Transcranial Magnetic Stimulation (TMS) as an Augmentation Agent in Treatment Resistant Bipolar II Depression

James G. Barbee, M.D., Jose Calderon-Abbo, M.D., Kimberly M. Lavigne, M.D., Joshua F. Jansen

TMS of New Orleans, 3439 Magazine St. New Orleans, LA 70115

Introduction/Hypothesis

Depressive symptoms in bipolar disorder produce a significant level of disability,[1] and seem to be the predominant phase of the illness.[2] Bipolar depression can be difficult to treat, and there is great need for techniques to improve rates of response.

Transcranial magnetic stimulation (TMS) has been reported to be effective in unipolar depression, but there are only a limited number of reports regarding its efficacy in bipolar depression.[3-5] Treatment techniques utilized to provide TMS in bipolar depression have also varied widely. We hypothesized that the addition of TMS to pharmacotherapy would improve the rates of response to medication treatment.

Methods

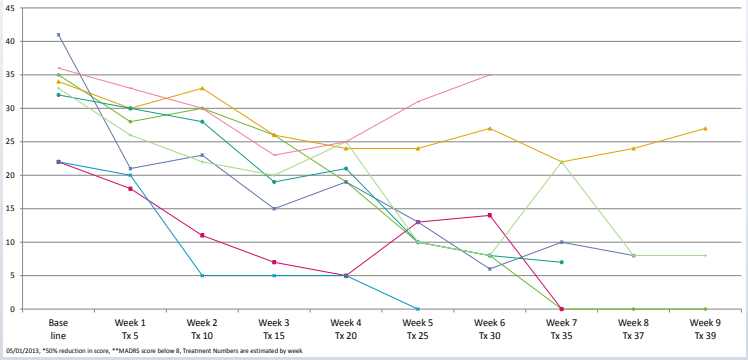
Eight patients (n=8) with bipolar II depression that had failed multiple medication trials were treated with TMS for at least 30 sessions and with medications; the latter were adjusted during the course of the treatment with TMS. TMS was given utilizing the Neuronetics device under the standard treatment conditions recommended by the manufacturer (stimulation of the left dorsolateral prefrontal cortex at 10 Hertz for 3000 pulses per treatment session).

The primary outcome measure was the Montgomery Asberg Depression Rating Scale (MADRS). Response was defined as a reduction of ≥ 50% reduction in baseline MADRS ratings, and remission by a MADRS score of ≤ 8. Ratings were obtained weekly by the same rater. Medication adjustments were done by this same clinician, who saw the patients on most of the treatment days.

Table 1. Patient Characteristics (n=8)

Mean Age (years)	46 (range 23-72)
Gender (%)	Male 75% Female 25%
Mean age of onset mood disorder (years)	20.1 (range 10-32)
Mean Number of lifetime depressive episodes	8.3 (range 1-30)
Mean Duration of current depressive episode (months)	43 (8-180)
Mean Duration of lifetime depressive episodes (months)	230 (60-600)
Mean Number of failed antidepressant/mood stabilizer trials prior to TMS therapy	14.9 (range 9-22)

Figure 1
Individual Transcranial Magnetic Stimulation MADRS scores
(n: 8, 6/8 response* 75%, 6/8 remission 75%**



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

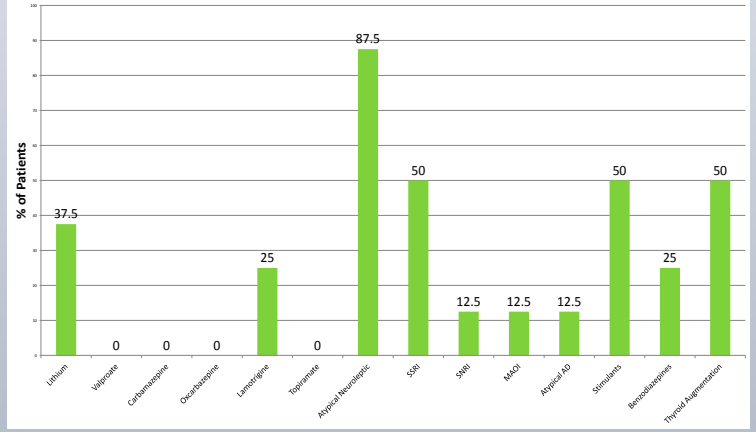
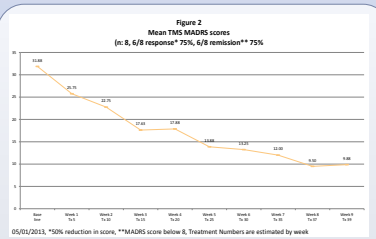


Figure 2
Mean TMS MADRS scores
(n: 8, 6/8 response* 75%, 6/8 remission 75%**



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

Results

Eight patients qualified for this analysis. Their median MADRS score at baseline (the first TMS session) was 31.8 (range 22-41); the average MADRS score at the conclusion of treatment was 10 (range 0-35). Additional characteristics of the patients and their illness appear in Table 1. Six of the eight patients (75%) achieved a MADRS score of ≤8, and were therefore classified as in remission. The weekly MADRS scores in each of the eight patients are depicted in Figure 2. The medications regimens of the patients at the time of the last TMS treatment appears in Table 2. TMS treatment was well tolerated. Hypomanic symptoms occurred with three of the eight patients, even while the patients were on mood stabilizers, requiring the cessation of TMS. The average number of treatments administered in these patients before hypomanic symptoms emerged was 6.67 (range 1-11). Retrospectively, one patient was likely having emergent symptoms of hypomania upon initiation of TMS that were not recognized. These patients were classified as responders since their depressive symptoms had resolved.

Conclusions

These results suggest a relatively robust efficacy of TMS in bipolar II depression when given with pharmacotherapy. It appears that the emergence of hypomania is a relatively common effect of treatment. The conclusiveness of this report is limited by the small number of subjects, the fact that the rater was not blinded to the treatment the patient was receiving, and the lack of a placebo comparison group trial. However, the relatively high response rate and good tolerability of TMS suggest that further study is indicated.

References

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