

## **Transcranial Magnetic Stimulation as an Adjunct to Cognitive Behavioral Therapy for Obsessive-Compulsive Disorder.**

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### **Abstract**

This randomized controlled trial investigated whether augmenting cognitive behavioral therapy (CBT) for obsessive-compulsive disorder (OCD) with repetitive transcranial magnetic stimulation (rTMS) over the supplementary motor area (SMA) enhances symptom reduction and modulates brain network connectivity. Eighty adults with moderate to severe OCD were randomized to receive 8 weeks of CBT plus real rTMS or CBT plus sham stimulation. Resting-state functional connectivity and Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) scores were assessed pre- and post-intervention. The combined therapy group exhibited significantly greater Y-BOCS reduction (mean  $\pm$  SD:  $14.2 \pm 4.5$  vs.  $9.1 \pm 5.0$  points;  $p < 0.001$ ) and higher response rates (65 % vs. 35 %;  $p = 0.005$ ). Network analysis revealed increased connectivity post-treatment in fronto-striatal and cerebellar-prefrontal circuits in the real rTMS group, which correlated with symptom improvement ( $r = 0.52$ ;  $p = 0.002$ ). These findings indicate that adjunctive rTMS significantly enhances CBT efficacy and facilitates favorable modulation of cortical-subcortical networks. The observed connectivity changes suggest neuroplastic mechanisms underpinning clinical gains and support integration of neuromodulation with psychotherapy as a novel and effective intervention for OCD.

### **Keywords**

Repetitive TMS; cognitive behavioral therapy; obsessive-compulsive disorder; network connectivity; randomized controlled trial.

### **Introduction**

Obsessive-compulsive disorder (OCD) is a chronic psychiatric condition characterized by intrusive thoughts and repetitive behaviors that markedly impair daily functioning. While cognitive behavioral therapy (CBT), particularly exposure and response prevention, is established as a first-line psychotherapeutic modality, a significant proportion of individuals experience residual symptoms or incomplete response. Furthermore, OCD has been consistently linked to

dysfunction within cortico-striato-thalamo-cortical (CSTC) circuits and associated neural networks, as elucidated by neuroimaging studies that reveal abnormal connectivity patterns across prefrontal, striatal, thalamic, and cerebellar regions. Thus, strategies targeting both behavioral and neurobiological domains may yield enhanced therapeutic outcomes.<sup>1-4</sup>

Repetitive transcranial magnetic stimulation (rTMS) has emerged as a non-invasive neuromodulatory intervention capable of influencing cortical and subcortical circuits implicated in psychiatric disorders. Recent meta-analytic evidence demonstrates moderate effectiveness of rTMS across various neural targets—such as the supplementary motor area (SMA), dorsolateral prefrontal cortex (DLPFC), orbitofrontal cortex, and medial prefrontal/anterior cingulate regions—for symptom reduction in OCD. Moreover, deep TMS targeting networks involving the prefrontal cortex and ACC has gained regulatory approval for treatment-refractory cases. Nonetheless, existing studies often examine rTMS in isolation, without integration within psychotherapeutic regimens.<sup>5-7</sup>

Cognitive-behavioral therapy applied alone can modulate brain network connectivity, inducing increased integration across classical CSTC circuits as well as ancillary regions such as cerebellum and prefrontal areas. These neuroplastic changes are associated with symptomatic gains, suggesting that combining CBT with neuromodulation might produce additive or synergistic effects. However, empirical investigation into the concurrent use of rTMS and CBT, as well as the resulting network-level changes, remains notably scarce.<sup>8-9</sup>

The present randomized controlled trial was designed to evaluate whether adjunctive rTMS delivered alongside a standardized CBT protocol enhances clinical outcomes and induces differential network connectivity changes compared to CBT with sham stimulation. The research aimed to elucidate both symptomatic and mechanistic effects of combining neurostimulation with behavioral therapy, thereby addressing gaps in integrative treatment approaches. This experimental framework offers the potential to optimize OCD treatment by targeting behavioral symptoms while reinforcing neuroplastic remodeling in relevant brain circuits.<sup>10</sup>

## **Methodology**

A single-blind randomized controlled experimental trial enrolled at Balochistan Institute of Psychiatry and Behavioural Sciences, Quetta 80 adults aged 18–60 years diagnosed with moderate to severe OCD, confirmed via structured clinical assessment and exceeding Y-BOCS threshold of 24. Participants were randomized equally to receive 16 sessions of manualized CBT over eight weeks alongside either real rTMS targeting the SMA using low-frequency protocol (1 Hz, 1200 pulses/session) or identical sham stimulation. Sample size determination via Epi Info<sup>TM</sup> was based on detecting a 30 % between-group difference in symptom reduction (90 % power,  $\alpha = 0.05$ ), yielding 40 participants per arm. Exclusion criteria included neurological comorbidities, current psychotropic medication changes, and contraindications to MRI or TMS. Resting-state functional MRI was performed pre- and post-intervention to assess network connectivity changes. Verbal informed consent was obtained following detailed explanation of study processes. Y-BOCS ratings and imaging analyses were conducted by blinded evaluators. Clinical outcomes were compared using independent-samples t-tests and chi-square tests; connectivity changes were examined via

network-based statistics, and correlations with symptom change assessed via Pearson's  $r$ , with statistical significance at  $p < 0.05$ .

## Results

**Table 1. Participant Baseline Characteristics**

Variable	CBT + Real rTMS (n=40)	CBT + Sham (n=40)	p-value
Age (years)	35.2 $\pm$ 9.1	36.5 $\pm$ 8.8	0.57
Gender (M/F)	22/18	21/19	0.83
Baseline Y-BOCS	28.4 $\pm$ 3.6	29.1 $\pm$ 4.0	0.42

**Table 2. Clinical Outcomes Post-Intervention**

Outcome	CBT + Real rTMS	CBT + Sham	p-value
Y-BOCS reduction	14.2 $\pm$ 4.5	9.1 $\pm$ 5.0	< 0.001
Response rate (%)	65 %	35 %	0.005

**Table 3. Network Connectivity Changes (Post-vs-Pre)**

Circuit	CBT + Real rTMS	CBT + Sham	p-value
Fronto-striatal connectivity	+0.22 $\pm$ 0.08	+0.08 $\pm$ 0.07	< 0.001
Cerebellar-prefrontal connectivity	+0.18 $\pm$ 0.06	+0.05 $\pm$ 0.05	< 0.001
Correlation with Y-BOCS change (r)	0.52	0.18	—

Real-rTMS combined with CBT yielded significantly greater symptom reduction and higher response rates than CBT with sham. Enhanced connectivity in fronto-striatal and cerebellar-prefrontal circuits was observed only in the real-rTMS group, and these changes correlated strongly with clinical improvement.

## Discussion

Adjunctive rTMS significantly enhanced the efficacy of cognitive behavioral therapy, as evidenced by greater reductions in Y-BOCS scores and higher response rates. This finding demonstrates that combining neurostimulation with psychotherapy yields superior symptomatic outcomes relative to CBT alone. The degree of improvement indicates clinical relevance and potential for meaningful impact in treatment protocols for moderate to severe OCD.<sup>11-13</sup>

The connectivity analysis revealed that real rTMS potentiated increases in fronto-striatal and cerebellar-prefrontal circuit integration—brain networks integral to cognitive control and habitual suppression. These network alterations likely reflect neuroplastic mechanisms enabling more adaptive regulation of intrusive thoughts and compulsive behaviors. Notably, these changes were absent in the sham group, underscoring the specific neuromodulatory effect of rTMS.<sup>14-16</sup>

The strong positive correlation between connectivity changes and symptom improvement suggests that neuroimaging markers may serve as predictive biomarkers of treatment response. This relationship offers a promising avenue for tailoring interventions based on individual neurofunctional profiles. It also affirms the mechanistic role of network modulation in therapeutic change.<sup>17-18</sup>

These results align with theoretical models asserting that OCD involves dysfunctional CSTC circuits and that therapeutic gains are mediated through restoration of network integration. The added modulation of cerebellar-prefrontal pathways suggests that ancillary circuits outside classical models are also engaged in recovery processes, potentially reflecting broad-based neural reorganization.<sup>19-20</sup>

Implementation of combined rTMS and CBT has significant clinical implications. This integrative approach may be particularly valuable in patients with partial response to CBT alone, providing an evidence-based augmentation strategy. Moreover, as rTMS protocols become more accessible and standardized, combining them with psychotherapeutic modalities may enhance personalization of treatment and reduce chronic symptoms.

Study limitations include modest sample size and single-site design, which may restrict generalizability. Future research should examine long-term maintenance of gains, cost-effectiveness, comparative efficacy across different rTMS targets, and integration with other therapeutic modalities. Broader multi-center trials and extended follow-ups will strengthen the evidence base.

## **Conclusion**

Adding rTMS to cognitive behavioral therapy produced significantly greater symptom reduction and favorable neuroplastic changes in brain connectivity compared to CBT with sham. These outcomes highlight the potential of combined neuromodulation and psychotherapy in optimizing OCD treatment. Continued research should explore long-term durability, scalability, and individual predictors of response.

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