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# Magnetic Seizure Therapy of Treatment-Resistant Depression in a Patient With Bipolar Disorder

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**Abstract:** Electroconvulsive therapy (ECT) is a highly efficacious treatment for severe depression. However, a disadvantage of ECT is the risk of cognitive side effects. Magnetic seizure therapy (MST) is a novel treatment modality, by which therapeutic seizures are induced using rapidly alternating strong magnetic fields. In this case study, we report on successful MST treatment of an episode of otherwise treatment-resistant depression in a patient with bipolar I disorder. Compared with published ECT results, MST seizures in this case report were of shorter duration, lower ictal electroencephalogram amplitude, and less pronounced postictal suppression. Furthermore, the patient did not experience subjective side effects and particularly recovered time to full orientation more quickly with MST than what has been previously described for ECT. Taken together, these results suggest that MST, compared with ECT, might have antidepressant effects and may have fewer clinical side effects.

**Key Words:** electroconvulsive therapy (ECT), magnetic seizure therapy (MST), depression, EEG, cognitive side effects

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Electroconvulsive therapy (ECT) is an important treatment approach in severely depressed patients.[1] Most importantly, it is the most effective treatment known for major depression.[2] The application of ECT sometimes results in severe cognitive side effects. Declarative memory impairment after ECT has often been reported and is well investigated.[3,4] Electroconvulsive therapy often results in a number of short- and long-time side effects including memory impairment for past and current events, which can last for several months after ECT treatment.[5]

Certain ictal electroencephalogram (EEG) measurements were associated with changes in several neuropsychological tests.[6] A few studies focused on the impact of sine and pulse waveforms on anterograde memory and other cognitive functions.[7] Other side effects of ECT include headache, muscle aches, nausea, and fatigue.[8–11] Electroencephalogram measures of ECT treatment were modestly associated with clinical outcome, greater ictal power, delta coherence, and postictal suppression predictors of greater therapeutic benefit.[12]

Magnetic seizure therapy (MST) is a novel method of convulsive therapy using rapidly alternating strong magnetic fields. It offers greater control of intracerebral current intensity than is possible with ECT.[13,14] The first use of therapeutic magnetic seizure induction in a psychiatric patient took place in Bern, Switzerland, in May 2000.[1]

We report on MST treatment in a 44-year-old male patient who has been experiencing bipolar disorder I since 1999. The index episode of depression was his eighth, and it started in October 2006. Patient attempted suicide with alcohol and benzodiazepine overdose. He was treated in an intensive care unit and needed artificial ventilation. Psychopathologic symptoms included sleep disturbance, low level of activities, agitated melancholia, joylessness, rumination, social retraction, hopelessness, and suicidal tendency.

He was subsequently admitted to a psychiatric hospital and received multiple-course cognitive-behavioral therapy and the following different psychotropic medication (high-dose rate and sufficient space of time): bromazepam, chlorprothixene, zopiclone, tranylcypromine, lamotrigine, and pregabalin. Four weeks before starting MST and 6 weeks after MST trials,treatment pharmaceuticals were changed to mirtazapine 30 mg, chloral hydrate 1000 mg, and prothipendyl 80 mg.

Depressive symptoms were rated with Hamilton Rating Scale for Depression (HRDS-21)[15] and Montgomery Åsberg Depression Scale (MADRS).[16]

## MATERIALS AND METHODS

This patient consented to participate in a clinical trial of MST at the University of Bonn, Department of Psychiatry and Psychotherapy, according to an approved study protocol, between September and October 2007. This patient is part of a larger sample (n = 10) in an open-label study without control group. The patient was chosen for a case study because he was the first to complete the study protocol.

Treatments were delivered with a magnetic stimulator (Tonica Elektronik A/S, Tonica MagPro MST, Denmark) and using a figure 8–shaped twin coil, containing 2 individual coils with a diameter of 13 cm. Current flows through the coil following the direction of the arrows, shown on the coil encapsulation. Induced current direction in the tissue is always the opposite of the coil current direction. During the stimulation, the center of the coil was placed at the vertex. The peak magnetic field induced approximately 2 T at the coil surface. The pulse has a dampened cosine wave form.

We chose the following stimulation parameters: stimulation frequency, 100 Hz; stimulation pulses, 400 to 600; stimulation amplitude, 100%; and duration of stimulation, 4 to 6 seconds. We stimulated the first and the second trials with 400 pulses and the following with 600. Seizures were elicited

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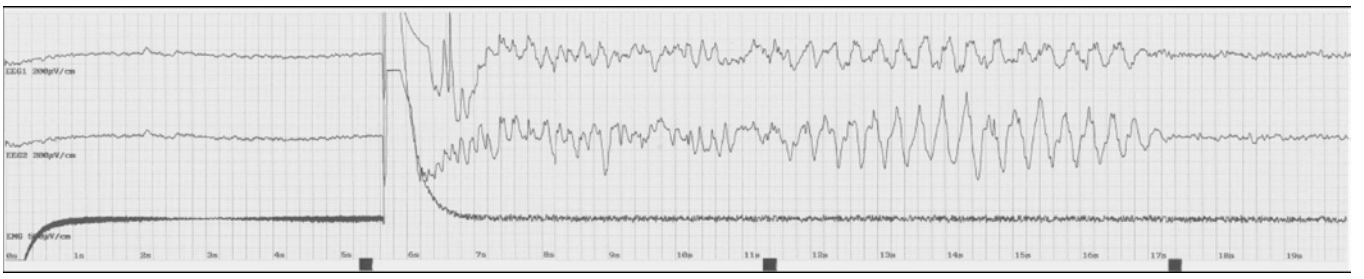

AQ2 **FIGURE 1.** First and second leads are bifrontal (paramount left and midway right) EEG recorded during MST. Third lead was to be electrocardiogram. Stimulation parameters are as follows: frequency, 100 Hz; pulses, 600; amplitude, 100%; and duration of stimulation, 6 seconds.

under general anesthesia (propofol). The patient was oxygenated during anesthesia with 100% $O_2$. He received earplugs to protect against the high-frequency clicking noise of the MST machine, and a rubber bite block was inserted to prevent dental damage. The right leg was cuffed before the administration of the muscle relaxant (succinylcholine). The motor activity of the right food was assessed visually to track the duration of motor seizures, and bilateral frontal-mastoid EEG recordings were obtained. A total of 9 MST sessions were conducted (2 per week).

The patient received between 100 and 180 mg propofol for anesthesia, except for the last session, which required 250 mg propofol because of pretreatment agitation. For muscle relaxation, the patient received between 50 and 100 mg succinylcholine.

The severity of his depressive symptoms was rated with the following neuropsychological scores: HRDS-21 and MADRS. Ratings were performed at baseline, twice during the treatment course, after the ninth MST session, and then after 3 and 6 weeks. The psychotropic medication continued unchanged until the final clinical assessment.

We measured the time between onset of anesthesia and recovery of full orientation after each induced seizure. Recovery of full orientation was assessed by asking the patient to open his eyes and state his name and by asking his chronological and local orientation.

The study has been approved by the local ethics committee of the University Hospital Bonn, Germany.

## RESULTS

All 9 MST treatments were well tolerated without any side effects such as headache, nausea, dizziness, or subjective or clinically observable cognitive symptoms. The visible duration of the tonic-clonic seizure took between 15 and 28 seconds (19.11 ± 4.1 seconds), and EEG alterations lasted between 18 and 28 seconds (21.6 ± 4.72 seconds). A representative seizure during MST treatment is presented in Figure 1. F1

At baseline, HRDS-21 was 31, then decreased to 25 and 24 during treatment, was 18 after the last MST trial, became 19 three weeks after, and escalated to 27 at 6 weeks follow-up. At baseline, MADRS score was 37, then decreased to 31 and 36 during the treatment, scored 16 after the end of the MST trial, became 17 three weeks after, and was 30 at 6-week follow-up. (Fig. 2). Clinically, his depression improved substantially. In F2 the second week of MST, he experienced sadness, sleep disorder, insensitiveness, and pessimism. Because MADRS

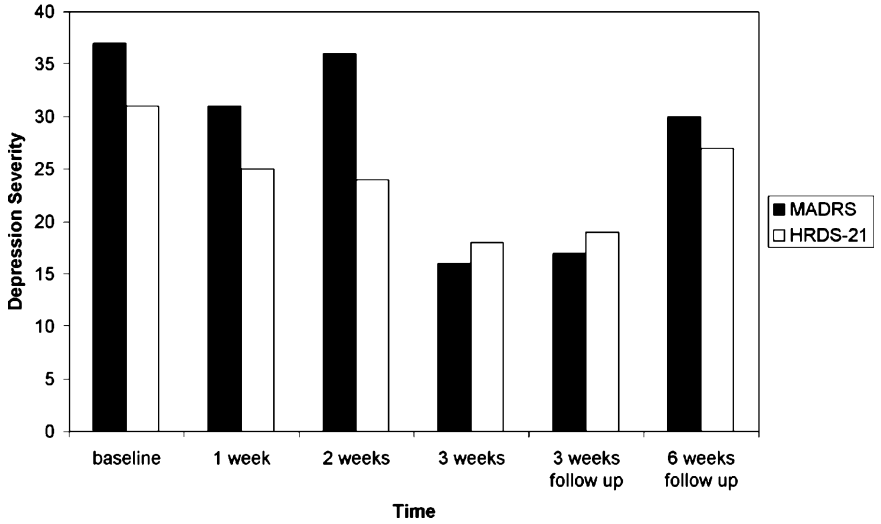


**FIGURE 2.** Rating of depressive symptoms: MADRS and HRDS-21.

score reflects those symptoms stronger, the sum score is higher in this questionnaire in comparison to the HDRS. However, the patient's overall condition was improved in week 2. The decrease of HAMD score from 37 to 18 is reflected as, in particular, improvement of fewer suicidal thoughts and sleep disorder, more physical ability, and less circadian variation.

The time to recover after the induction of seizure measured from the moment of spontaneous respiration took between 20 and 150 seconds, the time to open his eyes averaged 84 seconds, and the time to full orientation took between 48 and 150 seconds (ie, telling his name, medial 117 seconds; location, 116 seconds; age, 112 seconds; birthday, 117 seconds). The patient spontaneously reported distinct elevations of mood and drive (level of activity) continuing for 3 or 4 hours after each MST. Furthermore, he did not report on any subjective cognitive impairment after the MST treatments.

## DISCUSSION

We report on an uncomplicated course of MST in a patient with pharmacoresistent depression, producing a partial clinical response. In this single case study, MST was associated with faster recovery of full reorientation as compared with ECT treatments.[17,18] Similar to our findings, a previous case report by Kosel and colleagues[19] also reported that time of full orientation after MST was shorter as compared with what is expected with ECT. Furthermore, White and colleagues[18] found that MST was associated with a reduced time to orientation (4 ± 1 vs 18 ± 5 minutes) compared with ECT. In this case, we assessed the time to full orientation between 48 and 150 seconds.

Taken together, our results are in line with previous observations suggesting that MST may have some advantages over ECT in terms of subjective side effects.[20] Although retrograde amnesia often improves during the first few months after ECT, for many patients, recovery is incomplete, with prolonged amnesia regarding events that occurred close to the time of treatment.[21] Variations in ECT technique (eg, right unilateral electrode placement or ultrabrief pulse width) can reduce the incidence and severity of retrograde amnesia substantially.[22,23] For example, persistent loss of autobiographical memories 2 months after treatment is greater with bilateral than with right unilateral ECT.[24] These findings indicate that MST may be associated with more benign clinical acute cognitive side-effect profile than ECT.[25] Electrode placement and electrical dosage are strongly associated with the magnitude of acute, subacute, and long-term cognitive side effects.[22,26–28]

Compared with ECT, MST seizures in our case had shorter duration, lower ictal EEG amplitude, and less postictal suppression. Given the similar duration of clinical seizure symptoms in MST and ECT, evaluation of EEG suggests that the amplitude of the induced seizure activity may have been reduced with MST, contributing to a reduction of postictal suppression[1,14,18] and maybe to the reduction of cognitive impairment. Analysis of EEG recorded during and immediately after the treatments indicated that MST-induced seizures showed less robust ictal expression and less marked postictal suppression than did ECT. These measures have traditionally been viewed as markers for the clinical efficacy of ECT.[29–32] Whether these same relationships will pertain to MST is unknown. Subjectively, the MST treatment was tolerated well by the patient, and no side effects were reported, especially subjective cognitive impairments. This is another major difference to treatment with ECT.[14,17]

The efficacy of ECT is highly dependent on technique, with remission rates ranging from 20% to more than 80%, depending on the exact treatment parameters.[33]

This single case suggests that MST can be successfully applied in the treatment of depression with a beneficial side-effect profile. Obviously, further studies remain to be done to assess whether MST as an antidepressant treatment modality is of comparable clinical efficacy as ECT.

## REFERENCES


1. Lisanby SH, Schlaepfer TE, Fisch HU, et al. Magnetic seizure therapy of major depression. *Arch Gen Psychiatry.* 2001;58(3):303–305.
2. Krystal AD, West M, Prado R, et al. EEG effects of ECT: implications for rTMS. *Depress Anxiety.* 2000;12(3):157–165.
3. Datka W, Siwek M, Dudek D, et al. Working memory disturbances in patients with major depression after ECT treatment. *Psychiatr Pol.* 2007;41(3):339–349.
4. Tamaoki T, Motohashi N. Other treatments for depressive patients. *Nippon Rinsho*. 2007;65(9):1655–1659.
5. Dragovic M, Allet L, Janca A. Electroconvulsive therapy and determination of cerebral dominance. *Ann Gen Hosp Psychiatry.* 2004;3(1):14.
6. Azuma H, Fujita A, Otsuki K, et al. Ictal electroencephalographic correlates of posttreatment neuropsychological changes in electroconvulsive therapy: a hypothesis-generation study. *J ECT.* 2007;23(3):163–168.
7. Fujita A, Nakaaki S, Segawa K, et al. Memory, attention, and executive functions before and after sine and pulse wave electroconvulsive therapies for treatment-resistant major depression. *J ECT.* 2006; 22(2):107–112.
8. Dwork AJ, Arango V, Underwood M, et al. Absence of histological lesions in primate models of ECT and magnetic seizure therapy. *Am J Psychiatry.* 2004;161:576–578.
9. Coffey CE, Weiner RD, Djang WT, et al. Brain anatomic effects of electroconvulsive therapy: a prospective magnetic resonance imaging study. *Arch Gen Psychiatry.* 1991;48:1013–1021.
10. Devanand DP, Dwork AJ, Hutchinson ER, et al. Does ECT alter brain structure? *Am J Psychiatry.* 1994;151:957–970.
11. Agelink MW, Andrich J, Postert T, et al. Relation between electroconvulsive therapy, cognitive side effects, neuron specific enolase, and protein S-100. *J Neurol Neurosurg Psychiatry.* 2001; 71:394–396.
12. Perera TD, Luber B, Nobler MS, et al. Seizure expression during electroconvulsive therapy: relationships with clinical outcome and cognitive side effects. *Neuropsychopharmacology.* 2004;29(4): 813–825.
13. Lisanby SH. Update on magnetic seizure therapy: a novel form of convulsive therapy. *J ECT.* 2002;18(4):182–188.
14. Lisanby SH, Luber B, Schlaepfer TE, et al. Safety and feasibility of magnetic seizure therapy (MST) in major depression: randomized within-subject comparison with electroconvulsive therapy. *Neuropsychopharmacology.* 2003;28(10):1852–1865.
15. Hamilton M. Development of a rating scale for primary depressive illness. *Br J Soc Clin Psychol*. 1967;6:278–296.
16. Montgomery P, Åsberg M. A new depression scale designed to be sensitive to change. *Br J Psychiatry.* 1979;134:382–389.
17. Sackeim HA. Memory and ECT: from polarization to reconciliation. *J ECT.* 2000;16(2):87–96.
18. White PF, Amos Q, Zhang Y, et al. Anaesthetic considerations for magnetic seizure therapy: a novel therapy for severe depression. *Anesth Analog*. 2006;103(1):76–80.

19. Kosel M, Frick C, Lisanby SH, et al. Magnetic seizure therapy improves mood in refractory major depression. *Neuropsychopharmacology.* 2003;28(11):2045–2048.
20. Lisanby SH, Morales O, Payne N, et al. New developments in electroconvulsive therapy and magnetic seizure therapy. *CNS Spectr.* 2003;8(7):529–536.
21. Donahue AB. Electroconvulsive therapy and memory loss: a personal journey. *J ECT.* 2000;16:133–143.
22. Sackeim HA, Prudic J, Devanand DP, et al. Effects of stimulus intensity and electrode placement on the efficacy and cognitive effects of electroconvulsive therapy. *N Engl J Med*. 1993;328:839–846.
23. Sackeim HA, Portnoy S, Neeley P, et al. Cognitive consequences of low-dosage electroconvulsive therapy. *Ann N Y Acad Sci*. 1986; 462:326–340.
24. Lisanby SH, Maddox JH, Prudic J, et al. The effects of electroconvulsive therapy on memory of autobiographical and public events. *Arch Gen Psychiatry.* 2000;57:581–590.
25. Moscrip TD, Terrace HS, Sackeim HA, et al. Randomized controlled trial of the cognitive side-effects of magnetic seizure therapy (MST) and electroconvulsive shock (ECS). *Int J Neuropsychopharmacol.* 2006; 9(1):1–11.
26. Sackeim HA, Prudic J, Devanand DP, et al. A prospective, randomized, double-blind comparison of bilateral and right unilateral electroconvulsive therapy at different stimulus intensities. *Arch Gen Psychiatry.* 2000;57:425–434.
27. Sackeim HA. Acute cognitive side effects of ECT. *Psychopharmacol Bull*. 1986;22:482–484.
28. Sackeim HA, Luber B, Moeller JR, et al. Electrophysiological correlates of the adverse cognitive effects of electroconvulsive therapy. *J ECT.* 2000;16:110–120.
29. Nobler MS, Sackeim HA, Solomou M, et al. EEG manifestations during ECT: effects of electrode placement and stimulus intensity. *Biol Psychiatry.* 1993;34:321–330.
30. Krystal AD, Weiner RD, Coffey CE. The ictal EEG as a marker of adequate stimulus intensity with unilateral ECT. *J Neuropsychiatry Clin Neurosci*. 1995;7:295–303.
31. Folkerts H. The ictal electroencephalogram as a marker for the efficacy of electroconvulsive therapy. *Eur Arch Psychiatry Clin Neurosci*. 1996; 246:155–164.
32. Suppes T, Webb A, Carmody T, et al. Is postictal electrical silence a predictor of response to electroconvulsive therapy? *J Affect Disord*. 1996;41:55–58.
33. Lisanby SH. Electroconvulsive therapy for depression. *N Engl J Med*. 2007;357(19):1939–1945.

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