Transcranial Magnetic Stimulation-Induced Switch into Mania: A Report of Two Cases

Ornah T. Dolberg, Shaul Schreiber, and Leon Grunhaus

Background: Transcranial magnetic stimulation is a novel, experimental procedure in the treatment of psychiatric disorders, most notably mood disorders. Transcranial magnetic stimulation is currently being widely studied in other applications, and its efficacies and potential side effects are being investigated.

Methods: Transcranial magnetic stimulation was administered five times a week for 4 weeks.

Results: In this report, a manic episode followed treatment with transcranial magnetic stimulation in two patients.

Conclusions: Clinicians should be aware that, like with other antidepressive treatments, a switch into mania might complicate treatment with transcranial magnetic stimulation in bipolar patients. Biol Psychiatry 2001;49: 468–470 © 2001 Society of Biological Psychiatry

Key Words: Transcranial magnetic stimulation, bipolar affective disorder, major depressive disorder, antidepressants–adverse effects

Introduction

Transcranial magnetic stimulation (TMS) is a procedure in which a strong pulsed magnetic field is created by an electromagnet held close to the skull. The strong magnetic field pulses induce an electrical field, which can in turn cause excitable membranes, such as nerve cell membranes, to depolarize (Barker 1991).

Magnetic stimulation has several potential advantages over direct electric stimulation of the central nervous system, including greater safety, fewer side effects, and the ability to stimulate particular regions. A growing number of studies with single-pulsed TMS, slow TMS, and repetitive TMS support the beneficial effect of TMS in depression (Conca et al 1996; George et al 1997; Klein et al 1999; Pascual-Leone et al 1996; Triggs et al 1999). In the treatment of mania there are less data. Grisaru et al (1998) showed the beneficial effect of TMS in mania in 16 patients.

In this case report we describe two bipolar patients who developed a manic episode following a course of TMS for depression. These patients are part of a larger study exploring the efficacy of TMS in the treatment of bipolar depression.

All patients included in this study were given a detailed explanation of the procedure and signed an informed consent form.

TMS Procedure

Transcranial magnetic stimulation was administered five times a week for 4 weeks. The protocol includes 20 trains of 10 Hz, for a duration of 6 sec, with 30 sec between each train. Each patient received a total of 1200 magnetic pulses during each treatment day. All medications were discontinued before treatment, apart from valproic acid, which was given at doses aimed at blood levels of 75–100 mg/mL. (For full description of the procedure, please see Grunhaus at al 2000.)

Case Reports

Case 1

Patient 1 is a 46-year-old woman who has been suffering from bipolar affective disorder for the last 15 years. She has had at least five episodes of depression lasting 6 months or longer. Three of these episodes were followed by a manic episode. She was given several types of antidepressants as well as mood stabilizers. Admission was due to a 2 week-long episode of depression that began 2 weeks after the end of a manic episode. Patient 1 has been treated with valproic acid 800 mg/day (blood levels 75 mg/mL) and haloperidol 5 mg/day for the last couple of years. Haloperidol was discontinued when TMS was initiated. The patient started to develop psychomotor restlessness, pressured speech, insomnia, euphoric mood, and increased goal-directed activity at the end of the third week of treatment. By the end of the fourth and last week, these symptoms worsened. The patient presented with elevated mood, singing loudly, mostly during the night when she was busy cleaning the ward. She would enter the

From the Department of Psychiatry "C," Division of Psychiatry, Sheba Medical Center, Ramat-Gan, and Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel.

Address reprint requests to Ornah T. Dolberg, M.D., Sheba Medical Center, Out-Patient Day Hospital, Division of Psychiatry, Ramat-Gan 52621, Israel. Received September 20, 1999; revised October 17, 2000; accented October 25

Received September 20, 1999; revised October 17, 2000; accepted October 25, 2000.

bedrooms of other patients while they were sleeping to clean their belongings, which caused much consternation. Although strictly forbidden, she began using the ward's kitchen for cooking while declaring she needs no more than 3 hours of sleep and must make use of her free time. She was argumentative and the staff found her difficult to handle and control. Haloperidol was initiated and the manic episode abated within a month.

Case 2

Patient 2 is a 54-year-old male construction engineer who is married and has three children. He is known to be suffering from hypertension. His psychiatric history includes a previous depressive episode, which took place 22 years ago. He was treated with three types of antidepressants and psychotherapy and reached full remission. He also had at least three hypomanic episodes appearing after a prolonged euthymic period, with spontaneous recovery. For the last 18 months he has been suffering from a depressive episode, manifested by sleep disturbances, depressed mood, decreased interest, "negative" pessimistic thoughts, and a tendency to cry. The patient received a course of TMS. Five days following the end of this course patient 2 developed insomnia and a feeling of "internal boiling." The patient was talkative and his mood was elevated; he gave the physician advice on how to better use TMS, promising money and donations to the ward from the wealth he would soon acquire. Although in serious difficulties at work, he had several grandiose schemes on how to better his position, although he confessed it was hard for him to concentrate on even the simplest tasks he had to perform. He reported his great success with women and made sexual advances toward the treating physician. He felt his thinking was "sharp" and that his head was "buzzing with ideas." During this time he found it difficult to sit still. Treatment with valproic acid 800 mg/day was initiated. This episode lasted for approximately 2 months.

Discussion

Transcranial magnetic stimulation is a novel and experimental therapeutic modality in psychiatry, mostly in the area of mood disorders. In this report, two patients with bipolar disorder, treated with TMS for their depression, developed a manic episode during or shortly after treatment with TMS. This change was not due to the effects of medication, as the only medications allowed during this period were valproic acid and some benzodiazepines for insomnia. Patient 1 had previous manic episodes following treatment for depression, especially during the last 5 years of her illness. It is therefore likely that TMS caused an effect similar to that of previous administration of antidepressants. The causal relationship to TMS in patient 2 is not as strong; however, there is a strong temporal relationship between the TMS treatment and the onset of the manic episode. One of the adverse effects of antidepressants is the induction of a "switch" from depression to mania, especially in bipolar patients. This switch phenomenon has been reported to occur in anywhere from 50% to 100% of bipolar depressed patients (Wehr and Goodwin 1987). This phenomenon during TMS treatment was reported by Garcia-Toro (1999) to occur while treating a depressed bipolar patient. The patient manifested transient manic symptoms when TMS was first applied, but not during the second TMS trial. Nedjat and Folkerts (1999) reported on three healthy volunteers experiencing transient hypomanic symptoms with TMS application. The difference between our patients and those described is obvious. Although both report on transient symptoms, our patients experienced a full-blown manic episode following TMS application.

Further research is needed to understand the nature of the possible manic switch following TMS for depression. It can be a mere coincidence or the outcome of the action of a confounding factor. Most likely, however, it is a genuine complication of treatment with TMS, as is known to occur with other treatments of depression.

This study was supported by a National Alliance for Research on Schizophrenia and Depression Young Investigator's Award (OTD).

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