Research Article

Similar Outcomes in Treating Major Depressive Disorder With 10 Hz Repetitive Transcranial Magnetic Stimulation (rTMS) Versus Intermittent Theta Burst Stimulation (iTBS): A Naturalistic Observational Study

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Background: **Results reported in the existing literature have shown intermittent theta burst stimulation (iTBS) to be noninferior to 10 Hz repetitive transcranial magnetic stimulation (rTMS) in treating major depressive disorder (MDD) when targeted at the left dorsolateral prefrontal cortex. The goal of this naturalistic observational study was to further explore potential differences between these 2 treatment modalities in treating depression in a real-world cohort.**

Methods: **The participants were 105 patients, 18 years of age or older with a diagnosis of MDD who received standard clinical 10 Hz rTMS or iTBS treatment between 2016 and 2020. Clinical outcomes of depression treatment were assessed on the basis of changes in scores on the Patient Health Questionnaire-9 and on the Montgomery-Åsberg Depression Rating Scale.**

Results: **Reduction in depression symptoms was measured with the Patient Health Questionnaire-9 and Montgomery-Åsberg Depression Rating Scale from baseline to end of treatment, and no discernible differences in percent change, response, remission, or minimum clinically important difference were found between the 10 Hz rTMS and iTBS treatment groups.**

Conclusions: **Findings in an observational, real-world clinical sample showed no significant differences in outcomes between 10 Hz rTMS and iTBS targeted at the left dorsolateral prefrontal cortex in the treatment of MDD. Because of the shorter treatment time involved, the choice of iTBS may reduce hospital exposure and increase savings and the treatment capacity of clinics without sacrificing effectiveness.**

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KEY WORDS: depression, transcranial magnetic stimulation (TBS), intermittent theta burst stimulation (iTBS), clinical practice, observational study

Major depressive disorder (MDD) is a common mental disorder that is currently one of the leading causes of disability and disease burden in people across the globe.[1] As the development of innovative pharmacologic therapies for treatment-refractory depression has slowed, newer, noninvasive treatment modalities such as repetitive transcranial magnetic stimulation (rTMS) have increasingly become the focus of research as alternative therapy options. Transcranial magnetic

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stimulation (TMS) generates very brief, pulsed magnetic fields that travel through the scalp and skull to induce electrical currents in the cerebral cortex of the brain.[2] When applied repetitively and targeted precisely, these electrical currents can modulate activity and excitability in regions of the brain that are generally dysfunctional in people with depression without some of the adverse cognitive and memory impairments seen with electroconvulsive therapy or the systemic side effects of pharmacologic interventions.[2,3]

Within the past 25 years, a multitude of multisite, randomized as well as sham-controlled clinical trials, in addition to various meta-analyses, have established both the safety and efficacy of rTMS therapy for depression.[4–8] The standard of care for TMS treatment for depression has been 10 Hz rTMS, which was first cleared by the US Food and Drug Administration (FDA) in 2008 for treatment of MDD when targeted at the left dorsolateral prefrontal cortex (DLPFC), delivering 3000 pulses over 37.5 minutes.[9] More recently, a newer stimulation paradigm, intermittent theta burst stimulation (iTBS), was cleared by the FDA in 2018 for the treatment of MDD in adults when targeted at the left DLPFC, following the results of the THREE-D trial—a randomized noninferiority study—which found iTBS to be noninferior when compared with 10 Hz rTMS.[10,11] In iTBS, repeated short trains of pulsed magnetic fields are generated to induce electrical currents in the cortex, imitating endogenous theta rhythms associated with the initiation of long-term potentiation in neurons. This treatment approach is thought to be more efficient for achieving a therapeutic effect, delivering 600 pulses in just over 3 minutes, as opposed to the much longer 37.5-minute treatment protocol for 10 Hz rTMS.[12,13]

As the standard 10 Hz rTMS option involves a substantially longer treatment session than its newer and noninferior iTBS counterpart, the use of the standard rTMS option could potentially limit an institution's capacity to treat more patients, in addition to decreasing the institutions' ability to be compensated for those treatments.[11] In the dynamic and ever-changing era of COVID-19 (coronavirus disease 2019), hospitals have lost millions of dollars due to canceled procedures, and they continue to struggle with efficiency problems due to the unique workflow challenges posed by new sanitization protocols and protective measures. Optimizing treatment capacity is thus increasingly important in maintaining patient access to care and the financial viability of hospitals. Given these factors, it is imperative for clinicians and clinics to further investigate if 10 Hz rTMS and iTBS, delivered in a "real-world" outpatient setting, achieve comparable therapeutic benefits for treating MDD.

To better address questions concerning differences between these therapy modalities and the impact of those potential differences in a clinical setting, naturalistic observation studies allow for the inclusion of participants with a diverse range of comorbidities and who are receiving a variety of medications in realistic, standard-of-care treatment protocols, expanding the generalizability of the findings to everyday clinical practice and decision-making. For example, the THREE-D trial discussed above employed neuronavigational targeting, a technology rarely used in standard clinical TMS practice settings at present. In the single-site, naturalistic observation study described here, we examined the results of a retrospective chart review of 131 patients with MDD who received standard clinical 10 Hz rTMS or iTBS therapy targeted at the left DLPFC to better elucidate potential differences in clinical outcome between the 2 modalities.

METHODS

Patient Population

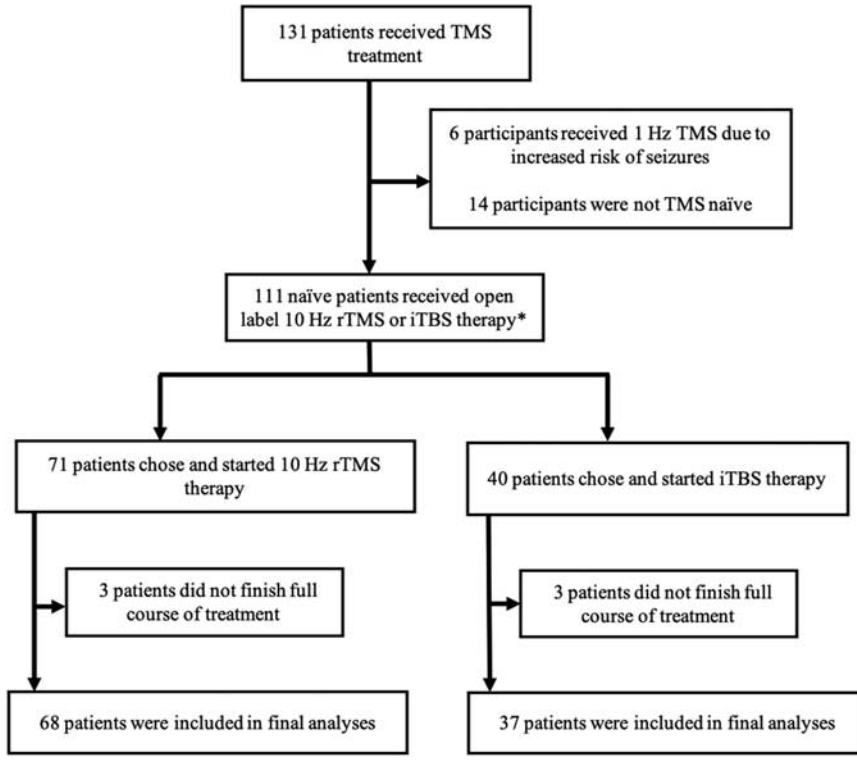
This analysis involved data acquired from a retrospective chart review of 131 participants who received standard clinical rTMS or iTBS targeted at the left DLPFC between December 2016 and February 2020. Inclusion criteria were being a patient 18 years of age or older with an existing diagnosis of MDD who had been referred to the interventional psychiatry service in the University of Iowa Hospitals and Clinics. The patients were evaluated by a physician with expertise in TMS and deemed appropriate candidates for TMS treatment based on an extensive diagnostic history and an examination including medication reconciliation, evaluation of previous treatment trials, and screening for *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (DSM-5) diagnostic categories. Patients were excluded from the study and from treatment if they were younger than 18 years old, had a diagnosis of epilepsy or other seizure disorder, had implanted ferromagnetic equipment in their face or skull near the rTMS stimulation target, or had previously received TMS treatment of some kind.

To preserve the generalizability of our study results to standard clinical practice, we did not exclude patients with other comorbid psychiatric disorders. In this naturalistic study, participants were allowed to continue taking their prescribed psychiatric medication throughout the duration of their TMS course. This study was approved by the Institutional Review Board at the University of Iowa. Figure 1 shows the outcomes of the 131 participants who received TMS treatment during the time frame of the study. We included 105 participants in our final analyses.

DLPFC-rTMS and -iTBS Technique

Before the FDA clearance of iTBS for use in MDD in 2018, patients primarily received 10 Hz rTMS stimulation. After the clearance of iTBS, the prescribing physician decided on 10 Hz rTMS versus iTBS therapy based on a discussion with the patient, taking into account factors such as the patient's schedule. Participants initially received stimulation with the Magventure MagPro X100 Figure 8 Butterfly Coil with Active Cooling (Magventure, Alpharetta, GA) at the left primary motor cortex to determine resting motor threshold via visual observation of right-handed thumb twitches in 3 of 5 trials.[14] Trained technicians then targeted the left DLPFC using either the Beam F3 method (n = 23) or 5.5 cm rule (n = 82).[14–16] Patients receiving 10 Hz stimulation received 3000 pulses at 120% the intensity of their motor threshold, in a 37.5-minute treatment session (4-s trains with a 26-s intertrain interval), while patients receiving iTBS received 600 pulses at 120% the intensity of

FIGURE 1. Disposition of study participants.



**Before Food and Drug Administration (FDA) clearance of iTBS in 2018, participants mainly received 10 Hz rTMS. After the FDA clearance, participants were able to chose between 10 Hz rTMS and iTBS therapy. iTBS indicates intermittent theta burst stimulation; rTMS, repetitive transcranial magnetic stimulation; TMS, transcranial magnetic stimulation.*

their motor threshold in just over 3 minutes (50 Hz triplets patterned into 5 Hz stimulation, 2-s trains with 8-s intertrain intervals). In our study, patients received a variable number of treatment sessions (average of 32) as clinically indicated, with treatments occurring for 5 consecutive days a week for 4 to 6 weeks, occasionally followed by a taper period of 1 to 3 weeks.

Clinical Assessments

All participants in this study underwent a baseline clinical assessment consisting of a self-report scale [Patient Health Questionnaire-9 (PHQ-9)] before starting treatment. After initial data collection had begun, an additional clinician-administered questionnaire [Montgomery-Åsberg Depression Rating Scale (MADRS)] was added, and 61 of the 68 10 Hz rTMS participants and 29 of the 37 iTBS participants had a baseline MADRS recorded before treatment as well. A consistent team of psychiatrists skilled in the administration of the MADRS performed all of the assessments for both treatment groups. The participants were assessed by the same psychiatrist whenever possible, although this was not always the case. The same team evaluated both treatment groups.

Participants completed these questionnaires at the initiation of treatment and at the end of each treatment week to track depression severity and improvement. The baseline score was ascertained on the first treatment visit, and the final score was determined at the final treatment visit. Scores from the PHQ-9 and MADRS were used to determine our primary and secondary outcome measurements to assess if there were differences in effectiveness between 10 Hz rTMS and iTBS to the left DLPFC for treating MDD.

The percent change in scores on the PHQ-9 and MADRS from baseline to end of treatment was calculated, as well as response and remission rates. Response for both the PHQ-9 and MADRS was defined as $> 50\%$ reduction in scale score relative to baseline,[17–19] and remission was defined as a score < 5 for the PHQ-9 and as a score < 10 for the MADRS.[20–22] Finally, comparisons were made using the minimum clinically important difference (MCID) metric. MCID is an increasingly studied outcome that represents the smallest change on a given scale capable of producing a clinically meaningful and observable improvement. For the PHQ-9, the research-validated MCID is a reduction of ≥ 5 points from baseline, and for the MADRS, the MCID is a reduction of ≥ 2 points from baseline.[17,18]

Data Analysis

Summary statistics were calculated for all measures of interest. Continuous measures are presented as means (SDs), and categorical measures are presented with counts and percentages. Assessments of differences on these measures between therapies used 2-tailed, independent sample t tests and 2-tailed Pearson χ^2 tests. Comparisons with P-values < 0.05 were considered statistically significant. All analyses were conducted using IBM SPSS Statistics (Version 26). The null hypothesis of our study was that there would be differences in clinical outcomes including response, remission, and MCID using changes on the PHQ-9 and MADRS between participants receiving 10 Hz rTMS or iTBS therapy for MDD. The co-primary outcomes of our study were the percent change from baseline to end of treatment on the PHQ-9 and the MADRS. Secondary outcomes of our study were response rate, remission rate, and MCID of treatment, using changes in overall score on both the PHQ-9 and MADRS from baseline to end of treatment.

RESULTS

Of the 131 patients who received TMS treatment for depression, 105 participants met the inclusion and exclusion criteria to be included in the analysis (Fig. 1): 68 of these participants (64.8%) completed a course of standard clinical 10 Hz rTMS, while 37 (35.2%) completed a course of iTBS. In total, the final patient population received on average 33.2 ± 5.10 treatment sessions. Table 1 displays the baseline demographic information on the 105 participants included in the final analyses. The only statistically significant difference between the 10 Hz rTMS and iTBS groups at baseline was the rate of posttraumatic stress disorder (PTSD) diagnoses, with 13 (19.1%) participants in the 10 Hz group and 5 (13.5%) participants in the iTBS group diagnosed with PTSD ($\chi^2 = 5.541$, $P = 0.019$).

TABLE 1. Baseline Demographic and Clinical Characteristics of Study Participants (N = 105)

	n (%)		
	10 Hz rTMS (n = 68)	***iTBS (n = 37)***	***P***
Age (mean ± SD)	53.47 ± 15.7	49.62 ± 17.337	0.251
Female	41 (60.0)	21 (57.0)	0.728
Baseline PHQ-9 (range: 0-27)	17.8 (4.9)	19.0 (4.4)	0.270
Baseline MADRS (range: 0-60)	30.3 (6.5)	28.4 (7.6)	0.326
Comorbid disorders			
Generalized anxiety disorder	46 (67.7)	16 (43.2)	0.178
Obsessive-compulsive disorder	7 (10.3)	2 (5.4)	0.921
Posttraumatic stress disorder	13 (19.1)	5 (13.5)	0.019*
Attention-deficit/hyperactivity disorder	9 (13.2)	3 (8.1)	0.155
Prior electroconvulsive therapy	20 (29.0)	8 (21.6)	0.393
Pharmacotherapy during TMS treatment			
Prescribed antidepressants	62 (91.2)	33 (89.2)	0.740
Prescribed benzodiazepines	41 (66.1)	17 (35.0)	0.161
Prescribed stimulants	14 (20.6)	11 (29.7)	0.928
Prescribed antipsychotics	27 (39.7)	13 (35.1)	0.756

*$P < 0.05$.
iTBS indicates intermittent theta burst stimulation; MADRS, Montgomery-Åsberg Depression Rating Scale; PHQ-9, Patient Health Questionnaire-9; rTMS, repetitive transcranial magnetic stimulation; TMS, transcranial magnetic stimulation.

Co-primary outcomes of our study, the percent change in scores on the PHQ-9 and MADRS from baseline to end of treatment, displayed no significant differences between 10 Hz rTMS and iTBS (Table 2). On the self-report PHQ-9, the percent improvement for 10 Hz rTMS was 41.9% (SD = 36.2), and for iTBS it was 39.9% (SD = 38.6); $F = 0.064$, $P = 0.683$ (Fig. 2A). For the clinician-reported MADRS, the percent improvement for 10 Hz rTMS was 44.4% (SD = 31.4), and for iTBS, it was 49.7% (SD = 27.3); $F = 1.410$, $P = 0.238$ (Fig. 2B). Figure 2C shows how the average PHQ-9 scores in both the 10 Hz rTMS and iTBS groups changed over time.

Validated clinical outcomes including response, remission, and MCID were also measured, using changes in scores from baseline to end of treatment on the PHQ-9 and the MADRS. Specifically, the response rate on the PHQ-9 in the 10 Hz rTMS group was 48.5% compared with 46.0% in the iTBS group: $\chi^2 = 0.064$, $P = 0.800$ (Table 2, Fig. 3A). Remission rates on the PHQ-9 in the 10 Hz rTMS group and iTBS group were 29.4% and 21.6%, respectively: $\chi^2 = 0.744$, $P = 0.389$ (Table 2, Fig. 3B). Finally, rates of those achieving an MCID on the PHQ-9 in the 10 Hz rTMS and iTBS groups were 70.6% and 64.9%, respectively: $\chi^2 = 0.364$, $P = 0.546$ (Table 2, Fig. 3C).

Response rates on the MADRS were 52.5% and 58.6% for the 10 Hz rTMS and iTBS groups, respectively: $\chi^2 = 0.301$, $P = 0.583$ (Table 2, Fig. 4A). Remission rates on the MADRS were 31.1% and 34.5% for the 10 Hz rTMS and iTBS groups, respectively: $\chi^2 = 0.100$, $P = 0.752$ (Table 2, Fig. 4B). Finally, rates of those achieving an MCID in the 10 Hz rTMS and iTBS groups were 86.9% and 93.1%, respectively: $\chi^2 = 0.770$, $P = 0.380$ (Table 2, Fig. 4C).

DISCUSSION

The findings from our naturalistic observation study demonstrate similar effectiveness and a lack of significant difference between left DLPFC 10 Hz rTMS and iTBS in reducing depression symptom severity. This was true when measured both by patient self-report and with a clinician-administered depression scale. No significant differences were found in overall percent change on the PHQ-9 and MADRS scales, as

TABLE 2. Changes in Clinical Outcomes From Baseline to End of Treatment

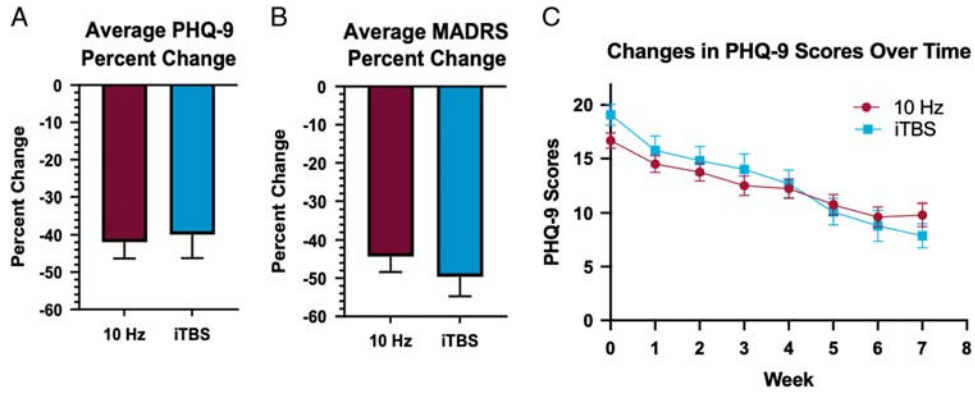
	n (%)		
	10 Hz rTMS	***iTBS***	***P***
Clinical Rating Scale			
PHQ-9 Self Rating Scale	N = 68	N = 37	
Percent improvement from baseline [mean (SD)]	41.9 (36.2)	39.9 (38.6)	0.683
Response rate	33 (48.5)	17 (46.0)	0.800
Remission rate	20 (29.4)	8 (21.6)	0.389
MCID rate	48 (70.6)	24 (64.9)	0.546
MADRS Clinician Rating Scale	N = 61	N = 29	
Percent improvement from baseline [mean (SD)]	44.4 (31.4)	49.7 (27.3)	0.238
Response rate	32 (52.5)	17 (58.6)	0.583
Remission rate	19 (31.1)	10 (34.5)	0.752
MCID rate	53 (86.9)	27 (93.1)	0.380

iTBS indicates intermittent theta burst stimulation; MADRS, Montgomery-Åsberg Depression Rating Scale; MCID, minimum clinically important difference; PHQ-9, Patient Health Questionnaire-9; rTMS, repetitive transcranial magnetic stimulation.

well as no differences in response rate, remission rate, or MCID as determined by changes from baseline to the end of treatment. Our study is among the first to directly compare 10 Hz rTMS and iTBS treatment protocols in a "real-world" naturalistic patient sample with standard-of-care treatment protocols commonly used in the United States. The outcomes of this study are consistent with those of previous studies suggesting that 10 Hz rTMS and iTBS have similar effectiveness in treating MDD.[11]

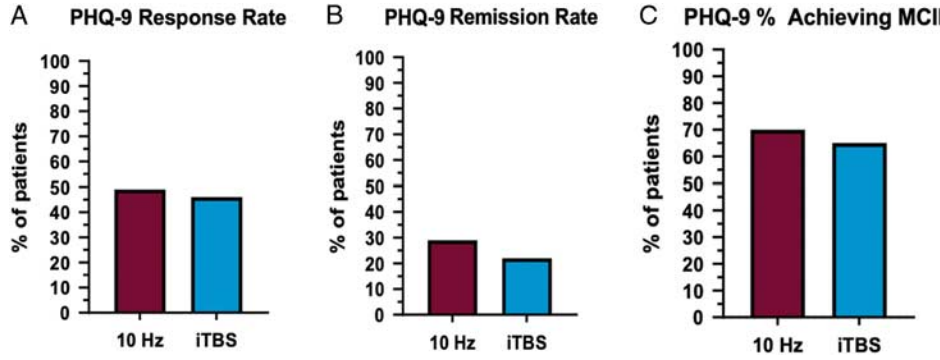
The 10 Hz rTMS group in our study had a 48.5% response rate and a 29.4% remission rate on the basis of the PHQ-9 compared with an iTBS response rate of 46.0% and remission rate of 21.6%. These

FIGURE 2. Changes in depression rating scales from baseline to end of treatment.



A, Average percent change in PHQ-9 scores from baseline to end of treatment in 10 Hz rTMS and iTBS groups. B, Average percent change in MADRS scores from baseline to end of treatment in the 10 Hz rTMS and iTBS groups. C, Depiction of average PHQ-9 scores in the 10 Hz rTMS and iTBS groups at weekly intervals from baseline to end of treatment. iTBS indicates intermittent theta burst stimulation; MADRS, Montgomery-Åsberg Depression Rating Scale; PHQ-9, Patient Health Questionnaire-9; 10 Hz, 10 Hz repetitive transcranial magnetic stimulation.

FIGURE 3. Percent of patients in the 10 Hz rTMS and iTBS groups meeting validated clinical outcome criteria on PHQ-9 scores.

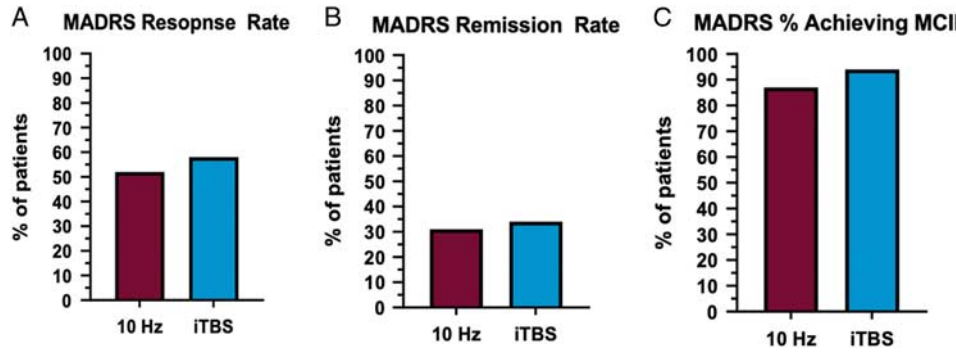


A, Percent of patients classified as responders: > 50% reduction from baseline scores at end of treatment. B, Percent of patients classified as reaching remission: final score < 5 on the PHQ-9. C, Percent of patients classified as having achieved an MCID: change ≥ 5 from baseline. iTBS indicates intermittent theta burst stimulation; MCID, minimum clinically important difference; PHQ-9, Patient Health Questionnaire-9; 10 Hz, 10 Hz repetitive transcranial magnetic stimulation.

response and remission rates track closely with the results of the THREE-D noninferiority trial, even though the THREE-D trial used a different primary outcome measure, the 17-item Hamilton Depression Rating Scale (10 Hz rTMS = 47% response and 27% remission: iTBS = 49% response and 32% remission).[11] The lower remission rate in the iTBS group as measured by the PHQ-9 was the largest discrepancy between treatment groups in our study; however, this discrepancy was not seen when using the MADRS depression rating scale, which found a remission rate of 34.5% in the iTBS group compared with a 31.1% remission rate in the 10 Hz rTMS group.

As TMS becomes an increasingly utilized noninvasive alternative to pharmacologic therapy in the treatment of MDD, it is crucial to compare the clinical effectiveness of different treatment options. Although

FIGURE 4. Percent of patients in the 10 Hz rTMS and iTBS groups meeting validated clinical outcome criteria on MADRS scores.



A, Percent of patients classified as responders: > 50% reduction from baseline scores at end of treatment. B, Percent of patients classified as reaching remission: final score < 10 on the MADRS. C, Percent of patients classified as having achieved an MCID: change ≥ 2 from baseline. iTBS indicates intermittent theta burst stimulation; MADRS, Montgomery-Åsberg Depression Rating Scale; MCID, minimum clinically important difference; 10 Hz, 10 Hz repetitive transcranial magnetic stimulation.

one must be cautious in making comparisons across studies, our findings suggest that rTMS outperforms second-line and third-line pharmacologic therapies for patients with treatment-resistant MDD when comparing response and remission rates.[23,24] Our findings are also consistent with the response and remission rates of rTMS treatment for MDD found in other clinical studies of 10 Hz rTMS for MDD.[25]

In addition to clinical effectiveness, our study also found that 94.6% of participants were adherent to a full TMS treatment course, which closely follows the findings of a multisite, observational, naturalistic study that found an 83% adherence rate to TMS.[25] We did not find any notable differences in self-reported adverse effects between the 2 TMS treatments we examined; however, adverse effects were not systematically assessed beyond those that led to treatment discontinuation. Within the 10 Hz rTMS group, 1 participant reported intolerable headaches from the TMS therapy, while another participant reported increased myoclonic jerks and auras outside of treatment. This latter case was complicated by the patient abruptly discontinuing benzodiazepine medication around the same time. One participant in the iTBS group reported intolerable pain at the stimulation site. There were no seizures or other serious adverse effects in either treatment group. With only 3 participants self-reporting intolerable effects serious enough to withdraw from treatment, we concluded that 10 Hz rTMS and iTBS are similarly safe and well-tolerated treatments for depression.[7,25–28]

Because tightly controlled, randomized clinical trials (RCTs) include more stringent treatment parameters and additional exclusionary criteria, it is important to contrast findings from such RCTs with those of observational studies such as the one presented here. Observational studies allow us to confirm findings from RCTs and explore their generalizability in real-world patient populations that may more closely align with typical practice settings, such as the inclusion of patients who may be taking a variety of medications or who may have multiple medical and psychiatric comorbidities. For example, concurrent use of medications like benzodiazepines while receiving rTMS treatment for depression has been associated with a blunted improvement in depression symptomatology, whereas psychostimulant medications have been linked to increased responsiveness to rTMS therapy in depressed subjects.[29] In light of these factors, it is reassuring to see the positive clinical outcomes of TMS delivered in clinical trial settings further confirmed in real-world observational studies like ours.

Although observational studies may extend the generalizability of study findings to patients who more closely resemble patient populations receiving TMS treatment in clinics across the nation, several limitations in studies such as ours should also be considered when interpreting results. One of those limitations is the lack of a placebo group. Several studies have already demonstrated the efficacy of rTMS compared with sham treatment for MDD,[7,9,26,27] and our observational study was focused on further exploring potential differences between the 2 groups we examined. Due to the observational nature of our study, we included patients with all levels of treatment resistance and with all potential comorbidities. For example, the rates of benzodiazepine and stimulant medication prescriptions among participants were 41.2% and 23.9%, respectively. In addition, there was a statistically significant difference in comorbid PTSD diagnoses between the 10 Hz rTMS and iTBS groups at 19.1% and 13.5%. Notably, existing research has demonstrated that a comorbid PTSD diagnosis may impact a person's response to TMS treatment for depression.[30,31] These reported limitations may reduce our ability to comment specifically on the effectiveness of TMS in treating MDD in isolation, as psychiatric comorbidities, increasing levels of treatment resistance, and concomitant medication use may either decrease or increase the effectiveness of TMS therapy for depression.

Within our naturalistic study paradigm, we did not randomly select patients to participate in our study, nor did we randomize patients to receive a specific treatment protocol. Participants sought TMS treatment and were involved in the decision-making process to identify the most appropriate protocol for themselves. In addition, the targeting method used to identify the left DLPFC stimulation site was not standardized in this population, with some patients receiving Beam F3 targeting and others receiving 5.5 cm rule targeting. Although some research suggests potential unique effects from one targeting method versus another, our sample showed similar overall treatment response between groups with no significant interaction

between treatment type (iTBS vs. 10 Hz) or targeting method (Beam F3 vs. 5.5 cm rule). Despite this, such factors could lead to a potential self-selection bias or other confound in our study, limiting our ability to evaluate the 10 Hz versus iTBS question in isolation from other factors. For example, without randomization, the drastic difference in treatment session lengths between 10 Hz rTMS and iTBS introduces the possibility that participants self-stratified into groups based on dimensions that could impact a person's responsiveness to treatment for depression, such as working status, disability, or other factors, further increasing possible confounding variables in our study.

A final limitation of our study was the lack of statistical power to detect small differences in clinical outcomes between 10 Hz rTMS and iTBS when treating MDD. A larger sample would have better allowed us to comment on the significance of the small differences in outcome measures we found. In the face of these limitations, we believe that increased research, including multisite trials directly comparing 10 Hz rTMS and iTBS, will help uncover potential differences or the lack thereof between these treatment modalities. Further comparisons of the 2 modalities in novel treatment paradigms will further illuminate possible discrepancies between the outcomes of these treatment modalities. Two such promising protocols include the Stanford Accelerated Intelligent Neuromodulation Therapy (SAINT) protocol, which provides a rapid and efficacious antidepressant iTBS treatment course over 5 consecutive days,[32] and the "19 Minute Dash Protocol," which reduces the 10 Hz rTMS protocol interstimulus interval from 26 to 11 seconds, allowing for faster and similarly effective 10 Hz rTMS treatment.[33]

CONCLUSIONS

Our study, one of the first to directly compare 10 Hz rTMS and iTBS treatment protocols in a "real-world" naturalistic patient sample, adds to the growing literature demonstrating a lack of discernible differences between these 2 treatment modalities in clinical effectiveness in the treatment of MDD. In the time of COVID-19, when hospitals face both tighter budgetary constraints due to canceled procedures and time constraints associated with the implementation of thorough sanitation protocols, the demonstration of comparable outcomes between these 2 protocols (iTBS being 10 times shorter than the standard of care without sacrificing effectiveness) becomes even more important. Using data from the THREE-D trial, a cost-analysis was completed comparing the prices of entire courses of treatment with 10 Hz rTMS versus iTBS.[34] Considering the shorter technician time required for the 3-minute iTBS sessions, in addition to the increased treatment capacity and ability to see more patients per day, iTBS could potentially save health care thousands of dollars per course of TMS treatment without sacrificing effectiveness in the treatment of depression. Our study found no significant differences in the treatment of MDD with 10 Hz rTMS or iTBS targeted at the left DLPFC. The era of COVID-19 has cut budgets and time to treat patients, and by implementing iTBS as a first-line TMS treatment option for depression, psychiatrists may increase patient access to effective treatment while simultaneously helping clinics save time and money.

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