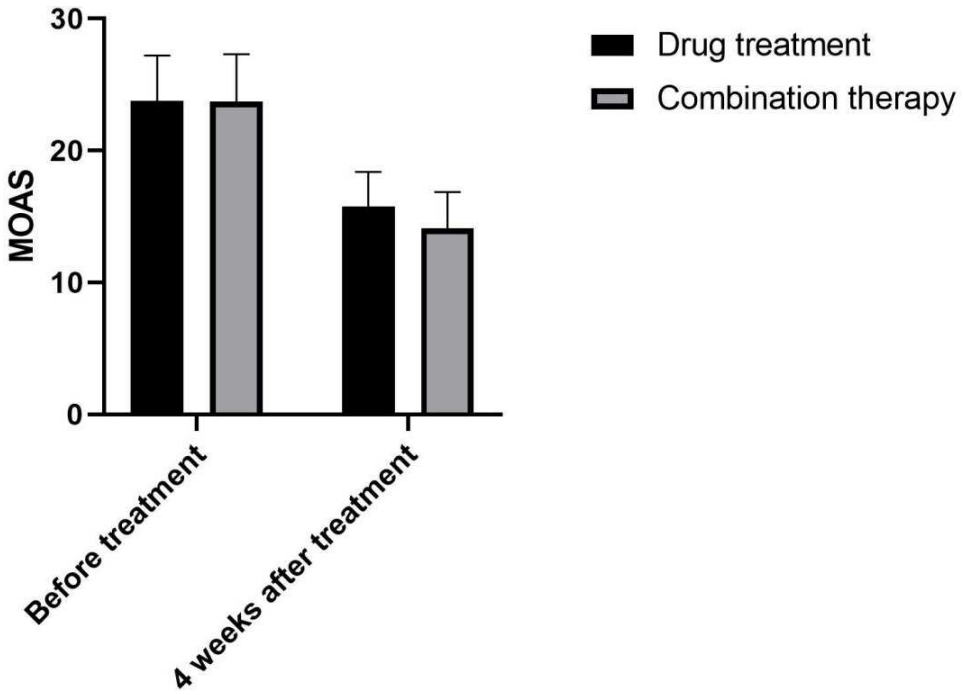

Fig. 2: Comparison of MOAS scores between the two groups before and after treatment.
Bar chart comparing the Modified Overt Aggression Scale (MOAS) total scores between the drug treatment group and the combination therapy group after the 4-week intervention. Consistent with table 3, the combination therapy group showed a significantly greater reduction in aggression, with a lower mean score (14.12 ± 2.75) than the drug treatment group (15.77 ± 2.62) at week 4 (P = 0.007). Data are presented as mean ± SD.

The pathogenesis of cognitive impairment in schizophrenia remains debated. A prevailing hypothesis posits that these deficits are core disease features established at initial onset and remain relatively static throughout its course. Furthermore, the cognitive course in patients is shaped by multiple factors, including disease heterogeneity, medication efficacy and concurrent conditions (Allott and Van Rheenen, 2020). Addressing cognitive impairment thus represents a promising therapeutic direction in schizophrenia.

Second-generation antipsychotics offer a modest cognitive advantage, including in working memory and processing speed, over first-generation ones, as noted in the 2022 EPA guidelines (Vita *et al*., 2022). However, the effect size of this improvement is small and no single drug can consistently show superiority in all cognitive domains. In addition, it is impossible to rule out whether cognitive improvement is a direct cognitive-promoting effect of the drug or an indirect effect caused by the reduction of psychotic symptoms. As a non-invasive brain stimulation technology, rTMS regulates the excitability of the target cortex by inducing weak electrical currents in specific brain areas and triggering a series of neurophysiological effects. Existing clinical evidence shows that rTMS can significantly improve the overall cognitive level of patients with cognitive impairment. At the same time, these improvements are not limited to a single cognitive domain, but widely cover memory, executive function and language ability (Xu *et al*., 2024; Yan *et al*., 2023).

This study used rTMS combined with risperidone to observe its effect on improving cognitive function and aggressive behavior in patients with schizophrenia. This study showed that after the same treatment cycle, the cognitive factor score of the combined treatment group was lower than that of the simple drug treatment group during the same period. It is speculated that the reason is that rTMS generates local induced currents through the dorsolateral prefrontal cortex, which is closely related to executive function and working memory and can regulate cortical excitability and neural plasticity, thereby improving the symptom dimension that is not well treated with drug treatment (Vergallito *et al*., 2024).

Table 4: Comparison of serum parameters between the two groups before and after treatment

Serum indicators	Drug treatment (n= 40)	Combination therapy (n= 40)	*t*	*P*
TNF-α (pg/mL)				
Before treatment	15. 22 ± 3. 14	15. 21 ± 3. 06	0.014	0.989
After treatment	12.76 ± 1.64	11.25 ± 1.81	3.910	<0.001
IL-8 (pg/mL)				
Before treatment	12.15 ± 2.47	12. 13 ± 2. 52	0.036	0.971
After treatment	13.52 ± 2.89	14.84 ± 2.67	-2.122	0.037
IL-10 (pg/mL)				
Before treatment	8.61 ± 1.46	8.46 ± 1. 32	0.482	0.631
After treatment	10.33 ± 2.62	11.66 ± 2.95	-2.132	0.036
IL - 18 (pg/mL)				
Before treatment	17.36 ± 5.42	17.20 ± 5. 39	0.132	0.895
After treatment	5.39 ± 1.12	4. 20 ± 1. 07	4.859	<0.001
BDNF (pg/mL)				
Before treatment	12. 13 ± 2. 21	12. 09 ± 2. 35	0.078	0.938
After treatment	13. 14 ± 2.4 4	14.39 ± 2.52	-2.254	0.027
PDGF-BB (pg/mL)				
Before treatment	12.13 ± 2.21	12.36 ± 2.27	-0.459	0.647
After treatment	13. 06 ± 2.4 2	13. 10 ± 2. 53	-0.072	0.943
HGF (pg/mL)				
Before treatment	12.87 ± 3. 77	12.90 ± 3.79	-0.035	0.972
After treatment	13.91 ± 3.84	14. 04 ± 3. 95	-0.149	0.882
FGF-2 (pg/mL)				
Before treatment	13.56 ± 3. 42	13.61 ± 3.44	-0.065	0.948
After treatment	11.95 ± 2.12	10.78 ± 2.36	2.333	0.022
VEGF-A (pg/mL)				
Before treatment	215.13 ± 22.41	215.82 ± 22.48	-0.137	0.891
After treatment	220.72 ± 23.25	235.36 ± 23.88	2.778	0.007

Note: $^{*}P < 0.05$; $^{**}P < 0.001$

In addition, the regulatory effect of rTMS on neural circuits may create a more favorable neurobiological basis for the pharmacological effects of risperidone, thereby producing a synergistic effect. This study also observed that the MOAS score of the combined treatment group was lower after treatment. The aggressive behavior of schizophrenia patients is related to impulse control, emotion regulation and executive function defects, all of which are closely related to the prefrontal cortex. Therefore, rTMS targeting the dorsolateral prefrontal cortex may indirectly reduce impulsive aggression by improving these top-level control functions. This study also observed that the combined treatment regimen can have a more significant effect on some specific cytokines than simple drug treatment.

Previous studies have shown that rTMS can regulate serum BDNF levels in patients and significantly reduce the levels of pro-inflammatory factors (Zhao *et al*., 2019). The present study demonstrates the significant advantages of rTMS combined with risperidone in improving cognitive function and aggressive behavior in schizophrenia. Furthermore*, Wu et al., (2025*) indicates that similar combinatorial therapeutic strategies are equally effective in treating somatic symptom disorders. Collectively, these findings point to a deeper conclusion: As a neuromodulation technique, the effects of rTMS may not be confined to the specific pathophysiological processes of individual diseases, but rather may modulate transdiagnostic, shared neural circuits—such as those underlying emotion regulation, cognitive control and somatosensory integration. Animal experiments have further confirmed that rTMS improves cognitive dysfunction by activating the BDNF/TrkB signaling pathway (Hou *et al*., 2023). The present study observed favorable shifts in serum inflammatory and neurotrophic biomarkers following combination therapy, providing direct evidence for the neuroprotective and anti-inflammatory effects of rTMS. In conjunction with the findings by Li *et al.,* (2023). that low-frequency rTMS combined with risperidone can modulate the gut microbiota in patients with chronic schizophrenia, it can be postulated that rTMS exerts a bidirectional regulation via the gut-brain axis. Specifically, the direct neuromodulation of the central nervous system and the indirect influence on the gut microecology jointly constitute this regulatory mechanism, ultimately synergizing to ameliorate psychiatric symptoms and cognitive function A possible speculative explanation for the lack of significant change in PDGF-BB and HGF levels, in contrast to the alterations observed in other biomarkers, may be attributed to their distinct biological roles and regulatory pathways. While biomarkers such as BDNF and certain inflammatory

cytokines are more directly involved in synaptic plasticity and acute neuroinflammatory responses—processes that rTMS is postulated to modulate—PDGF-BB and HGF are primarily associated with vascular remodeling, angiogenesis and longer-term tissue repair mechanisms. The intervention period or the specific parameters of rTMS used in this study might have been insufficient to induce measurable changes in these latter pathways. Based on the role of rTMS in regulating BDNF and inflammatory factors alone, it can exert a neuroprotective effect, thereby further improving the symptoms of schizophrenia.

Limitations

This study was a single-center, small-sample study (n=80) and the sample source was only the neurology department of a single hospital. There may be selection bias in the patients' baseline characteristics, making it difficult to extrapolate the results to schizophrenia patients in different regions and different medical settings and limiting external validity. rTMS treatment is a non-invasive procedure and patients can be grouped based on slight perceptual judgments during treatment, which may produce a subjective expectation effect and interfere with the objective assessment of cognitive function and aggressive behavior. This study has certain limitations. Its brief duration and absence of long-term follow-up prevent assessment of the combined therapy's sustained benefits. Although randomization ensured baseline comparability, potential influences of interindividual variability on cognitive and serum biomarker outcomes were not fully addressed. The lack of blinding (both participants and assessors were aware of treatment allocation) may have introduced bias in subjective outcome assessments, such as PANSS scores and aggressive behavior ratings.

CONCLUSION

This study demonstrated that, compared to risperidone monotherapy, the combination of risperidone with high-frequency rTMS targeting the left DLPFC for 4 weeks led to significantly greater improvements in cognitive function and more substantial reductions in aggressive behavior in patients with schizophrenia. These clinical benefits were paralleled by more favorable modulation of key serum biomarkers, including a greater reduction in pro-inflammatory factors (TNF-α, IL-8, IL-18) and a more pronounced increase in anti-inflammatory (IL-10) and neurotrophic (BDNF, VEGF-A, FGF-2) factors. The lack of significant change in PDGF-BB and HGF suggests that the observed benefits may be mediated through specific inflammatory and neuroplasticity pathways rather than broader angiogenic or tissue repair mechanisms. These findings support the potential of adjunctive rTMS as a strategy to enhance therapeutic outcomes in schizophrenia, particularly for cognitive deficits and behavioral dysregulation that show limited response to antipsychotic medication alone. However, the conclusions are tempered by the study's limitations, including its single-center design, modest sample size, short duration and lack of blinding, which highlight the need for larger, longer-term and methodologically rigorous trials to confirm these preliminary results and elucidate the underlying mechanisms.

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Authors' contribution

Si Zhou and Hongyan Tu: Designed the study and drafted the original manuscript; Hongyan Tu and Jijin Lin; Collected the patients' data and handled the statistical analysis; Si Zhou: Responsible for reviewing and editing.

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Data availability statement

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethical approval

This study was approved by the ethics committee of The Third People's Hospital of Fuyang District (Approval no. 22-FY-EC-23). Signed written informed consents were obtained from the patients and/or guardians. This study was conducted in accordance with the Declaration of Helsinki.

Conflict of interests

The authors declared no conflict of interest.

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