

ISSUP 2026 VIRTUAL EVENT

Efficacy of Repetitive Transcranial Magnetic Stimulation (rTMS) for Craving Reduction & Relapse Prevention in AUD and OUD

A Double-Blind, Sham-Controlled Randomised Trial in a Nigerian Tertiary Care Setting

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INTRODUCTION & RATIONALE

Background & Problem Statement: The Challenge of Addiction

Global & Regional Burden

- Rising prevalence of AUD & OUD in Nigeria, driven by socioeconomic pressures and limited access to care
- Substantial global morbidity, mortality, and economic impact (\$2.5B annual loss in Nigeria)

The Relapse Crisis

- Core issue: Intense, persistent craving acts as the key motivator for drug use and primary predictor of relapse
- Standard pharmacotherapy & CBT face high relapse rates (>50% within 1 year)

Neurobiological Dysregulation

- Executive Control Network failure: Hypoactivity in the left DLPFC impairs top-down inhibitory control
- Brain reward circuitry becomes hyperactive, hindering the patient's capacity to resist cravings

THEORETICAL FRAMEWORK

Hypothesis & Neuromodulation Mechanism (rTMS)

Mechanism of Action: High-Frequency rTMS

- High-Frequency Stimulation (10 Hz):
Delivers repetitive magnetic pulses over the left Dorsolateral Prefrontal Cortex (DLPFC)
- Cortical Excitability: Enhances prefrontal neural activity and neuroplasticity
- Restoring Executive Control: Re-establishes top-down inhibitory modulation over hyperactive mesolimbic reward circuits
- Target Outcome: Reduces craving intensity and suppresses impulsive drug-seeking behavior

Study Objective & African Context

- Critical Gap: Scarcity of neuromodulation RCTs for SUDs in Africa. Need for validation in specific cultural, genetic, and environmental contexts
- Primary Objective: Evaluate the efficacy of 10 Hz rTMS over left DLPFC as an adjunct to CBT for sustained craving reduction & relapse prevention
- Study Hypothesis: Active rTMS + CBT will achieve significantly lower craving scores and lower 12-month relapse rates compared to Sham rTMS + CBT

THEORETICAL FRAMEWORK

Hypothesis & Neuromodulation Mechanism (rTMS)

Target Cohort

- Severe AUD and OUD patients at Monarch Specialist Hospital, Kaduna, Nigeria

STUDY DESIGN & ELIGIBILITY

Methodology: Trial Design & Participant Selection

Study Architecture

Double-blind, randomised, sham-controlled trial conducted over 26 months (Monarch Specialist Hospital, Kaduna)

Sample Size (N=300)

Calculated via G*Power (Power 0.95, $\alpha=0.05$, $f=0.25$). 300 participants randomized (150 Active, 150 Sham)

Blinding & Allocation

Computer-generated randomization (Stat Trek); concealed opaque envelopes. Patients & raters double-blinded

Eligibility Criteria

Inclusion Criteria:

- Adults ≥ 18 yrs meeting DSM-5 criteria for severe AUD or OUD
- Baseline Visual Analog Scale (VAS) craving score $> 50/100$
- Desirous of abstinence; proficient in English/Hausa; written consent

Exclusion Criteria:

- Seizure history, metallic cranial implants, active suicidality, severe comorbidity
- Medications lowering seizure threshold or primary polysubstance use

STUDY DESIGN & ELIGIBILITY

Methodology: Trial Design & Participant Selection

Confounding Control:

- CBT Standardized: All patients received weekly 60-min individual CBT sessions
- Psychotropic changes excluded (4 cases withdrawn, ITT maintained)

INTERVENTION & METRICS

Intervention Protocol & Standardized Measurement

rTMS Technical Parameters

- Equipment: Magstim Rapid2 stimulator with figure-of-eight coil
- Target Site: Left DLPFC via 5 cm rule (marked cap, 45° angle to midsagittal line). Single operator (AAY) for consistency
- Dose / Parameters: 10 Hz frequency, 110% resting motor threshold (RMT)

- Session Structure: 75 trains (4s ON, 26s OFF) = 3,000 pulses/session (20 mins)
- Schedule: 5 sessions/week for 4 weeks (20 total sessions)
- Sham Protocol: Same coil location angled at 90° (identical acoustic/scalp sensation without cortical stimulation)

INTERVENTION & METRICS

Intervention Protocol & Standardized Measurement

Validated Assessment Metrics

- Craving Assessment Timepoints: Baseline (T0), Post-treatment (T1), 3-mo (T2), 6-mo (T3), 12-mo (T4)
- Visual Analog Scale (VAS): 0-100mm self-report scale measuring real-time craving intensity
- Obsessive Compulsive Drug Use Scale (OCDUS): Multi-item interviewer-rated scale measuring obsession, compulsion, and interference

- Relapse Criterion: Any self-reported substance use OR positive urine drug screen (AUD) / breathalyser test (AUD)
- Statistical Rigor: ITT analysis (SPSS v29.0), 2-way RM-ANOVA, Kaplan-Meier survival curves, Cox Proportional Hazards

TRIAL RESULTS - BASELINE

Baseline Characteristics: Rigorous Randomization Balance

Characteristic / Metric	Active rTMS (n = 150)	Sham rTMS (n = 150)	p-value (Significance)
Age, years (Mean ± SD)	38.4 ± 9.1	39.1 ± 8.7	0.52 (NS)
Gender: Male, n (%)	112 (74.7%)	115 (76.7%)	0.78 (NS)
Gender: Female, n (%)	38 (25.3%)	35 (23.3%)	0.78 (NS)
Substance: Alcohol (AUD), n (%)	75 (50.0%)	75 (50.0%)	1.00 (NS)
Substance: Opioid (OUD), n (%)	75 (50.0%)	75 (50.0%)	1.00 (NS)
Baseline Craving VAS (Mean ± SD)	82.3 ± 11.5	80.9 ± 12.2	0.31 (NS)
Baseline OCDUS Score (Mean ± SD)	22.1 ± 4.8	21.7 ± 5.1	0.49 (NS)

NB: Zero significant baseline differences across groups. Patient completion rate was 94.3% (283/300 completed 12-month follow-up; low attrition with no systematic bias).

TRIAL RESULTS - RELAPSE RATES

Primary Outcome 1: Marked & Sustained Relapse Reduction

Follow-up Point	Active rTMS	Sham rTMS	p-value
3-Month Prevalence	18.3% (26/142)	46.8% (66/141)	< 0.001
6-Month Prevalence	25.4% (36/142)	63.1% (89/141)	< 0.001
12-Month Cumulative	31.7% (45/142)	72.3% (102/141)	< 0.001

Survival Analysis (Time to First Relapse)

- Kaplan-Meier Log-Rank Test: $\chi^2 = 55.4$, $p < 0.001$
- Significantly longer time to relapse in active rTMS group
- Consistent therapeutic efficacy across AUD and OUD subgroups

40.6%

Absolute Risk Reduction (ARR)
12-Month Relapse Risk Difference
(72.3% sham vs 31.7% active)

56.2%

Relative Risk Reduction (RRR)
Relapse risk cut by more than half

2.5

Number Needed to Treat (NNT)
95% CI: 2.1 - 3.1 (Only 2.5 patients treated to prevent 1 relapse)

0.34

Hazard Ratio (HR)
95% CI: 0.24 - 0.48 (66% reduction in instantaneous relapse risk)

TRIAL RESULTS - CRAVING TRAJECTORIES

Primary Outcome 2: Long-Term Craving Reduction

Assessment Timepoint	Active rTMS (Mean VAS)	Sham rTMS (Mean VAS)
Baseline (T0)	82.3	80.9
Post-Treatment 4-Wk (T1)	35.0	55.0
3-Month Follow-up (T2)	30.0	65.0
6-Month Follow-up (T3)	32.0	68.0
12-Month Follow-up (T4)	33.0	70.0

Two-Way Repeated-Measures ANOVA

- Significant Time Effect: $F(4, 1192) = 520.44, p < 0.001, \eta^2 = 0.64$ (Massive overall craving drop)
- Significant Group Effect: $F(1, 298) = 110.25, p < 0.001, \eta^2 = 0.27$ (Active rTMS superior)
- Time $\times$ Group Interaction: $F(4, 1192) = 95.30, p < 0.001, \eta^2 = 0.24$
- Observer-Rated OCDUS Concordance: Identical pattern of statistical significance ($F = 82.16, p < 0.001, \eta^2 = 0.22$)
- Craving Trajectory Dynamics: Active group craving remained suppressed at ~30-33 VAS points out to 12 months, while Sham craving rebounded back toward baseline (70 VAS)

DISCUSSION

Discussion: Scientific Synthesis & Clinical Synergy

Neuroplasticity & Sustained Effect

- 4-week high-frequency rTMS protocol induces durable synaptic neuroplasticity in prefrontal circuits
- Sustained 12-month suppression proves rTMS provides long-term neurobiological modulation beyond initial treatment

Synergy with Psychotherapy

- Craving reduction creates a crucial 'window of opportunity' for cognitive engagement
- Restoring executive control allows patients to effectively apply CBT coping strategies without being overwhelmed by intense cravings

Hard Clinical Endpoints

- Moves beyond transient craving surrogates to prove direct impact on hard clinical outcomes (relapse prevention)
- NNT of 2.5 represents exceptional clinical utility compared to standard pharmacotherapies

LMIC CONTEXT & IMPLEMENTATION

Feasibility, Implementation & Cultural Dynamics in LMICs

Resource & Cost Realities

- Capital cost (\$30k-\$50k) is highly cost-effective against Nigeria's \$2.5B annual addiction burden
- Protocol optimization can leverage existing generator backup and clinical infrastructure

Task-Sharing Model

- rTMS can be safely administered by psychiatric nurses/technicians under physician supervision
- Requires 1-week theory, 2-week practical training; regional hubs in teaching hospitals

Destigmatization Effect

- Frame as medical brain stimulation reduced moral stigma, driving strong recruitment
- High 94.3% protocol adherence achieved in tertiary care setting

Socio-Cultural Enablers

- Communal family support enhanced patient compliance during 20 daily sessions
- Spiritual/religious coping (~40% participants) complemented medical treatment seamlessly

LIMITATIONS & FUTURE WORK

Methodological Limitations & Future Research Roadmap

Study Limitations

- 5 cm Anatomical Targeting: Scalp measurement used rather than MRI-guided neuronavigation (mitigated via rigorous cap standardization)
- Single-Center Design: Conducted at one tertiary hospital in Kaduna; multi-center expansion needed for national generalizability
- Follow-up Duration: 12-month follow-up is substantial, but chronic relapsing nature of SUDs warrants 3-5 year longitudinal tracking
- Urban Selection Bias: 85% of sample lived within 50 km of center; rural accessibility remains an issue

Future Research Agenda

- Protocol Optimization: Test session doses (10 vs 20 vs 30) and intensities (90-120% RMT)
- Maintenance Schedules: Evaluate periodic booster sessions (monthly/biweekly) for long-term retention
- Mechanistic & Biomarker Studies: Integrate fMRI connectivity, cortisol, and BDNF biomarkers
- Health Economics: Formal cost-effectiveness analyses to support health insurance reimbursement

POLICY FRAMEWORK

Actionable Policy & Clinical Recommendations

Government & Policy Action

- Integrate rTMS into National Mental Health Policy as adjunctive treatment for AUD/OD
- Include rTMS in National Health Insurance Authority (NHIA) basic benefit packages
- Establish NAFDAC regulatory pathways for medical neurodevices

Institutional & Service Models

- Colocate rTMS units in existing addiction treatment centers using Hub-and-Spoke models
- Phase national rollout: 2-3 tertiary centers in Year 1, expanding to 37 federal hospitals in 5 yrs
- Prioritize severe AUD/OD patients with high baseline craving (>50 VAS)

Sustainability & Funding

- Form Public-Private Partnerships (PPPs) and leverage WHO mhGAP framework
- Pursue international research grants (NIH Fogarty, Wellcome Trust)
- Negotiate 40-60% tiered equipment pricing for low-resource settings

CONCLUSION & SUMMARY

- ✓ Level-I Clinical Evidence: Adjunctive high-frequency (10 Hz) rTMS over left DLPFC produces profound, durable reductions in craving and relapse for AUD and OUD
- ✓ Substantial Effect Size: 12-month relapse cut from 72.3% to 31.7% (NNT = 2.5, HR = 0.34)
- ✓ Proof of Feasibility: Demonstrates that advanced, non-invasive neuromodulation is highly effective, feasible, and acceptable in Nigerian and African clinical settings
- ✓ Call to Action: Advocates for national policy integration, health insurance coverage, and structured capacity building to transform addiction care

Thank you for your attention!

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