Intermittent Theta Burst Stimulation (iTBS) Has Similar Efficacy to 10 Hz Repetitive Transcranial Magnetic Stimulation (rTMS) in Treating Major Depressive Disorder

University of Iowa Carver College of Medicine
University of Iowa Health Care

Nathen Spitz[1], Patrick Ten Eyck[2], Krystal Nizar[1], Nicholas Trapp[1]

1. University of Iowa Carver College of Medicine Department of Psychiatry
2. University of Iowa Institute for Clinical and Translational Science

Introduction

- Major depressive disorder is a leading cause of disability and disease burden across the globe[1].
- A 2018 study found that 10 Hz repetitive transcranial stimulation (rTMS) which delivers 3000 pulses in 37.5 minutes, and intermittent theta burst stimulation (iTBS), a newer modality that delivers 600 pulses in 3 minutes, to be non-inferior when stimulating the left dorsolateral prefrontal cortex (DLPFC) while treating major depressive disorder[2,3].

In this study we aim to further elucidate and examine if there are any potential differences between 10 Hz rTMS and iTBS in treating major depressive disorder.

Methods

- **Subjects**: This retrospective cohort study consisted of 105 patients (age ≥ 18) with diagnoses of major depressive disorder who were recruited during evaluation for TMS therapy at the University of Iowa Hospitals and Clinics between December 2017 and February 2020.
- **Treatment:** Patients received open-label 10 Hz rTMS or iTBS therapy targeted at the left DLPFC at 120% their resting motor threshold for 20-36 TMS treatments.

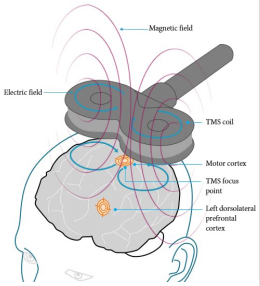

Figure 1. A cartoon used with permission that depicts a transcranial magnetic stimulator (TMS) coil targeting the dorsolateral prefrontal cortex (DLPFC)[4].

Validated outcomes were defined by the literature as:

	PHQ-9	MADRS
Response[5,7]	> 50% reduction from baseline	> 50% reduction from baseline
Remission[6,8]	Final score < 5	Final score < 10
Minimum Clinically Important Difference[5,7]	> 5 pt reduction from baseline	> 2 pt reduction from baseline

Figure 1. This chart characterizes various validated depression rating scale outcomes for both the Patient Health Queistionnaire-9 (PHQ-9) and the Montgomery–Åsberg Depression Rating Scale (MADRS) .

Patient Demographics

	10 Hz rTMS (n = 68)	iTBS (n = 37)
Age	53.47 ± 15.7	49.62 ± 17.337
Women	41 (60.0%)	21 (57.0%)
Men	27 (40.0%)	16 (43%)
Baseline PHQ-9 (range 0 – 27)	17.8 (4.9)	19.0 (4.4)
Baseline MADRS (range 0 – 60)	30.3 (6.5)	28.4 (7.6)
Baseline GAD-7 (range 0 – 21)	17 (4.1)	13.6 (5.2)
Comorbid Disorders		
Generalized Anxiety Disorder	46 (67.7%)	16 (43.2%)
Obsessive Compulsive Disorder	7 (10.3%)	2 (5.4%)
Post-Traumatic Stress Disorder	13 (19.1%)	5 (13.5%)
Attention Deficit Hyperactivity Disorder	9 (13.2%)	3 (8.1%)
Prior electroconvulsive therapy	20 (29.0%)	8 (21.6%)
Pharmacotherapy during TMS treatment		
Benzodiazepines	45 (66.1%)	13 (35.0%)
Antipsychotics	27 (39.7%)	13 (35.1%)
Stimulants	14 (20.6%)	11 (29.7%)

Figure 3. This data table depicts demographics of the 105 patients included in the final analyses of the Patient Health Questionnaire-9 (PHQ-9) comparing 10 Hz and iTBS therapy in treating major depressive disorder.

Changes in Depression Scales between 10 Hz and iTBS

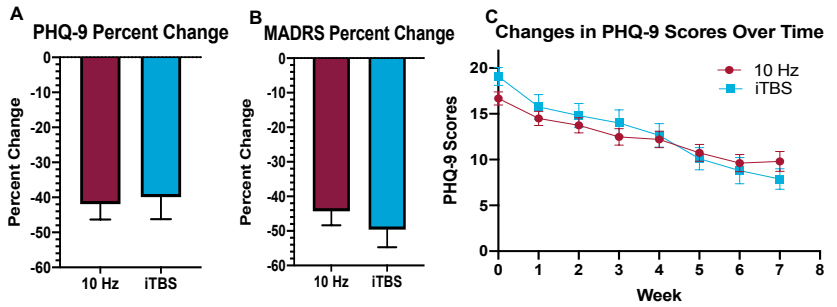

Figure 4. (A) Percent change (negative value indicates improvement) in self-reported Patient Health Questionnaire-9 (PHQ-9) score from baseline to TMS course completion. t(105) = -0.270, p = 0.788. **(B)** Percent change in the clinician administered Montgomery–Åsberg Depression Rating Scale (MADRS) from baseline to completion. , t(103) = 0.362, p = 0.718. **(C)** Changes in PHQ-9 scores from baseline (week 0) to Week 7 for both 10 Hz rTMS and iTBS. The n throughout the weeks ranged from 62 to 41 for 10 Hz and 26 to 16 for iTBS.

Comparisons between 10 Hz and iTBS on validated outcomes

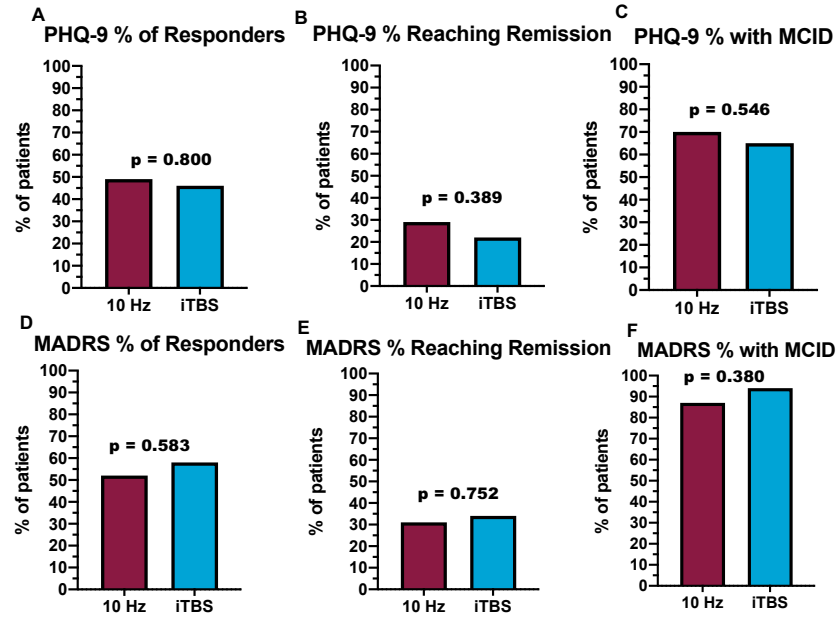

Figure 5. (A) Depicts the percent of patients that were classified as responders (greater than 50% reduction from baseline) on the PHQ-9 at the end of treatment. *n* = 105. **(B)** Displays the percent of patients that were classified as reaching remission (score less than 5) on the PHQ-9 at t he end of treatment. *n* = 105. **(C)** Shows percent of patients that were classified as having a minimum clinically important difference (MCID) which was classified as having a change ≥ 5 from baseline at the end of treatment. *n* = 105. **(D)** Details the ercent of patients that were classified as responders (greater than 50% reduction from baseline) on the MADRS at the end of treatment. *n* = 90. **(E)** Represents the percent of patients that were classified as reaching remission (score less than 10) at the end of treatment on the MADRS. *n* = 90. **(F)** Demonstrates the percent of patients that were classified as having a minimum clinically important difference (MCID) that was classified as having a change ≥ 2 from baseline at the end of treatment. *n* = 90.

Conclusions

- We found **no statistically significant differences** in depression rating scales or validated clinical outcomes between 10 Hz rTMS and iTBS when targeted at left DLPFC for treatment of major depressive disorder.
  - Supports findings from Blumberger *et al.* (2018)[3].
- With iTBS treatment sessions delivering pulses for just over 3 minutes, compared to 37.5 minutes with 10 Hz rTMS, emphasizing iTBS could greatly increase clinics' capacity to treat patients and reduce time burden on patients.

Strengths and Limitations

- This retrospective cohort review examines real-world clinic outcomes and is more generalizable to real-world clinic populations.
- With open-label study design, we did not have matched cohorts and could not control for variables like: number of treatment sessions, comorbid diagnoses, or other pharmaceuticals that may influence treatment outcomes.

Further Directions:

- Investigate potential differences in symptom specific improvement of major depressive disorder between 10 Hz rTMS and iTBS and at different time points.
- Collaborate with Dr. Nolan Williams at Stanford to build a cohort of TMS patients with naturalistic follow-up to examine differences in duration of benefit of both 10 Hz rTMS and iTBS for major depressive disorder.

References

1. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. (2018). ***The Lancet.*** 392(10159): 1789-1858.

2. George M.S *et al.* (2010). ***Arch Gen Psychiatry.*** 67(5):507–16.

3. Blumberger *et al.* (2018). ***The Lancet.*** 391(10131):1683-1692

4. Transcranial magnetic stimulation (TMS) for depression. (2018). ***PsychSceneHub.***

5. Lowe *et al.* (2004). ***Medical Care.*** 42(12): 11194-11201.

6. Kroenke *et al.* (2001). ***J. Gen. Internal Medicine.*** 16:60.

7. Duru *et al.* (2008). ***Current Medical Research and Opinion.*** 24(5): 1329-1335.

8. Hawley *et al.* (2002). ***Journal of Affective Disorders.*** 72(2): 177-184.