A Retrospective Analysis of Transcranial Magnetic Stimulation Right Dorsolateral Prefrontal Cortex (RDLPFC) Treatments for Patients with Generalized Anxiety Disorder

Kimberly Cress MD, Kerstin Brown, Beth Landry and Roxane Zotyka Sugar Land, TX

Abstract

Introduction: TMS Therapy is approved for Unipolar, Non-Psychotic Major Depressive Disorder, but shows great promise for the treatment of Generalized Anxiety Disorder (GAD). Our experience in treating patients with GAD with low-frequency, RDLPFC TMS therapy has shown significant improvement of anxiety symptoms as well as depressive symptoms in those who have comorbidity.

Methods: 20 patients a primary diagnosis of Generalized Anxiety Disorder were treated with low-frequency, right-sided TMS therapy between 2011 and 2015. Patient diagnoses of GAD were based on DSM-IV and DSM-V criteria. Patients were treated only on the RDLPFC with a 1 Hz per second protocol for either 1,600 or 2,400 pulses. All 20 patients experienced mild to severe anxiety based on the Beck Anxiety Inventory (BAI) and 11 of 20 patients experienced moderate to severe depression based on the Beck Depression Inventory (BDI II) symptom scales. The primary and secondary clinical outcomes for the treated sample were the response and remission rates at the end of the acute phase of treatment compared to baseline using the Beck Anxiety Inventory (BAI) scale and the Beck Depression Inventory (BDI II), respectively. Response rates were determined based upon a minimum 50% reduction in symptom score compared to baseline for the BAI and BDI. Remission rates were determined by a symptom score of ≤ 7 on the BAI scale and ≤ 13 on the BDI scale. All pre-treatment, intra- and post-treatment data was input into a proprietary patient database (TMS TrakStar™) which facilitated retrospective TMS data reporting and documentation. Scores were performed prior to and at the end of the acute treatment phase. Those available for follow-up were assessed up to 12 months post-treatment.

Results: The study population included 13 (65.0%) females and 7 (35.0%) males with an average age of 39.9 (range 22 – 56). The mean number of TMS treatment sessions was 37.4 (±10.1) with a range of 1,600 to 2,400 pulses administered daily. 14 of 20 patients (70.0%) demonstrated a 50% improvement in the BAI symptom score, establishing treatment response at the end of the acute phase. 12 of 20 patients (60.0%) reported BAI symptom scores at or below 7, establishing remission at the end of the acute phase. Total mean baseline BAI score was 19.0 (±10.7) and improved to a mean 7.8 (±6.8) at the end of treatment. BDI results (N=20) significantly improved from a mean 22.5 (±12.0) at baseline to a mean of 9.5 (±6.7) at the end of treatment, resulting in BDI response and remission rates of 80.0% and 70.0%, respectively. Follow-up data was collected on 16 patients who achieved remission in the acute phase and were available for follow-up assessment (Table 3). Data demonstrates a long duration of benefit based on BAI symptom scores with 68.8% of patients remaining in remission up to 12 months post-acute treatment.

Discussion: TMS therapy is FDA-approved for the treatment of Major Depressive Disorder but shows strong evidence in the treatment of Generalized Anxiety Disorder. Literature for this indication is limited for those diagnosed with GAD or those with a comorbidity of depression. Thus, future studies should be considered.

Disclaimer: Abstract has been changed to reflect new data since submission.

Table 1: Demographic, Clinical Characteristics and Treatment Variables of Patient Population (N=20)

Demographic Variables	
N (%) females	65.0 %
Mean Age (years ± SD)	39.9 ±12.8
Age Range	22 - 56
Pharmacotherapies in Current Episode	3.9
Mean (SD) TMS Sessions during Acute Phase	37.4 (±10.1)
Baseline Symptom Scores	
BAI- Total score mean	19.0 *(Moderate Anxiety)*
BDI II - Total score mean	22.5 *(Moderate Depression)*

Methods

All patients had an initial evaluation with an attending psychiatrist with a considerable knowledge of treatment-resistant depression, anxiety disorders and TMS therapy. A history of previous antidepressant therapy was obtained. TMS sessions were conducted 5 days per week with a mean of 37.4 treatments (range 21-48) per acute phase. All treatments were initiated using the NeuroStar TMS Therapy System (Neuronetics, Inc., Malvern, PA, USA). Patients were administered an off-label protocol of stimulation at 110% of motor threshold; pulse frequency of 1 pulse per second, 1,600 or 2,400 pulses per treatment session. However, TMS dosing and duration of treatment varied based on clinical history, severity of disease and clinical progression. The primary clinical outcomes for the treatment sample were the response and remission rates at the end of the acute phase of treatment compared to baseline based on the Beck Anxiety Inventory and Beck Depression Inventory scales. Response rates were determined based on a minimum 50% reduction in symptom score compared to baseline. Remission rates were determined based on a symptom score of ≤ 7 and score of ≤ 13 for BAI and BDI II, respectively. Secondary clinical outcomes were response and remission rates, specifically in those with secondary diagnoses of MDD recurrent who suffer from moderate to severe depression, based on the Beck Depression Inventory symptom scale. Other clinical outcomes included long-term durability outcomes up to 12 months post-acute phase for those patients available for follow-up assessment.

Results

Primary efficacy endpoints, Figure 1, are presented. At the end of the acute phase of treatment, patients displayed a 70.0% response and 60.0% remission based on the BAI symptom scale. BDI II results also showed similar efficacy, with an 80.0% response rate and 70.0% of patients achieving remission. Durability data, Table 3, for those patients that complied with follow-up visits, demonstrates long-term preservation of clinical benefit up to 12 months post-acute treatment. 100% of patients completed treatments without complaint, non-serious or serious adverse events other than transient headache, easily managed with over-the-counter analgesics.

Results Highlight: Response and Remission Rates of Patients with GAD and Moderate to Severe Depression

We retrospectively evaluated our patient population and assessed those with a secondary diagnosis of Major Depressive Disorder who experienced moderate and severe depressive symptoms at baseline, based on the Beck Depression Inventory, to further demonstrate low-frequency RDLPFC TMS therapy as an effective treatment option for those with high symptom severity.

Table 2 presents response and remission rates of the sub-sample. Of the total patient population (N=20) 11 patients had secondary diagnoses of MDD. 3 of 11 patients (27.3%) had BDI symptom scores of 20-28 (moderate depression) with an average baseline score of 22.7 (±5.7). At the end of the acute phase, 100.0% of patients achieved remission with a mean endpoint score of 9.8 (±4.5). 8 of 11 patients (72.7%) had BDI symptom scores of 29-63 (severe depression) with an average baseline score of 35.1 (±10.9). At the end of the acute phase, response and remission rates were 75.0% and 50.0%, respectively, with a mean endpoint score of 10.4 (±6.8).

These results support the use of low-frequency RDLPFC TMS therapy for treatment of Generalized Anxiety Disorder. The data also demonstrates the efficacy of RDLPFC TMS therapy as a viable treatment option for those with a comorbidity of depression and those with moderate to severe depressive symptoms.

Figure 1: Primary Efficacy Outcomes of RDLPFC Treatment in GAD

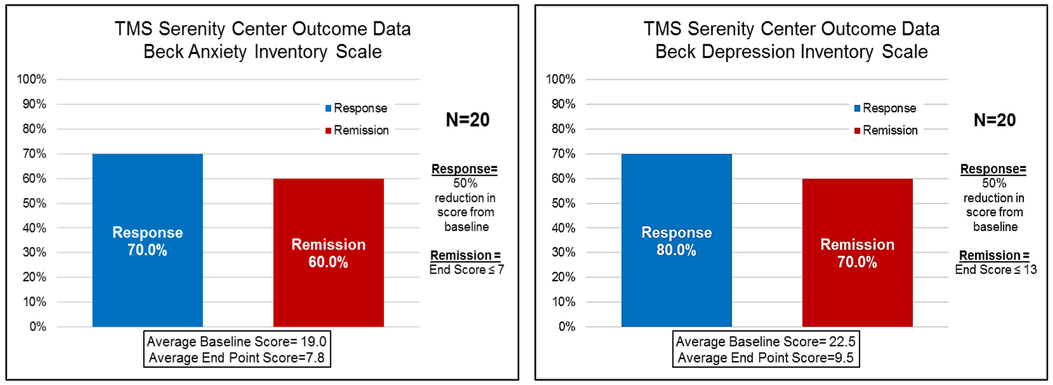

Table 2: Response and Remission Rates of Patients with Moderate and Severe Depression Based on Beck Depression Inventory Symptom Scale

Total N=11	**Moderate Depression N=3**	**Severe Depression N=8**
Baseline (SD)	22.7 (±5.7)	35.1 (±10.9)
Endpoint (SD)	9.8 (±4.5)	10.4 (±6.8)
Response (%)	100.0	75.0
Remission (%)	100.0	50.0

Table 3: Durability Results for Patients that Complied with Follow-Up Requirements

Symptom Scale	Baseline	6 to 12 Months
Beck Anxiety Inventory (BAI)	N=20 Average Baseline Score (SD): 19.0 (±10.7) Average Endpoint Score (SD): 7.8 (±6.8) **Remission Rate: 60.0%** **Response Rate: 70.0%**	N=16 Average Symptom Score at Follow-up (SD): 7.4 (±6.8) Average Months (SD): 11.8 (±8.8) **Remission Rate: 68.8%** **Relapse Rate: 37.5%**
Beck Depression Inventory (BDI II)	N=20 Average Baseline Score (SD): 22.5 (±12.0) Average Endpoint Score (SD): 9.5 (±6.7) **Remission Rate: 70.0%** **Response Rate: 80.0%**	N=16 Average Symptom Score at Follow-up (SD): 5.7 (±5.2) Average Months (SD): 10.7 (±8.4) **Remission Rate: 87.5%** **Relapse Rate: 12.5%**

Conclusion

Transcranial Magnetic Stimulation shows significant promise in the treatment of Generalized Anxiety Disorder using low-frequency RDLPFC stimulation. Acute response and remission rates demonstrated over a 50% improvement in symptom severity for patients with primary diagnoses of Generalized Anxiety Disorder on the Beck Anxiety symptom scale. Our results also demonstrate the efficacy of using low-frequency, right-side TMS therapy for the treatment of depression, specifically in those who present with high degree of symptom severity at baseline. Follow-up findings demonstrated long duration of benefit with BAI and BDI of 68.8% and 87.5%, respectively, at up to 12 months remaining in remission. Data on low-frequency RDLPFC TMS therapy is limited, but supports that of low-frequency, right-sided treatment for those who suffer from GAD and/or present with a comorbidity of depression. Further studies should be considered and discussion should include clinical diagnostic tools to identify those who may benefit from low-frequency RDLPFC treatment.