Optimizing the Response to TMS in Major Depression through Intensive Concomitant Medication Management

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Introduction/Hypothesis

Transcranial Magnetic Stimulation (TMS) is a new FDA-approved technology for treatment resistant major depression. Two major sham-controlled trials of TMS monotherapy separately showed a remission rate of 14% in one study,[1] and a response rate of 39% at 6-weeks in another study.[2] In the NIMH-sponsored STAR-D study of major depression, remission rates to medications and/or cognitive behavioral therapy progressively decreased from about 30% (level 1) to 10% (level 4). Comparing these results to those from TMS studies suggests similar outcomes for the two approaches, although the outcomes with TMS are hardly compelling when patients are faced with the current high cost of the procedure, often without insurance coverage.

There have been few reports on the concomitant use of TMS and antidepressants.[3] Studies give little details on the pharmacotherapy used, and do not appear to have incorporated newer pharmacologic strategies for depression, such as agents with a rapid onset of action (e.g., atypical neuroleptics),[4] or those reported to be especially effective in individuals with resistant depression (e.g., monoamine oxidase inhibitors).[5]

We hypothesized that the combination of TMS with intensive pharmacotherapy administered by a physician skilled in both technologies would result in a superior outcome. Rating scales were utilized to monitor the response and guide medication adjustments.

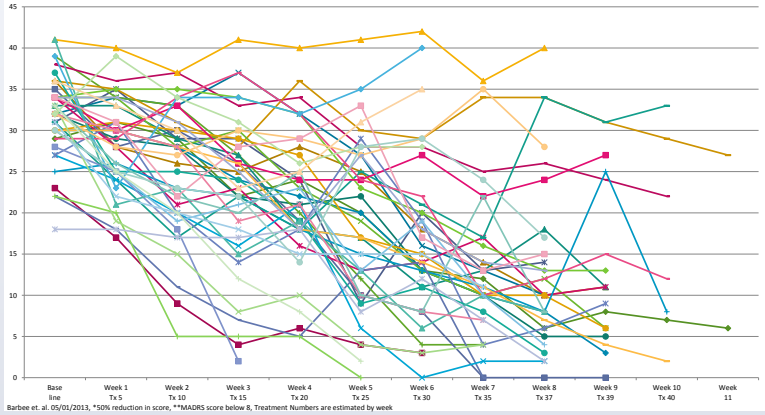
Methods

Forty-three patients with chronic treatment-resistant major depression and multiple failed antidepressant/augmentation trials received at least 30 sessions of TMS. TMS was administered utilizing the device manufactured by Neuronetics, and applied according to the guidelines recommended by the manufacturer. The primary outcome measure was the Montgomery Asberg Depression Rating Scale (MADRS). Response was defined as a ≥ 50% reduction in the MADRS score, and remission as a MADRS score of ≤ 8. Ratings were obtained weekly.

Table 1. Patient Characteristics (n=43)

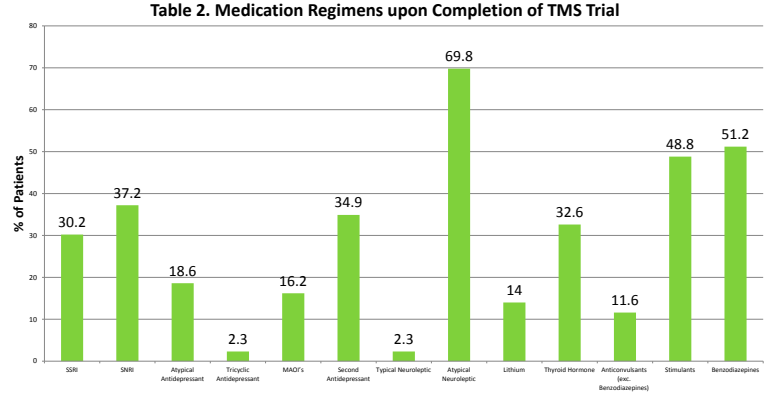
Mean Age (years)	46.5 (range 17-92)
Gender (%)	Male 53% Female 47%
Mean age of onset mood disorder (years)	20.9
Mean Number of lifetime depressive episodes	4.7 (range 1-30)
Mean Duration of current depressive episode (months)	66.4 (range 2-300)
Mean Duration of lifetime depressive episodes (months)	175 (range 8-600)
Mean Number of failed antidepressant trials prior to TMS therapy	8.4 (range 2-26)
Mean Number of failed augmentation trials prior to TMS therapy	8.6 (range 2-20)
Number of patients that had a trial of Electroconvulsive Therapy	5
Mean MADRS score at baseline	31.79 (range 18-41)

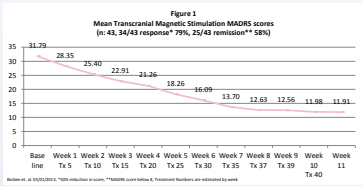
Figure 1
Individual Transcranial Magnetic Stimulation MADRS scores
(n: 43, 34/43 response* 79%, 25/43 remission 58%)**



Barbee et. al. 05/01/2013, *50% reduction in score, **MADRS score below 8, Treatment Numbers are estimated by week

Table 2. Medication Regimens upon Completion of TMS Trial





Results

Forty-three patients qualified to be included in this interim analysis (unipolar depression n=35, bipolar II depression n=8). The patient demographics and characteristics of their illness are summarized in Table 1.

The average number of TMS sessions per patient was 36.5 (range 15 to 81). A wide variety of FDA-approved antidepressants and augmentation agents were used in the course of treatment. The medication regimen for each patient at the time of completing TMS appears in Table 2. At the time of completion of TMS treatment, patients were on an average of 4.1 (range 2-7) psychiatric medications (including benzodiazepines and hypnotics).

Under these conditions, the response rate was 79% and the remission rate was 58%. Four patients showed no improvement. The mean weekly MADRS score appear in Figure 1. The weekly MADRS scores for each patient during TMS appear in Figure 2.

TMS treatment was well tolerated. Three patients with bipolar II depression became hypomanic during treatment and terminated further TMS treatments. There were no additional dropouts for any reason.

Conclusions

TMS when given with intensive pharmacotherapy management produced much higher response and remission rates than those reported in the literature for treatment resistant depression either with TMS alone, medications alone, or the combination of an antidepressant with TMS. These results suggest the value of a high level of physician involvement for timely pharmacologic management in patients receiving TMS, and the use of standardized rating scales in driving this process. These findings should be considered as exploratory, as there are multiple methodological limitations to be considered. These include the lack of placebo or sham controls, and the fact that the rater was not blinded to the treatment. These findings need further replication. Interactions between TMS and specific antidepressant and/or augmentation strategies warrant further investigation.

References

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