Outcomes and feasibility from the first TMS specific web-based intervention

Kayla Evans[1], Lauren Valencia LCSW[1], C. Dean Cochran[2], Michelle Cochran MD, DFAPA[3]

[1]NeuroScience & TMS Treatment Center, Nashville, TN. USA, [2]Centre College, Danville, KY. USA,
[3]Vanderbilt University Medical Center, Nashville, TN. USA

Abstract

Background: The authors sought to review the feasibility of an intervention combined with transcranial magnetic stimulation (TMS) for patients with Major Depressive Disorder (MDD) and assess outcomes on a self-rated measure of mood.
Methods: A post hoc analysis was performed with de-identified data from patient users of the workbook. A subset of data was identified, n=20, and analyzed. This subset of patients had verified daily workbook use and a complete data set (diagnosis, demographics, medication history, TMS treatment protocols, number of delivered TMS sessions, weeks of workbook participation, etc.).
Results: Overall patient PHQ-9 outcomes for the group were: Remission = 60%, Response = 85%, Nonresponse = 15%. The analysis showed that use of the workbook is feasible by a TMS operator and patients with electronic tablets and smartphones. Demographics of the patients were 50% (10/20) female, and 50% (10/20) male, with an average age of 33 years old, (range: 18-58). All patients had a primary diagnosis of Major Depressive Disorder, recurrent, severe and were quite treatment-resistant with an average number of antidepressants used prior to TMS initiation of 6.2 antidepressants (range of 4-18), and the average number of augmenting agents (antipsychotics, stimulants, anti-anxiety, folate supplements, e.g.) of 7.3 (range 1-20). The patients had an average of 41 (range 26-59) treatments and an average workbook use of 10.25 weeks (range 8-14 weeks of use). Of the patients treated throughout their TMS course with the standard protocol (10/20), PHQ-9 outcomes were: Remission = 80%, Response = 90%, Nonresponse = 10%.
Conclusion: This study showed that the HIPAA compliant, web-based workbook can feasibly be used by TMS operators in combination with TMS Treatment for depressed patients. The interpretation of the reported outcome results is limited by the small number, the post hoc nature of the data analysis, and the lack of a randomized comparator group. A randomized clinical trial to test this workbook against nonconcurrent TMS and online CBT or other interventions, with specific education to improve operator and patient utilization, might answer if this combined intervention can improve outcomes for patients compared to standard TMS treatment.

Introduction

For over a decade, repetitive transcranial magnetic stimulation (TMS) has become an acceptable treatment for Major Depressive Disorder (MDD). In 2010, CBT was been found to be a feasible treatment to offer with TMS.[1] Multiple treatments and interventions have been reported which could augment the effectiveness of the treatment: cognitive behavioral therapy, behavioral activation, cognitive-emotional reactivation, lightbox therapy.[2,3,4,5] Of these study reports, psychotherapy provided by a licensed counselor reported the greatest outcomes.[2] Intuitively, it seems that adding any form of therapy to TMS treatment for a patient would result in better outcomes, yet there is a low likelihood of implementing psychotherapy combinations within the US, as costs are higher and reimbursement for the combined treatment on the same day within the same office is unlikely without more robust scientific evidence. Online CBT delivered via smartphone applications have been shown to improve depression,[6] although it has not been studied with TMS.

A TMS specific, web-based, HIPAA compliant workbook was developed for patients, operators, and clinicians and launched in April 2019. The intervention was developed to provide therapeutic tools and a standardized format for TMS operators and patients during the course of TMS for Major Depressive Disorder. The web-based workbook mimics online CBT and behavioral activation. In addition, the workbook helps educate the patient about TMS and many other mood interventions (sleep hygiene, nutrition, exercise, etc.). The workbook is self-explanatory for patients, clinicians, and operators if they read the content.

The user agreement of the web-based HIPAA compliant intervention allows for the collection of de-identified data for analysis of outcomes for the intervention overall and specific practices individually. Prior to the collection of this data, there was no training available to optimize the online workbook. To date, there had been no feasibility data nor outcome data from the patient or operator users. In this study, the authors sought to review the feasibility of use for the web-based intervention combined with TMS for patients with recurrent, severe, Major Depressive Disorder, and to assess outcomes on a self-rated measure of mood with this combination care.

Method

A post hoc analysis was performed with de-identified data from nine separate practices who used the web-based workbook (Apr 2019 – Feb 2020). To be included in this analysis, patient data had to be complete: diagnosis, de-identified (continued above)

Funding Information

This study was paid for by the NeuroScience and TMS Treatment Centers.

Method continued

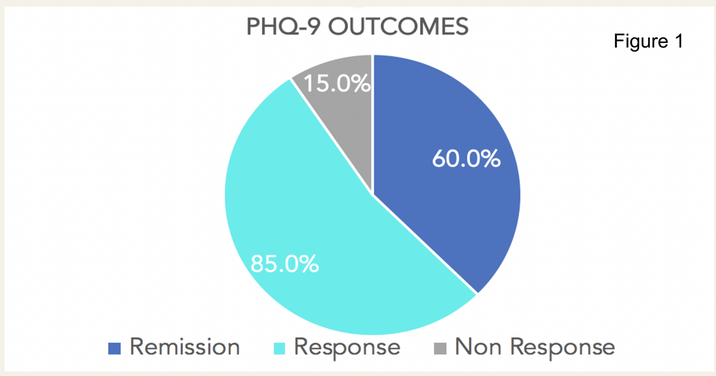
demographics (sex, age), medication history, TMS treatment protocols, placement of TMS coil, number of delivered TMS sessions, Patient Health Questionnaire-9 (PHQ-9) item scales (reference Spitzer,1999) at regular intervals (initial, and with TMS #5, #10, #15, #20, etc.) and workbook use confirmation. Workbook use was defined as the patient read or had the TMS Operator read the material to them. In addition, we excluded patients who had been treated with TMS in a prior episode. Most patient data was found to be missing in eight of the practice locations which used the workbook since April 2019. The use of the workbook was sporadic by patients in these eight groups. Missing data could not be gathered at the time of this analysis. An analysis of the patients with complete datasets (n=20) were all from the author's practice. In this subset, it could be confirmed that patients read or had the workbook read to them by the TMS operator and all parts of the data set were complete. The collected data was organized into .csv files and an Excel spreadsheet for analysis, and statistical studies & graphs were produced using Excel and RStudio.

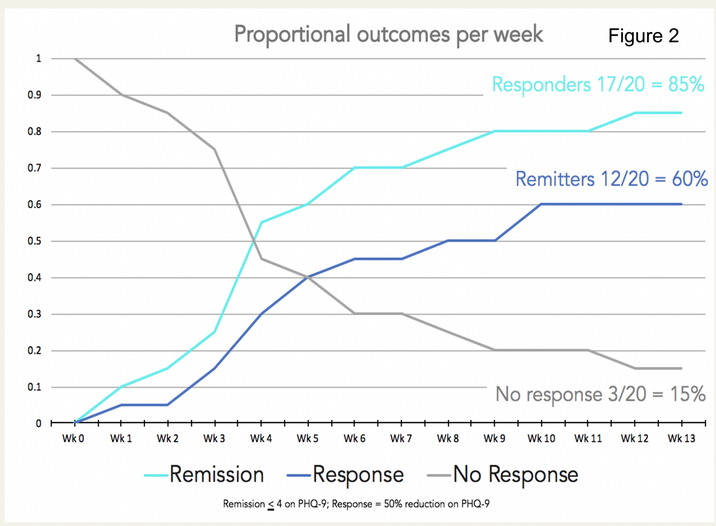
Results

It was found that when patients had not read the standardized section of the workbook upon arrival for treatment, the Operator could have the patient log into the online workbook and read the exercise to the patient during the TMS session. It is important to note that wearing proper ear protection did not impair the use of the workbook. Standing close to the patient and reading to them was a feasible means of delivering content.

Overall patient PHQ-9 outcomes: Remission = 60%, Response = 85%, Nonresponse = 15% *(Figure 1).* These outcomes were from the patients which had a complete dataset (10/20 females, 10/20 males, with average age =33 years old, range 18- 58). All patients had a primary diagnosis of Major Depressive Disorder, recurrent, severe. The analysis revealed that the group was very treatment-resistant with an average number of 6.2 (range 4-18) failed medication trials before TMS began. In addition, these patients had a high average number of prior augmenting agents of 7.3 (range 1-20), (e.g. antipsychotics, stimulants, anti-anxiety, mood stabilizers, folate supplements).

The patient's average number of TMS treatments was 40.9 and the average workbook use was 10.25 weeks (range 8-14 weeks). Despite the severity of treatment resistance, there was a trend towards more response and remission with the increased use of the workbook and increased TMS sessions *(Figure 2).*





On further analysis of the group, ten patients were treated throughout their course of TMS with the FDA cleared standard protocol for depression over LDLPFC 10Hz (4 sec on, at least 10 sec off) for 3000 pulses with a NeuroStar or MagVenture FDA cleared device. The treatment location, LDLPFC, was determined using the Modified Beam protocol to find F3.[7] Of the patients treated with the standard protocol, PHQ-9 outcome: Remission = 80%, Response = 90%, Nonresponse = 10%. Ten patients were treated with Nonstandard protocols. Eight of these (8/10) did not respond to standard protocol and, after 36 TMS sessions, were switched to non-standard protocols which included: 1) Additional Pulses (7/10) up to 5000 per TMS session with Remission 29% (2/7) and Response 86% (6/7), Non-response 14% (1/7); and 2) Bilateral (1/10): RDLPFC 1Hz 1800 pulses then, standard LDLPFC 10Hz, this patient had Non-response 100% (1/1). Two (2/10) did not tolerate the standard protocol at the beginning of the TMS course (reporting discomfort and severe anxiety), resulting in a change to RDLPFC 1 Hz 1800 pulses protocol - Remission of 100% (2/2).

Discussion/Conclusion

This analysis shows that it is possible to have TMS operators use an online workbook with patients receiving TMS treatment for depression. When patients had not read the session material prior to their session, the TMS operator could read the materials to the patients.

In this subset of patients with verified complete data, the outcomes were high. Specifically, the reported outcomes of these patients are higher than naturalistic data reported in the literature and the results showed similar outcomes to published literature combining psychotherapy and TMS[2] and better than that combining behavioral activation with TMS.[3] These high outcomes were achieved combining the online TMS specific workbook and TMS, without the need for a licensed therapist. Validating this data with a clinical trial could help clinical practices save money and improve patient outcomes with TMS.

While these high outcomes may have resulted from combining workbook use with TMS, a number of other factors could have led to improved outcomes, including but not limited to 1) a longer length of TMS treatment than the usual 36 treatments (average in this subset of 41 TMS sessions/ 10.25 weeks); 2) improved clinical management by an experienced TMS clinician and TMS operators; and 3) improved accountability of patients within the author's practice. In addition, placebo effects may have produced an effect, as the patient population was a motivated group who used a purchased web-based program with the intent to improve their TMS outcome.

While the interpretation of these results is limited by the obvious post hoc nature of the data analysis, the small study population, and the lack of a control/comparator group, these results could contribute to two bodies of growing evidence: 1) those studies supporting the combined effects of therapeutic techniques with concurrent TMS, and 2) those studies showing extending beyond 36 standard treatments improve outcomes. As the goal remains to improve outcomes for patients, a randomized clinical trial to test this TMS-specific, web-based, HIPAA compliant workbook versus TMS alone would answer if this combined intervention can improve outcomes for patients compared to standard TMS treatment. A trial of this nature would also provide a means to hone education, enhance program content, and improve data collection for patients and prescribers and operator users.

References

1. Vedeniapin, A, Cheng, L, and George, MS. Feasibility of Simultaneous Cognitive Behavioral Therapy and Left Prefrontal rTMS for Treatment Resistant Depression. *Brain Stimulation.* 2010 October 3 (4), 207-210.
2. Donse, L, Padberg, F, Sack, AT, Rush, AJ, and Arns, M. Simultaneous rTMS and psychotherapy in major depressive disorder: Clinical outcomes and predictors from a large naturalistic study. *Brain Stimulation.* 11, 2018, 337-345.
3. Russo, G, Tirrell, E, Busch, A, and Carpenter, L.L. Behavioral activation therapy during transcranial magnetic stimulation for major depressive disorder. *Journal of Affective Disorders*. 2018 April 236:101-4.
4. Isserles, M, Rosenberg, O, Dannon, P, Levkovitz, Y, Kotler, M, Deutsch, F, Lerer, B, and Zangen, A. Cognitive-emotional reactivation during deep transcranial magnetic stimulation over the prefrontal cortex of depressive patients affects antidepressant outcome. *Journal of Affective Disorders*. 128, 2011, 235-242.
5. Mania, I, and Kaur, J. Bright Light Therapy and rTMS; novel combination approach for the treatment of depression. *Brain Stimulation*, Volume 12, Issue 5, 2019, 1338-1339.
6. Firth, J, Torous, J, Nicholas, J, Carney, R, Pratap, A, Rosenbaum, S, Sarris, J. The efficacy of smartphone-based mental health interventions for depressive symptoms: a meta-analysis of randomized controlled trials. *World Psychiatry*. 2017;16:287–298.
7. Mir-Moghtadaei, A., Caballero, R., Fried, P., Fox, M. D., Lee, K., Giacobbe, P., Downer, J. (2015). Concordance between Beam F3 and MRI neuro-navigated target sites for repetitive transcranial magnetic stimulation of the left dorsolateral prefrontal cortex. *Brain Stimulation, 8,* 965-973

Contact Information

Michelle R. M. Cochran, M.D.
Email: drcochran@TMSworkbook.com
Web: www.TMSworkbook.com

Conflicts of Interest

- Dr. Cochran is the owner and author of Train Your Brain: Your record of Care with TMS, www.TMSworkbook.com.
- Dr. Cochran is on the speaker's bureau for NeuroStar/Neuronetics and has done market research for MagStim and NeuroStar/Neuronetics.
- Dr. Cochran owns a practice, NeuroScience and TMS Treatment Centers which purchased both a MagVenture device and two NeuroStar devices which are used with patients.
- Lauren Valencia, LCSW is one of the authors of Train Your Brain, TMSworkbook.com and works with Dr. Cochran
- Kayla Evans is a TMS operator in Dr. Cochran's practice.
- C. Dean Cochran is Dr. Cochran's son and a Data Science Analytics major at Centre College, Danville, KY.