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PULSE

A Monthly Update on Advances in Neuromodulation

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Patient-Reported Outcomes Following Accelerated vs. Standard TMS With the H1 Coil for Major Depression: A Multisite Randomized Trial

Clara D. T. Nguyen, MD, MPH reviewing Tendler et al., Brain Stimulation, 2026 Feb.

In this multisite randomized trial of adults with moderate-to-severe MDD, both the accelerated H1-coil TMS (ACC-iTBS) and standard once-daily high-frequency (SOC-HF) showed improvements in mood symptoms and quality of life based on 104 participants' patient-reported outcomes (PROs). While there were no significant between-group differences noted, ACC-iTBS resulted in PROs indicating faster relief of symptoms over a 6-week period.

While TMS has shown to be safe and efficacious for the treatment of MDD, logistical barriers such as work/school schedules and transportation can make daily treatment for

IN THIS ISSUE:

several weeks challenging to accommodate. Accelerated TMS treatment schedules may help mitigate these barriers by condensing treatment into a shorter time frame. In this study, the authors evaluated the effects of an accelerated versus standard TMS dosing schedule, specifically using patient-reported outcomes, extending findings from a previously published FDA-regulated trial in which the primary endpoint was clinician-rated depressive symptoms (HAM-D).

The study screened 150 patients age 22-86 years from 7 sites in the United States and 1 in India between May 2024 and February 2025. To be eligible, patients were required to have failed 1-4 antidepressant trials during the current depressive episode, maintained stable antidepressant dosing for at least 2 months prior to randomization, and a minimum score of 20 on HAM-D at screening and at subsequent assessment ≥7 days later. The accelerated protocol (ACC-iTBS) was delivered at 110% RMT using 50 Hz triplet bursts at 5 Hz, with five sessions per day across six treatment days followed by a four-week continuation phase of twice-daily weekly sessions, totaling 38 sessions and 68,400 pulses across 10 visit days. The standard-of-care protocol (SOC-HF) was delivered at 120% RMT using 18 Hz stimulation once daily, five days per week for four weeks with a two-week continuation phase, totaling 24 sessions and 47,520 pulses across 24 visit days. Clinicians administered the Clinically Useful Depression Outcome Scale- Daily Version (CUDOS-D) and Clinically Useful Anxiety Outcome Scale-Daily Version (CUXOS-D) daily to assess for PROs while the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q) was assessed only at baseline and the 6-week endpoint.

Following a 6-week course, depression response measured by CUDOS-D was 70.0% in ACC-iTBS and 75.6% in SOC-HF while depression remission was 57.5% and 58.5% respectively. Anxiety response measured by CUXOS-D was 70.0% in ACC-iTBS and 75.6% in SOC-HF while anxiety remission was 67.5% and 69.0% respectively. Quality of life improved from 37.8% and 38.7% at baseline to 70.0% and 70.5% after 6 weeks in the ACC-iTBS and SOC-HF groups, respectively. Differences in these scales did not rise to the level of statistical significance, indicating the accelerated TMS protocol resulted in similar PROs for depression, anxiety, and quality of life when compared to the standard treatment. The only significant difference observed was in median time to CUDOS response, which was shorter in the accelerated group than in the standard group (11 vs. 16 days, $p = 0.0377$). No serious adverse effects occurred in any of the 104 patients. One limitation is that participants were not blinded to treatment allocation, as the differing visit frequencies between the two protocols made masking infeasible. Of note, this study was designed and conducted by BrainsWay, the manufacturer of the TMS system used in the treatment arms.

Impact: This study demonstrates ACC-iTBS and SOC-HF show comparable efficacy in the treatment of moderate-to-severe MDD, as measured by patient-reported outcomes. Utilizing an accelerated schedule may reduce the scheduling burden that patients face, resulting in similar improvements in symptoms and quality of life in a shorter period.

Tendler, A., Roth, Y., Bates, M. et al. Patient-reported outcomes following accelerated vs. standard TMS with the H1 coil for major depression: A multisite randomized trial. Brain stimulation, 19(2), 103048 (2026). https://doi.org/10.1016/j.brs.2026.103048

Perioperative HF-rTMS to DLPFC Reduces Postoperative Delirium in Older Adults Undergoing Major Non-Cardiac Surgery

Sheyna M. Nathwani, MD, reviewing Gao et al., Brain and Behavior 2026 Jan.

In this double-blind, sham-controlled RCT, perioperative HF-rTMS targeting the left DLPFC was associated with a significant reduction in postoperative delirium among older adults undergoing major non-cardiac surgery. Findings also suggest rTMS may influence a broader range of early perioperative symptoms—including pain intensity, sleep disturbance, frailty, and anxiety and depressive symptoms—indicating potential multidimensional benefits during the immediate postoperative period.

Postoperative delirium (POD) remains one of the most challenging perioperative complications in older adults, associated with longer hospital stays and elevated long-term risks, including prognosis, mortality, and subsequent cognitive decline. Incidence of POD ranges from 5–50% in older adults undergoing major surgery. Although non-pharmacological strategies are considered the most effective approach to POD, the rapid growth of the geriatric surgical population underscores the need for perioperative, evidence-based strategies to reduce incidence of POD. HF-rTMS can enhance prefrontal excitability and modulate neuroplasticity, with prior studies demonstrating

cognitive benefits in conditions such as mild cognitive impairment and Alzheimer's disease. This RCT evaluates whether preoperative HF-rTMS applied to the left DLPFC could reduce POD in older adults undergoing major non-cardiac surgery.

Investigators conducted a prospective, double-blind, sham-controlled trial enrolling 254 adults aged 60 or older undergoing elective non-cardiac surgery. Participants were randomized 1:1 to receive two sessions of active-rTMS or sham-rTMS—one the day before surgery, and one the day of surgery (before surgery), spaced at least 12 hours apart. Active stimulation consisted of 10 Hz rTMS delivered at 110% of the RMT (2-second trains with 20-second inter-train intervals), totaling 1080 pulses over 20 minutes. Stimulation targeted the left DLPFC, located 5 cm anterior to the parasagittal area from the RMT. For sham stimulation, the coil was tilted by 90 degrees to mimic active-rTMS acoustic and procedural cues. The primary outcome was POD incidence within seven postoperative days, assessed twice daily on postoperative days 1, 3, and 7, using validated Confusion Assessment Method protocols. Secondary outcomes included delirium subtype and severity, pain intensity, sleep quality, anxiety and depressive symptoms, frailty, and postoperative nausea and vomiting. Analyses followed an ITT framework, with per-protocol analyses performed for sensitivity.

Among 249 participants included in the ITT analysis, POD incidence was 8.1% in the active-rTMS group compared with 28.8% in the sham-rTMS group (relative risk 0.22; 95% CI 0.10-0.46; p<0.001). Similar findings were observed in the per-protocol analysis, where POD occurred in 8.2% of participants receiving active-rTMS and 28.5% receiving sham-rTMS (relative risk 0.29; 95% CI 0.15–0.56; p<0.001). Among participants who developed POD, delirium severity scores did not differ significantly between groups (p=0.27). Higher MMSE score emerged as an independent protective factor for POD (aOR 0.57; 95% CI 0.44–0.73; p<0.001). Several secondary outcome differences were observed at early postoperative time points. On postoperative day 3, active-rTMS was associated with significantly lower anxiety and depression scales (both p<0.001), with effects persisting through postoperative day 7. Pain scores were significantly lower in active-rTMS compared to sham-rTMS on postoperative day 1 (p<0.001) and day 3 (p<0.001). Similarly, sleep dysfunction scores were significantly lower in the active-rTMS group on postoperative day 1 (p<0.001) and day 3 (p<0.001), although differences were no longer sustained by day 7 (pain p=0.023; sleep p=0.017). Frailty scores were significantly lower in the active-rTMS group on postoperative day 1 (p<0.001) and day 7 (p<0.001), though these differences were not maintained on day 3 (p=0.037). Rates of postoperative nausea and vomiting were similar between groups at all time points, and no serious adverse reactions or safety concerns occurred in either group.

Impact: This prospective randomized, double-blind, sham-controlled trial demonstrates that brief preoperative HF-rTMS targeting the left DLPFC can reduce the incidence of POD in older adults undergoing non-cardiac major surgery. The findings also highlight the potential of preoperative rTMS as a non-pharmacologic strategy for improving early postoperative pain, sleep, frailty, and mood. Larger multisite trials with longer follow-up are warranted to clarify long-term neurocognitive outcomes and determine how rTMS compares with established delirium-prevention strategies.

Gao WB, Wang WH, Zhou ST, Lu ZW, Xiang X, Hu J, Jin TY, Ni CB, Yao M, Ni HD. Efficacy of Repetitive Transcranial Magnetic Stimulation on Postoperative Delirium in Elderly Patients Undergoing Non-Cardiac Major Surgery: A Randomized Controlled Trial. Brain Behav. 2026 Feb;16(2):e71242. doi: 10.1002/brb3.71242. PMID: 41612909; PMCID: PMC12856374.

Digital Mental Health Coaching Interventions Demonstrate Promising Data Supporting an Adjunctive Role to rTMS for MDD

Praveen P. Rajaguru MD, MPH reviewing Rosenberg et al., Journal of Affective Disorders, 2026

In this pilot RCT evaluating adjunctive digital mental health coaching during rTMS for MDD, both coach-supported digital cognitive behavioral therapy (iCBT) and coach-supported narrative psychoeducation (iNarratives) produced comparable reductions in depressive symptoms during a six-week rTMS course. Among 36 participants receiving rTMS, depression severity decreased significantly over time (p < 0.001) but did not differ between the two coaching conditions. Benchmarking analyses suggested that rTMS combined with these coaching interventions produced steeper reductions in depressive symptoms compared with a historical rTMS-only cohort of 29 patients.

rTMS has demonstrated efficacy in treating MDD. However, remission rates are roughly 20-30%, with over 50% of responders expected to relapse after one year. Strategies that enhance treatment

engagement or augment therapeutic effects may help maximize treatment response. Psychotherapeutic interventions may have complementary benefit but are not easily accessible. Digital mental health programs supported by human coaching may offer a more scalable supplementary approach. This RCT compared clinical outcomes of coach-supported digital iCBT and iNarratives interventions delivered during rTMS for MDD, while also comparing with expected outcomes of rTMS alone.

Inclusion criteria were diagnosis of MDD, prior lack of antidepressant treatment response, right-handedness, and age 18-75. Exclusion criteria were comorbidities interfering with rTMS response and rTMS contraindications. Forty adults were included and 35 completed the study. rTMS course lasted at least 30 sessions (5 sessions weekly for 6 weeks), and parameters for each session were 3000 pulses of 10 Hz rTMS administered to the left DLPFC targeted with the Beam F3 method with a train duration of 40s and inter-train interval of 11s. Participants were randomized to either coach-supported internet-based cognitive behavioral therapy (iCBT), or coach-supported narrative psychoeducation (iNarratives). iCBT was delivered using the This Way Up Anxiety and Depression Program involving self-paced CBT lessons. iNarratives comprised a series of mental health videos (Stories of the Mind), created by the Public Broadcasting Service (PBS) in the USA. Both groups completed weekly video visits from trained study coaches that adhered to standardized procedures. Depression severity was assessed using the HAM-D as the primary outcome, with other secondary psychometrics and multilevel models also used to assess depressive symptoms. Benchmarking analyses were also used to compare outcomes in this sample with a separate sample of 29 patients who received rTMS without coaching.

Depression severity improved significantly during the six-week rTMS course across both intervention groups (main effect of time $p < 0.001$). No significant difference was observed between the iCBT-with-coaching and iNarratives-with-coaching conditions in HDRS symptom reduction (Group X Time $\chi2(1) = 0.19$, $p = .662$) or response rates ($\chi2= 0.20$, $p = .654$). Secondary analyses showed varying secondary effects across interventions. The iNarratives group had greater improvements in positive emotion ($\chi2(1) = 3.75$, $p = .053$) and reductions in functional impairment ($\chi2(1) = 3.93$, $p = .047$), whereas the iCBT group showed lower dropout rates from the coaching program ($\chi2(1) = 8.34$, $p = .004$). Exploratory benchmarking analyses comparing the RCT participants (N = 36) with a historical rTMS-only cohort (N = 29) revealed a significant Group × Time interaction ($\chi2(1) = 4.24$, $p = .039$), suggesting greater reductions in depression severity among patients receiving rTMS combined with coaching interventions.

Impact: These findings suggest that coach-supported digital mental health interventions can be feasibly and effectively integrated into rTMS treatment for MDD, possibly with benefits beyond treating with rTMS alone. They also suggest similar efficacy in MDD symptoms across the iCBT (CBT) and iNarratives (supportive psychotherapy) approaches, with the iNarratives group showing relatively greater benefit for creating positive emotions and improved functional impairment. A notable limitation of the study is the use of a benchmarking sample that differed from the RCT cohort. Future studies may incorporate waitlist control groups to better isolate the effects of digital mental health coaching, recruit larger and more diverse samples, explore other forms of psychotherapeutic adjuncts, and experiment with the temporal relationship between interventions.

Rosenberg BM, Barnes-Horowitz NM, Ngo D, et al. Does mental health coaching improve efficacy of transcranial magnetic stimulation for major depression? A pilot randomized controlled trial and benchmarking study. J Affect Disord. 2026;402:121366. doi:10.1016/j.jad.2026.121366

Early Skew Towards Positive Emotional Processing Bias May Predict Clinical Response to rTMS in MDD

Praveen P. Rajaguru MD, MPH reviewing Sarrazin et al., Molecular Psychiatry, 2026

In this prospective, open-label study of iTBS for MDD, early shifts toward positive emotional processing were reported as predictive of antidepressant response after four weeks of treatment. Among 49 adults receiving iTBS to the left DLPFC, those who ultimately responded demonstrated significantly greater early increases in behavioral and neural measures of positive bias during facial emotion recognition tasks. This may support a similar neurocognitive mechanism of action for rTMS as is observed in other treatments for MDD.

A hallmark of MDD is negatively biased emotional processing that may be a downstream effect of decreased regulatory control from the DLPFC. Cognitive neuropsychological models of various treatments for MDD including antidepressants posit that effective treatments reverse these biases as one of the early predictors of clinical improvement. However, this hypothesis has not yet been tested with regards to rTMS. This study examined whether observable early behavioral and neural changes in positive emotional bias during rTMS (specifically iTBS) treatment for MDD would predict subsequent clinical response.

Forty-nine adults with MDD were included in the study. Inclusion criteria were age 18-65, HAM-D >14, and diagnosis of MDD; exclusion criteria included ongoing substance use, manic or psychotic symptoms, current SI, or contraindications to rTMS. These 49 adults received open-label iTBS to the left DLPFC for 20 sessions over four weeks (1,800 pulses per session at 100% RMT). Positive bias measurements were obtained at baseline and after approximately one week of treatment, assessed using a Facial Expression Recognition Task (FERT) and task-based fMRI during presentation of positive vs negative faces. Positive bias was defined as a 1) FERT outcome of increased response rate or 2) fMRI outcome of increased blood-oxygen level dependent (BOLD) response in exposure to positive vs negative faces. Clinical response was defined as ≥50% reduction in Hamilton Depression Rating Scale (HAM-D) score at week four.

Thirty-three of 49 participants (67%) met criteria for clinical response. Responders demonstrated greater early increases in behavioral positive bias as measured by FERT testing compared with non-responders. Specifically, responders had a greater tendency to classify ambiguous facial expressions as happy (Clinical Response X Time interaction: $F(1,44) = 10.5$, $p = 0.002$). Logistic regression demonstrated that early positive bias predicted treatment response even when controlling for demographics, medication, and baseline HAM-D ($\beta = 2.18$, odds ratio 3.39, 95% CI 1.5–9.7). Analysis of fMRI data showed that clinical improvement correlated with increased positive vs negative emotional activation in the anterior cingulate cortex (peak $t = 5.35$, $p = 0.045$). Additional associations were observed in default mode network regions including the precuneus and angular gyrus (peak $t = 5.70$, $p = 0.008$), suggesting wider spread effects across brain regions. Machine learning models incorporating these behavioral and neural bias measures explained substantially greater variance in future treatment response ($R^2 = 0.52$) than models using only clinical variables ($R^2 = 0.19$).

Impact: These findings suggest that rTMS may create early shifts toward positive emotional processing, which may predict positive clinical outcomes. However, because depressive symptoms also improved significantly by the second week of treatment, the temporal and causal relationship between these neurobehavioral changes and clinical improvement remains unclear. The absence of a control group further limits interpretation of the findings. Regardless, this study contributes to ongoing efforts to identify predictive biomarkers of rTMS response, with the goal of improving patient selection and optimizing treatment strategies.

Sarrazin V, Suen P, Cavendish B, et al. Positive bias in brain and behaviour as a mechanism of transcranial magnetic stimulation depression treatment. Mol Psychiatry. Published online February 12, 2026. doi:10.1038/s41380-026-03485-8

cTBS (continuous theta burst stimulation)
DBS (deep brain stimulation)
dTMS (deep transcranial magnetic stimulation)
ECT (electroconvulsive therapy)
HFL (high frequency left, 10 Hz stimulation to left DLPFC)
HF-rTMS (high frequency repetitive transcranial magnetic stimulation; 10 Hz unless otherwise stated)
iTBS (intermittent theta burst stimulation)
MST (magnetic seizure therapy)
TBS (theta-burst stimulation; TMS delivered as triplet burst pulses at 50 Hz, repeated at 5 Hz)
TENS (transcutaneous electrical nerve stimulation)
TMS (transcranial magnetic stimulation)
rTMS (repetitive transcranial magnetic stimulation)
tDCS (transcranial direct current stimulation)
tACS (transcranial alternating current stimulation)
TPS (transcranial pulse stimulation)

BOLD (blood oxygen level dependent)
DTI (diffusion tensor imaging)
EEG (electroencephalography)
EMG (electromyography)
fMRI (functional magnetic resonance imaging)
MRI (magnetic resonance imaging)
MT (motor threshold)
RMT (resting MT)

ADHD (attention-deficit/hyperactivity disorder)
AUD (alcohol use disorder)
GAD (generalized anxiety disorder)
MDD (major depressive disorder)
OCD (obsessive compulsive disorder)
PTSD (post-traumatic stress disorder)
SUD (substance use disorder)
TRD (treatment resistant depression)

BAI (Beck Anxiety Inventory)
BDI (Beck Depression Inventory)
CGI (clinical global impression scale)
HAM-A (Hamilton Anxiety Rating Scale)
HAM-D / HDRS (Hamilton Depression Rating Scale)
MADRS (Montgomery-Asberg Depression Rating Scale)
MoCA (Montreal Cognitive Assessment)
PANSS (Positive and Negative Symptom Scale)
QIDS (Quick Inventory of Depressive Symptomatology)
YBOCS (Yale-Brown Obsessive Compulsive Scale)

ANOVA (analysis of variance)
AUC (area under the curve)
CI (confidence interval)
FDA (United States Food and Drug Administration)
ICA (independent component analysis)
ITT (intention to treat)
OR (odds ratio)
PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)
RCT (randomized controlled trial)
ROC (receiver operating characteristic)
SMD (standard mean difference)

BA (Brodmann area)
DLPFC (dorsolateral prefrontal cortex)
DMPFC (dorsomedial prefrontal cortex)
M1 (primary motor cortex)
mPFC (medial prefrontal cortex)
OFC (orbitofrontal cortex)
SMA (supplementary motor area)