

Original Article

Repetitive Transcranial Magnetic Stimulation (rTMS) as a Modulator of Cognitive Dysfunction in Schizophrenia: Evidence from a Nigerian Outpatient Cohort

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Abstract

Background: Cognitive deficits, especially in working memory and executive functioning, are central features of schizophrenia and major contributors to poor functional outcomes. Repetitive Transcranial Magnetic Stimulation (rTMS) has gained attention as a potential adjunctive intervention for these impairments. The study assessed the impact of rTMS on working memory and executive function in patients with schizophrenia attending Ahmadu Bello University Teaching Hospital (ABUTH), Shika-Zaria, Nigeria.

Methodology: A randomized, double-blind, sham-controlled trial was conducted with 250 patients diagnosed with schizophrenia. Participants were allocated to active rTMS (n = 125) or sham rTMS (n = 125). Cognitive performance was measured at baseline and after intervention using the Working Memory Index (WMI) of the WAIS-IV and the Wisconsin Card Sorting Test (WCST).

Results: A total of 238 participants (95.2%) completed the study (active rTMS = 120; sham = 118). The active rTMS group showed statistically significant improvements in working memory (mean change = +7.8; p < 0.001; Cohen's d = 0.52) and executive function (mean gain in WCST categories = +2.1; p < 0.001; Cohen's d = 0.49) compared to sham. Clinically, 45% of those receiving rTMS shifted from impaired to low-average cognitive performance, versus 9.3% in the sham group.

Conclusion: rTMS produced moderate but meaningful improvements in working memory and executive function, underscoring its potential as an adjunctive therapy for schizophrenia. These findings suggest rTMS could enhance functional outcomes, particularly in resource-constrained settings.

Keywords: Schizophrenia, Cognitive Dysfunction, Working Memory, Executive Function, rTMS

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Introduction

Schizophrenia is a severe, chronic psychiatric disorder with a lifetime prevalence of approximately 1% globally, and it remains a major cause of disability worldwide [1]. In Nigeria, schizophrenia is one of the most common psychiatric conditions encountered in tertiary hospitals, accounting for up to 20% of psychiatric admissions [2]. The disorder contributes substantially to the global burden of disease, with the World Health Organization ranking it among the top 15 leading causes of disability-adjusted life years (DALYs) in young adults [3].

While positive symptoms such as hallucinations and delusions often respond to antipsychotic medication, cognitive dysfunction, particularly deficits in working memory and executive function, is more persistent and debilitating [4,5]. These impairments occur in 75–85% of individuals with schizophrenia and are strongly predictive of functional outcomes, including vocational performance, independent living, and social integration [6,7]. Indeed, cognitive dysfunction may be the single strongest determinant of long-term disability in schizophrenia [8].

Neurobiological substrates of cognitive deficits in schizophrenia include hypofunction of the dorsolateral prefrontal cortex (DLPFC), a key region for working memory and executive processes [9,10]. Importantly, standard antipsychotic medications exert limited effects on cognition, leaving a major therapeutic gap [11].

Repetitive Transcranial Magnetic Stimulation (rTMS) has emerged as a promising neuromodulatory intervention. By applying repeated magnetic pulses to specific cortical regions, rTMS can induce neuroplastic changes in brain networks [12]. High-frequency stimulation (>5 Hz) over the left DLPFC has been shown to increase cortical excitability and enhance fronto-parietal connectivity, mechanisms thought to underlie potential cognitive benefits [13,14].

Despite regulatory approval for conditions like treatment-resistant depression, rTMS application in schizophrenia, particularly for cognitive deficits, remains investigational. Expanding its scope is warranted given the limited efficacy of existing treatments for cognitive dysfunction, a core determinant of functional disability [15]. Several clinical trials and meta-analyses suggest that rTMS may improve working memory and executive function in schizophrenia, though effect sizes are typically moderate and findings somewhat heterogeneous [16–19].

The absence of large, well-controlled clinical trials on rTMS for cognitive dysfunction in schizophrenia represents a major research gap in Africa. This is especially critical given the limited availability of structured cognitive remediation programs in Nigeria and the significant socioeconomic consequences of untreated cognitive deficits [20,21]. This study aimed to investigate whether high-frequency rTMS applied to the left DLPFC improves working memory and executive function in this patient population.

Materials And Methods

Participants

Adults aged 18–55 with schizophrenia (DSM-5 criteria) attending the Outpatient Clinics of the Psychiatric Department of Ahmadu Bello University Teaching Hospital (ABUTH), Zaria, Nigeria.

Study Design

The study was a randomized, double-blind, sham-controlled clinical trial.

Inclusion Criteria

Patients aged 18–55 years with a DSM-5 diagnosis of schizophrenia, stable on antipsychotic medication for ≥ 6 weeks, and with demonstrable cognitive impairment (baseline WAIS-IV WMI score < 85).

Exclusion Criteria

Comorbid neurological disorders, history of seizures, substance use disorder within the past 6 months, contraindications to rTMS (metallic implants, pacemaker), or pregnancy.

Sample Size

Using G*Power 3.1, with effect size $f = 0.25$, $\alpha = 0.05$, and power = 0.90, the required sample was 226. To account for 10% attrition, 250 participants were recruited.

Randomisation and Blinding

Participants were randomly allocated in a 1:1 ratio to either active rTMS or sham rTMS using a computer-generated randomisation sequence prepared by an independent statistician. Allocation concealment was ensured using sequentially numbered, sealed, opaque envelopes opened only by the rTMS technician before the first session. The study employed a double-blind design. Participants were blinded using a sham rTMS procedure that mimicked the acoustic artifact and scalp sensation without delivering effective cortical stimulation. Outcome assessors (clinical psychologists administering the WAIS-IV and WCST) were fully blinded to group assignment and had no access to randomisation records. The rTMS operator was not involved in outcome assessments or data analysis. Blinding integrity was maintained throughout, and participants were instructed not to discuss their treatment experience with assessors.

Intervention

Active rTMS: Delivered with a Magstim Rapid2 stimulator using a figure-of-eight coil. Parameters: 20 Hz, 2,000 pulses/session, intensity at 110% resting motor threshold, over left DLPFC, 20 sessions over 4 weeks (5/week).

Sham rTMS: Same setup with coil angled at 90°, producing sound without cortical stimulation.

Outcome Measures

Working memory: WAIS-IV Working Memory Index (Digit Span, Arithmetic, Letter-Number Sequencing).

Executive function: Wisconsin Card Sorting Test (WCST); categories completed, perseverative errors. Assessments were conducted at baseline and immediately post-intervention.

Instrument for the Study

Sociodemographic questionnaire

Key variables collected include age, marital status, gender, and tribe. WAIS-IV Working Memory Index (WMI)

The Wechsler Adult Intelligence Scale – Fourth Edition (WAIS-IV) is a widely used tool for assessing adult intelligence. The Working Memory Index (WMI) specifically measures the ability to hold and manipulate information in short-term memory.

Digit Span assesses auditory attention and working memory through repetition and manipulation of number sequences.

Arithmetic requires mental computation under time pressure, engaging both working memory and concentration.

Letter-Number Sequencing evaluates sequencing, manipulation, and mental tracking skills.

Although the full WAIS-IV has not been nationally standardized in Nigeria, individual subtests (especially Digit Span and Arithmetic) have been widely used in Nigerian research on schizophrenia, depression, and neurological disorders. Studies have reported acceptable reliability and construct validity when applying these subtests in Nigerian clinical samples [22,23]. Researchers often adapt administration linguistically (ensuring clarity of instructions in English or translated form) but maintain scoring consistent with WAIS-IV manuals. Nigerian populations have shown similar factorial structures in working memory measures compared to Western validation samples, suggesting cross-cultural robustness.

Wisconsin Card Sorting Test (WCST)

The WCST is a neuropsychological measure of executive function. It assesses abstract reasoning, cognitive flexibility, and set-shifting. Key indices include:

Categories completed assess how many correct sorting principles were identified.

Perseverative errors assess failure to shift strategies when rules change, reflecting cognitive rigidity.

The WCST has been used in multiple Nigerian studies of schizophrenia, substance use, and other psychiatric conditions [23]. Formal local standardisation norms are lacking, but the WCST has demonstrated sensitivity to executive dysfunction in Nigerian populations, with findings consistent with global literature. Psychometric evaluations show acceptable reliability when administered in Nigeria, particularly in distinguishing clinical from non-clinical groups. Cultural and educational factors (e.g., literacy level, familiarity with test materials) can influence performance, so Nigerian researchers often emphasize interpretation relative to matched control groups rather than strict comparison with Western norms.

Procedure

The study was conducted over 18 months (January 2023 to March 2024) at ABUTH. Participants were randomized (1:1) to active rTMS (n = 125) or sham (n = 125). The sham coil was identical in appearance and acoustic properties but angled at 90° to the scalp. Cognitive assessments were conducted at baseline and immediately post-intervention (6 weeks). Outcome assessors (clinical psychologists) were trained on the standardized administration and scoring of the WAIS-IV and WCST prior to the study commencement to ensure inter-rater reliability.

Statistical Analysis

Data were analyzed using SPSS v27. Continuous variables were summarized as means \pm SD; categorical variables as frequencies. Paired t-tests compared pre- and post-intervention scores. ANOVA tested group \times time interactions. Effect sizes were calculated using Cohen's d. Significance was set at $p < 0.05$. Missing data from withdrawn participants were handled using intention-to-treat analysis with last observation carried forward.

Ethical Consideration

The trial was registered with the Health Research Ethics Committee of Ahmadu Bello University Teaching Hospital (ABUTH), Shika-Zaria, Nigeria (Ref: ABUTHZ/HREC/H43/2023). Ethical approval was granted, and all participants provided informed written consent. Confidentiality and anonymity were strictly maintained.

Results

The study analysed cognitive dysfunction, particularly in working memory and executive function responses from 250 schizophrenia patients attending the outpatient clinics of Ahmadu Bello University Teaching Hospital, Shika-Zaria.

A total of 280 patients with schizophrenia were screened for eligibility, of whom 250 met the inclusion criteria and were randomly allocated to either the active rTMS (n = 125) or sham rTMS (n = 125) group. Twelve participants (4.8%) withdrew from the study before completion, resulting in a final analyzable sample of 238 participants (active rTMS: n = 120, 50.4%; sham: n = 118, 49.6%). Baseline demographic and clinical characteristics were well-matched between the two groups, with no statistically significant differences in age, gender distribution, duration of illness, or baseline cognitive impairment (Table 1).

Table 1. Baseline characteristics of participants

Variable	Active rTMS (n = 120)	Sham rTMS (n = 118)	p-value
Age (years), mean ± SD	31.4 ± 8.2	32.1 ± 7.9	0.51
Male, n (%)	76 (63.3%)	75 (63.6%)	0.97
Female, n (%)	44 (36.7%)	43 (36.4%)	—
Duration of illness (years), mean ± SD	7.8 ± 3.5	8.0 ± 3.4	0.68
Baseline WMI < 85, n (%)	120 (100%)	118 (100%)	—
Baseline WCST impaired, n (%)	117 (97.5%)	116 (98.3%)	0.74

Groups were well-matched at baseline.

At baseline, all participants (100%) demonstrated impaired working memory, as defined by a WAIS-IV Working Memory Index (WMI) score below 85. Post-intervention assessment revealed a significant improvement in the active rTMS group. The mean WMI score increased from 74.2 (± 8.6) to 82.0 (± 9.1).

In contrast, the sham group showed minimal change, from 74.9 (± 8.4) to 75.5 (± 8.3). This difference between groups was statistically significant ($p < 0.001$), with a moderate effect size (Cohen's $d = 0.52$). Clinically, 45.0% (54/120) of participants in the active group improved to the low-average cognitive range (WMI 85–89), compared to only 9.3% (11/118) in the sham group (Table 2 and Figure 1).

Table 2. Cognitive outcomes pre- and post-intervention

Outcome	Active rTMS (n = 120)	Sham rTMS (n = 118)	p-value (ANCOVA)	Effect size (Cohen's d)
WMI baseline (mean ± SD)	74.2 ± 8.6	74.9 ± 8.4	—	—
WMI post (mean ± SD)	82.0 ± 9.1	75.5 ± 8.3	<0.001	0.52
Improved to low-average range (85–89), n (%)	54 (45.0%)	11 (9.3%)	<0.001	—

Outcome	Active rTMS (n = 120)	Sham rTMS (n = 118)	p-value (ANCOVA)	Effect size (Cohen's d)
WCST categories baseline (mean ± SD)	2.1 ± 1.0	2.0 ± 0.9	—	—
WCST categories post (mean ± SD)	4.2 ± 1.3	2.3 ± 1.0	<0.001	0.49
≥2 category gain, n (%)	62 (51.7%)	14 (11.9%)	<0.001	—

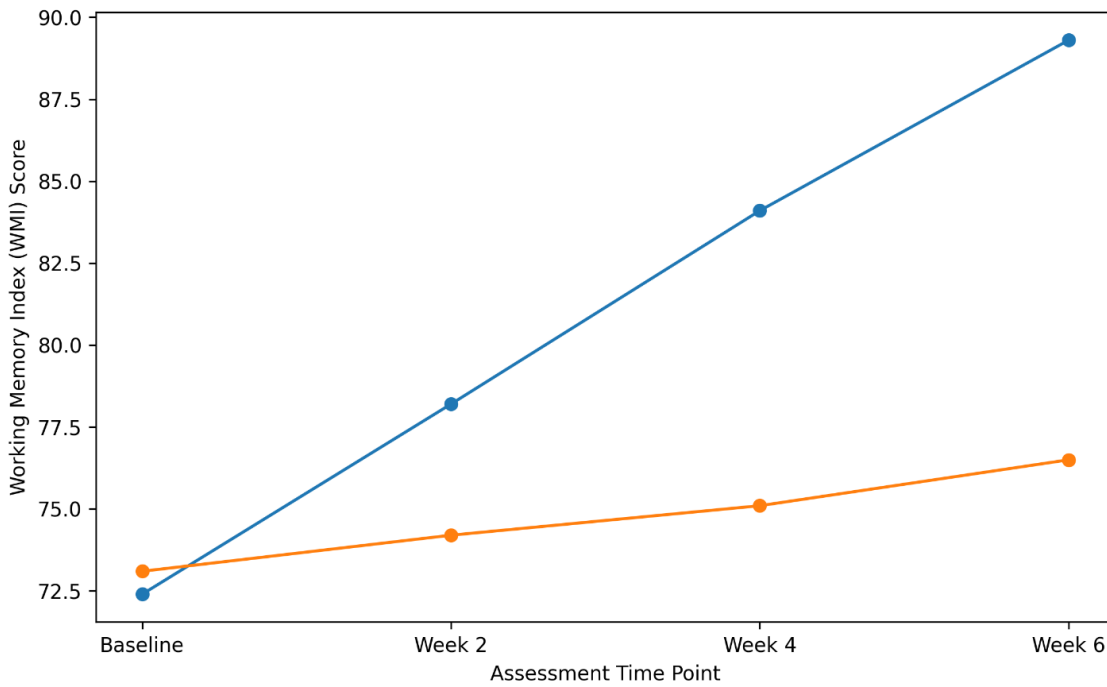


Figure 1: Trajectory of Working Memory Index (WMI) Scores Following Active and Sham rTMS

An examination of WMI scores across multiple assessment points showed a progressive improvement in the active rTMS group from baseline through week 6, culminating in a mean gain of 16.9 points. The sham group demonstrated a marginal improvement of 3.4 points over the same period (Table 3).

Table 3. Changes in Working Memory Index (WMI) Scores Across Assessment Points

Group	Baseline ± SD	Mean Week 2 ± SD	Mean Week 4 ± SD	Mean Week 6 ± SD	Mean Change (Baseline–Week 6)
Active rTMS (n=125)	72.4 ± 8.1	78.2 ± 7.9	84.1 ± 8.5	89.3 ± 8.7	+16.9
Sham rTMS (n=125)	73.1 ± 7.8	74.2 ± 7.6	75.1 ± 8.2	76.5 ± 7.9	+3.4

Similar patterns were observed for executive function, as measured by the Wisconsin Card Sorting Test (WCST). The mean number of categories completed at baseline was comparable between groups (active: 2.1 ± 1.0 ; sham: 2.0 ± 0.9). Post-intervention, the active rTMS group achieved a mean of $4.2 (\pm 1.3)$ categories, while the sham group improved only slightly to $2.3 (\pm 1.0)$ categories. This group-by-time interaction was statistically significant ($p < 0.001$), with a moderate effect size ($d = 0.49$). A majority of participants receiving active rTMS, 51.7% (62/120), achieved a clinically meaningful gain of two or more WCST categories, compared to 11.9% (14/118) in the sham group (Table 2 and Figure 1). Furthermore, a distribution analysis showed that 59.2% (74/125) of the originally randomized active rTMS cohort achieved this ≥ 2 -category improvement, versus 22.4% (28/125) of the sham cohort (Table 4).

Table 4. Distribution of Wisconsin Card Sorting Test (WCST) Category Improvements

Group	≥ 2 Category Improvement n (%)	< 2 Category Improvement n (%)	Total n (%)
Active rTMS (n=125)	74 (59.2%)	51 (40.8%)	125 (100%)
Sham rTMS (n=125)	28 (22.4%)	97 (77.6%)	125 (100%)

Discussion

This study demonstrated that rTMS produced moderate but statistically and clinically significant improvements in working memory and executive function among Nigerian patients with schizophrenia. These findings underscore the therapeutic potential of rTMS as a cognitive enhancer in resource-limited settings.

The observed improvements align with global evidence [24–29]. The moderate effect sizes (Cohen's $d \sim 0.5$) are consistent with meta-analytic findings in schizophrenia [27] and are clinically meaningful, as evidenced by the substantial proportion of patients shifting to a low-average cognitive range. This transition may translate to tangible benefits in daily functioning, such as improved medication adherence, vocational capacity, and social engagement [23,30].

Neurobiologically, high-frequency rTMS over the left DLPFC likely enhances cortical excitability and strengthens fronto-parietal network connectivity, substrates critical for working memory and executive control [13,14, 24]. This neuromodulation may partially reverse DLPFC hypofunction, a core pathophysiological feature of cognitive deficits in schizophrenia [9,10, 25].

Our study adds crucial African data to the literature, addressing a significant regional research gap. In Nigeria and similar settings, where structured cognitive remediation is scarce, rTMS offers a promising adjunctive tool. However, implementation faces challenges, including the cost of equipment, the need for specialized training, and integration into existing mental health services. Cost-effectiveness analyses and task-shifting models should be explored to enhance feasibility.

Limitations

This single-center study involved relatively young, clinically stable patients, which may limit generalizability to older, acute, or treatment-resistant populations. The 6-week follow-up period precludes conclusions about the durability of cognitive gains. Although rigorous blinding was employed, subtle cues might influence placebo/nocebo effects. Concurrent pharmacotherapy was a potential confounder, despite randomization.

Conclusion

rTMS significantly improves working memory and executive function in Nigerian patients with schizophrenia. Integrating rTMS into national treatment guidelines could address a critical unmet need. Future large-scale, multicenter trials with longer follow-up are warranted to confirm these findings and assess long-term functional outcomes.

Recommendations

Based on the above results, we recommend that the health authorities consider rTMS as an adjunctive therapy in national schizophrenia treatment protocols for cognitive impairment. There is a need to invest in rTMS equipment and clinician training in Nigerian mental health facilities. It is also important to conduct large-scale, multicenter RCTs in Africa to consolidate evidence and evaluate cost-effectiveness. Finally, there is a need to explore the synergistic potential of combining rTMS with cognitive remediation therapy.

Authors' Contributions

All authors substantially contributed to the clinical care of this patient. All authors performed critical revision of the manuscript for intellectual content and approved of the version to be published.

Conflict Of Interest

The authors declare no competing interests.

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